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Abstract Book

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ORAL ABSTRACT SESSION 1: BIOLOGY OF THYMIC MALIGNANCIES
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O1.01

PROGRAMMED DEATH RECEPTOR LIGAND-1 (PD-L1) EXPRESSION IN A THYMOMA TISSUE MICROARRAY (TMA)

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Background: Thymic epithelial tumors (TETs) are rare and include thymomas and thymic carcinomas. TETs contain lymphocytic infiltrates, and as they arise from an immune organ confer a unique tumor microenvironment. Tumor expression of the immune checkpoint ligand, PD-L1, is a known mechanism for immune evasion. Here, we evaluated TET expression of PD-L1.

Methods: A TMA was constructed from 69 TETs and 17 thymic controls (C) (including 9 paired normal thymuses adjacent to tumor), at Stanford University. Each TET and C was represented by triplicate cores in the TMA. The pathologist (E.J.S.) was blinded to clinical data and sample identity. The TMA was stained with a monoclonal antibody (clone 15, Sino Biological) to human PD-L1 using human placenta for staining titration. To distinguish PD-L1 expression on epithelial cells from that on lymphocytes, a CK5/6 cytokeratin stain was used. An intensity scale of 0, 1, 2, and 3 representing no, equivocal, weak, and intermediate-strong staining, respectively, was used. Since both TETs and Cs stained for PD-L1 at least to some degree, TETs and Cs were classified as "PD-L1 high" if all representative cores in the TMA stained 3 on epithelial cells, while the remaining which did not fit this criteria were classified as "PD-L1 low." A nonparametric permutation test was used to compare the PD-L1 intensity on epithelial cells between TETs and Cs and the Fisher's exact test was used to correlate PD-L1 staining with WHO histology. A two-sided p-value ≤0.05 was considered statistically significant.

Results: Characteristics for 69 patients: 36M/33F; mean age 54 years (2-86); WHO histology: 8 A, 17 AB, 14 B1, 18 B2, 7 B3, 4 C. PD-L1 high scores were significantly more frequent in TETs than Cs (68.1% vs. 17.6%, respectively, p=0.004). Majority of PD-L1 staining was found on epithelial cells and present in > 50% of these cells. PD-L1 staining was both membranous and cytoplasmic. Only 14.8% (n=8/54) of TETs had PD-L1 staining of an associated lymphocytic infiltrate. There was also a significant correlation of PD-L1 and histology, with more aggressive histologies containing a higher percentage of PD-L1 high scores: B3>B2>C>B1>AB>A (p=0.035). In an unadjusted analysis, PD-L1 high versus PD-L1 low TETs demonstrated no difference in recurrence-free survival (RFS; p=0.2) and overall survival (OS; p=0.83). However, when adjusted for age and gender, PD-L1 high TETs had a worse OS (HR 5.40, 95% 1.13-25.89, p=0.035) and a trend for worse RFS (HR 2.94, 95% CI 0.94-9.24, p=0.064).

Conclusions: This is the largest set of TETs ever studied for PD-L1 expression to our knowledge and the first to be correlated with clinical data. All TETs expressed PD-L1 in our TET TMA. Though benign thymus also stained for PD-L1, TETs stained more intensely for PD-L1. PD-L1 expression is a potential biomarker for benefit to anti-PD1/PD-L1 therapies. Our findings lend support to a clinical trial targeting PD1/PD-L1 in this rare tumor type.

Disclosure: No significant relationships.

Keyword: PD-L1, PD-1, thymoma

ORAL ABSTRACT SESSION 1: BIOLOGY OF THYMIC MALIGNANCIES
September 5, 2014 11:45-12:45

O1.02

QUANTITATIVE MEASUREMENT OF PROGRAMMED DEATH LIGAND-1 (PDL-1) IN THYMIC NEOPLASMS

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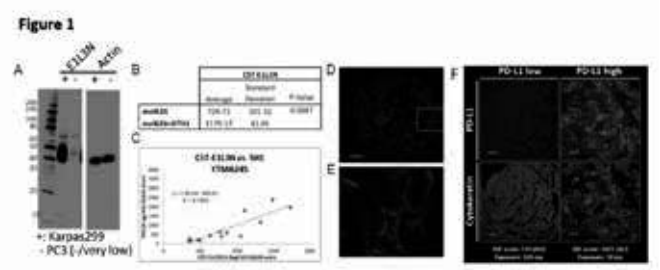
Background: Thymic epithelial neoplasms (TENs) are rare mediastinal lesions with variable malignant potential and limited therapeutic options. Compounds targeting immune inhibitory molecules (e.g. CTLA-4 and PD-1/PD-L1) have shown promising results opening new avenues for effective anti-cancer immunotherapy. Programmed Death-1 pathway is a major immune evasive mechanism in various solid tumors and is an active area of drug development. PDL11 appears to be predictive of response to drugs targeting the PD-1 pathway. Herein, we validated an assay for PD-L1 measurement in formalin-fixed paraffin-embedded (FFPE) tissue and determined the relationship between PD-L1 levels and key clinico-pathological variables.

Methods: We measured PDL-1 protein levels in 31 TENs from Yale New Haven Hospital between 1997-2012 represented in a tissue microarray (TMA). PD-L1 protein levels were determined in FFPE tissue samples using a Rabbit monoclonal antibody E1L3N and automated quantitative immunofluorescence (QIF). Antibody validation included immunoblot experiments and QIF analysis of human placenta and mel624-transfected with PD-L1 as positive controls. TENs cases with PD-L1 levels above the dynamic cut point determined by using Join point software were considered as high expressers. Clinico-pathological variables studied included age, gender, tumor size, development of myasthenia gravis, recurrence, WHO histotype and Masaoka stage. The limited number of cases in the cohort and the small number of events precluded any survival analysis.

Results: Results of antibody validation using immunoblot and QIF experiments using human placenta and mel624-transfected with PD-L1 are shown in figure 1. In TENs samples, PDL-1 signal was measured in the tumor compartment defined by pan-cytokeratin. 11/29 (38%) patients with TENs had high PDL-1 expression. Correlation with clinic-pathological variables did not show any significant associations. (Table 1). Evaluation of PD-L1 in a larger cohort of TENs from Cleveland clinic is underway.

Conclusions: PD-L1 protein levels can be reproducibly measured using QIF in FFPE samples. Over one third of patients with TENs show elevated PD-L1 protein levels. PD-L1 could be involved in the tumor-induced immune tolerance in patients with TENs. These observations support the exploration of the possible therapeutic role of PD-1 inhibitors in TENs.



(A) Western blot of positive and negative cell line controls (B) average quantitative scores of PD-L1 expression in mel624 and mel624-transfected with PD-L1 as positive controls. (C) regression of quantitative scores of antibody used in this study with previously published specific anti-PD-L1 antibody clone 5H1 (118). (D,E) Image of tissue microarray histospot of placental tissue (D) and at higher magnification (E) Red=PD-L1, Blue=DAPI. (F)A representative histospot of PDL-1 high and low TEN patient sample

Table 1. Clinicopathological characteristics by PD-L1 status in the Yale Thymic Epithelial Neoplasms Series

	PD-L1 low	PD-L1 high	*P* value
Age (years)			
< 50	6	8	**0.038**
≥ 50	12	3	
Gender			
Female	10	7	0.67
Male	8	4	
Tumor size (mm)			
< 50	4	6	0.05
≥ 50	6	1	
Myasthenia gravis			
No	12	4	0.11
Yes	6	7	
WHO histology			
A, B1, B2, B3	12	10	0.43
C	3	1	
Masaoka stage			
I-II	10	5	0.87
III-IV	7	4	
Recurrence			
No	12	7	0.53
Yes	4	4	

Disclosure: No significant relationships.

Keywords: Thymic epithelial tumors, Programmed death Ligand-1, Biomarker, Immunotherapy

ORAL ABSTRACT SESSION 1: BIOLOGY OF THYMIC MALIGNANCIES
September 5, 2014 11:45-12:45

O1.03

ADVANCES IN MICRORNAS EXPRESSION PROFILING OF THYMIC EPITHELIAL TUMORS

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Background: An increasing interest is deserved to tumor-specific microRNA as relevant regulatory factors involved in tumor biology. MicroRNAs develop from pre-miRNAs to mature miRNAs, and different methodologies and approaches (Radovich et al, 2012 ASCO Annual Meeting) are currently applied to characterize relevant microRNAs in Thymic Epithelial Tumor (TET). Our aim was to characterize whether different mature MicroRNA (miRs) are expressed in Thymoma (T) vs Thymic carcinoma (C) and in different WHO subtype subgroups. According to our previous data (ITMIG Annual Meeting, Bethesda 2013), 14 miRs were found significantly deregulated (9 up- and 5 down-regulated) in TET vs Normal (N) matched thymus.

Materials and methods: MicroRNA expression profiling was performed by microarray analysis of Formalin Fixed Paraffin Embedded (FFPE) tissue from two patient cohorts (54 thymic tumor samples and 12 matched normal counterparts). Scanning and image analysis were performed by Agilent DNA Microarray Scanner . Following to the TET *vs* N comparison already presented, we compared the miR signature of T vs C, and the miR signature of WHO histotype subgroups (A/AB/B1 vs B2/B3 vs C) characterized by well know different clinical behavior according to literature data (Okumura et al 2002, Ströbel et al 2010, Harnath et al 2012). Reverse Transcription and RT-qPCR quantification of miRs were performed to validate selected miR expression. Unsupervised two-way hierarchical clustering and Principal Component Analysis were applied to evaluate the data. In silico prediction pathway analysis on deregulated miRs in tumor vs normal samples was performed using Diana miR-path program.

Results: Commonly deregulated miRs in distinct WHO histotype subgroups vs N tissue were found as well as specifically deregulated miRs in clinically distinct histotype subgroups and in Thymoma (T) *vs* Carcinoma (C) (Ganci et al, 2014). Particularly, by comparing the miR signature of specific histotype groups vs normal tissues (A/AB/B1 vs N, B2/B3 vs N, C vs N,) we identified a group of 9 most significant miRs in a group of 22 common deregulated microRNA. Moreover, we evidenced 15 miRNAs (11 down- and 4up-regulated) distinguishing T vs C. The differential expression of three such miRNAs (miR-128, miR-142-5p and miR-181c-5p) was validated by RT-qPCR in a subgroup of representative samples . Next, we performed comparisons between TET histotype subgroups. In particular we compared C vs B2/B3, or C vs A/AB/B1 or B2/B3 vs A/AB/B1 subtypes, thus identifying miRNAs differently associated to histotype groups. By *in silico* pathways prediction analysis, cell adhesion and motility pathways as well as cancer phenotype- related pathways appear to be targeted from deregulated miRs. It is worth to note that, among miRs down-regulated in thymic carcinoma, we found some miRs putatively targeting BIRC3, SCYA20 and MYC, a group of thymic carcinoma-associated genes recently identified by Huang et al. (2013).

Conclusion: Our data indicate that TET are characterized by a complex molecular miR network. MiR deregulation may contribute to the different oncological behavior of thymoma subtypes and thymic carcinoma.

Disclosure: No significant relationships.

Keywords: Thymic carcinoma, Thymoma, Thymic epithelial tumors, MicroRNA

ORAL ABSTRACT SESSION 1: BIOLOGY OF THYMIC MALIGNANCIES
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O1.04

GENETIC PROFILING OF THYMIC CARCINOMA USING TARGETED NEXT-GENERATION SEQUENCING

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Background: Thymic carcinoma is a rare tumor of thymic epithelial origin. Several efforts have been made to identify the tumorigenesis of thymic carcinoma, but little is known about the molecular mechanism. There is no effective treatment except for complete resection, and the prognosis of advanced cases is poor. Recently, sequencing technology has progressed remarkably. Next-generation sequencing has enabled whole-exome sequencing and targeted sequencing more easily than before. This method is effective and ideal for rare tumors like thymic carcinoma to analyze the molecular mechanism of oncogenesis. To identify the mutations associated with tumorigenesis, we analyzed genetic profile of thymic carcinoma using targeted Next-Generation Sequencing.

Methods: This study included 12 thymic squamous cell carcinoma including 10 tumor / normal tissue pairs. DNA was extracted from fresh frozen tissue. We performed targeted sequencing about 409 cancer related genes, using Ion AmpliSeq Comprehensive Cancer Panel and Ion PGM Sequencer (Life Technologies).

Results: The individual sample underwent on average 4,881,951 mapped sequence reads with a 114 bp mean read length. The average base coverage depth was 311 reads, and uniformity of coverage was 92.8%. Sequencing identified 1,039 variants in 294 genes per sample on average, and we filtered the variants using Ingenuity Variant Analysis (QIAGEN) and compared the sequence of the tumor to the matched normal tissue. And then, we excluded the SNVs which are Tolerated in SIFT, Benign in PolyPhen-2, and Neutral in PROVEAN. In ten tumor / normal pairs, candidate mutations were identified in 9 of 10 patients. We confirmed 25 mutations in 24 genes, including six tyrosine kinase genes (KIT, DDR2, PDGFRA, ROS1, IGF1R). One tumor contained a three-codon in-frame deletion in exon 11 of KIT (c.1667_1669delTTG), resulting in a deletion of valine at position 556 (V556del). The mutation was confirmed by Sanger sequencing.

Conclusion: We performed genetic profiling of thymic carcinoma using targeted next-generation sequencing. The mutation status of thymic squamous cell carcinoma is highly heterogeneous. We identified KIT exon 11 deletion mutation in one case. It's an activating mutation of KIT and this mutation is sensitive to Imatinib in patients with GIST and thymic carcinoma.

Disclosure: No significant relationships.

Keywords: sequencing, Thymic carcinoma

ORAL ABSTRACT SESSION 2: SURGICAL TREATMENT September 5, 2014 15:45-16:45

ORAL ABSTRACT SESSION 2: SURGICAL TREATMENT
September 5, 2014 15:45-16:45

O2.01

THYMOMA PATIENTS WITH PLEURAL DISSEMINATION: NATIONWIDE RETROSPECTIVE STUDY OF 136 CASES IN JAPAN

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Background: Thymoma is a rare mediatinal tumor with reltively slow growth. However, advantage-stage cases with pleural dissemination are occasionally encountered. The outcome of surgical resection for thymomas with pleural dissemination has not been clearly determined.

Methods: We retrospectively investigated the clinical records of 2,835 patients with thymic epithelial tumors that were treated from 1991 to 2010 in 32 institutions that participated in the Japanease Association for Research on Thymus. In this study, we analyzed the clinico-pathologic factors and prognosis of thymoma patients with plearal dissemination who underwent surgical resection.

Results: The thymomas with pleural disseminations numbered 148 cases (5.2% in the 2,835 thymic epithelial tumors). Surgical resection was performed in 136 cases. Pathologic Masaoka stages were classified as 4A (n=118) and 4B (n=18). In Masaoka stage 4A disease, the small number of disseminated pleural nodules (10 or fewer) was related to the curative resection. The prognosis was also better in these cases than in those with greater than 10 disseminated pleural nodules (certified during the operation; p=0.0057). Patients who underwent macroscopic total resection of disseminated nodules had a better prognosis than those with residual tumors (p=0.037). In stage 4A cases with complete resection (n=42), the efficacy of adjuvant chemotheray, radiotherapy, or both was not demonstrated.

Conclusions: Macroscopic total resection of tumors appears to be a promising prognostic factor in Masaoka stage 4A thymomas. The number of disseminated pleural nodules correlated with resectability.

Disclosure: No significant relationships.

Keywords: macroscopic total resection, surgical resection, pleural dissemination, Thymoma

ORAL ABSTRACT SESSION 2: SURGICAL TREATMENT
September 5, 2014 15:45-16:45

O2.02

SURGICAL MANAGEMENT OF RECURRENT THYMIC TUMORS:AN ANALYSIS BASED ON THE JAPANESE NATIONWIDE DATABASE

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Background: There is no standard treatment for recurrent thymic epithelial tumors. Although the efficacy has not been validated based on the large series studies, surgical resection is sometimes employed for patients with recurrent thymic tumors. The aim of this study was to evaluate the surgical outcomes for recurrent thymic epithelial tumors based on the Japanese nationwide database.

Methods: A Japanese nationwide registry study of thymic epithelial tumors was carried out by the Japanese Association for Research on the Thymus (JART). From the database of patients whose thymic epithelial tumors were treated surgically from 1991 through 2010, the cohort who developed recurrence after the initial resection was extracted. Clinicopathological factors were reviewed, and the prognostic factors for postrecurrence survival of re-resected cases were examined.

Results: Twenty-eight hundred and thirty-five patients who underwent surgical resection of thymic epithelial tumors were registered to the database. Among these patients, 420 (14.8%) experienced recurrence. One hundred and sixty-two patients were treated surgically (the surgery group) and 243 were treated non-surgically for recurrent disease (the non-surgery group). In fifteen patients, presence of surgical treatment was unknown. The median follow-up period after diagnosis of recurrence was 59.8 months among those 405 patients and 73.3 months among the 267 surviving patients. The 5- and 10-year postrecurrence survival rates were 82.7% and 68.2%, respectively, in the surgery group and 43.5% and 25.4%, respectively, in the non-surgery group ($p < 0.001$). An analysis of the completeness of re-resections showed a survival advantage among the patients treated with R0-1 and R2 resections compared to that observed in the non-surgery group ($p < 0.001$, $p = 0.004$). A significant survival advantage was also noted among the patients treated with R0-1 resection compared to that observed in the non-surgery group for thymomas and thymic cancers, resepectvely ($p < 0.001$, $p = 0.014$). Meanwhile, survival of the patients treated with R2 resection was intermediate between that with R0-1 resection and that in the non-surgery group for thymomas, although the difference between the patients treated with R2 resection and the non-surgery group was not significant for either histology ($p = 0.143$ and 0.809, respectively). According to univariate analyses, female sex as well as the early pathological Masaoka stage, WHO histologic type (non-thymic cancer), absence of preoperative treatment and short disease-free interval (DFI) was significantly favorable factors for survival in the surgery group. And according to the multivariate analysis, the WHO histologic type and DFI were identified to be independent prognostic factors.

Conclusions: The surgical outcomes of recurrent thymic epithelial tumors are favorable in selected patients. The role of re-resection may be limited in the setting of thymic cancer and/or a short DFI.

Disclosure: No significant relationships.

Keywords: recurrence, reresection, thymic cancer, Thymoma

ORAL ABSTRACT SESSION 2: SURGICAL TREATMENT
September 5, 2014 15:45-16:45

O2.03

DOES THE WHO HISTOLOGICAL CLASSIFICATION PREDICT OUTCOMES AFTER THYMOMECTOMY?

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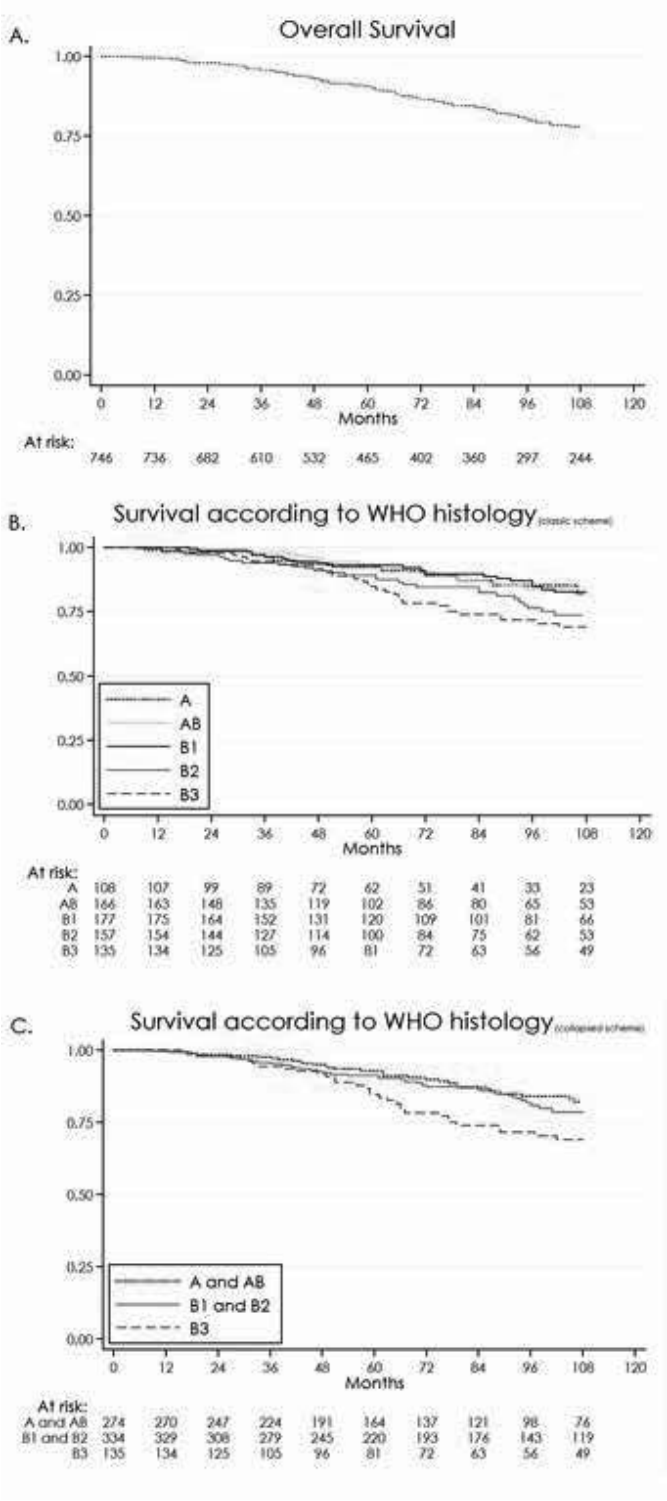
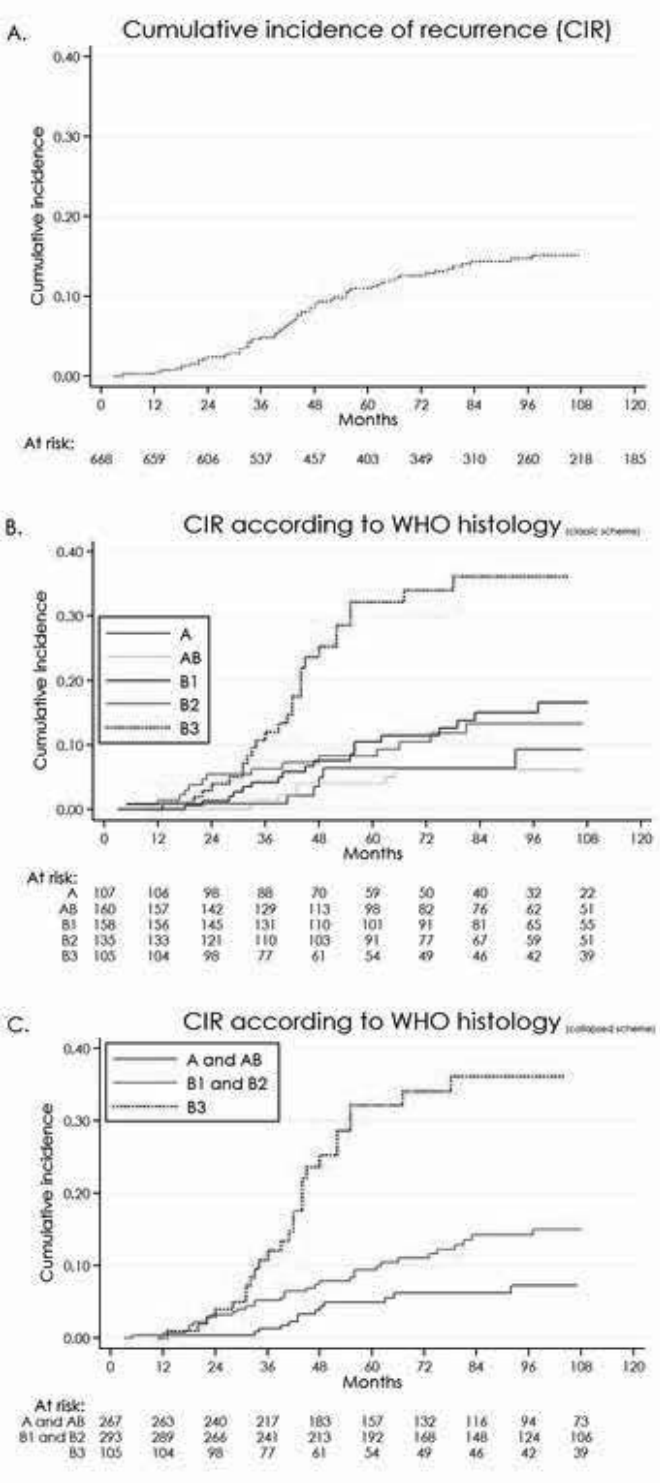
Background: The World Health Organization (WHO) thymoma histological classification clinical value remains controversy. In this study, we evaluated its prognostic significance in patients with thymoma treated with radical intent.

Methods: Six high-volume Italian Thoracic Surgery Institutions collaborated with their own retrospective anonymized datasets. Demographic, clinical, pathological and treatment data were examined. A WHO histological classification (WHO-HC) collapsed scheme (A/AB and B1/B2 types merged) was proposed and compared to the traditional one. Predictors of survival were assessed using Cox model with shared frailty. Competing-risk regression models were performed to identify the association between individual factors and cumulative incidence of recurrence (CIR).

Results: Between 1990 and 2011, 750 thymomas were operated in participating Centres. Myasthenia Gravis was observed in 363 (48%) patients. A complete resection was achieved in 676 (91%) cases. One hundred and nine patients (15%) had a WHO-HC A type, 166 (22%) AB, 179 (24%) B1, 158 (21%) B2 and 135 (18%) B3, respectively. The 5-year OS (Fig.1) and CIR (Fig.2) for all cases was 91% and 0.11, respectively. Five-year survival rates by WHO-HC in collapsed scheme were A/AB 93%, Early-B 90% and Advanced-B 85%. Masaoka stage only, demonstrated to be an independent predictor for survival and recurrence. WHO-collapse scheme showed a weak significance in influencing recurrence development (P= 0.09).

Conclusions: Our results put in evidence a WHO-HC lack of significance in influencing prognosis, even if proposed collapsed scheme revealed a good stratification of risk to relapses and better correlation with patients' clinical characteristics





Disclosure: No significant relationships.

Keyword: Thymoma, Histology, WHO Classification, Survival, Recurrences

ORAL ABSTRACT SESSION 2: SURGICAL TREATMENT
September 5, 2014 15:45-16:45

O2.04

IMPACT OF THE ITMIG CRITERIA ON DIAGNOSIS IN THE FRENCH NETWORK OF THYMIC EPIHELIAL TUMOURS.

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The French National Cancer Institute (INCa) has promoted since 2012 the constitution of a nationwide network for thymic epithelial tumors (TET), "RYTHMIC", with a national multidisciplinary tumor board. Systematic review (after the board) of all patients' slides has been performed by a panel of expert histopathologists, of whom three had been involved in the ITMIG histopathological proposals linked to the 2004 WHO classification. In each case, additional immunohistochemistry was performed systematically with antibodies against CD5, CD20, Cytokeratins (KL1 or AE1/AE3), TdT, and if needed p63, CD117, CD1a; diagnosis was made by consensus on multihead microscope and videoprojection.

We report the results of the first 125 consecutive cases that were included in the French Pathology Network RYTHMIC-Pathology. Cases were classified for histology and stage whenever it was possible, taking into account WHO 2004 and ITMIG proposals for histological typing and staging. There were complete concordance with the initial pathological and stage diagnoses in 74 cases (59%). 39 cases (31%) were discordant considering either stage and/or histology. In 12 cases (10%), there were strong difficulties for the panel for a consensus diagnosis.

Major discrepancies between initial and panel diagnoses were observed in 4 cases for which treatment impact concerned adjuvant radiotherapy : initial thymic carcinoma with a thymoma A panel diagnosis; initial AB stage II with a panel AB stage III diagnosis; Initial B3 stage IIB with a panel Thymic carcinoma stage III; initial micronodular thymoma IIB with a panel Thymic carcinoma stage IIB. Minor discrepancies mainly concerned downstaging stage IIA to panel stage IIB (5 cases), upstaging stage IIB to panel stage IIA (3 cases), initial diagnosis of B1 with a B2 panel diagnosis (5 cases), initial B2 with a B2/B3 diagnosis (4 cases), initial B2 to AB (3 cases).

Difficult cases without strong panel consensus were mainly linked to the discussion between B3 and thymic carcinoma (8 cases) with some of the cases classified as "B3/Thymic squamous cell carcinoma borderline TET". Rare cases (3) concerned differential diagnosis between type A and B3 or between type AB and type B thymoma.

Our series underline that panel diagnosis and ITMIG proposals may modify staging and histotyping of TET by defining more precisely the histological and stage criteria. Furthermore, our series demonstrate the importance of CD5, CD20 and CD117 staining for the

correct classification of TET. Our results suggest the relevance of an expert panel diagnosis for better decision-making about post-operative radiotherapy to avoid over- or undertreatment of the patients.

Disclosure: No significant relationships.

Keywords: diagnostic, Thymic epithelial tumors, histopathology, stage

ORAL ABSTRACT SESSION 3: DIAGNOSIS AND TUMOR AGGRESSIVENESS September 6, 2014 11:15-12:15

ORAL ABSTRACT SESSION 3: DIAGNOSIS AND TUMOR AGGRESSIVENESS September 6, 2014 11:15-12:15

O3.01

CLINICAL FEATURES OF POSTTHYMECTOMY MYASTHENIA GRAVIS

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Objective: The aim of this study was to assess the clinical features of the patients with myasthenia gravis occurring after resection of thymoma.

Methods: Between 1986 and 2012, a total of 391patients underwent resection of thymoma, excluding patients with type C thymoma and patients who underwent incomplete resection. We retrospectively reviewed the patients who were diagnosed as myasthenia gravis after thymoma resection.

Results: Postthymectomy myasthenia gravis was found in 11 (2.8%) of 391 thymoma patients who received complete resection. The patients included 9 male and 2 female with a median age of 42 (range, 27~60) years at the time of thymoma resection. Masaoka-Koga stages of initial thymomas were stage I in 7 patients, stage IIb in 1 patient, stage III in 1 patient and stage IVa in 2 patients. WHO histologic types were type B1 in 4 patients, type B2 in 4 patients, type AB in 1 patient, type B3 in 1 patients and type B2+B3 in 1 patient. The interval between thymectomy and the onset of myasthenia gravis was 5 to 96 months. There were 2 patients (0.7%) of postthymectomy myasthenia gravis in the extended thymectomy group (n=279) and 9 patients (8.0%) in the limited thymectomy group (n=112); resection of the thymoma with the surrounding thymus and fatty tissue, leaving residual thymic tissue. Six patients (54.5%) of 11 patients had thymoma recurrence at the time of myasthenia gravis diagnosis.

Conclusion: The prevalence of postthymectomy myasthenia gravis is higher in the patients underwent limited thymectomy than the patients underwent extended thymectomy. In addition, more than half of patients with postthymectomy myasthenia gravis had thymoma recurrence. Therefore, postthymectomy might be caused by the remnant thymic tissue after thymoma resection or thymoma recurrence.

Disclosure: No significant relationships.

Keyword: postthymectomy myasthenia gravis

ORAL ABSTRACT SESSION 3: DIAGNOSIS AND TUMOR AGGRESSIVENESS September 6, 2014 11:15-12:15

O3.02

IMPACT OF VEGF, VEGFR, PDGFR, HIF AND ERCC1 GENE POLYMORPHISMS ON THYMIC MALIGNANCIES OUTCOME

Rossana Berardi[1], Alessandro Brunelli[2], Silvia Pagliaretta[1], Vittorio Paolucci[1], Alessandro Conti[3], Gaia Goteri[4], Majed Refai[2], Cecilia Pompili[2], Giulia Marcantognini[1], Francesca Morgese[1], Zelmira Ballatore[1], Agnese Savini[1], Mariagrazia De Lisa[1], Miriam Caramanti[1], Matteo Santoni[1], Paola Mazzanti[1], Azzurra Onofri[1], Armando Sabbatini[2], Stefano Cascinu[1]
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Background: we aimed to analyze genotypes of *VEGF-A*, *KDR*, *Flt4*, *PDGFRα*, *HIF-1α* and *ERCC1* in thymomas and thymic carcinomas and their potential correlation with the risk of thymic tumors and/or with the outcome of these patients.

Methods: The genomic DNA of 57 consecutive patients (43 thymomas and 14 thymic carcinomas) who underwent total thymectomy at our Institution was extracted from paraffin-embedded tissue. We selected polymorphisms in the following genes: HIF1-α (rs2057482T>C, rs1951795A>C, rs2301113C>A, rs10873142C>T, rs11158358G>C, rs12434438G>A, rs11549465C>T, rs-11549467G>A), VEGF-A (rs2010963G>C, rs699947A>C), VEGFR-2 (rs2305948C>T, rs1870377T>A), VEGFR-3 (rs307826T>C, rs307821C>A), PDGFR-α (rs35597368C>T) and (ERCC1 (rs11615A>G). Gene polymorphisms were determined by Real-Time PCR using TaqMan assays.

Results: The allele frequency of PDGFR-α rs35597368 T was significantly higher than general population (94.7% vs 86.7%, p=0.036), while the frequency of alleles HIF1-α rs2057482C (78.1% vs 90.3%), rs1951795C (69.3% vs 86.7%), rs2301113A (69.6% vs 82.7%), rs10873142T (70% vs 86.7%), rs11158358C (75.4% vs 88.2%), rs12434438A (66.7% vs 84.5%), rs11549465C (85.1% vs 92.5%) were significantly lower than in general population. VEGFR-3 rs307821C was significantly higher in thymomas vs. thymic carcinomas (79.5% vs 72%, p=0.0371). The following factors were significantly correlated with a better overall survival: VEGFR-3 rs307826C, VEGFR-2 rs1870377A, PDGFR-α rs35597368T/C, HIF1-α rs2301113C, rs2057482C/T, rs1951795C, rs11158358G/C and rs10873142T/C, ERCC1 rs11615A ($p<0.05$).

Conclusion: Our results suggest, for the first time, that inherited abnormalities in PDGFR-α, HIF-1α and VEGFR-3 pathways influence the risk and aggressiveness of thymic tumors. These results should be prospectively validated in order to optimize the diagnosis and treatment of these patients.

Disclosure: No significant relationships.

ORAL ABSTRACT SESSION 3: DIAGNOSIS AND TUMOR AGGRESSIVENESS September 6, 2014 11:15-12:15

O3.03

EXPRESSION OF RAGE AND HMGB1 IN TETS, THYMIC HYPERPLASIA AND REGULAR THYMIC MORPHOLOGY

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Recently, a role of the receptor for advanced glycation endproducts (RAGE) in myasthenia gravis was described. RAGE and its ligand high mobility group box 1 (HMGB1) play key roles in autoimmunity and cancer. To test whether these molecules are involved in patients with thymic abnormalities we applied immunohistochem-

ical analysis in 33 cases of thymic epithelial tumors, comprising 27 thymomas and 6 thymic carcinomas, and 21 nonneoplastic thymuses. Both molecules were detected in neoplastic epithelial cells: RAGE staining was most intense in WHO type B2 thymomas and thymic carcinomas ($p<0.001$). HMGB1 nuclear staining was strongest in A and AB, and gradually less in B1=B2>B3>thymic carcinoma ($p<0.001$). Conversely, HMGB1 cytoplasmic staining intensities were as follows: A and AB (none), B1 (strong), B2 (moderate), B3 and thymic carcinoma (weak); ($p<0.001$). Fetal thymic tissue showed a distinct expression of RAGE and HMGB1 in subcapsular cortical epithelial cells which was found in 50% of myasthenic patients. Furthermore RAGE and HMGB1 were expressed in thymocytes, macrophages, Hassall's corpuscles, thymic medulla, and germinal center cells in myasthenic patients. Immunohistochemistry results were complemented by systemic measurements (immunosorbent assay): serum levels of soluble RAGE were significantly reduced in patients with epithelial tumors ($p=0.008$); and in invasive tumors ($p=0.008$). Whereas RAGE was equally reduced in thymic hyperplasia and epithelial tumors ($p=0.003$), HMGB1 was only elevated in malignancies ($p=0.036$). Results were most pronounced in thymic carcinomas. Thus, RAGE and HMGB1 are involved in the (patho-)physiology of thymus, as evidenced by differentiated thymic and systemic expression patterns that may act as diagnostic or therapeutic targets in autoimmune disease and cancer.

Disclosure: No significant relationships.

Keywords: regular thymic morphology, TETs, HMGB1, RAGE

ORAL ABSTRACT SESSION 3: DIAGNOSIS AND TUMOR AGGRESSIVENESS
September 6, 2014 11:15-12:15

O3.04

GLUT-1 IMMUNOHISTOCHEMICAL EXPRESSION IN THYMIC EPITHELIAL TUMORS ACCORDING TO WHO HISTOLOGICAL TYPE

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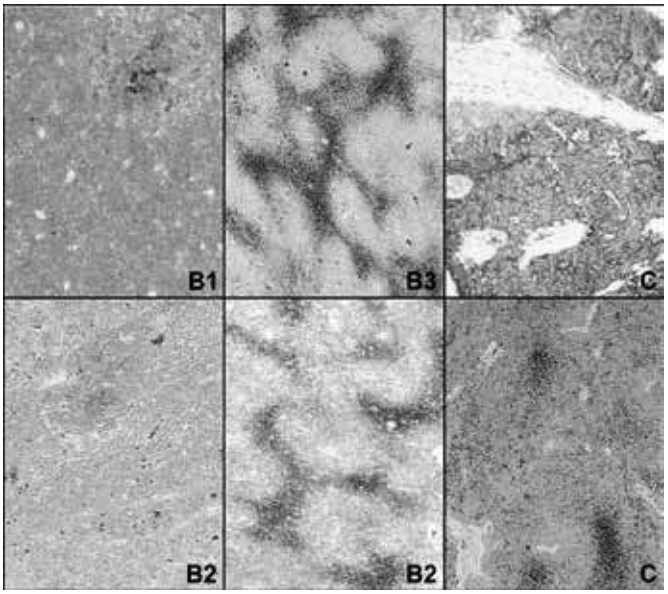
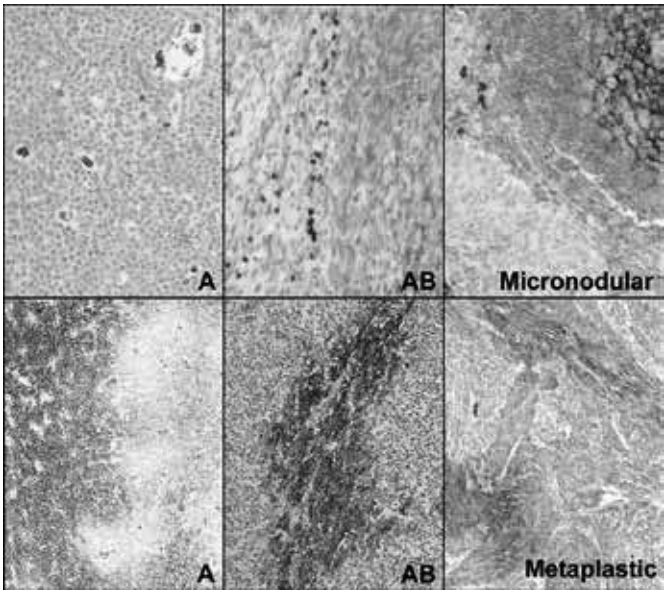
Background: Expression of glucose-transporter-1 (Glut-1) has been reported as a useful marker for the differential diagnosis between B3 thymomas and thymic carcinomas. Rythmic-pathology is a group of expert pathologists reviewing thymic epithelial tumors that are clinically discussed at French national multidisciplinary tumor boards.

Methods: Immuno-histochemical expression of Glut-1 was reviewed by the Rythmic-pathology group in a series of 94 successive cases with confirmed diagnosis from surgical specimen. Immunostaining was performed, with polyclonal rabbit antibody (RP128-05 Diagnostic-biosystems), on a whole section of one representative paraffin block from each case. Pattern and intensity (strong/moderate/weak) of Glut-1 expression were assessed and compared in each WHO histological subtype. In cases with combined histology, only the main subtype present on the slide was considered. Erythrocytes were used as positive internal controls.

Results: Expression was membranous and cytoplasmic, and mainly restricted to epithelial cells. Immature T-lymphocytes were negative.



A diffuse, moderate or strong staining was observed in most thymic carcinomas (C, 20/23). In B3 thymomas and cases with intermediated features between B3 thymoma and thymic carcinoma, a strong or moderate zonal staining was observed at distance from vessels and fibrous septa (9/11). This pattern sometimes created the aspect of an anastomosing network in large cellular lobules.In B1 thymomas, immunostaining highlighted foci of medullary differentiation and was otherwise restricted to scattered cells (7/9). B2 thymomas (n=25) were heterogeneous with a spectrum of patterns between those of B1 and B3 thymomas.



Type A thymomas presented diffuse and weak positivity (3/5) except for one aggressive case with lung invasion in which diffuse positivity was moderate/strong. In AB thymomas (n=17), immunostaining was observed in spindle cell areas and ranged from weak and focal positivity, to diffuse positivity. In micronodular thymo-

mas (n=3), epithelial cells were negative or weakly positive, while B-lymphocytes were weakly positive and follicular dendritic cells were strongly highlighted. A single metaplastic thymoma displayed diffuse and moderate positivity.

Conclusion: The pattern of Glut-1 expression globally depends on histological types. However, in our experience, the immunostaining heterogeneity does not allow a definite sub-classification in every single case. A comparative study of Glut-1 expression in aggressive versus conventionnal type A thymomas appears warranted.

Disclosure: No significant relationships.

Keywords: Thymic carcinome, Thymoma, Immuno-histochemistry, Glut-1

ORAL ABSTRACT SESSION 4
STAGE PREDICTION AND MULTIMODALITY THERAPY
September 6, 2014 15:30-16:30

ORAL ABSTRACT SESSION 4: STAGE PREDICTION AND MULTIMODALITY THERAPY
September 6, 2014 15:30-16:30

O4.01

COMPUTED TOMOGRAPHY (CT) CHARACTERISTICS ASSOCIATED WITH MASAOKA-KOGA PATHOLOGIC STAGE IN THYMOMA

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Introduction: Preoperative CT imaging is key for the management of thymic malignancies (TMs), especially in making the decision of whether a patient should proceed to surgery. Several groups have examined preoperative CT characteristics that associate with pathologic stage, histology, and surgical resectability. Here, we present Stanford University's experience.

Methods: The inclusion criteria was as follows: 1) diagnosis of a TM (thymoma, thymic carcinoma, or thymic carcinoid), 2) primary definitive surgery performed at Stanford, and 3) available preoperative CT imaging for review. Since 1997, we identified 224 patients with TMs who were seen at Stanford. Of these, 106 patients had a TM-related surgery, 33 had missing preoperative CTs (not routinely uploaded until 2008), and 50 met all inclusion criteria. For those patients who received preoperative chemotherapy, post-treatment imaging was examined. The radiologist (D.T.) who was blinded to clinical data examined CT variables as defined by the International Thymic Malignancy Group (ITMIG) prospective database including: size of longest diameter of lesion, contour, internal density, calcification, infiltration of mediastinal fat (iMF), abutment of $\geq$50% of mediastinal vessels, vascular endoluminal invasion, abutment/invasion of adjacent mediastinal structures, elevated hemidiaphragm (eHD), pleural effusion, pleural nodules, mediastinal lymph node enlargement, and suspected extra-thoracic metastases. A proportional odds regression was used to analyze the univariate association of these variables with pathologic Masaoka-Koga stage and WHO histology (low-risk=A/AB/B1; intermediate-risk=B2/atypical carcinoid; and high-risk=B3/C). P-value <0.05 significant. A Lasso regularized general transformation model was used to develop a prediction model for staging with all variables.

Results: Of the 50 TMs, there were 20 pathologic stage I, 4 IIA, 5 IIB, 12 III, 6 IVA, and 3 IVB and 21 low-risk histologies, 15 intermediate-risk and 14 high-risk. In a univariate analysis for stage, the following CT characteristics were associated with a higher stage: invasion of mediastinal structures OR=4.11/p=0.026), vascular endoluminal invasion (OR=12.43/p=0.001), eHD (OR 6.66/p=0.013), and pleural nodule(s) (OR 5.07/p=0.045). There was a trend for higher stage with a lobulated tumor (p=0.096) and abutment of mediastinal vessels (p=0.077). In a multivariate analysis for stage, vascular endoluminal invasion was the most important for predicting for a higher stage followed by eHD, pleural nodule(s), lobulation, invasion of mediastinal structures, and iMF. There were less compelling associations with histology, none of which reached statistical significance. In a univariate analysis, iMF (p=0.063) and abutment of mediastinal vessels (p=0.061) trended for associating with higher-risk histologies.

Conclusions: Certain preoperative CT characteristics as defined by ITMIG predict for Masaoka-Koga pathologic stage in our cohort, particularly separating stage I/II disease from stage III/IV disease. Vascular endoluminal invasion appeared to be the most important CT characteristic in our cohort. Preoperative CT features were not important in predicting for histology, but this could be confounded by inclusion of post-neoadjuvant therapy CTs. Our study is limited by its retrospective nature and small sample size; however, it shows that a group of CT characteristics as defined by ITMIG can assist in the management of TMs.

Disclosure: No significant relationships.

Keyword: computed tomography, thymoma, Masaoka-Koga stage, WHO histology

ORAL ABSTRACT SESSION 4: STAGE PREDICTION AND MULTIMODALITY THERAPY
September 6, 2014 15:30-16:30

O4.02

THE BENIGN THYMECTOMY RATE AT A QUATERNARY REFERRAL HOSPITAL: DOES MRI HAVE POTENTIAL TO REDUCE IT?

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Purpose: To ascertain the benign thymectomy rate at our institution, clinical and imaging features that prompted surgery, and whether preoperative MRI could have averted a significant number of these benign thymectomies.

Materials and Methods: The benign thymectomy rate was ascertained by electronic data base query of thymectomies performed at from 2016-2012, yielding 160 cases, 124 of which had available imaging. Preoperative clinical and CT imaging features were assessed by review of the in-house electronic medical record by 2 thoracic surgeons and 2 pathology-blinded radiologists, respectively.

Results: The benign thymectomy rate of 20.0% (32/160; CI: 14.1-27%) and non-therapeutic thymectomy rate of 43.8% (70/160; CI: 35.9-51.8%) were primarily due to concern for thymoma. Cysts and thymic hyperplasia comprised 91% of resected benign lesions (53% and 38% respectively). 96%(28/29) of subjects with thymic bed cysts or thymic hyperplasia underwent sternotomy. Comparison of thymic bed cysts, thymic hyperplasia, and other lesions yielded significant differences in morphology (p < .0001), homogeneity of attenuation (p < .0001), and location with respect to midline (p < .0001). A saccular shape was exclusive to cysts. Quadrilateral, triangular, bilobed, and bipyramidal shapes were exclusive to thymic hyperplasia. Gross fatty intercalation was 100% specific to hyperplasia (p < .0001). 10/10 cysts, 3/10 hyperplasia, and 22/104 remaining lesions were homogeneous in attenuation. Thymic cyst mean attenuation was 23 +/- 23 HU, ranging up to 58 HU. 90% (9/10) of thymic hyperplasia were midline in location. 50% (5/10) of thymic cysts were midline and 32% of other lesions were midline.

Conclusion: Given the known superior capability of MRI to dis-

tinguish between thymic cysts, hyperplasia, and tumor, when compared with CT, a preoperative MRI should be considered prior to thymic mass resection to exclude benign thymic cysts and hyperplasia, in an effort to lower the benign thymectomy rate and its associated morbidity.

Disclosure: No significant relationships.

Keywords: MRI, thymic hyperplasia, thymic cyst, Thymectomy

ORAL ABSTRACT SESSION 4: STAGE PREDICTION AND MULTIMODALITY THERAPY
September 6, 2014 15:30-16:30

O4.03

VARIATION IN RESPONSE TO NEOADJUVANT CHEMOTHERAPY ACROSS WHO HISTOLOGICAL SUBTYPES OF THYMOMA

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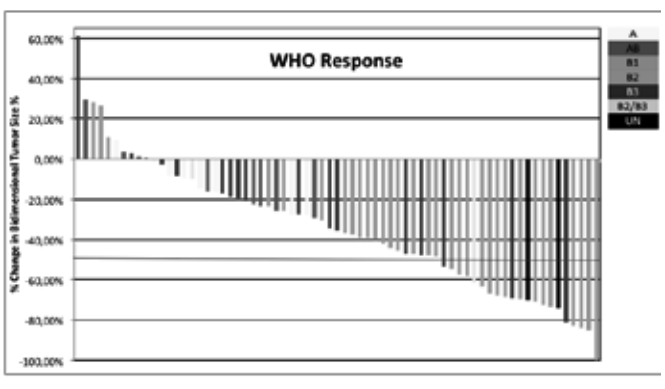
Introduction: Thymomas are rare tumors which are generally considered to be chemosensitive; however, the response to therapy can be quite variable across different patients. There is considerable heterogeneity among thymomas, as reflected in the WHO histologic classification, and we sought to assess whether response to chemotherapy correlated with histologic subtype.

Methods: Retrospective cohort study of patients with thymoma treated with neoadjuvant chemotherapy followed by surgery. Response to therapy was evaluated using RECIST and WHO criteria.

Results: From 1994 and 2013, 71 patients with biopsy-proven thymoma had neoadjuvant chemotherapy followed by surgery and 69 were evaluable. Most patients were clinical Masaoka stage III (n=36, 52%) or IVA (n=31,45%). The most frequent histologies were B2 (n=21, 30%) and B3 (n=16, 23%). The most common chemotherapy regimens included cisplatin, cyclophosphamide, doxorubicin (CAP, n=48, 70%), and platinum/etoposide (EP, n=14, 20%). R0 resection was achieved in 58%(n=40). Across all patients, overall response rate (CR+PR) was 26% by RECIST and 30% by WHO. Overall response rates were highest in B1 histology (58%), followed by B2 (38%), but 0% in A and AB. Bidimensional tumor size reduction for CAP chemotherapy was 38%, and 25% for EP. Mean tumor size reduction was 48.% for B1 and 47% for B2 and lower for A (12%) and AB (10%), $p<0.05$.

Conclusion: Response to neoadjuvant chemotherapy may vary markedly across different histologic subtypes of thymoma. B1 and B2 thymomas exhibited the greatest response to neoadjuvant chemotherapy. Further studies are needed to explore the mechanisms underlying the variation in chemosensitivity.

Figure 1 – Tumor response by WHO histologic classification



*UN= unknown

Disclosure: No significant relationships.

Keywords: Neoadjuvant Chemotherapy, Thymoma

ORAL ABSTRACT SESSION 4: STAGE PREDICTION AND MULTIMODALITY THERAPY
September 6, 2014 15:30-16:30

O4.04

RYTHMIC: INSIGHTS IN THE MANAGEMENT OF ADVANCED THYMIC EPITHELIAL TUMORS

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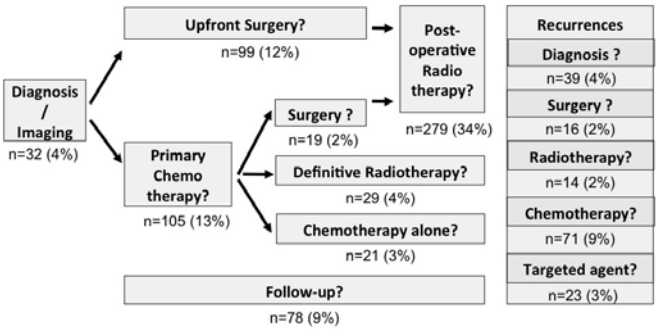
Introduction: RYTHMIC (Réseau tumeurs THYMiques et Cancer) is the French nationwide network for thymic malignancies. Starting January 2012, all patients diagnosed with thymic tumor had to be enrolled, as part of good clinical practice recommended by the French National Cancer Institute.

Methods: RYTHMIC database is hosted by the French Thoracic Cancer Intergroup, and prospectively collects clinical, imaging, treatment, and follow-up data of patients discussed at national reference multidisciplinary tumor board (MTB) meetings. Data cutoff was June 1st, 2014 for this analysis.

Results: Over the study period, 825 questions were raised at the MTB meetings, discussing the management of 627 patients with thymic tumor (Figure 1). Among assessable cases, Masaoka-Koga stage III-IV tumors accounted for 50% of cases; histology was of higher grade (thymoma B2, B3, C) in these cases ($p<0.001$). As previously reported, the most frequent topic requiring multidisciplinary discussion was post-operative radiotherapy (279 (34%) questions). First-line treatment of locally-advanced disease, and management (diagnosis and treatment) of recurrent disease led to raise 174 (21%), and 163 (20%) questions at the MTB meetings, respectively, 197 (24%) of which were about the modalities of systemic treatment. The most frequently proposed chemotherapy regimen and targeted agent were combination of cisplatin, adriamycin, and cyclophosphamide (35% of cases), and sunitinib (6% of cases), respectively. In the majority (72%) of cases, sunitinib was proposed after the results of a phase II trial were presented at the 2013 World Conference on Lung Cancer, reporting on a significant clinical activity of this agent in thymomas and thymic carcinomas (Thomas et al. J Thorac Oncol 2013;8:S268).

Conclusion: RYTHMIC is an exhaustive registry of thymic malignancies, which provides with unique insights in the management of advanced and recurrent thymic malignancies with systemic agents. Meanwhile, limited data on this subset of patients has been made available in the literature so far, as clinical trials were conducted in small numbers of patients, and existing databases enrolled a majority of surgically resected, early-stage tumors. Of more importance, RYTHMIC allows rapid implementation of new results in clinical practice, while ensuring patients an equal access

to therapeutic innovation. Supported by Institut National du Cancer



Disclosure: No significant relationships.

Keywords: Targeted treatment, Chemotherapy, Tumor Board, Thymoma

POSTER SESSION 1 - September 5, 2014

Poster Display Time: 10:00 – 16:00
Poster Setup Time: 08:00 – 10:00
Poster Take Down Time: 16:00 – 17:00

POSTER SESSION 1 - September 5, 2014 10:00-16:00

P1.01

THE BENEFITS OF THYMECTOMY IN THE EVOLUTION OF MYASTHENIA GRAVIS

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Objective: The goal of the study was to analyze the 5-year evolution of patients with non-thymomatous myasthenia gravis that underwent thymectomy and to compare the results with the evolution of the patients with non-thymomatous myasthenia that had conservative treatment. Methods: We used a match-pair design to study two groups of patients that were diagnosed with non-thymomatous seropositive myasthenia gravis between 2002 and 2004 in the Neurology Clinic of the Fundeni Clinical Institute. The first group (MGT) had 50 patients that underwent a thymectomy between the years 2002-2004. The second group (MGNT) contained also 50 patients that had the same diagnosis as the first group and had conservative treatment for personal reasons. The match pair criteria were: sex, age at onset, type of onset, Osserman classification stage at diagnosis and the duration of time from onset until positive diagnosis. The two groups were compared from the point of view of the QMG score, of the necessity of cortisone and anticholinesterasic medication, of the complications due to the usage of cortisone for long periods of time, of the number of relapses and of the complete stable remissions at 5 years. All the thymectomised patients had unilateral thoracoscopic thymectomy.

Results: Both groups had a majority of women (MTG-88%, MGNT-86%), young of age, 20-39 years old (MGT-70%, MGNT-68%). Initial ocular onset was the most frequent, being followed by the bulbar onset (MGT-28%, MGNT-24%) and then by the spinal onset (MGT-24%, MGNT-18%). From the point of view of the Osserman classification at diagnosis there was a predominance of class IIb–IIIb, for both groups. The time interval that passed between the onset and positive diagnosis had a medium of 11 months for both groups. The medium QMG score, the medium usage of cortisone and anticholinesterasic were significantly lower in the MGT group compared to the MGNT group (p<0,0005). The complete stable remission at 5 years was achieved in 68% of the patients in the MGT group compared to under 5% in the MGNT group.

Conclusions: All the analyzed variables are arguments that prove the benefits of thymectomy in non-thymomatous myasthenia gravis with achieving the complete stable remission at 5 years for more than half of our patients. Thymectomy is an important link in the complex treatment of myasthenia gravis, with major results on long term.

Disclosure: No significant relationships.

Keywords: treatment, complete stable remissions, Thymectomy, Myasthenia gravis

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P1.02

RESULTS OF EXTENDED INTRATHORACIC LYMPHADENECTOMY IN COURSE OF THYMECTOMY FOR THYMIC CARCINOMA.

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Objectives: The need and extent of lymphadenectomy in course of thymectomy for thymic carcinomas is a matter of debate. TNM-based classifications evidenced the prognostic relevance of nodal involvement. We report a series of extended intrathoracic lymphadenectomies (EIL) for thymic carcinomas (TC), describing the outcomes and its possible prognostic role.

Methods: From 2000 to 2011, 13 patients (M/F=6/7, mean age 55.3±11.1 years) with TC underwent extended thymectomy for TC plus EIL (including anterior mediastinal nodes, bilateral lower and higher paratracheal, aorto-pulmonary-window, para-aortic nodes). Nodal involvement was suspected on the basis of preoperative work up (PET-CT scan was performed in 6 patients). Tumor characteristics, surgical procedures (access type, extended resection rate and type), number of lymph-nodes harvested, post-operative complications, disease-free and overall survival are reported. Actuarial-survival was calculated with the Kaplan-Mayer method, differences in survival between groups were calculated with Log-rank-test.

Results: 3 patients underwent neo-adjuvant chemotherapy. Surgical access was sternotomy (n=9), hemi-clamshell (n=3), cervico-sternotomy (n=1). Macroscopic complete resection was achieved in all cases. Extended resection was needed in 7 patients for a total of 10 adjunctive procedures: upper right lobectomy (n=1), lung wedge resection (n=3), pericardial resection+reconstruction (n=3), anonymous vein resection and reconstruction (n=2), resection of pleural implants (n=1). Besides the aforementioned stations, dissection was extended to hilar nodes (2 cases), carinal (3), retrotracheal (3) and left prescalene lymph nodes (1). 291 lymph nodes were removed (mean=22). Postoperative complications were laryngeal paralysis (n=2), atrial fibrillation (n=2), pleural effusion (n=2), bleeding needing reoperation (n=1), sepsis (n=1). Mean post-operative stay was 7 days (range 5-14). 11 patients underwent post-operative radiotherapy. Nine tumors presented a low-grade histology (7 well-differentiated squamous-cell carcinomas, 2 Mucoepidermoid carcinomas), high-grade histology was represented by clear cell (n=1), undifferentiated (n=1) and lymphoepitelioma-like carcinoma (n=2). Nodal involvement was confirmed in 7 cases (53%). Yamakawa N-stage was N0 (n=6), N1 (n=2), N2 (n=4), N3 (n=1). Multistation involvement (n=5: 2 stations in 4 cases, and 3 stations in 1 case) and skip metastases (n=2) were observed. Disease-free-survival and overall-survival were 27±0.6 months and 36±0.9 months respectively. Recurrence occurred in 9 patients (5 distant, 2 regional, 2 local recurrences). Disease-free-survival and Overall 5-year survival rates were 42.85% and 57.14% respectively. N0 Patients showed a better 5-years-DFS and OS than N+ patients (83.3% vs. 14.3%, p=0.0040; 80.0% vs. 28.6%, p=0.0079 respectively).

Conclusions: EIL showed that TC has a high tendency to interest intrathoracic lymph nodes. Since presence of nodal metastases affect the prognosis, preoperative work-up (including PET-CT) should identify nodal involvement in order to select patients that would benefit from multimodality treatment and eventually from extensive surgery.

Disclosure: No significant relationships.

Keywords: preoperative staging, extended resection, lymphadenectomy, Thymic carcinoma

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P1.03

PEMETREXED IN PATIENTS WITH THYMIC MALIGNANCIES PREVIOUSLY TREATED WITH CHEMOTHERAPY

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Purpose: Thymic malignancies are rare, with limited published trials of chemotherapy activity. Pemetrexed, a multitargetedantifolate, was shown to have single agent activity in a prospective phase II trial[1] for previously treated thymoma and thymic carcinoma patients. We performed a retrospective analysis of pemetrexed activity in patients with thymic malignancies.

Methods: Patients with unresectable histologically confirmed invasive, recurrent, or metastatic thymoma or thymic carcinoma seen at the Stanford Cancer Center between January 2005 and November 2013 were identified, and those who were treated with pemetrexed in the second line setting and beyond were included in this analysis.

Results: A total of 81 thymic malignancy patients were identified, of whom 16 received pemetrexed. There were 10 patients (62.5%) with thymic carcinoma and 6 patients (37.5%) with thymoma. Among the 6 patients with thymoma, best response was 1 (17%) with a partial response (PR) and 5 (83%) with stable disease (SD). At a median follow-up of 21.2 months, the median PFS in the thymoma patients was 13.8 months (95% CI, 4.9 to 22.6 months) and the median OS was 20.1 months (95% CI, 16.4 to 23.9 months). Among the 10 patients with thymic carcinoma, best response to treatment was 1 (10%) PR, 5 (50%) SD, and 4 (40%) had progressive disease (PD). At a median follow-up of 13.5 months, the median PFS in patients with thymic carcinoma was 6.5 months (95% CI, 0.2 to 12.8 months) and the median OS was 12.7 months (95% CI, 2.9 to 22.5 months).

Conclusions: This small retrospective study demonstrates pemetrexed activity and disease stabilization in thymic malignancies with a clinically meaningful duration, and supports previous reports of pemetrexed efficacy in these rare diseases. Reference: 1. Loehrer PJ, Yiannoutsos CT, Dropcho S, et al. A phase II trial of pemetrexed in patients with recurrent thymoma or thymic carcinoma. ASCO Annu Meet Proc 2006; 24:7079.

Disclosure: No significant relationships.

Keywords: Thymoma, Thymic carcinoma, Chemotherapy

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P1.04

CAPECITABINE PLUS GEMCITABINE AS SECOND LINE THERAPY IN THYMIC EPITHELIAL TUMORS

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Background: Thymic epithelial tumors (TETs) are rare malignancies, with an estimated incidence of about 3 cases per 100,000 inhabitants. No standard treatment is available for recurrent disease. In 2005, a multi-institutional phase II trial was started on the combination of gemcitabine and capecitabine in pretreated patients with TETs. Final results of this phase II study are presented.

Methods: Eligibility criteria for the study were mainly the following: histologic diagnosis of TET by central review; at least one prior systemic chemotherapy treatment; progressive disease. Treatment consisted of oral capecitabine (650 mg/mq twice daily on days 1–14) and i.v. gemcitabine (1000 mg/mq on days 1 and 8) every 3 weeks. The radiographic response rate was chosen as primary end point and employed to calculate the study sample. Secondary end points were progression-free survival, toxicity, and overall survival.

Results: Thirty patients (18 men, 12 women; median age 57 years, range 48–61 years) were enrolled in this phase II trial from November, 2005 to June 2013. The majority of patients (73%) had thymoma, while the remaining had thymic carcinoma. Of note, 63% of patients showed disease progression within 2 months from the last dose of the last systemic received therapy. The most important grade 3 toxicity was neutropenia in eight patients. Twelve patients had a response (three complete responses and eight partial responses). Among thymic carcinoma patients, we observed three partial responses. Median PFS was 11 months (95% CI 3–17 months). The PFS for patients with thymoma and thymic carcinoma was respectively 11 months (95% CI 6–17 months) and 6 months (95% CI 3–11 months). Thirteen patients are dead at the time of the analysis (median OS, 16 months).

Conclusions: Capecitabine and gemcitabine is an highly active combination therapy in thymic epithelial tumors and should be routinely included in the managment of recurrent/metastatic disease.

Disclosure: No significant relationships.

Keywords: THYMIC EPITHELIAL TUMOR, capecitabine, gemcitabine, second line therapy

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P1.05

TIME CHANGE IN MANAGEMENT AND OUTCOME FOR THYMIC MALIGNANCY IN CHART RETROSPECTIVE DATABASE

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Thymic malignancies are relatively rare and indolent disease. The Chinese Alliance for Research of Thymomas (ChART) retrospectively collected 1693 patients treated at 10 institutions during 1994-2012. Histology was closely related to stage, with 67.7% thymomas in stage I-II but 80% thymic carcinomas above stage III. Overall 10-year survival (OS) was 76.4%, with 17% recurrence. Masaoka stage, WHO histology, and complete resection were identified as independent risk factors for OS, while MG or adjuvant therapies did not affect prognosis. Comparison was made between two time groups (Group A:1994-2003, Group B:2004-2012), similar in sex, age, MG, staging, and histology. There was a significant increase in minimally invasive approaches (0% vs. 24.2%, $p<0.05$) and decrease in lateral thoracotomy (41.6% vs. 25.6%, $p<0.05$). Significant increase in complete resection was observed in thymic carcinomas (62% vs. 83.3%, $p<0.05$), but not in thymomas (89.8% vs. 92.3%, $p>0.05$). Significantly more patients in Group B had surgery alone (29.9% vs. 48.5%, $p<0.05$), without adjuvant radiation (41.6% vs. 25.7%, $p<0.05$). This was observed in all A/

AB and stage I-II B1-3 thymomas. Similar change was seen in stage I-II thymic carcinomas, with decreased use of adjuvant chemotherapy. Management remained similar for stage III tumors. Overall recurrence decreased significantly in Group B (25.4% vs. 14.5%, p<0.05), although follow-up was also shorter. The decrease was both in thymic carcinomas (53.2% vs. 35.4%, p<0.05) and thymomas (16.1% vs. 9.1%, p<0.05), mainly in B1-3 (26.6% vs. 12.7%, p<0.01) but not in A/AB thymomas (3.1% vs. 1.9%, p>0.05). Five-year OS were similar between the two groups in stage I-II tumors (95.9% vs. 92.9%, p>0.05), despite of a significant decrease in adjuvant radiation (57.4% vs. 25.8%, p<0.001). OS was significantly increased in stage III tumors (67.1% vs. 81.5%, p<0.05). OS was similar in stage III thymomas (78.9% vs. 82.3%, p=0.658) though adjuvant radiation decreased (70% vs. 53.3%, p=0.16), owing to a significant increase in complete resection (73.9% vs. 89.5%, p=0.037). OS of stage III thymic carcinomas improved (45.8% vs. 60.7%, p=0.077) along with increased resection rate (59.4% vs. 75%, p=0.086). Consensus could be reached as follows: Both stage and histology should be considered when deciding management strategy for thymic malignancies, and complete resection is of critical importance. Stage I-II tumors could be removed via minimally invasive procedures, with optimal result after complete resection and without adjuvant therapies. For stage III B thymomas, improved survival is possible if complete resection could be achieved, and role of adjuvant radiation is still questionable. Most thymic carcinomas are in advanced stage. Effective induction may be needed to help increase resection rate and thereby, long-term survival.

Type	Stage	Group	OR only (%)	Adj Rt (%)	Adj Chemo (%)	Recurr (%)
A/AB	all	A B	31.4 81.1*	65.7 14.7*	4.3 4.5	3.1 1.9
B1-3	I-II	A B	27.9 62.3*	69.8 34.5*	7% 4.2	15 3.4*
	III	A B	25 27.6	62.5 64.6	20.8 12.7	28.6 13.9
C	I-II	A B	15.4 35.3*	84.6 52.9*	41.7 23.2*	16.7 20.5
	III	A B	6.2 25	59.4 54.5	56.2 52.7	62.8 36.6*

Disclosure: No significant relationships.

Keywords: adjuvant therapy, histology, stage, surgery

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P1.06

EIGHT YEARS OF EXPERIENCE WITH DA VINCI ROBOTIC-ASSISTED THYMECTOMIES

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Introduction Nowadays, Video-Assisted Thoracoscopic Surgery (VATS) is widely incorporated. Robotic systems, such as the da Vinci® System (Intuitive Surgical, Inc, US), offer an excellent visualization of the operative field in combination with a nearly unlimited range of movements of the instruments (Endowrist® technology). These advantages enable to perform more complex thoracoscopic interventions. The aim of present study is to review the experience at the Antwerp University Hospital with the da Vinci Robotic System within the field of thoracoscopic thymectomies. Materials and Methods This is a retrospective review of a single centre experience, using the da Vinci robotic system to assist in thoracoscopic resection of the thymus. Results Since 2003, the da Vinci robotic system has been implemented in our hospital; the first robotic assisted thymectomy was done in 2006. Since than, a total of 47 patients (19 males, 28 females; age 17 – 79, mean 40 years) underwent a da Vinci-assisted VATS thymectomy. One patient was converted to median sternotomy, due to severe obesity and inadequate single lung ventilation. Only 19 patients were admitted to the Intensive Care Unit (ICU), with a mean ICU stay of 1.5 days. Mean hospital stay was 9 days (4-29 days). There was no operative mortality. The majority of the patients suffered from myasthenia gravis (n=27). Five patients needed plasmapheresis in the immediate preoperative period. Only one patient with myasthenia gravis could not be weaned from the ventilator in the operative theatre, but was extubated shortly after admission to the ICU. All other patients had a good recovery from anesthesia. At least 15 patients with myasthenia had clear improvement of their symptomatology during follow up (0 – 8 years, mean 3 years). After histologic evaluation, 24 patients were found to have thymic hyperplasia, in 5 patients the thymus seemed to be normal, and in 2 patients a benign cystic lesion of the thymus was found. Sixteen patients were treated for a thymoma; in one patient even two separate thymomas were found. Seven patients with a thymoma suffered from myasthenia gravis. The thymoma's were WHO type A (n=3), type AB (n=3), type B1 (n=4) and B2 (N=7); according to the Masaoka-Koga classification 11 patients were in stage 1, 3 patients in stage 2a and 2 in stage 2b. The latter 5 patients were treated with adjuvant radiotherapy, as well as one patient were the capsula was opened (diagnosis of thymoma made by open surgical biopty). Recurrent disease was suspected in one patient, however without histological proof and with stable findings during follow up. All other patients remained disease-free (follow up 0 – 7 years, mean 2,4 years). Conclusion Robotic-assisted VATS thymectomy is feasible and safe. Although preparation for the procedure is time-consuming due to the installation and the sterile draping of the robotic system, the operative procedure itself is facilitated and reduced due to the excellent three dimensional visualization and movement of the robotic instruments. Although the hospital stay seems rather long, patients and surgeons feel at ease with this minimal invasive procedure.

Disclosure: No significant relationships.

Keywords: da Vinci, Thymectomy, Thymoma, Myasthenia gravis

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P1.07

EFFECTIVENESS OF EVEROLIMUS PLUS SOMATOSTATIN ANALOGS IN THYMIC EPITHELIAL TUMORS

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Background: New options are available in heavily pretreated advanced or recurrent thymic epithelial malignancies. The mTOR complex is also a potential target in TETs, as it is linked to downstream signaling of cytokines and growth factors involved in the biology of these tumors. After publication of two TET cases that showed a prolonged (>2 years) disease stabilization with everolimus plus octreotide LAR, we tested this combination in a phase II study.

Methods: This phase II study is an open-label, nonrandomized, Ital-

ian single center study. Adult patients with histologically confirmed TET, that is metastatic and measurable according to RECIST criteria, were enrolled, previous chemotherapeutic regimens, including platinum agent as first line. Treatment consists of oral everolimus (10 mg daily) and octreotide LAR (30 mg every four weeks). Treatment is continued until RECIST progression. The primary end point is response rate; secondary end points are safety, progression-free survival (PFS) and overall survival (OS). Tumor assessment is performed every eight weeks and safety every 14 days. Toxicity is assessed using the National Cancer Institute Common Toxicity Criteria (version 4.0). In the first stage, 15 patients have to be enrolled. If three or more responses are observed, the design calls for an additional 20 eligible patients to be accrued.

Results: Six patients were enrolled (median age, 54 years, range 49-58, 1 F and 5 M). Three patients with thymic carcinoma, one with B2 thymoma and 2 with B2-B3 were enrolled. A partial response was observed in 2 patients, while stable disease was observed in 4 patients. No grade 3-4 toxicity has been oberved. After a median follow up time of 3 months (range, 3-6), no patient has either died or progressed.

Conclusions: Preliminary data of this ongoing phase II study are extremely encouraging. Mature results are awaited.

Disclosure: No significant relationships.

Keywords: target therapy, everolimus, somatostatin analogs, Thymic epithelial tumors

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P1.08

CAPECITABINE AND GEMCITABINE AS 2ND LINE THERAPY IN THYMIC EPITHELIAL TUMOURS - RETROSPECTIVE DATA

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Background: In a recently published phase II trial, capecitabine and gemcitabine (CAP-GEM) was an effective second line therapy in patients with thymic epithelial tumours (TETs), with an overall response rate of 40%. On this basis, CAP-GEM is the standard second line therapy for patients with TETs at our institution. The aim of the present study was to investigate the effect of CAP-GEM in the clinical setting and to compare response rate to data from a recently published phase II trial.

Patients and Methods: This is a retrospective study investigating response rates in the first 6 patients with TETs treated with CAP-GEM at our institution. Patients eligible for therapy with CAP-GEM had histologically or cytologically verified TET, were progressing after first line chemotherapy, had PS ≤ 2, had sufficient organ function, and could not be treated with definite surgery or radiotherapy.

Results: The first 6 patients treated with CAP-GEM had a median age of 61 (range: 38-76). Three patients (50%) had type B2, two patients (33%) had B3 and one patient (17%) had thymic carcinoma. All patients had previously been treated with cisplatin, doxorubicine, cyclophosphamide and vincristine. Three patients had previous received more than one line of systemic therapy. Patients received a median of 7 cycles (range: 6-11) of CAP-GEM. Partial response was observed in 2 patients (RR: 33%), 3 patients (50%) had stable disease, and one patient (17%) had progressive disease. One patient underwent radical surgery after 6 cycles of CAP-GEM.

Conclusion: CAP-GEM is a well-tolerated regiment with a reasonable activity as second line therapy in patients with inoperable TETs. We found a response rate comparable to data from a recently published phase II trial.

Disclosure: No significant relationships.

Keywords: capecitabine, gemcitabine, Retrospective, Second line chemotherapy

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P1.09

IS DIAGNOSTIC VAT THYMECTOMY AN ACCEPTABLE FIRST-LINE APPROACH TO THE SUSPICIOUS MEDIASTINAL MASS?

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Introduction: The incidental early stage thymic mass presents a diagnostic challenge. Right-sided Video Assisted Thoracoscopic (VAT) thymectomy is an attractive but potentially morbid solution. The aim was to show that it can be safely applied as a first line modality in those with undiagnosed thymic enlargement with acceptable long-term results.

Methods: Forty-two patients were identified (23 male, median age 53 IQR: 41-65 years) in a 14 year experience who had computerised tomographic evidence of an enlarged, possibly malignant thymic mass but no tissue diagnosis prior to undertaking VAT thymectomy through a right-sided approach. The clinical outcomes of both benign and malignant diagnoses were compared.

Results: Pre-operative myasthenic symptoms were present in 19 patients (45%) whilst 15 (36%) were asymptomatic. Benign lesions were resected in 26 patients (62%): thymic hyperpalasia (54%), thymic cyst (35%), lipoma (8%), and xanthogranulomatous inflammation (3%). Of the 16 malignant patients, 82% had thymoma (two had Masaoka stage I, 10 stage II, and one stage III.), 6% thymic carcinoma, 6% teratoma and 6% seminoma. Eight patients required subsequent radiotherapy for R1 resection. The median hospital stay was significantly shorter in the benign group: 4 vs 5 days (p=0.046). One patient in both groups required conversion to open sternotomy. There was no other significant morbidity in the benign group. Two patients in the malignant group had significant morbidity (1 myocardial infarction and 1 pulmonary embolism). In the malignant group, there were no cases of tumour recurrence or mortality at median follow up of 5.6 years (IQR: 4.2-10.2 years).

Conclusion: Right sided diagnostic VAT thymectomy is a safe and effective first line approach to suspected malignant thymic enlargement. At five year follow-up there were no cases of recurrence in the malignant group, thus R0 resection may not be a necessity in these cases.

Disclosure: No significant relationships.

Keywords: Thymoma, VAT, Thymectomy

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P1.10

THE ASSESSMENT OF SURGICAL ACCESS TO THE EFFECTIVENESS OF THYMOMA TREATMENT

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Background: Thymoma is a neoplasm in which surgical resection is the treatment of choice.

Methods. A group of 124 patients with diagnosis of the thymoma which had surgical resection in the period of time between January 2004 and December 2013 was evaluated. Patients were devided in two 5- year periods 2004-2008 and 2009-2013. Overall survival rate was evaluated according to surgical technique and Masaoka staging system and was compared in periods. In first period of time between 2004 and 2008, 39 patients had sternotomy, 6 had thoracotomy and 3 had VATS thymectomy. The Masaoka staging in sternotomy was 4 in I, 30 in II, 4 in III and 1 in IV. In thoracotomy was 6 in II. In VATS thymectomy group was 1 in I and 2 in stage II. In second period of time between 2009 and 2013, 53 had sternotomy, 14 had thoracotomy and 9 had VATS thymectomy. The Masaoka staging in sternotomy was 7 in I, 40 in II, 3 in III and 3 in stage IV. In thoracotomy Masaoka distribution was 3 in I, 9 in II, 2 in III. In VATS group was 9 in II. Overall 92 patients (74,2%) had sternotomy, 20 patients (16,1%) had thoracotomy and 12 patients (9,7%) had VATS thymectomy. The distribution of Masaoka staging system was 15 in I (12,1%), 96 (77,4%) in II, 9 (7,2%) in III and 4 (3,2%) patients in stage IV.

Results: Five-year survival rate for patients with Masaoka histopathological diagnosis was: 2004-2008 I – 98,4%, II – 96,5%, III/IV – 90,1% and 2009-2013 I – 98,9%, II – 96,7%, III/IV – 89,3%. Five-year survival rate in first group for patients who had sternotomy was 98,1%, thoracotomy – 90,2% and VATS thymectomy 82,8%. Whereas survival rate in second group was: sternotomy – 98,7%, thoracotomy 94,6%, VATS 84,8%

Conclusion: Surgery remains the gold standard for thymoma and the overall survival rate is satisfying. The early-stages of thymoma in Masaoka staging have a better prognosis and it is confirmed in both periods. Although minimally invasive treatment of thymoma should be considered in early-stage tumors, it is still controversial and requires a long-term observations.

Disclosure: No significant relationships.

Keywords: Thymoma, VATS, minimally invasive thymectomy, surgery

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P1.11

SINGLE-CENTRE 20-YEAR EXPERIENCE WITH SURGICAL TREATMENT OF THYMIC TUMOURS.

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Background: Large single-centre institutional series on thymic tumours are scarce. Complete resection remains the mainstay of successful treatment. Characteristics and survival were reviewed in all patients treated in our institution between 1993-2013.

Methods: Hospital databases revealed 134 patients with pathologically-proven thymic tumour. Follow-up (median 63 months) was through patient notes and by telephone contact with the general practitioner.

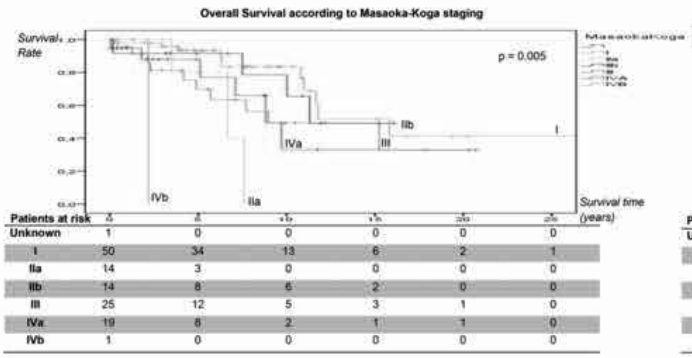
Results: Patients were classified in Masaoka-Koga stages: I: 37%; IIa: 10%; IIb: 10%; III: 20%; IVa: 14%; IVb: 3%; unknown: 5%. According to the WHO classification, pathological subtypes were A: 14%; AB: 19%; B1: 16%; B2: 23%; B3: 11%; thymic carcinoma: 17%. Parathymic syndromes were diagnosed in 45 patients: myasthenia gravis (84%); pure red-cell aplasia (4%); hypogammaglobulinemia (2%); and others (9%). 124 patients (93%) underwent surgery with complete resection in 104 (84%). Surgical approach was: sternotomy (n = 79); thoracotomy (n = 35); cervicotomy (n = 2); other/unknown: (n = 8). In 73 patients (59%) no biopsy was taken prior to surgical resection, 25 were treated with induction chemotherapy, 36 received adjuvant radiotherapy. In hospital mortality was 0.81%. 35 patients died during follow-up (13 of tumour or treatment-related causes). Overall and recurrence-free survival at 5, 10, and 15 years were 86%; 64%; 47% and 67%; 49%; and 31%, respectively. The survival curves were significantly different according to the Masaoka-Koga staging ($p < 0.01$) and so are the recurrence-free survival curves according to the WHO classification ($p < 0.05$). The overall survival according to the WHO classification was not significantly different ($p > 0.05$). (Figure) There was a significant association, using the Pearson's Chi square test, between WHO classification and Masaoka-Koga stages I-IIa-IIb versus III-IVa-IVb ($p < 0.01$). (Table)

Conclusions: Operability and complete resectability of thymic tumours in our experience is highly correlated with prolonged overall and recurrence-free survival. Masaoka-Koga stage is an important predictor for survival and shows a significant association with WHO classification.

Masaoka-Koga staging and WHO classification

	WHO classification						
Masaoka-Koga Staging	A	AB	B1	B2	B3	TC	Total
I, IIa, IIb	12	22	12	20	7	5	78
III, IVa, IVb	7	3	7	11	8	14	50
Total	19	25	19	31	15	19	128

a.



Patients at risk	0	5	10	15	20	25
Unknown	1	0	0	0	0	0
I	50	34	13	6	2	1
IIa	14	3	0	0	0	0
IIb	14	8	6	2	0	0
III	25	12	5	3	1	0
IVa	19	8	2	1	1	0
IVb	1	0	0	0	0	0

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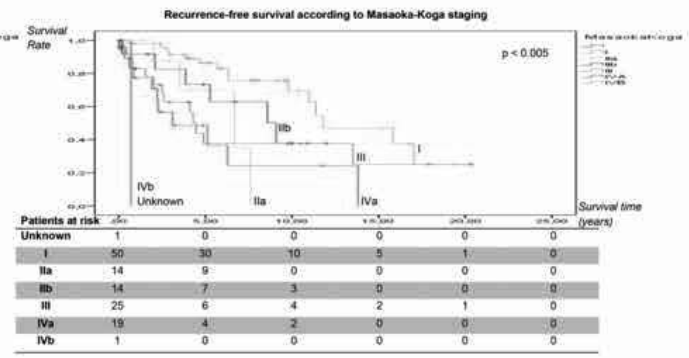
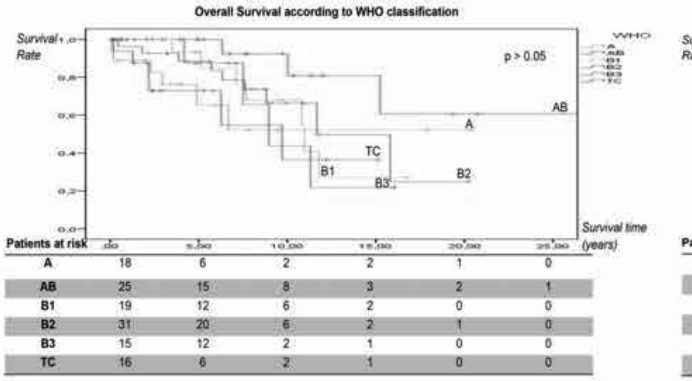


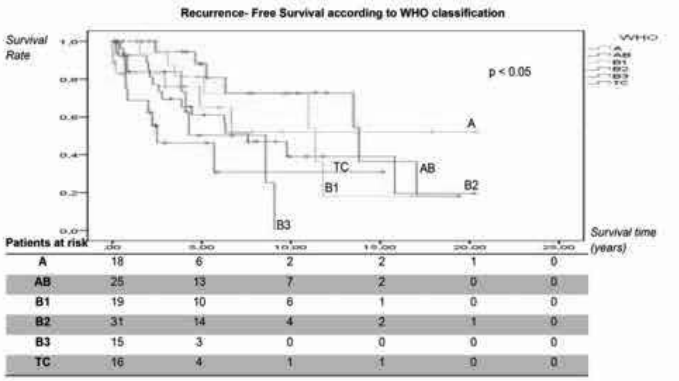
Patients at risk	0	5.00	10.00	15.00	20.00	25.00
Unknown	1	0	0	0	0	0
I	50	30	10	5	1	0
IIa	14	9	0	0	0	0
IIb	14	7	3	0	0	0
III	25	6	4	2	1	0
IVa	19	4	2	0	0	0
IVb	1	0	0	0	0	0

c.



Patients at risk	0	5.00	10.00	15.00	20.00	25.00
A	18	6	2	2	1	0
AB	25	15	8	3	2	1
B1	19	12	6	2	0	0
B2	31	20	6	2	1	0
B3	15	12	2	1	0	0
TC	16	6	2	1	0	0

d.



Patients at risk	0	5.00	10.00	15.00	20.00	25.00
A	18	6	2	2	1	0
AB	25	13	7	2	0	0
B1	19	10	6	1	0	0
B2	31	14	4	2	1	0
B3	15	3	0	0	0	0
TC	16	4	1	1	0	0

Disclosure: No significant relationships.

Keywords: Classification, Survival, Thymic carcinoma, Thymoma

POSTER SESSION 1 - September 5, 2014 10:00-16:00

P1.12

INDUCTION THERAPY VS INITIAL SURGERY IN ADVANCED THYMIC TUMORS:PERIOPERATIVE AND ONCOLOGICAL OUTCOME

Giovanni Leuzzi[1], Mirella Marino[2], Gabriele Alessandrini[1], Isabella Sperduti[3], Felicita Corzani[1], Enrico Melis[1], Virna Cerasoli[1], Daniele Forcella[1], Sandro Carlini[1], Paolo Visca[2], Maria Teresa Ramieri[4], Anna Ceribelli[5], Francesco Facciolo[1]
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Objective: Despite the intense debate concerning the management of advanced thymic tumors (ATTs), no specific oncological strategies have been yet recommended. In this setting, we report our mono-centric 13-yrs-experience to investigate this issue.

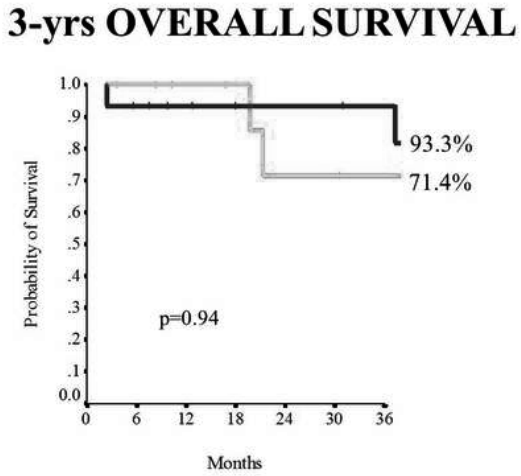
Methods: From 01/2001 to 12/2013, the clinical data of 28 patients treated for ATTs (Masaoka stages III-IV) were retrospectively reviewed. Eleven potentially non-resectable patients (Group A) underwent induction chemotherapy followed by surgery, while immediate surgery was performed in 17 patients (Group B). The end-point was to compare the two groups on: 1) surgical resectability; 2) postoperative course; 3) disease-free survival; 4) overall survival. The Mann-Whitney and Fisher's exact tests were used to evaluate the associations. Survival analysis was performed by Kaplan-Meier method and log-rank test.

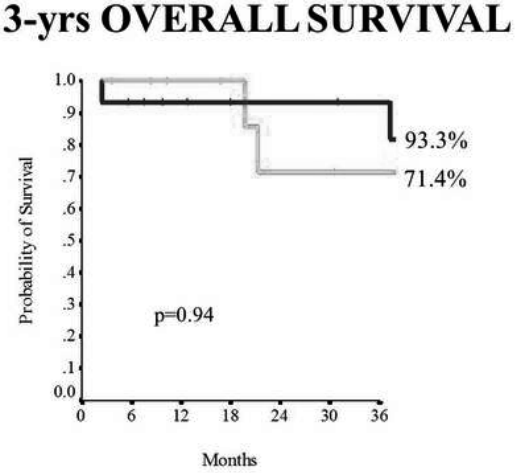
Results: The main features of the sample are summarized in Table 1 (Fig.1). WHO histological classification included two A, four AB, one B1, ten B2, one B2/B3, three B3, six C and one NETT. Both groups were comparable in terms of age, gender, clinical stage, clinical tumor size, histology and adjuvant therapy. Length of surgery was statistically longer in Group A (p=0.015). R0 resection was similarly achieved in both groups (p=0.99). Postop complications occurred in 8 cases of Group A and 9 of Group B (p=0.43). Median postoperative stay was 9 and 7 days for Group A and B, respectively (p=0.08). The 3-yrs overall survival was 71.4% for Group A and 93.3% for Group B (p=0.84, Fig.2). On the other hand, 3-yrs disease-free survival was 40.5% and 53.7% for Group A and B, respectively (p=0.67, Fig.2). Statistical analysis showed Masaoka stage as unique predictor of relapse (p=0.03).

Conclusions: Our results suggest that initial surgery in ATTs is associated to similar perioperative and oncological outcome compared with induction therapy plus surgery. Further studies based on larger series are needed to better investigate the role of multimodality treatment in ATTs.

Table 1

	Group A Induction therapy + surgery (n=11)	Group B Surgery (n=17)	p-value
Age (years)	54.64 ± 9.99	60.44 ± 16.09	0.22
Gender			
Female	4 (36%)	8 (47%)	0.71
Male	7 (64%)	9 (53%)	
Smoker			
No	4 (41%)	7 (36%)	0.51
Yes	7 (59%)	10 (64%)	
Clinical stage			
III	6	11	0.06
IVa	5	2	
IVb	0	4	
Clinical tumor size (cm)	7,82 ± 4.37	6.51 ± 2.51	0.51
WHO Histology			
A/AB/B1	1 (9%)	6 (35%)	0.19
B2/B3/C/NETT	10 (91%)	11 (65%)	
Combined resection (pleura,pericardium,lung)			
No	4 (36%)	11 (65%)	0.14
Yes	7 (64%)	6 (35%)	
Lung resection			
No	2	6	0.15
Wedge	7	11	
Lobectomy	2	0	
Length of Surgery (min)	361.36 ± 176.26	217.33 ± 66.01	**0.01**
R0 resection			
No	2 (18%)	2 (12%)	0.99
Yes	9 (82%)	15 (88%)	
Masaoka stage			
III	8	14	0.44
IVa	3	2	
IVb	0	1	
Pathological tumor size (cm)	9.60 ± 4.95	7.77 ± 2.83	0.54
Adjuvant therapy			
No	5 (45%)	10 (67%)	0.43
Yes	6 (55%)	5 (33%)	





Disclosure: No significant relationships.

Keywords: multimodality treatment, thymic tumors, induction therapy, advanced thymoma

POSTER SESSION 1 - September 5, 2014 10:00-16:00

P1.13

LONG LASTING MANAGEMENT OF FUNCTIONAL NEUROENDOCRINE THYMIC CARCINOMA

Margaret Ottaviano[1], Claudia Von Arx[1], Stefano De Falco[1], Carlo Buonerba[1], Piera Federico[1], Filomena Calabrese[1], Lucia Nappi[1], Pasquale Rescigno[1], Vincenzo Damiano[2], Giovannella Palmieri[1]
[1]Aou Federico Ii Rare Tumors Referal Center Campania Region, Oncology, Naples/ITALY, [2]Aou Federico Ii, Oncology, Naples/ITALY

Background: We describe two rare tumor cases of functional neuroendocrine thymic carcinoma. Due to their rarity, nowadays there are no guide-lines for the management of this kind of neoplasia and the associated syndromes.

Materials and Methods*: One* patient was a 49-year old woman with a diagnosis of functional neuroendocrine small cell thymic carcinoma in a MEN 1 syndrome, judge inoperable. The other patient is a 40-years old man, with diagnosis of functional neuroendocrine thymic carcinoma, discovered for an associated Cushing'Syndrome ACTH dependent, went to no radical surgery. Both of them, were so candidate to a systemic therapy associated to somatostatin analogues to control the paraneoplastic syndrome, never interrupted. The first line chemotherapy based on Carboplatin-Etoposide did not reach the control disease, second line chemotherapy based on CAP schedule (Doxorubicin-Cisplatin-Cyclophosphamide), reached a complete response in the male patient. After progression disease, both of them underwent to a target therapy with everolimus 10 mg/daily, obtaining stable disease for more than one year, and after other progression, they were candidate to sunitinib 50 mg/daily, obtaining stable disease for more than one year.

Results: The female patient died after five years from diagnosis, the male patient is still alive, with a stable disease, after five years from diagnosis.

Conclusion*:* We present our experience of long lasting management of functioning neuroendocrine thymic carcinoma, with the use of somatostatin analogues for the control of associated functioning syndromes and the target therapy (mTOR inhibitor and TKI inhibitor) as a promising new strategy of treatment.

Disclosure: No significant relationships.

Keywords: Neuroendocrine thymic carcinoma, TKI inhibitor, mTOR inhibitor, somatostatin analogs

POSTER SESSION 1 - September 5, 2014 10:00-16:00

P1.14

THYMIC MALIGNANCIES: CLINICAL SPECTRUM AND MULTIDISCIPLINARY APPROACH IN A TERTIARY CARE INSTITUTE.

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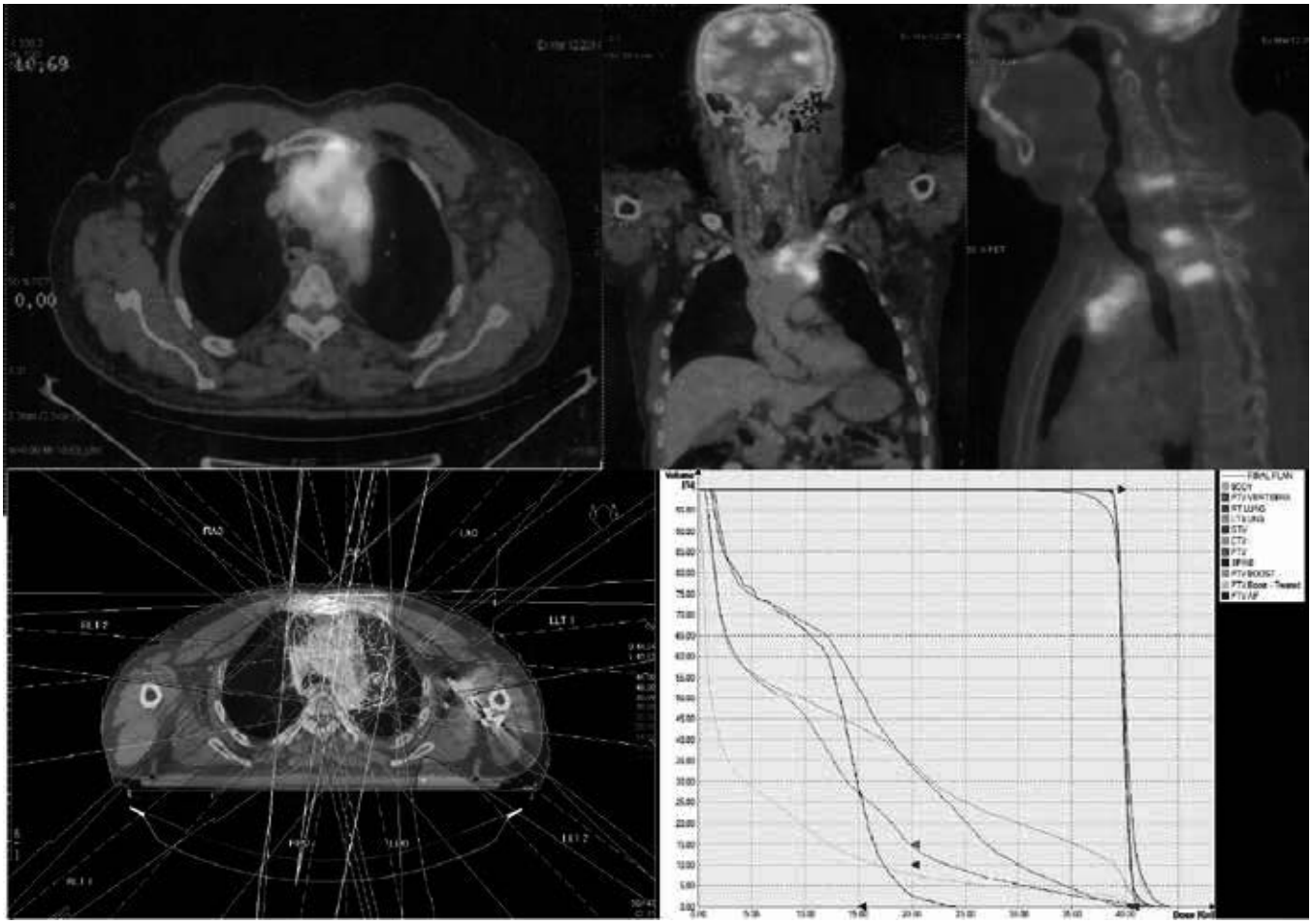
Aim: To evaluate the clinical presentation, combined therapeutic approaches and specifically the role of radiotherapy in thymic carcinoma.

Background: Thymic carcinomas are rare and invasive mediastinal neoplasm with high risk of metastasis, differ morphologically and biologically and management remains still controversial. Locally advanced tumors have a relatively high risk of recurrence and decreased rates of long term survival. Multimodal aggressive approach can improve complete resection rates and long-term out comes.

Material and Methods: The clinical and pathologic data of thymic malignacies were retrospectively reviewed from 2005 to 2014 and out of 17 patients only 7 were evaluable at the time of this study. The presenting age group ranges from 45 to 70 years. Ten patients were clinically staged as Masaoka stage III. Three patients had brain metastasis and 2 had bony/vertebral metastasis on presentation. The pathological subtypes were squamous cell carcinoma and poorly or undifferentiated carcinoma. The treatment modalities used: surgery (5), surgery followed by PORT (2), radiotherapy (3), chemo RT (2), and palliative therapy (5). Twelve cases were inoperable and received radiotherapy or chemoradiotherapy. Seven cases underwent resection; total resection in 2 cases and subtotal in 5 cases. The median dose of radical RT received was 60 Gy. Whole Brain RT with 30 Gy/10#/2 weeks in brain metastasis and palliative RT of 20 Gy/5#/1week or 8 Gy /1# in bony metastasis, were delivered. Systemic chemotherapy with cisplatin or carboplatin and etoposide, upto 6 cycles was the regimen used.

Results: The median survival was 38 months. Patients with brain and bone metastasis expired within 3-22 months. Overall survival was 52%. A number of cases did not report for proper follow up in time. Patients with complete resection and patients receiving radical RT with chemotherapy had better disease control. The recent case with vertebral metastasis received IMRT to the local disease and the bony lesion as well followed by systemic chemotherapy and bisphosphonate therapy having better symptom control.

Conclusion: Over the past 5-10 years radiotherapy has evolved from 2D to 3D Conformal to IMRT and IGRT. Conformal techniques have good result in terms of better coverage of target volume and sparing of normal tissue and better tolerance. Chemotherapy and Radiotherapy definitely add to overall survival, local control and symptomatic relief in palliative setting.Thymic malignancies need multidisciplinary approach but poor referral and follow up still remain a concern in our setup.



Disclosure: No significant relationships.

Keywords: Thymic carcinoma, Chemotherapy, Palliative therapy, Radiotherapy

POSTER SESSION 1 - September 5, 2014 10:00-16:00

P1.19

EFFECTIVENESS OF VIDEOTHORACOSCOPIC THYMECTOMY IN MANAGEMENT OF MYASTHENIA GRAVIS.

Wojciech Zurek[1], Malgorzata Bilinska[2], Sebastian Szczyrba[2], Witold Rzyman[1]
[1]Medical University Of Gdansk, Department Of Thoracic Surgery, Gdansk/POLAND, [2]Medical University Of Gdansk, Department Of Adult Neurology, Gdansk/POLAND

Myasthenia gravis (MG) is an autoimmune neuromuscular disease with fluctuating muscle weakness and fatigue. Muscle weakness is caused by circulating antibodies (Antiacetylcholine Receptor Antibodies – AChRAB) that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors at neuromuscular junctions. The possible source of antigen for AChRAB are myoid cells of thymus gland. Up to 65-75% of patients have thymus hyperplasia, 10-30% have thymoma. Surgical removal of the thymus in majority of patients results in improvement of symptoms. There is a number of surgical approaches for thymectomy: transsternal, transcervical and videothoracoscopic.

Aim: The aim of this paper was to analyse the effectiveness of videothoracoscopic thymectomy in the treatment of MG.

Material: 42 patients, aged 16 to 52 years with generalised form of MG according to Osserman classification, with thymic hyperplasia in computerised tomography (CT) were accepted for evaluation. All of them had videothoracoscopic thymectomy performed in the years 2002 – 2013 in the Department of Thoracic Surgery, Medical University of Gdansk. The mean time from onset of symptoms to surgery was 19 months. The mean time from surgery to the clinical evaluation was 35 months. Two different severity scores (Osserman Score and Oosterhuis Index) served as criteria for the course of the disease. All patients had CT of mediastinum after surgery. The serum level of AChRAB before and after thymectomy was compared. Medication before and after surgery was the other factor analysed.

Results: Post-operative complications were diagnosed in 5 patients (11,9%): pleural hematoma treated videothoracoscopically in 1 patient, myasthenic crisis treated in ICU in 2 patients, temporary palsy of right phrenic nerve in 1 patient, conversion to sternotomy due to intraoperative haemorrhage in 1 patient.

Class of MG Before surgery / After surgery

Class IIA 21 (50%) 35 (85%)
Class IIB 12 (29%) 7 (17%)
Class IIC 1 (2%) 0 (0%)
Class III 8 (19%) 0 (0%)

Class of MG before and after thymectomy according to Osserman classification The clinical state of muscle weakness according to Oosterhuis Index was assessed before and after thymectomy and was as follows:

Class 0 – 0% / 19%

Class 1 – 14% / 28 %

Class 2 – 35% / 39%

Class 3 – 32% / 8%

Class 4 – 19% / 6%.

The mean serum level of AChRAB before and after surgery was respectively 14,58 nmol/L and 12,34 nmol/L. P=0,2 (Wilcoxon signed-rank test). The medium dose of acetylcholinesterase inhibitors taken after surgery diminished statistically (p=0,53). There was no residual mass in mediastinum in follow – up chest CT In 91% of patients. In 9% of patients there was negative contrast enhancing mass in mediastinum.

Conclusions: Videothoracoscopic thymectomy is a safe surgical approach with potential to removal of the entire thymus gland.

Improvement in Osserman classification and Oosterhuis Index with lower level of AChRAB was noticed after surgery.

Unbiased neurological evaluation of this group of patients is difficult because of its heterogenity.

The effectivness of videothoracoscopic thymectomy requires randomized controlled trials.

Disclosure: No significant relationships.

Keywords: improvement, videothoracoscopic thymectomy, Myasthenia gravis

POSTER SESSION 2 - September 6, 2014

Poster Display Time: 10:00 – 16:00
Poster Setup Time: 08:00 – 10:00
Poster Take Down Time: 16:00 – 17:00

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.01

FUNCTIONAL MR IMAGING CAN IMPROVE CHARACTERIZATION OF ANTERIOR MEDIASTINAL LESIONS.

Johan Coolen[1], Frederik De Keyzer[1], Eric Verbeken[2], Christophe Deroose[3], Johan Vansteenkiste[4], Dirk De Ruysscher[5], Walter De Wever[1], Stephanie Peeters[5], Christophe Dooms[4], Paul De Leyn[6], Kristiaan Nackaerts[4], Johny Verschakelen[1], Steven Dymarkowski[1], Dirk Van Raemdonck[6]
[1]University Hospitals Of Leuven, Radiology, Leuven/BELGIUM, [2]University Hospitals Of Leuven, Pathology, Leuven/BELGIUM, [3]University Hospitals Of Leuven, Nuclear Medicine, Leuven/BELGIUM, [4]University Hospitals Of Leuven, Pneumology, Leuven/BELGIUM, [5]University Hospitals Of Leuven, Radiation Oncology, Leuven/BELGIUM, [6]University Hospitals Leuven, Thoracic Surgery, Leuven/BELGIUM

Purpose: Invasive surgical procedures (mediastinoscopy and -tomy) are at the moment the cornerstone of mediastinal oncologic staging, but can lead to patient discomfort and morbidity. In this study, we attempted to use a noninvasive MR imaging approach to differentiate benign from malignant anterior mediastinal lesions and at the same time attempt to provide an imaging-based preoperative evaluation of lesion resectability.

Materials and Methods: 60 consecutive patients (28 male, 32 female), with a suspicious anterior mediastinal lesion on clinical or on imaging-based (CT, PET or EBUS) examinations, were included. Additional to the anatomical MRI sequences on a 3 Tesla scanner, both a DCE- and a DWI-acquisition were performed one day prior to surgery. All MR images were evaluated by visual inspection and by calculating the ADC values (mean) of the whole lesion and of the suspect zone (based on b1000 DWI and ADC map). Finally, the DCE curves were calculated and visually evaluated. Histological examinations of operative specimens served as reference.

Results: A total of 27 benign and 33 malignant lesions were included in this study. In total 51 patients were diagnosed correctly and 9 incorrectly (4 FN and 5 FP) using a combination of DWI-MRI calculation (b1000 and ADC map) with DCE-MRI (sensitivity 87.9%, specificity 81.5% and accuracy 85.3%). Diagnosis based on the mean ADC calculated from the whole lesion was rather disappointing (sens. 63.6%, spec. 66.7% and acc. 65.0%) and showed an optimal threshold of $2x10^{-3}mm^2/s$ between benign and malignant lesions. However, the ADC calculation of the target zone evaluation alone was markedly better (sens. 78.8%, spec. 92.6% and acc. 85.0%) with an optimal cut-off value of $1.15x10^{-3}mm^2/s$. Over all patients, a very good correlation was found between MR signs of local invasion and surgical resectability (kappa 0.85, $p<0.0001$).

Conclusion: In the hard-to-image anterior mediastinal region, noninvasive imaging techniques (DWI- and DCE-MRI) might provide additional information for preoperative lesion characterization and assessment of lesion resectability. Volume and especially heterogeneity of the mediastinal lesion seem to preclude a simple whole-lesion delineation for diagnosis, but a combination of DWI and visual DCE-interpretation, or a targeted zone delineation allow better accuracies.

Clinical Relevance: MR imaging using DW- and DCE-MRI analysis could help to improve lesion characterization, can facilitate to assign the most appropriate biopsy site and might help to noninvasively predict lesions resectability prior to surgery.

Disclosure: No significant relationships.

Keywords: anterior mediastinal lesions, DWI and DCE-MRI, Functional MR imaging

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.02

A SURVEY OF CURRENT CLINICAL MANAGEMENT OF THYMIC CARCINOMAS AMONG ITMIG PHYSICIANS

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Introduction: Thymic carcinomas (TC) are rare malignancies of the thymus for which management recommendations are largely based on small retrospective series. In order to identify areas of agreement and variability in current clinical practice, we surveyed the membership of the International Thymic Malignancy Interest Group (ITMIG) with 12 vignettes of typical clinical scenarios.

Methods: A 16 question electronic survey was designed and approved by the members of the Thymic Carcinoma Working Group. Five-hundred and sixty-five ITMIG members were invited. Questions were directed at the diagnostic workup (n=1), definitive treatment approach (n=4), postoperative management (n=2), surgery options (n=2) chemotherapy options (n=1), and radiation therapy options (n=2).

Results: One-hundred and one ITMIG members replied to the questionnaire. Among the responders there were 60 surgeons, 18 medical oncologists, 14 radiation oncologists and 11 physicians from other specialties. Responders had completed their specialty training ≤5 years ago in 14%, 6-20 years in 58%, and >20 years in 28%. North America (37%), Europe (43%) and Asia (20%) were all well represented. Approximately two thirds had a medium to high experience level in treating patients with thymic tumors (<6 patients per year =33%, 7 to 24 patients=49%, or >25 patients=17%). There was general agreement (>60%) regarding 1) need for adjuvant treatment (radiation therapy +/- chemotherapy) for stage III TC, 2) the use of definitive chemoradiation for the treatment of unresectable localized TC, 3) 3D conformal radiation therapy or intensity modulated radiation therapy for R1 resections, and 4) trimodality treatment of stage IVA TC with limited pleural metastasis with neoadjuvant chemotherapy followed by surgery and radiation. Areas of controversy included 1) need for histological confirmation of TC prior to total thymectomy (core biopsy = 38%, total thymectomy without biopsy = 54%), 2) role of adjuvant radiation therapy for stage II TC with more experienced physicians recommending adjuvant radiation therapy over observation, 3) role of surgical management of stage IVA TC with multiple pleural metastasis (>5) with surgeons more likely to recommend complete thymectomy with total pleurectomy as compared to medical oncologists (32% vs 0%), 4) type of chemotherapy for unresectable IVB disease with less experienced physicians recommending CAP therapy (<6 pts/yr=50%, 7-24pts/yr=35%, >25pt/yr=18%) and 5) treatment of patients with TC who present with cervical lymph node involvement with medical oncologists more likely to recommend chemotherapy only, surgeons more likely to recommend multimo-

dality therapy with surgery, and radiation oncologists more likely to recommend chemoradiation.

Conclusions: The results of the questionnaire provide a description of the management of TC by ITMIG members. Although there was agreement in some areas, clinical practices vary widely based on experience level, location, and specialty. The areas of controversy identified a clear need for collaborative research to identify optimal evaluation and treatment strategies.

Disclosure: No significant relationships.

Keyword: thymic carcinoma, survey, clinical management

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.03

PURE RED CELL APLASIA ASSOCIATED WITH THYMOMA: A CASE SERIES

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[1]King'S College London, Guy'S Campus, Division Of Asthma, Allergy And Lung Biology, London/UNITED KINGDOM, [2]Guy'S And St Thomas' Nhs Foundation Trust, Department Of Thoracic Surgery, London/UNITED KINGDOM,[3]Guy'S And St Thomas' Nhs Foundation Trust, Cancer Centre, London/UNITED KINGDOM

Intoduction: Acquired pure red cell aplasia (PRCA) is a rare disorder of erythropoiesis, with preserved granulopoiesis and megakaryopoiesis. Less than 10% of patients with PRCA have an associated thymoma. The associated anaemia is thought to be due to an immune phenomenon and may respond to immunosuppressive medication.

Method: We retrospectively reviewed the case notes of patients with PRCA and thymoma treated at our institution.

Results: Between 2004 and 2014, 5 patients were diagnosed with PRCA and a thymoma at our institution (3 male, 2 female). The median age at PRCA diagnosis was 55 years. Two patients were diagnosed with a thymoma in the course of investigations for PRCA, whereas three patients developed PRCA after the diagnosis of thymoma was made. Three patients underwent surgical excision of their thymoma (one required induction CAP chemotherapy and post-operative radiotherapy) and were given a Masaoka staging of I, IIb and III respectively. One patient underwent surgical exploration with resection abandoned due to the extent of the disease. She later went on to have Dotatate therapy. The fourth patient had extensive disease on imaging and proceeded to CAP chemotherapy with initial partial response to stable disease. Histological examination showed 1 AB, 1 B1, 1 B2 and 2 B3 thymomas. All 5 patients had bone marrow examinations confirming PRCA. Marrow karyotype was normal in all cases. PRCA therapy varied with three patients receiving immunosuppressive therapy (one with cyclosporin only, one with cyclosporin and oral corticosteroids and one with oral corticosteroids and erythropoietin). One patient could not receive prolonged immunosuppressive therapy due to multiple other co-morbidities. The fifth patient's anaemia resolved spontaneously. At last follow-up, only the patient who did not receive immunosuppressants remains transfusion-dependent. No adverse effects were observed in the patients who received prolonged immunosuppression.

Conclusion: PRCA is one of the rare paraneoplastic syndromes associated with thymomas and should be considered in patients with anaemia in conjunction with a thymoma. Surgical resection aside, treatments to restore erythropoiesis usually involve prolonged immunosuppression with some patients remaining transfusion-dependent despite the above. In view of their rarity and association with complex paraneoplastic syndromes, thymomas should ideally be managed by a multi-disciplinary team in a tertiary care setting.

Disclosure: No significant relationships.

Keywords: paraneoplastic syndromes, pure red cell aplasia

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.04

DISCOVERY OF THE ECTOPIC MEDIASTINAL FOCI OF THE THYMIC TISSUE IN THYMOMAS WITH THE USE OF THE NEW IMMUNOHISTOCHEMICAL REACTION

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Background: The incidence and clinical importance of the ectopic foci of the thymic tissue in thymomas has never been studied, before. The aim of the study is to analyze the results of discovery of the ectopic mediastinal foci of the thymic tissue in thymomas with and without myasthenia gravis (MG) with use of the new immunohistochemical (IHC) reaction.

Material and Methods: The study group included patients operated on for thymomas with and without MG in the period 2000-2013. Extended transsternal or videothoracoscopic thymectomy was performed in all patients with removal of the adipose tissue of the neck, perithymic, right and left pericardiophrenic, aorta-caval and aorta-pulmonary window areas. The mediastinal fatty tissue was subsequently stained with Hematoxillin-eosin (HE) and studied with light microscopy. The results were positive in case of discovery of the Hassall bodies. Subsequenty IHC was performed with use of the Anti-Pan Keratin (CK-PAN) (AE1/AE3/PCK26) Primary Antibody (Isotype IgG_1) (Ventana Medical Systems) including the mousy monoclonal antibodies directed against the epitope present on the human epithelial cytokeratins. Differences in proportion of patients with Hassall bodies and IHC with CK-PAN between patients with and without MG were assessed using two-sample test of proportions. Differences in ectopic foci incidence were checked by chi^2test or Fisher exact test if needed.

Results: There were 43 patients, 34 of them with MG-associated thymomas and 9 with thymomas without MG. The Hassall bodies were found in 1/9 (11.1%) patients with thymoma without MG and in 15/34 (44.1%) with thymomas with MG (p=0.069). The IHC with CK-PAN was positive in 4/9 (44.4%) patients with thymoma without MG and in 22/34 (64.7%) with thymomas with MG (p=0.268). The highest incidence of the ectopic foci was found in the perithymic and the aorta-pulmonary window(okienko) areas (60.5% and 53.6% for IHC, and 58.3% and 27.0% for IHC, respectively) but they were also found in all other areas of the anterior and middle mediastinum. The incidence of ectopic foci in different areas of the fatty tissue of the neck and mediastinum were not different between patients with and without MG. The incidence of the ectopic thymic foci was not influenced by age, sex, histology of the thymus, the WHO type of thymoma and the Massaoka stage.

Conclusions: Immunohistochemistry proved to be useful in discovery of the ectopic mediastinal thymic foci in thymomas.

The incidence of the ectopic foci was higher in case of thymomas associated with MG vs thymomas without MG, however the differences were not statistically significant.

Our preliminary results support the use of extended thymectomy for thymomas with and without MG although further studies with larger number of patients are necessary to confirm these results.

Disclosure: No significant relationships.

Keywords: ectopic thymic tissue, Myasthenia gravis, Thymoma

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.05

ITMIG DEFINITION OF MEDIASTINAL COMPARTMENTS

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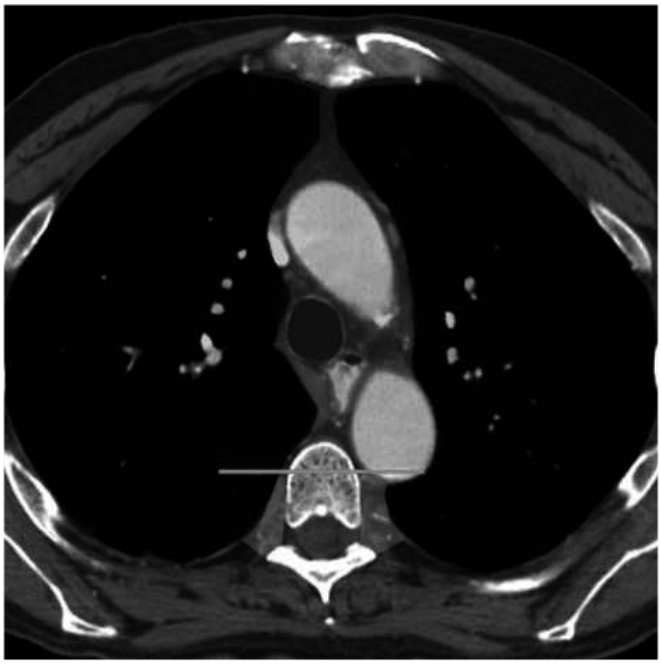
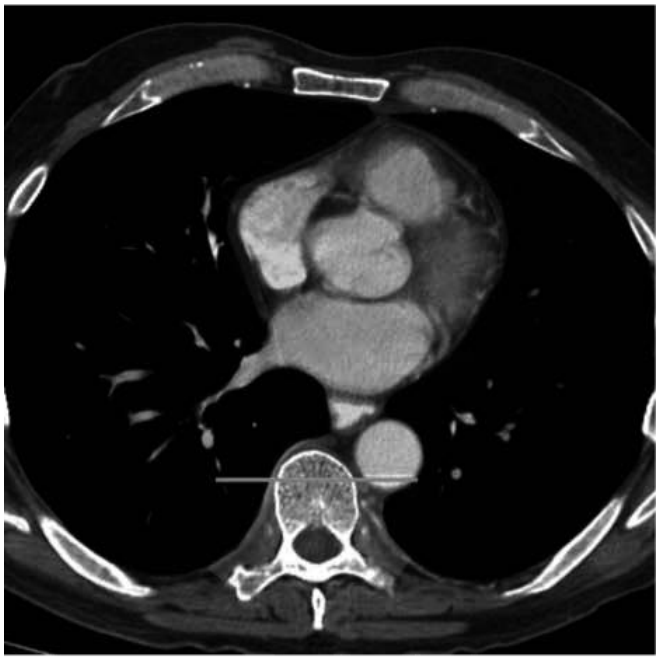
Division of the mediastinum into compartments is used to help narrow the differential diagnosis of newly detected mediastinal masses, to assist in planning biopsy and surgical procedures, and to facilitate communication among clinicians of multiple disciplines. Several traditional mediastinal division schemes exist based upon arbitrary landmarks on the lateral chest radiograph. We describe a modern, computed tomography (CT)-based mediastinal division scheme, which has been accepted by the International Thymic Malignancy Interest Group as a new standard. This clinical classification defines a prevascular (anterior), a visceral (middle) and a paravertebral (posterior) compartment, with anatomic boundaries defined clearly by CT. We anticipate that this system will improve tumor localization, help generate a focused differential diagnosis and assist in tailoring biopsy and treatment plans. In addition, this system should facilitate communication among surgeons, oncologists, radiologists, and pathologists worldwide, with the added benefit of ultimately helping to create meaningful prevalence studies across institutions.





Disclosure: No significant relationships.

Keyword: Mediastinum; compartments; CT

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.06

D2-40: A GOOD IMMUNOHISTOCHEMICAL MARKER FOR B2 THYMOMAS

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Background: Clinical stage, resectability and histological subtype of thymoma are the most important prognostic factors in the disease. Due to great heterogeneity of morphology in routine H&E staning, proper classifying of thymomas can be challenging. Immunohistochemical markers for cortical or medullar epithelial cells could be helpful. D2-40 is an antibody, that recognizes podoplanin, transmembrane glycoprotein found in various normal and neoplastic cells including lymphatic endothelium, mesothelial cells, stromal reticular cells and follicular dendritic cells of lymphoid tissue. The antibody is widely used by pathologists in diagnostics of mesothelioma, lymphatic-derived tumors or lymphatic invasion by neoplastic cells. Some authors report relationship between D2-40 expression and stage of thymoma or poor clinical outcome of the disease, but no correlation with histological subtype.

Materials and Method: 59 thymic epithelial tumors (53 thymomas and 5 thymic carcinomas, TC) were analyzed for expression of podoplanin using of D2-40 antibody. The extent and the type of reaction (membraneous or cytoplasmic) were assessed. Lymphatic vessels, remnants of normal thymus or lymphoid follicles in the stroma represented an internal positive control of reaction. The histological subtype of tumor was established according to WHO classification (2004) and the stage of thymomas under Masaoka staging system. Results Group of thymomas encompassed 3 type A, 12 AB, 6 B1, 11 B2, 2 B3, 2 micronodular, 1 metaplastic and 17 combined thymomas including B2B3 (11), B1B2 (4) and B1B2B3 (1) and AB/micronodular type (1). Three of 5 TCs revealed squamous and 1 neuroendocrine differentiation. One carcinoma was not spec-

ified. Positive anti-D2-40 reaction was observed in 1 (33%) type A thymoma, 3 (25%) AB, 2 (40%) B1, 12 (100%) B2, 9 (82%) B2B3, 3 (75%) B1B2, 1 (100%) B1B2B3 and 1 (100%) metaplastic type. Neither pure B3 and micronodular thymomas nor TCs revealed expression of podoplanin. B2 (pure or combined) presented almost exclusively membranous type of reaction unlike with other types of tumors (A, AB, B1 and metaplastic). Mean area of tumor positive for D2-40 was: <1% for type A and AB, 10.2% for B1, 16.67% for B2, 24.64% for B2B3, 15.75% for B1B2, 20% for B1B2B3 and 2% for metaplastic type. There were 6 tumors in the 1st, 36 in the 2nd, 6 in 3rd and 4 in 4th stage. The stage of disease could not be determined in 7 tumors. Four tumors (67%) of stage 1, 19 (53%) of stage 2, 4 (67%) of stage 3 and 4 (100%) of stage 4 expressed podoplanin. Mean area of tumor that disclosed reactivity was: 18.33%, 9.61%, 15.33% and 17.75% respectively. Reaction in tumor cells had variable intensity, but usually weaker than in control tissues.

Discussion: Results of our study revealed that positive, membranous reaction with D2-40 antibody in neoplastic cells that involves over 10% of area of tumor strongly suggests B2 component. Either cytoplasmic reaction or reactivity in lymphoid stroma is not diagnostic. There were no relationship between the reactivity and tumor stage.

Disclosure: No significant relationships.

Keywords: immunohistochemistry, D2-40, Thymoma

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P2.07

POSITRON EMISSION TOMOGRAPHY IN THYMIC LESIONS' SURGERY. A PROSPECTIVE STUDY.

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Aim: To evaluate the utilization of positron emission tomography (PET) scan with fluorine-18 fluorodeoxyglucose (FDG) in the selection of the surgical approach for thymic lesions.

Material and Methods: Seventeen consecutive patients with thymic pathology, underwent PET-FDG after being evaluated by computed tomography (CT), since 2011. The Standard Uptake Value (SUV) max of the lesion, as well as the SUV of the mediastinum, were estimated. The ratio SUVmax Lesion/Mediastinum was the caliber for selecting thoracoscopic thymectomy (TT) or thymectomy via median sternotomy (TMS), as the therapeutic procedure. If the ratio SUVmax L/M < 1, thoracocscopic thymectomy was preferable. If the ratio was, 1 < SUVmax L/M < 2, the selection was depended on the lesion's dimensions (TT was preferred for lesions < 4 cm). If the ratio was SUVmax L/M > 2, a median sternotomy was the approach of choice.

Results: There were 12 male and 5 female patients, with a mean age of 41.1 y.o. In 10 patients the ratio SUVmax L/M showed up > 1, while in 4 patients was higher than 2. The histopathology revealed 5 thymomas, 2 thymolipomas, 5 true thymic hyperplasias, 1 non seminomatous tumour, 1 silicone indused lemphadenopathy while 1 patient is waiting for TT and another one (type C thymoma by fine needle biopsy), for TMS. The mean SUVmax for thymomas was 3.02+-1.67, for thymolipomas was 1.48+-0.26, for true thymic hyperplasias was 1.82+-0.42, while the non seminomatous' tumour SUVmax was 12.4. There have been performed 4 TTs, 1 Transcervical approach and 9 TMSs. R0 resection was achieved in all 14 patients, have undergone operation, so far. All patients had an uneventful postoperative course and the mean duration of hospital stay was 4 days for TTs and 7 days for TMSs.

Conclusions: There is no imaging modality sufficient by itself to identify the nature of thymic lesions. The intensity of FDG uptake is useful for predicting the grade of malignancy, and high FDG uptake may reflect the invasiveness of the malignant nature in thymic epithelial tumors. The creation of a scale of "metabolic biopsy" with the use of the ratio SUVmax L/M, will allow the use of TT to a larger patient population, following of course, the surgical oncology guidelines for the removal of thymic lesions.

Disclosure: No significant relationships.

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P2.08

EBV-ASSOCIATED THYMIC LYMPHOEPITHELIOMA-LIKE CARCINOMA (LELC) : A CASE SERIES .

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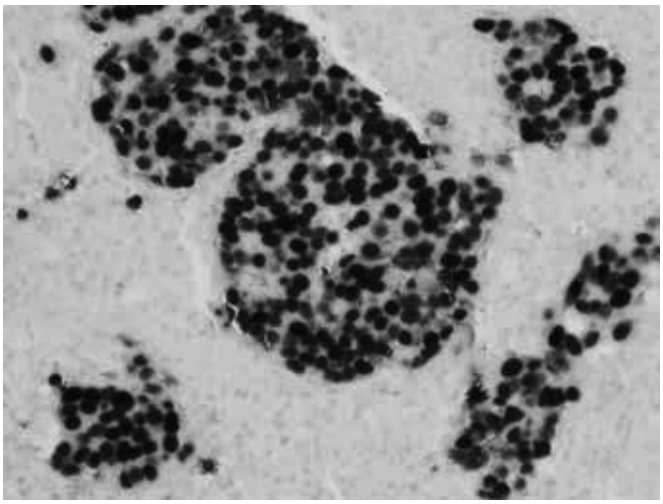
Background: Thymic carcinoma (TC) consists of only 1% of all thymic neoplasms , by themselves uncommon. A few distinctive TC variants are known, one of them is LELC, occurring in young adults. Association of the latter entity with EBV has been described.

Methods: Tumoral EBV expression, assayed by in-situ hybridization (ISH) in 1 case (see picture below); by immunohistochemistry (IHC) in two . IHC included MNF116, CD5, CD3, TdT, CD1A , c-Kit and Ki67. Presence of somatostatin receptors was evaluated by PET Ga68 DOTANOC-octreotate scan.

Results: During the years 2011-2013 we have treated three young (16-21 years old) male patients with similar clinical attributes. All presented with an advanced disease: Masaoka-Koga Stage Iva/b and high tissue Ki67 proliferation index. All responded to 1st-line platinum/etoposide, or CAP (doxorubicin combination) but relapsed thereafter. Two were given radiation to the primary mediastinal tumor. Further chemotherapy included CHOP (1 case) and capecitabine combined with either cisplatin, gemcitabine or irinotecan and oxaliplatin in different cases. Sunitinib and everolimus yielded no benefit. Two patients, having positive octreotate scans, were treated by octreotide depot and enjoyed a clinical benefit and objective stability. Two patients received peptide-receptor radionuclide (Lutecium 177) therapy (PRRT) conferring partial response in one case. Two patients have expired 18 and 25 months from diagnosis, while one is surviving, with disease, 30+ months.



Conclusion: Despite the dismal prognosis in thymic carcinoma at large and in LELC patients as well, our experience indicates that meaningful palliation and apparent survival prolongation are feasible. Biologic tumor targets such as SSTR, notable in this small series. and potential others should be explored for personalized therapy in the context of an orphan disease. The underlying role of EBV is currently unknown; however, a Phase I trial in nasopharyngeal carcinoma with the related vaccinia Ankara has been reported (Hui EP et al, 2013). Further collaborative research effort is warranted.

Disclosure: No significant relationships.

Keywords: SSTR, lymphoepithelioma-like, thymus, EBV

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P2.09

MEDULLARY APLASIA: A SEVERE CONDITION ASSOCIATED TO THYMIC EPITHELIAL TUMOR (TET)

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Background: Thymic epithelial tumors constitute a wide category of rare neoplasia with a large spectrum of pathologic characteristics and clinical presentations. Hematological complications such as pure red cell aplasia (PRCA) and aplastic anemia are documented in about 15% of patients with TET. Amegakaryocytic thrombocytopenia is not a well studied paraneoplastic syndrome of thymic cancers, owing to its rarety.

Materials and Methods: We report four cases of TET complicated with PRCA and amegakaryocytic purpura and consequent complete bone marrow failure observed at "Centro di Riferimento Tumori Rari" in Naples.

Results: Study Population is composed by 2 women and 2 men; all the patients had Thymoma B2 or B3 sec. WHO 2004, three patients with stadium IVB sec Masaoka and one IVA. They were diagnosed as PRCA and amegakaryocytic thrombocytopenia during treatment for primitive tumor at about 3 years from the diagnosis of TET. They had no benefit from treatment with high-dose corticosteroids and Immunoglobulins. Several immunosuppressive therapies were performed after the diagnosis of complete medullary aplasia: all the patients were treated with cyclosporine A; One patient with Tacrolimus; One patient with Alemtuzumab and plasmapheresis. Neverthless three patients died for severe infections, particularly: one died for respiratory infections, one for viral myocarditis and one for viral encephalitis; the last patient is still in course of treatment.

Conclusions: PRCA, amegakaryocytic thrombocytopenia and medullary aplasia are life-threatening conditions that influence significantly prognosis of patients affected by TET, and require intensive multidisciplinary approach for the management of associated hemorrhagic and infective complications.

Disclosure: No significant relationships.

Keywords: Amegakaryocytic thrombocytopenia, pure red cell aplasia, MEDULLARY APLASIA, THYMIC EPITHELIAL TUMOR

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P2.10

EVALUATION OF RESECTABILITY OF THYMOMAS VIA CINE MRI

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Thymomas are slow-growing tumors of the anterior mediastinum with the highest prevalence at the age of 40-60 years. There is a strong association with paraneoplastic syndroms especially the neuromuscular junction disorder myasthenia gravis not uncommonly producing the first clinical symptoms with weakness of voluntary muscles. When the suspicion of a thymoma arises on a CT scan the next diagnostic step consists of obtaining a tissue sample either by complete surgical excision or biopsy. A precise histopathologic examination of the specimen establishes the diagnosis of thymoma and the tumor is staged according to the widely accepted Massaoka staging system. The latter classifies thymomas according to the extent of tumor mass and the presence of invasion into adjacent structures or the occurrence of metastases. While tumor stage at the time of diagnosis comprises an independent predictor of long-term survival, resectability of tumor mass has also been shown to be crucial for the prognosis of the patient. Thymomas that extend to adjacent structures like the pericard, the pleura or big vessels comprise a special challenge for surgeons as they potentially face an unresectable tumor that has already invaded deeply into adjacent organs or vessels. At the interface between tumor and these organs CT scan imaging of the thorax often does not provide enough information upon which a valid statement can be made whether a complete resection will be possible or not. In these cases we propose the application of a novel imaging technique. Cine MRI is a method where MRI imagines are obtained ECG triggered, finally allowing for the assessment of moving organs. While the patient holds her/his breath a set of MRI imagines is acquired over the period of several cardiac circles. Each cardiac circle is divided into 20 segments or frames. The information of several imagines of the same frame is fused creating a sharply delineated clear result for each frame. In the end, the sequence of these individual frames can be displayed like a movie (cine). These movies can be very helpful specifically in the assessment of the interface between thymoma and mediastinal organs like the heart or big vessels. A tumor that seems so slide smoothly along the surface of the pericardium during the cardiac circle is likely to be easily accessible for complete resection. In contrast to this, a different approach is warranted for patients where the tumor seems to adhere to cardial tissue on Cine MRI imaging. In this case neoadjuvant therapy to first reduce tumor size in order to increase the chance of a complete resection might be the better option.

Disclosure: No significant relationships.

Keywords: Therapy, Resectability, Thymoma, Cine MRI

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P2.11

RESULTS OF MULTIMODALITY TREATMENT FOR THYMIC CARCINOMA AND THE CURRENT CHALLENGE

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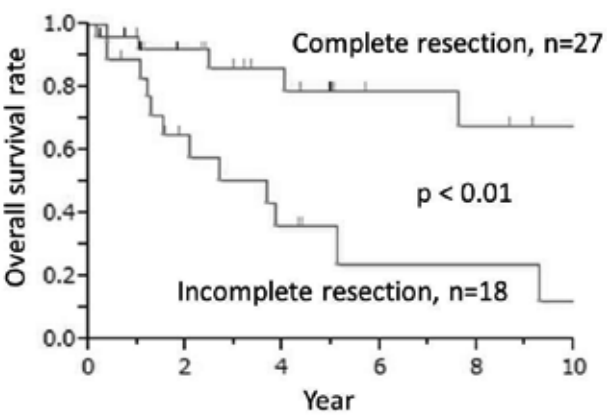
Osaka University Graduate School Of Medicine, Department Of General Thoracic Surgery, Suita, Osaka/JAPAN

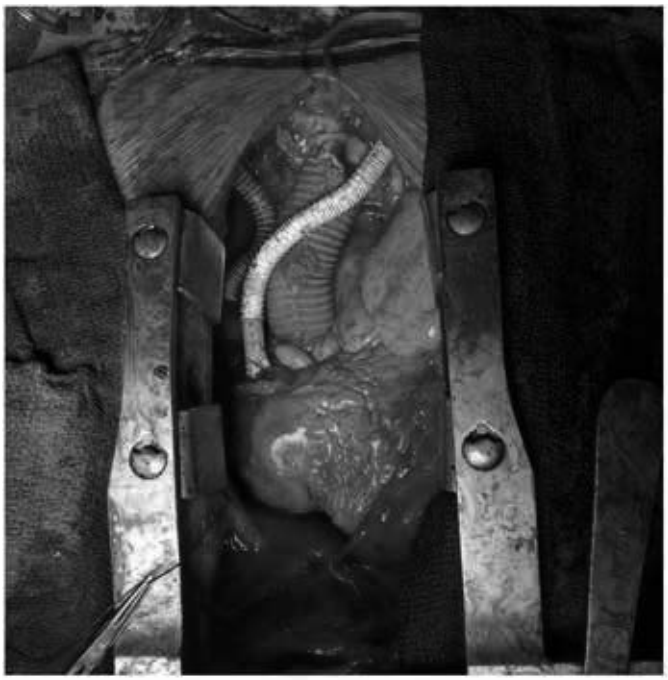
Background: Thymic carcinoma is frequently found as a locally advanced disease. Complete resection is practically recommended as a radical treatment, if possible. Otherwise, chemotherapy and irradiation are indicated for unresectable cases, while there is no standard treatment. We have challenged aggressive multimodality strategy including preoperative chemoradiation followed by extended resection with neighboring organs, occasionally using cardiopulmonary bypass (CPB).

Objective and Methods: We retrospectively analyzed 45 thymic carcinoma patients who underwent surgical intervention in our institute to clarify the outcome and the efficacy of the multimodality treatment for thymic carcinoma. Stage was classified as Masaoka I in 2, II in 1, III in 21, IVa in 6, and IVb in 15 patients. Histological diagnosis was reported as squamous cell carcinoma in 25, neuroendocrine carcinoma in 10, and others in 10 patients. Statistical analyses for survival were performed using Kaplan-Meier method and log-rank test.

Results: The 5-year and 10-year overall survival (OS) rates were 59.9% and 40.4%, respectively. A complete resection was achieved in 27 patients and the 5-year OS was 79.2%, which was significantly better as compared to 36.2% for the patients' group with an incomplete resection ($p<0.01$, Fig.1). Preoperative therapy was indicated in 15 patients; 10 chemoradiation and 5 chemotherapy alone in 5. The complete resection rate was 60% after preoperative therapy. The 5-year OS was 84.6% and 49.6% in patients with and without preoperative therapy, respectively, while there was no significant difference. According to the histology, patients with squamous cell carcinoma showed a tendency to be better outcome and the 5-year OS was 71.4%, though it was 40.6% in patients with non-squamous cell carcinoma ($p=0.08$). Recently, we encountered two patients who underwent a complete resection using CPB due to the direct invasion into the aorta after preoperative chemoradiation therapy (Fig.2). These patients survive without recurrence for 52 and 14 months.

Conclusion: Multimodality treatment for advanced thymic carcinoma is feasible. Recent progress of safe extended surgery in addition to effective chemotherapy and irradiation may contribute to the improvement of the outcome, since only a complete resection is an independent prognostic factor and the local control is essential in thymic carcinoma.





Disclosure: No significant relationships.

Keywords: surgery, multimodality, Thymic carcinoma

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P2.12

PRURITUS AS A PARANEOPLASTIC SYMPTOM OF THYMOMA

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Introduction: Pruritus in malignancy is most strongly associated with Hodgkin's disease (HD), afflicting 30% of patients and acting as a paraneoplastic symptom for up to 5 years prior to diagnosis. Here, we report pruritus as a paraneoplastic symptom for two patients with thymoma.

Case 1 is a 36 year-old woman who presented with generalized pruritus without rash during her second pregnancy and her symptoms did not resolve after delivery. A trial with antihistamines and topical steroids did not help. She had a normal physical exam without lymphadenopathy or hepatosplenomegaly; no evidence of thyroid disease; normal complete blood count and differential (CBC+diff) and kidney and liver function; normal lactate dehydrogenase and erythrocyte sedimentation rate; negative hepatitis panel; and a right upper quadrant ultrasound without cholelithiasis or cholestasis. When the patient had a chest x-ray (CXR) >14 months from the onset of pruritus, it showed an anterior mediastinal mass. CT chest demonstrated a 5.1 cm mediastinal mass that abutted but did not appear to invade the great vessels. Chest MRI revealed no fat plane between the mediastinal mass and pericardium, clini-

cally concerning for Masaoka-Koga stage III disease. A CT-guided fine needle aspiration was nondiagnostic. Because of the concern for HD given the pruritus, a repeat core biopsy was performed and was also nondiagnostic but immunohistochemistry staining for HD was negative. The patient underwent 2 cycles of cisplatin, cyclophosphamide, and doxorubicin (CAP) chemotherapy for presumed thymoma. Her pruritus resolved 3 days after her first cycle and did not return. She had significant decrease in the size of the mediastinal mass and after one more cycle of CAP, she had a median sternotomy and complete thymectomy. Pathology demonstrated a Masaoka-Koga stage II WHO type B2 thymoma, without a clearly defined capsule and microscopic foci of tumor in the mediastinal fat, but margins were negative. The patient did not receive post-operative radiation given the R0 resection.

Case 2 is a 60 year-old woman who presented with 12 months of intermittent pruritus without rash in the upper extremities and back. A physical exam was normal and she had a normal CBC+diff except for mild leukocytosis and normal kidney function. She had a screening CXR for work that showed a large right anterior mediastinal mass. CT chest revealed an 11.8 cm well-circumscribed mediastinal mass. A CT-guided core biopsy confirmed thymoma. Clinically, she had a Masaoka-Koga stage I or II thymoma and the decision was made to forego neoadjuvant chemotherapy. She had a median sternotomy, complete thymectomy, and wedge excision of a right upper lobe (RUL) lung nodule. Pathology demonstrated a fully encapsulated Masaoka-Koga stage I WHO type AB thymoma and the wedge lung biopsy showed an organizing pneumonia pattern. The pruritus resolved promptly after surgery and did not return.

Conclusions: We report, to our knowledge, the first cases of pruritus as a paraneoplastic symptom of thymoma. Pruritus is more frequently associated with another anterior mediastinal malignancy, HD. In our cases, pruritus was present for >12 months prior to diagnosis and resolved promptly after treatment.

Disclosure: No significant relationships.

Keyword: pruritus, paraneoplastic, thymoma

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P2.13

PELVIC METASTASIS FROM THYMIC CARCINOMA: A CASE REPORT

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Introduction: Thymic epithelial tumors are rare and more often localized. Metastatic sites of thymic carcinoma (Masaoka-Koga stage IVb) included mainly lung, liver and brain.

Case report: We report a 64 year-old woman's case with an initial diagnosis of thymoma B3 treated by pre-operative chemo-radiotherapy followed by complete resection. Six years later parietal and pleural tumors were detected by CT scan and [18F]FDG-PET/CT. These lesions were resected and were confirmed as metastasis of mixed thymoma B3 and thymic carcinoma. Eleven years after initial diagnosis of thymoma a pelvic mass was detected by [18F] FDG-PET/CT (SUVmax 8.4) and confirmed by MRI . The patient was asymptomatic. A laparotomy confirmed an isolated peritoneal 60 mm tumoral mass localized on left part of the douglas' pouch. The lesion was completely resected. Pathological analysis concluded to a metastasis of the previously diagnosed thymic carcinoma.

Discussion: Peritoneal and/or ovarian metastasis from thymic malignancies are very rare. Four cases had been reported in the literature. There were observed with different thymic histological subtype (carcinoma, B1, neuroendocrine) and were always associated with loco-regional extension and/or distant metastasis.

Conclusion: To our knowledge this is the first report of an isolated pelvic metastasis from thymic carcinoma. Efficacy of [18F]FDG-PET/CT is well established in patients with thymic epithelial tumors to detect and localize mediastinal recurrence. Our case report emphasizes also the utility of [18F]FDG-PET/CT for metastasis detection and long term follow-up.

Figures: Baseline thoracic CT scan (2002), [^{18}F]FDG-PET/CT (2013), Pelvic MRI (2013), Histological features of the pelvic metastasis

Disclosure: No significant relationships.

Keywords: Thymic carcinoma, positron emission tomography, pelvic metastasis, Thymoma

POSTER SESSION 2 - September 6, 2014 10:00-16:00

P2.14

THYMOMA AND THYMIC CARCINOMA: A MULTIVARIATE ANALYSIS OF PROGNOSTIC FACTORS IN 220 PATIENTS

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Objective: The diversity of the biological, oncological and histological features of thymoma and thymic carcinoma generate difficulties for researchers to establish main prognostic factors. Retrospective analysis of 220 patients with thymoma and thymic carcinoma was conducted at the Department of Thoracic Surgery, Ruhrlandklinik Essen, Germany from January 1998 to July 2013. The goal of the analysis was to determine prognostic factors in this patient population. Thymomas and thymic carcinomas are rare malignant tumors and have a low prevalence.

Methods: 220 patients (137 male and 83 female) diagnosed with thymoma and thymic carcinoma and subjected to surgical treatment were reviewed retrospectively for the 15 year period. The mean age of the patients was 56.37 ± 15.06. Influences of age, Masaoka-Koga stage, WHO histological type, completeness of resection and Myasthenia Gravis were analyzed. The surgical treatment included sternotomy (191), thoracotomy (12), VATS (13) and sternotomy+thoracotomy (4). Total tumor removal included R0 resections (85%), microscopic incomplete resections (R1) (12.7%) and macroscopically incomplete resections (R2) (2.3%). Myasthenia Gravis was observed in 18.2% of patients.

Results: The 5-year overall survival rate (OS) after complete resection was 92.5% and was significantly higher than after incomplete resection (78.5% (R1) and 60% (R2); $p < 0.05$). The 5-years OS of early Masaoka-Koga stage I (92.7%) and II (89.8%) were significantly higher than advanced stages III (61.4%) and IV (40.0%), $p<0.05$). WHO type A (23.6%), AB (16.8%) and B1 (12.7%) tumors have better prognosis than other types B2 (10%); B3 (10%), C (26.9%). Survival rate in WHO (A, AB, B1) was 93.2% in WHO (B2, B3) 51.3.% and in WHO (C) the rate was 18.9% ($P<0.05$). Age, Myasthenia Gravis and type of surgical treatment didn't have statistically significant influence on 5-year survival rate.

Conclusions. From the 5 variables analyzed in the present study only Masaoka-Koga stage, WHO histological type and completeness of resection proved to be significant prognostic factors that affect the 5-year survival rate.

Disclosure: No significant relationships.

Keyword: Thymoma, thymic carcinoma, prognostic factors

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P2.15

PRIMARY MEDIASTINAL MALIGNANT LYMPHOMA. A CLINICOPATHOLOGICAL STUDY.

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Background: Majority of the primary mediastnal malignant lymphoma is aising from the thymic region. The thymus is likely to be involved by the large B cell lymphoma (PBML) or the classical Hodgkin lymphoma (cHL). To determine therapeutic strategy, we need the correct diagnosis of the subtype of the malignant lymphoma.

Materials and Methods: We retrospectively collected medical records of the patients with the malignant lymphoma of the anterior mediastinum from 1998 to 2014 in our hospital.

Results: Twenty-one patients were eligible for the diagnostic criteria with the age ranging from 19 to 72 year-old. Eleven men and 10 women were included. The pathological diagnoses of the subtype were PBML in 10 patients, the nodular sclerosis type of cHL in 8 patients, the T-lymphoblastic leukemia / lymphoma in 1 patient, the follicular lymphoma in 1 patient, and the grey-zone lymphoma in 1 patient. Mean diameter of the mediastinal tumor was 103 mm and 102 mm in PBML and cHL patients, respectively. One patient with cHL had suffered from B-symptoms. Mean values of serum LDH, CRP, sIL2-Receptor of PBML patients were 325 U/L, 3.1 mg/dL and 2002 U/L, respectively. Those of cHL patients were 225 U/L, 2.1 mg/dL, and 948 U/L, respectively. Serum LDH of PBML patients were significantly higher than that of cHL patients (p=0.008). Six patients were pathologically diagnosed with percutaneous needle biopsy. We performed surgical resection of the tumor on other patients to determine the final diagnosis.

Conclusion: We suggest that serum titer of LDH might help us distinguish PBML from cHL. The final diagnosis was determined with the pathological examination of the biopsied specimen which was often retrieved by surgical resection.

Disclosure: No significant relationships.

Keywords: classical Hodgkin lymphoma, Large B cell lymphoma, Mediastinum, malignant lymphoma

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P2.16

RADIOGRAPHIC ASSESSMENT OF TREATMENT RESPONSE OF THYMIC NEOPLASMS USING MODIFIED RECIST CRITERIA

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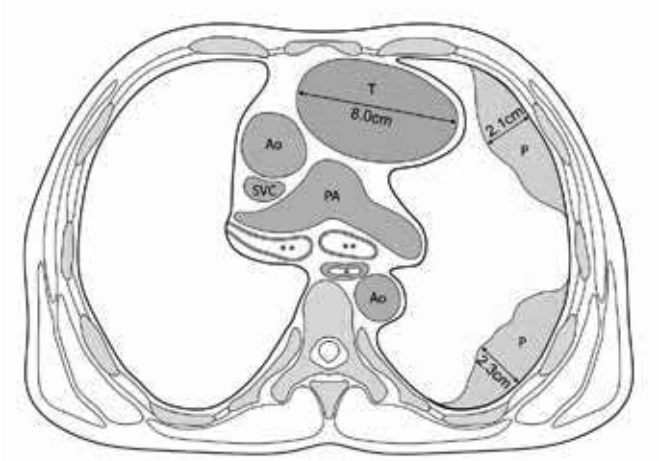
Imaging evaluation is essential in diagnosis, staging and assessment of treatment response in thymic epithelial malignancies and computed tomography is the imaging modality of choice for evaluating thymoma. There is variability in the medical community in how these tumors are measured for treatment response. Accurate measurement of tumor response to treatment is important not only for assessment if therapy is to be continued for the individual patient, but also for drug trials in which new chemotherapy regimens are assessed for their effectiveness. In this presentation we will emphasize how advanced disease should be measured to provide an accurate and universal measurement method that can be consistently performed minimizing intra- and interobserver variability in routine film interpretation and in clinical trials.



Disclosure: No significant relationships.

Keyword: Thymic Neoplasm, ITMIG, response measurement

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P2.17

IMAGING APPROACH TO ANTERIOR MEDIASTINAL MASSES

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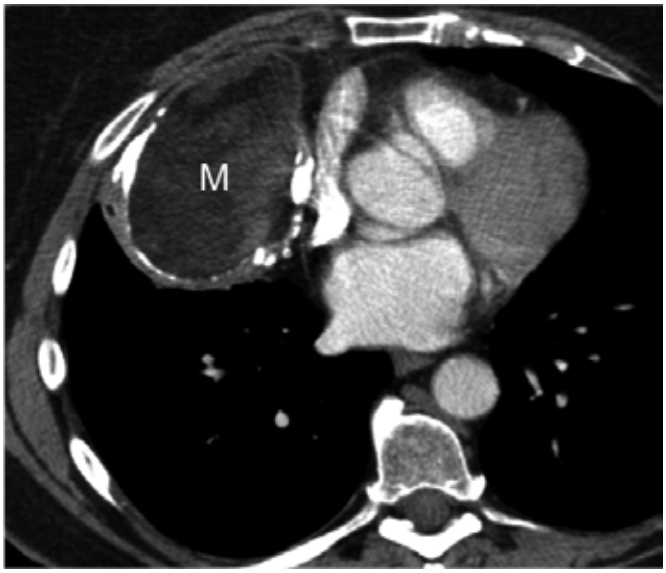
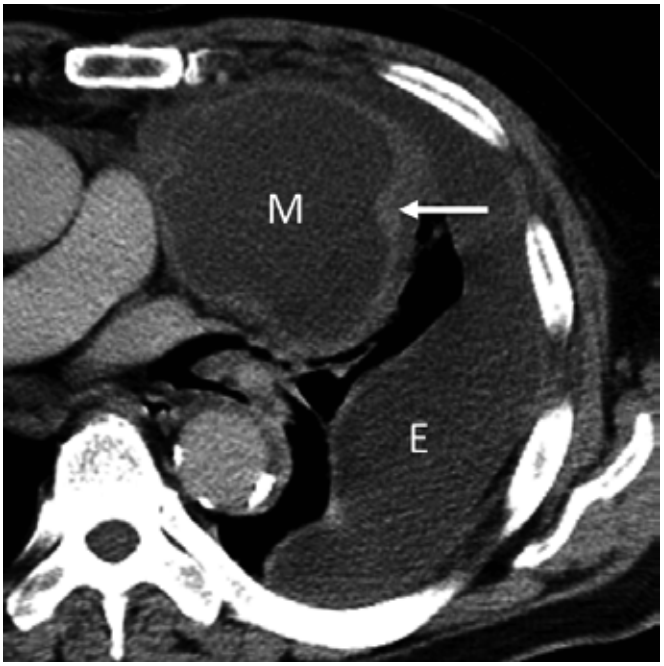
Mediastinal masses are relatively uncommon, yet include a large variety of entities. A structured approach will be presented to facilitate evaluation of patients with anterior mediastinal tumors. The approach will focus first on the more common tumors and on imaging features that strongly suggest a particular diagnosis. Some lesions can be reliably identified by imaging alone, including substernal goiters, benign teratoma, and benign cysts. However, many anterior mediastinal tumors exhibit suggestive but inconclusive imaging features; when the imaging correlates with the typical clinical features a presumptive diagnosis can be quite reliable. This underscores the need for a discussion between the clinician and the radiologist when evaluating most anterior mediastinal tumors. The suggested approach therefore

is to initially rule in or out those lesions that can be reliably identified purely on the basis of characteristic imaging features. Less conclusive imaging features should be correlated with specific clinical features; in many cases this will strongly suggest a particular diagnosis and a further evaluative or treatment strategy.





Disclosure: No significant relationships.

Keyword: Mediastinum; Anterior; Imaging; CT; MRI

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P2.18

MYASTHENIA GRAVIS APPEARING AFTER THYMECTOMY HERALDING RECURRENT THYMOMA

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Thymoma is an uncommon neoplasm of the anterior mediastinum with a strong association with myasthenia gravis (MG). 30-50% of thymoma patients have MG. In 1.5-28% of cases MG first appears after removal of a thymoma. We present a case of a 72-year-old female Caucasian patient who presented with new onset of MG 6 months after a two-stage resection of a B2 thymoma (stage III according to Masaoka-Koga) which was detected during investigation for autoimmune hemolytic anemia. MG was associated with a local intrapericardial recurrence of the tumor which was resected by median sternotomy. No adjuvant therapy was given. Literature research showed two previous cases of recurrent thymoma associated with new onset of MG. Both patients had metastatic disease, one in the lung, the other in the liver while our patient had a locally recurrent thymoma. New onset MG after thymectomy may be the first clinical sign of local recurrent or metastatic disease and should be extensively investigated. If feasible, repeat resection is the treatment of choice.

Disclosure: No significant relationships.

Keywords: Thymectomy, Recurrent Thymoma, Myasthenia gravis

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P2.19

P63 EXPRESSION IN SUBTYPES OF THYMIC EPITHELIAL TUMOURS AND SIGNIFICANCE IN DIFFERENTIAL DIAGNOSIS

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Background: World Health Organization (WHO) classification of a thymoma was universally accepted in clinical diagnosis and closely related with prognosis of patients. Due to various reasons, pathologists often had trouble with exact classification, and lacking available markers to solve this problem. P63 was found to be expressed in epithelial cells of various tumors, including thymic epithelial tumours. However, detailed research between the expression of P63 and thymomas was finite. Methods: The expression of P63 was examined in 134 cases of thymomas and thymic carcinomas by Immunohistochemistry (IHC), and the results were compared with the initial and reviewed diagnoses of all the subjects.

Results: Immunoreactivity for this marker was seen in 126 cases, with a distinctive pattern in each subtype and the results referring to P63 were consistent with the reviewed diagnoses. In addition, easily misdiagnosed subtypes were also indicated in the present study with the growth pattern showed by P63 expression.

Conclusion: In view of the validity of P63, which was expressed in all the types of TET and showed a good and clear tumour cells number and distribution, in discerning subtypes of thymomas, P63 was recommended as a regular marker for thymomas.

Disclosure: No significant relationships.

Keyword: Thymoma, IHC, p63, WHO Classification

Author Index

Authors highlighted in bold = Presenting Author of this Abstract

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