



Cytopathology of thymic epithelial neoplasms

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A cytologic diagnosis of thymoma is extremely challenging. In part, this is because the tumor is uncommon and aspirates are infrequently encountered, a technically proficient interventional radiologist is needed, epithelial cells may be difficult to recognize in lymphoid rich aspirate smears, and there is inherent sampling error in a tumor that frequently displays heterogeneous histopathology. Critical to the cytologic diagnosis of most WHO Type B thymomas is the recognition of a distinct population of epithelial cells mixed with lymphocytes. This is more easily accomplished using Papanicolaou or H&E stains, and often requires a cytokeratin stain for verification (in the correct clinical-radiologic context) because these cells are cytologically bland and have a varying amount of cohesiveness. WHO Type A thymoma may contain only epithelial cells and thus mimic a spindle cell neoplasm, or mesothelial cell clusters. Limitations of the cytologic method include an unproven ability to definitively separate thymoma into specific WHO subtypes using cytology alone, and to determine capsular invasion. Non-neuroendocrine thymic carcinomas mimic their extra-thymic counterparts in cytologic aspirates, and their malignant nature is usually readily recognizable. Thymic neuroendocrine carcinomas (NEC) are also cytologically identical to their more common pulmonary sites of origin, but identification of moderately-differentiated NEC is generally not possible.

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This presentation will focus of the cytopathology of epithelial tumors of the thymus, which include thymoma and thymic carcinoma. The former category contains several histologic subtypes, whereas the latter contains several well-known carcinomas that much more commonly arise in extra-thymic locations such as squamous cell carcinoma, adenocarcinoma, and clear cell carcinoma. In the latest WHO classification, neuroendocrine carcinoma is also included under the broad class of thymic carcinoma, but I will discuss the cytopathology of this group of neoplasms separately in this presentation. In addition to cytopathologic description, some of the pitfalls and limitations derived from the application of fine-needle aspiration (FNA) biopsy to these neoplasms will be mentioned with particular reference to the correlative

histopathology of the various subtypes of thymoma. Minimal discussion will occur regarding the clinical, radiographic, and biologic activity of thymic epithelial neoplasms.

Thymoma

A *specific* cytologic diagnosis of thymoma is among the most difficult attempted in FNA cytopathology. One reason is that few individuals encounter on any regular basis the cytology of thymoma since it accounts for less than 1% of human neoplasms. Another is that proper and adequate sampling is extremely important in the FNA diagnosis of this tumor. The latter is highly dependent on the technical skill of the interventional radiologist attempting to procure this cellular material. Additionally, many of the features that assist in the histopathologic diagnosis of thymoma, such as organotypical differentiation, lobule formation, and dilated

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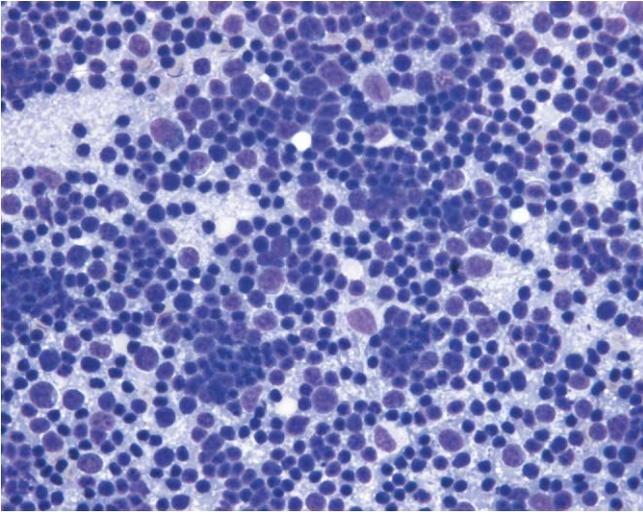


Figure 1 Thymoma, WHO Type B1. A polymorphous population of lymphocytes in a dissociated pattern is present with a predominance of small lymphocytes. The larger cells with identifiable cytoplasm may possibly represent epithelial cells (or large lymphocytes), but without a cytokeratin stain this is difficult to prove. Romanowsky stain.

perivascular spaces (or marked cystic transformation), are completely missing from aspirate slides. Hassall's corpuscles are extremely uncommon in thymoma, and one should not expect to encounter them in smears. The cytopathology literature occasionally contains references to the phrase "malignant thymoma." What most authors really mean to convey by using this phrase is a thymoma that has invaded beyond its fibrous capsule, so-called *invasive thymoma*. Malignant thymoma is an archaic diagnostic label which has been applied indiscriminately in the past and should not be used in either cytologic or tissue diagnoses. Certainly any attempt to distinguish an invasive from a noninvasive thymoma is impossible using cytopathology (or core needle biopsy for that matter) since the cell morphology can be identical to both. Secondly, FNA slides cannot evaluate spatial relationships to determine presence or absence of capsular invasion in any neoplasm. In this discussion, I will use diagnostic terms from the most recent WHO¹ and Suster–Moran² classifications of thymic epithelial neoplasms.

Aspirates of thymoma vary from case to case depending on area sampled, what cell type (epithelial or lymphoid) is most common, whether epithelial cell nuclei are spindle-shaped or rounded, and even whether fluid from an area of cystic change has been aspirated. In the latter case, where only cyst fluid is obtained, one can expect the cytopathology to be nondiagnostic. In a well-performed FNA biopsy, the slides from a thymoma regardless of histologic subtype are moderately cellular or even hypercellular. Smears from WHO Type B (lymphocyte-rich or lymphocytic) thymoma are filled primarily with lymphocytes, whereas epithelial cells are the predominant cell type in slides of WHO Type A (spindle cell) thymoma.

Most thymomas fall into WHO Type B histologic subtype. The large number of lymphocytes found in these aspirates is a heterogeneous group with small round lymphocytes being most common and larger transformed lymphocytes constituting a smaller percentage (Figure 1). Secondary lymphoid follicle formation may occur within thymoma (especially in myasthenia gravis patients). FNA biopsies that sample only these structures will produce smears identical to those of reactive lymphoid tissue, and one finds in addition to a polymorphous population of lymphocytes, the presence of tingible-body macrophages, dendritic-lymphocytic aggregates, and follicular center cell fragments. Critical to the cytologic diagnosis of thymoma is the recognition of a second distinct population of epithelial cells admixed with lymphocytes.^{3–5} Depending on histologic subtype (WHO Type B1, B2, or B3), epithelial cells exist in differing amounts from being relatively inconspicuous and infrequent in smears (WHO Type B1) to being the predominant cell type (WHO Type B3). Epithelial cells in all forms of Type B thymoma typically can exist in tightly clustered microfragments in which it can be difficult to appreciate individual cell morphology (Figure 2). In WHO Type B1 thymoma, groups of epithelial cells are widely scattered in slides that on initial examination appear to be those of a lymph node aspirate because of the overwhelming lymphoid population. Such epithelial cell clusters in WHO Type B1 thymoma are small and inconspicuous, and characteristically closely commingled with lymphocytes (Figure 3). I find Romanowsky stained smears to be particularly difficult in attempting to find these epithelial cell groups. Papanicolaou stained smears in my experience (particularly those that are re-hydrated smears so that red cells are lysed)

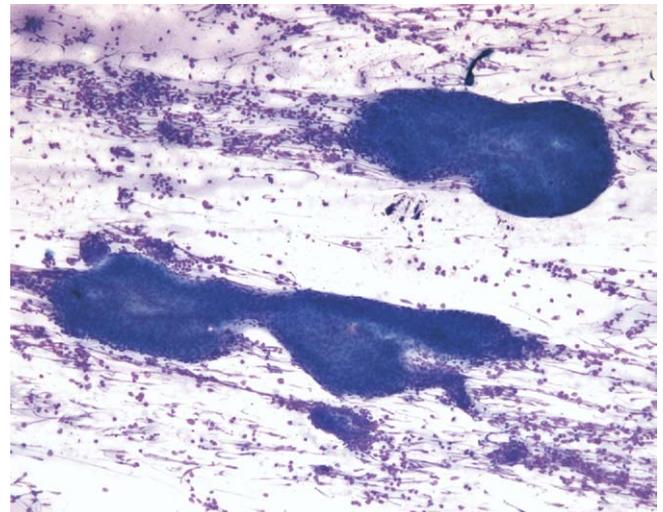


Figure 2 Thymoma. Two discrete tightly clustered aggregates of epithelial cells are set in a background of lymphocytes with smearing artifact—a common phenomenon in mediastinal aspirates. Note that it is not possible to examine individual cell morphology within these thick clusters, however this combination of epithelial and lymphocytic cells in smears from an anterior mediastinal mass is good evidence of thymoma. Romanowsky stain.

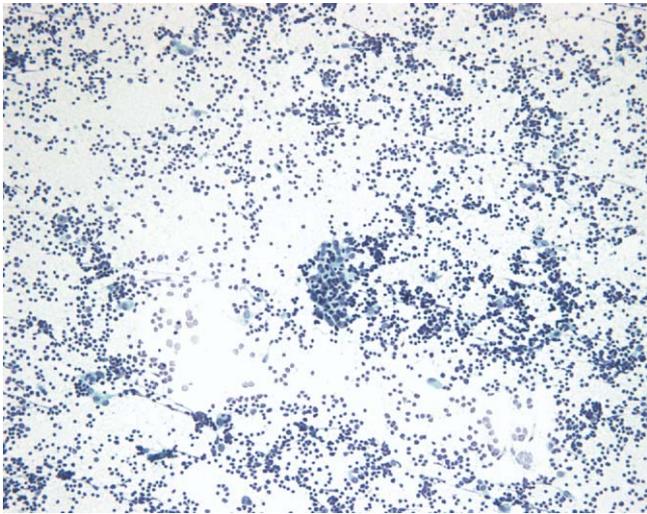


Figure 3 Thymoma, WHO Type B1. Numerous lymphocytes are present in this field that contains a single cluster of epithelial cells in the center. Note that lymphocytes have penetrated into the cluster center. Papanicolaou stain.

allow an easier recognition of epithelial cells. With this stain cell cytoplasm and nuclear detail do not blend with the surrounding lymphocytes to the same degree as occurs with Romanowsky stained slides (Figure 4). In some cases of WHO Types B1 and B2 thymoma, epithelial cell groups are more loosely aggregated, and rarely, one may encounter epithelial cells singly. Epithelial cells are much more noticeable in WHO Types B2 and B3 thymoma. In these subtypes, they can be seen in a dissociated arrangement with single epithelial cells scattered among a polymorphous population of lymphocytes, or even having a loose syncytial arrangement with lymphocytes composing only a fraction of the existing cells (Figure 5).

The cytologic morphology of epithelial cells in WHO Types B1 and B2 thymoma is one of isomorphic cells with

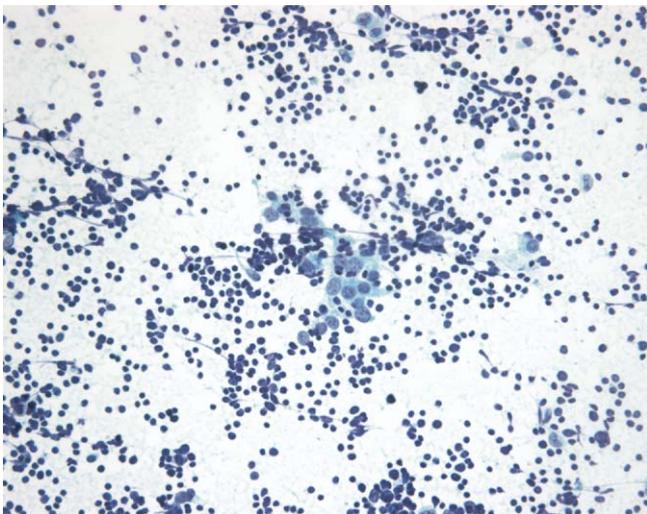


Figure 4 Thymoma, WHO Type B1. The centrally located loose cluster of epithelial cells is easily recognized as such. Note the absence of cytologically malignant features. Papanicolaou stain.

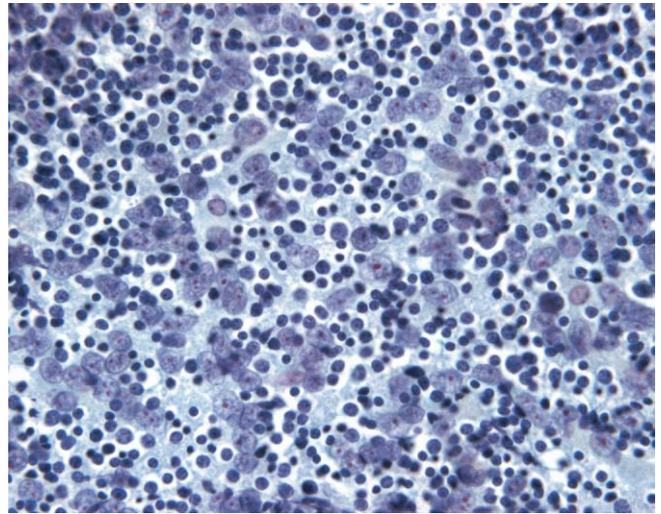


Figure 5 Thymoma, WHO Type B2. Instead of a distinct cell aggregate the larger epithelial cells are haphazardly scattered among lymphocytes. Papanicolaou stain.

rounded to slightly oval nuclei, and no morphologic features suggesting an overt malignancy. Nuclei display smooth or slightly irregular nuclear borders (Figure 6). Evenly dispersed finely granular chromatin is better appreciated in Papanicolaou stained preparations. Nucleoli are small, sometimes distinct, and epithelial cell cytoplasm is meager to moderate in amount. It usually has a finely granular wispy character. Cytoplasmic borders are inconspicuous as the cytoplasm from one cell merges with that of the next creating a syncytium (Figure 7). Cell borders in epithelial aggregates often have a frayed edge with short cytoplasmic prolongations. Aspirates of WHO Type B3 (Atypical Thymoma in the Suster–Moran classification) are rarely en-

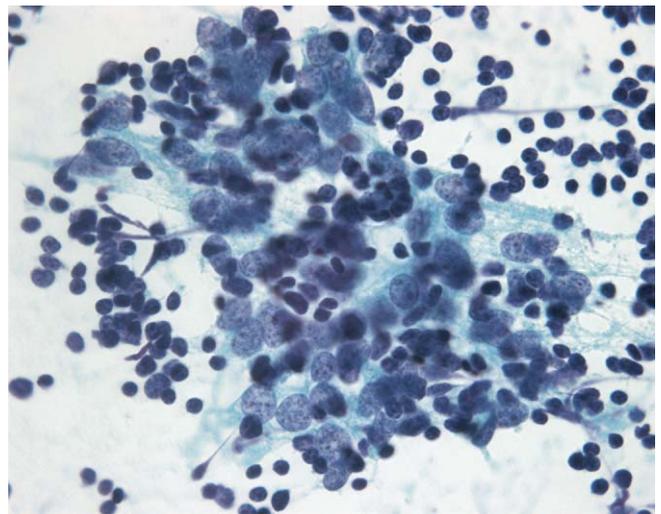


Figure 6 Thymoma, WHO Type B1. Lymphocytes having extremely hyperchromatic small nuclei mix with larger euchromatic epithelial cell nuclei. The latter exhibits round to oval smooth contours, and evenly dispersed punctate nucleoplasm. Discrete nucleoli are not evident. Papanicolaou stain.

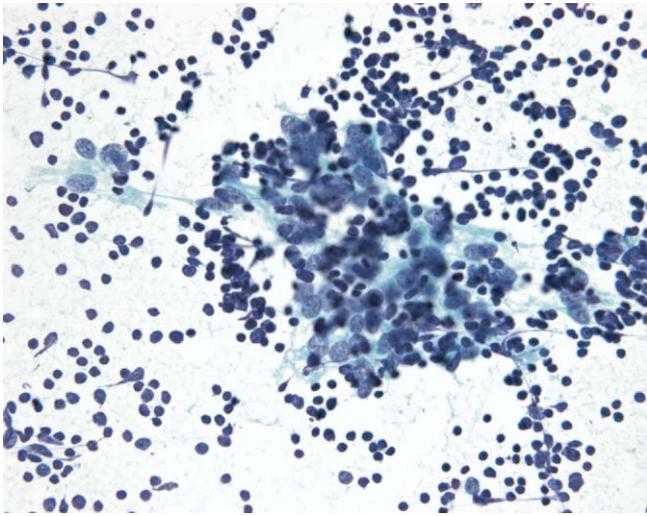


Figure 7 Thymoma, WHO Type B1. Epithelial cell cytoplasm appears as a loose wispy syncytium with a fibrillar quality to cytoplasmic processes as they radiate from the cell cluster. Papanicolaou stain.

countered. The few cases we have encountered show large thick opaque clusters containing many overlapping epithelial cells (Figure 8). In areas where a monolayer of cells exists epithelial nuclei are large, almost 3x the diameter of surrounding lymphocytes, with discrete small nucleoli and finely granular chromatin. A marked difference between WHO Type B2 and B3 epithelial cell nuclei is not appreciated in smears (Figure 9). The major distinction seems to be in the lower fraction of lymphocytes present, but even this is difficult to quantify in FNA slides.

Aspirates of WHO Type A (spindle cell) thymoma are highly cellular. Epithelial cells are distributed as discrete closely aggregated groups, and as single cells (Figure 10). Infrequently, one can find epithelial cell aggregates in a whorled arrangement (Figure 11), or with a fascicular storiform-like pattern mimicking the architectural patterns that are sometimes seen in tissue sections of this subtype (Figure 12). Cells are relatively uniform in size. Nuclei have smooth fusiform or oval contours with fine chromatin, and no visible (or barely perceptible) nucleoli (Figure 13). Cytoplasm is moderate in amount without sharp borders. Similar to the cytoplasm of epithelial cells in WHO Type B thymomas it often has ragged randomly branching processes at the edge of cell clusters. Bare nuclei are particularly noticeable in this thymoma subtype, whereas lymphocytes are sparse (Figure 14). WHO Type A thymoma has been reported to show glomeruloid bodies, glandular structures, rosettes, and perivascular spaces in tissue sections; only rarely, if at all, will these be appreciated in cytologic preparations. In all subtypes of thymoma, it is exceedingly rare to come across typical mitotic figures in aspirate slides. Background necrosis is very uncommon also.

I am unaware of any published papers that profess an ability to reliably correlate the cytopathology of thymoma with any of the specific thymoma histopathologic subtypes

as delineated by the WHO classification. Chhieng and co-workers, using a lymphoid to epithelial cell ratio on needle aspirates, were unable to find a cytologic feature that correlated significantly with any classification scheme using the older Bernatz and Müller–Hermelink classifications.⁶ Although the WHO classification claims that there is a definite histologic difference between WHO Type B1 and B2 thymoma for instance, with the former having smaller epithelial cells with smaller nuclei and smaller nucleoli,¹ this is not a distinction that anyone has reported is possible in cytologic preparations. Moreover, because it is not infrequent for there to be histopathologic transitions in thymoma (mixture of B1, AB, B2, and B3 subtypes) even within the same mass,⁷ it would be imprudent to attempt this on FNA biopsies that sample only a small fraction of the tumor. In my own experience I believe it unwise to confidently attempt to classify a thymoma into a specific histologic subtype using cytology alone. One should inform the clinician in a note as to the cellular appearance of the aspirate (primarily lymphoid/epithelial/mixed/or spindle), but that should be the extent of the exercise. If a pathologist is able to confidently issue a diagnosis of thymoma from an FNA biopsy, that should suffice for appropriate further management of the patient.

Cytologic pitfalls in the diagnosis of thymoma

Critical to the cytologic diagnosis of thymoma is the ability to recognize a dual population of epithelial cells and lymphocytes in the correct clinical and radiologic setting. This can be difficult. For example: (1) the spindle cells in WHO Type A thymoma can sometimes imitate flat sheets of normal mesothelial cells (Figure 15) or a bland spindle cell neoplasm such as solitary fibrous tumor; (2) normal dendritic-lymphocytic aggregates (as seen in reactive lymphoid

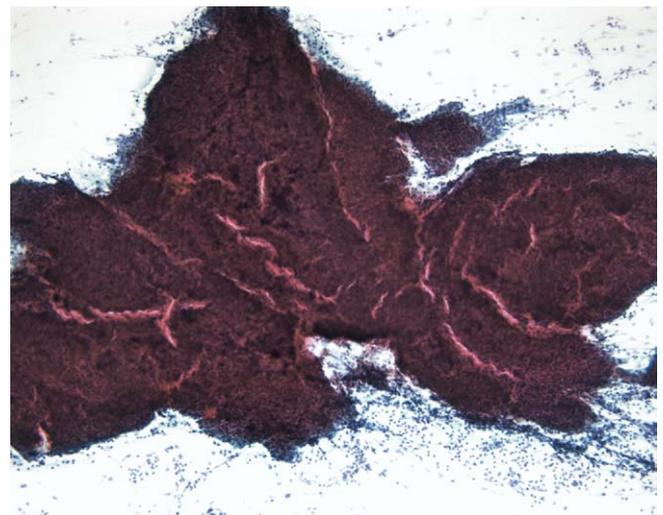


Figure 8 Atypical thymoma, WHO Type B3. An extremely large epithelial cell microfragment is seen. Smaller clusters must be examined to view individual cell morphology. Papanicolaou stain.

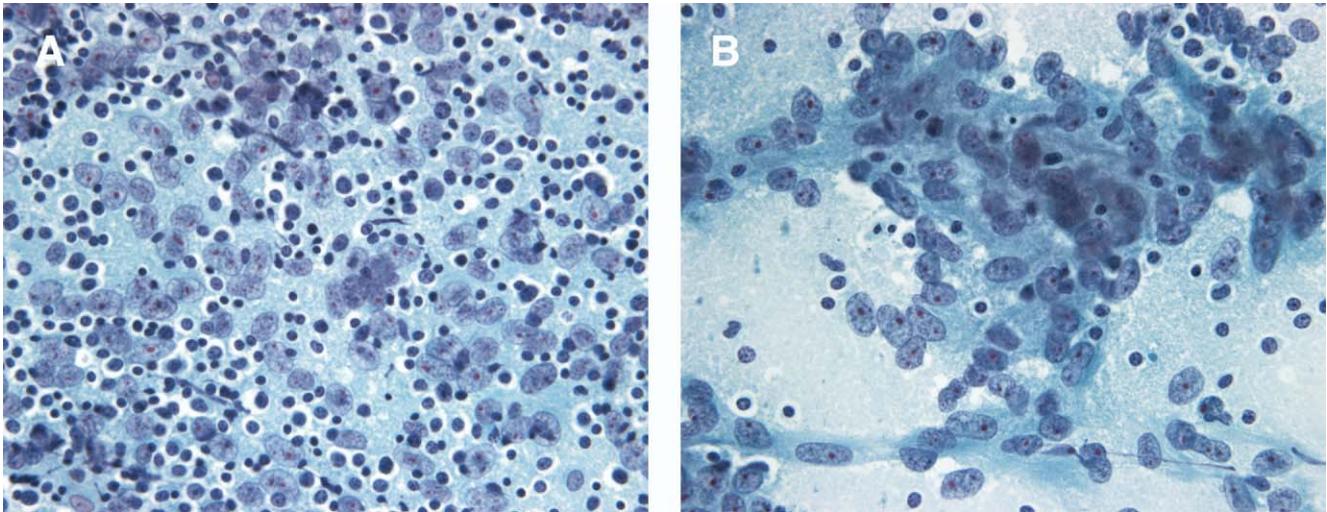


Figure 9 (A) Thymoma WHO Type B2. A heterogeneous population of lymphocytes is sprinkled into this syncytial clustering of epithelial cells. The latter have enlarged slightly irregular large nuclei, and distinct enlarged nucleoli. The nuclear-cytoplasmic ratio is only minimally increased. (B) Atypical thymoma, WHO Type B3. An almost mirror image has epithelial cells in a loose collection with a lesser number of lymphocytes. The distinct nucleoli and nucleomegaly of epithelial cells from both these images cytologically straddle the border of malignancy. Papanicolaou stain.

hyperplasia) may imitate clusters of thymic epithelial cells in a densely lymphoid population of WHO Type B1 thymoma resulting in a false diagnosis of reactive lymphoid tissue (Figure 16); (3) the abundant lymphoid population of WHO Types B1 and B2 thymoma can easily obscure epithelial cells creating the false impression of a lymphoproliferative neoplasm; (4) slides from mediastinal aspirates are often subjected to crush and smearing artifact (secondary to fibrosis within the mass) falsely creating a spindle cell population out of rounded lymphocytes; and (5) lack of epithelial cells [sampling error] combined with immature

appearing lymphoid cells can lead to an erroneous diagnosis of lymphoma.⁸ Thus, immunophenotyping is often required to clearly identify epithelial cells as such. Cytokeratin stain should be performed on all aspirates (either directly on smears or to a cell block preparation) if thymoma is a serious diagnostic consideration.

Because tissue architecture of thymoma is poorly represented on cytologic smears, the differential diagnosis of thymoma is dependent on whether the dominant cell is a lymphocyte or an epithelial cell. Hodgkin lymphoma and non-Hodgkin lymphomas are the main entities to be excluded in lymphocytic thymoma smears. Epithelial cells are absent in each of these entities, but entrapped or adjacent

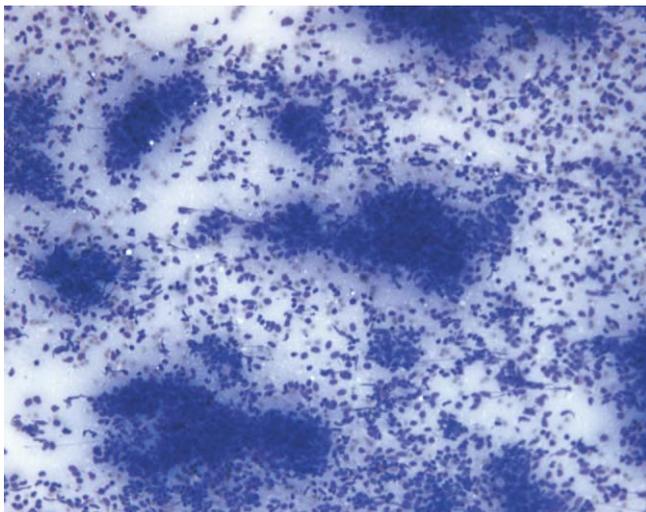


Figure 10 Thymoma, WHO Type A. Epithelial cells are dispersed in several discrete clusters as well as single cells. The latter have nuclei that have been stripped from their cytoplasmic attachment. Although at this low power these bare nuclei simulate lymphocytes, they represent epithelial cells. Romanowsky stain.

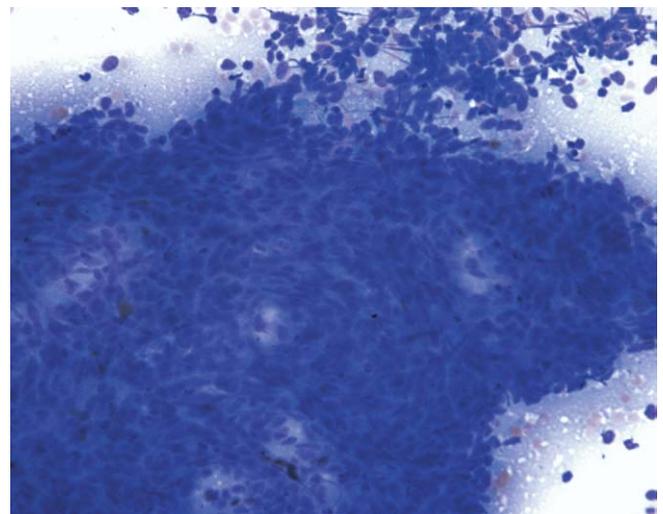


Figure 11 Thymoma, WHO Type A. A whorled arrangement of spindle shaped epithelial cells is seen. Lymphocytes are absent. Romanowsky stain.

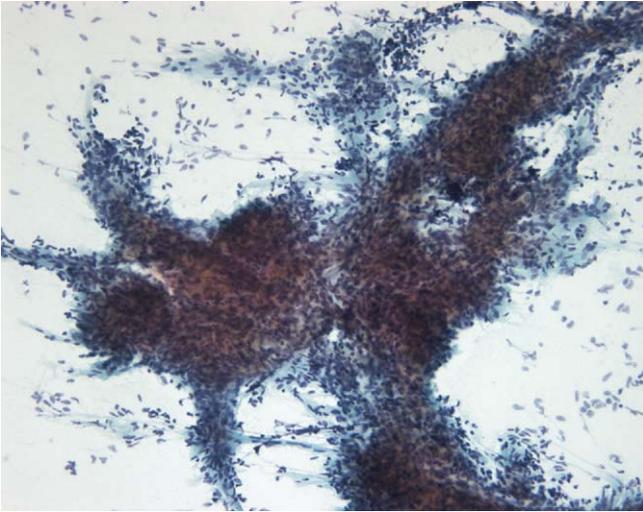


Figure 12 Thymoma, WHO Type A. Spindle cells are closely arranged in intersecting fascicles producing a storiform effect. Papanicolaou stain.

thymic tissue may be aspirated to confound the cytologic picture, and erroneously diagnose a lymphoma as a thymoma. The lymphoid population in thymoma is cytologically polymorphous with a range of lymphocyte sizes and appearances, unlike that of most non-Hodgkin lymphomas. However, it is mandatory that lymphocyte-rich aspirates from the anterior mediastinum be submitted for immunophenotyping in most cases. Aspirates of Hodgkin lymphoma require a careful search for Reed–Sternberg cells and variants.

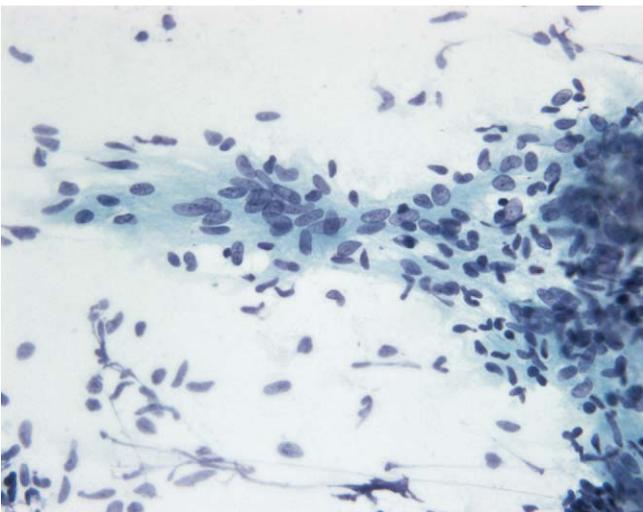


Figure 13 Thymoma, WHO Type A. The edge of a cluster shows the blandness of these cells with relatively isomorphic nuclei having spindle to oval shapes and evenly dispersed fine nucleoplasm. Nucleoli are not evident, and only a few dot-like lymphocytes are seen. Papanicolaou stain.

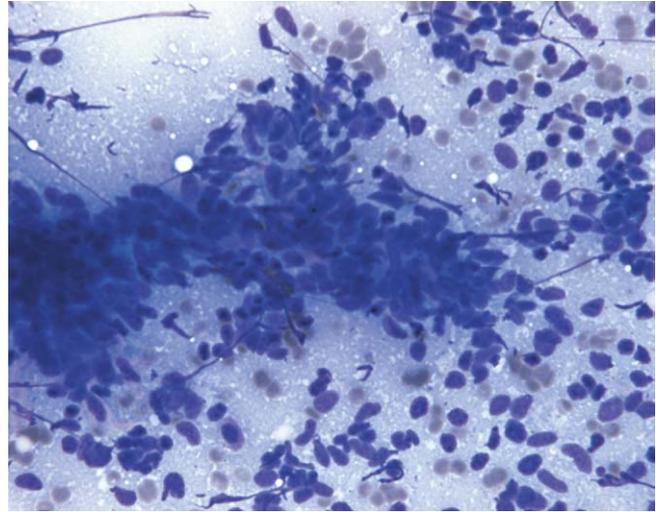


Figure 14 Thymoma, WHO Type A. At the edge of a cluster are many bare oval and spindle shaped epithelial cell nuclei. Romanowsky stain.

Thymic carcinomas

The WHO has classified thymic carcinoma into 10 histologic subtypes excluding neuroendocrine carcinomas. Primary carcinomas of the thymus are rare. Aspirates from the vast majority of carcinomas from the anterior mediastinum are actually of pulmonary derivation. Because the cytopathology of most thymic carcinomas is identical to that of their pulmonary counterparts, the clinical, radiographic, and sometimes gross features must be evaluated very carefully and completely before designating the carcinoma as being of thymic origin. Histologic variants of thymic carcinoma include: squamous cell, sarcomatoid, mucoepidermoid, basaloid, clear cell, adenocarcinoma, papillary adenocarcinoma, carcinoma with t(15;

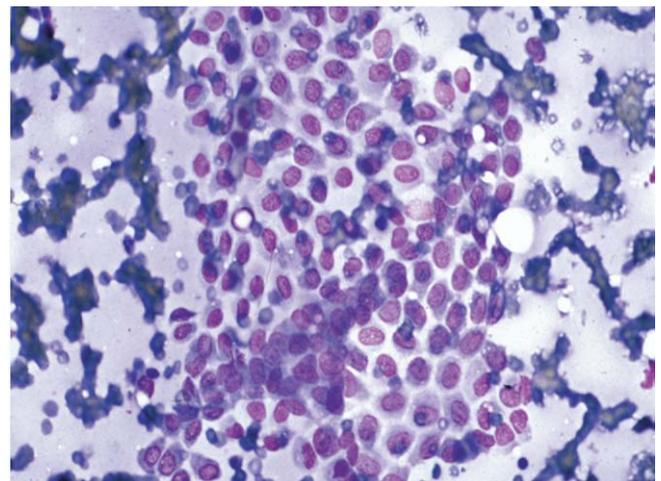


Figure 15 Benign mesothelial cells. An almost flat sheet of mesothelial cells can superficially imitate a spindle cell thymoma. This cluster lacks the marked nuclear overlapping typical of thymic epithelial cells, and has well-developed clear spaces around most cells. Romanowsky stain.

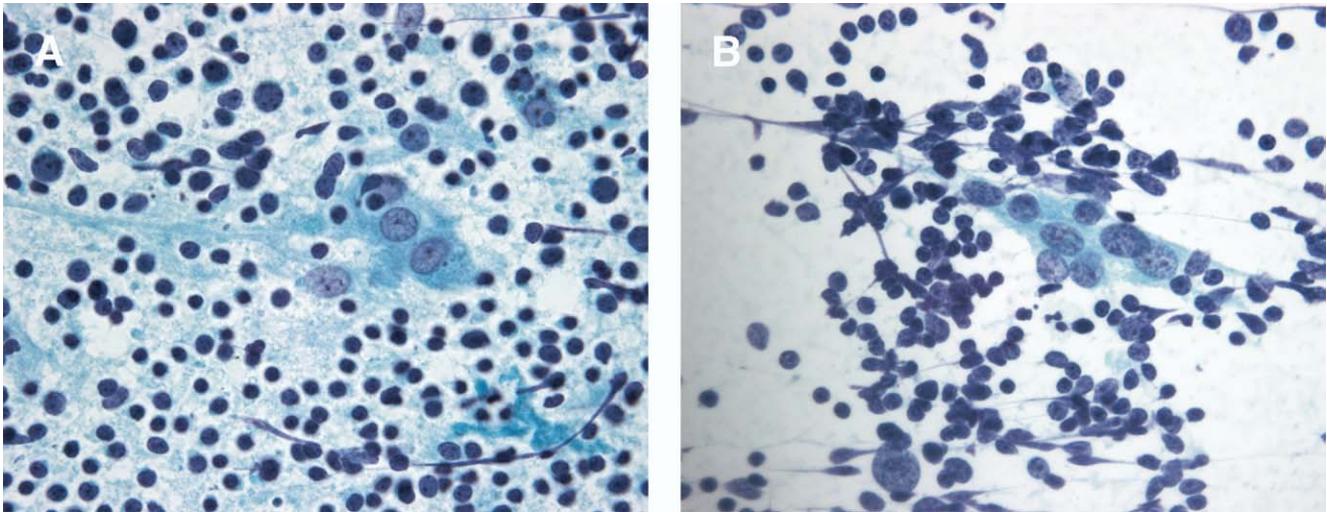


Figure 16 (A) Reactive lymphoid hyperplasia. This dendritic-lymphocytic aggregate contains 3 follicular dendritic cells in the center with long thin cytoplasmic extensions. The bland oval nuclei match those of thymic epithelial cells. Lymphocytes are in the background. (B) Thymoma, WHO Type B1. Note the marked similarity between these two images. Cytokeratin stain is often needed to make a distinction between the two. Papanicolaou stain.

19) translocation, undifferentiated, and lymphoepithelioma-like carcinoma.¹ No substantial series of thymic carcinoma cytopathology exists. Most reports consist of one to two cases. Smear background often has some degree of necrosis (unlike most aspirates of thymoma). Unlike the epithelial cells in thymoma, those of thymic carcinoma display overt malignant features. Similar to their appearance in extra-thymic sites, cells are large and smeared in clusters and as single forms (Figure 17). In general, they have enlarged nuclei, coarse chromatin, discrete macronucleoli, and a moderate amount of cytoplasm. Depending on the subtype the cytoplasm may be focally keratinized (squamous cell carcinoma), meager in amount

(basaloid), spindle shaped (sarcomatoid carcinoma), or vacuolated (clear cell carcinoma) (Figure 18).

Lymphoepithelioma-like carcinoma is among the more common thymic carcinomas in North American patients. Tight clusters of large malignant cells are surrounded and focally infiltrated by small mature lymphocytes. In smaller clusters epithelial cells containing a small amount of cytoplasm are more loosely aggregated allowing for scrutiny of individual cells. These show large rounded nuclei overlapping one another in a syncytial fashion. Nuclei have smooth contours with fine granular chromatin, and single discrete nucleoli. In some

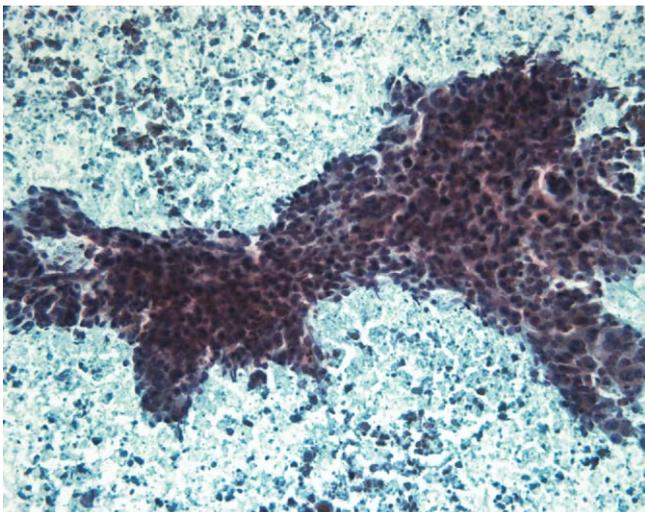


Figure 17 Thymic carcinoma. A microfragment of malignant epithelial cells lies in a necrotic background. The thickness of the fragment precludes detailed evaluation of individual cell morphology, but even at this magnification one can appreciate the large cell size and high nuclear-cytoplasmic ratio. Papanicolaou stain.

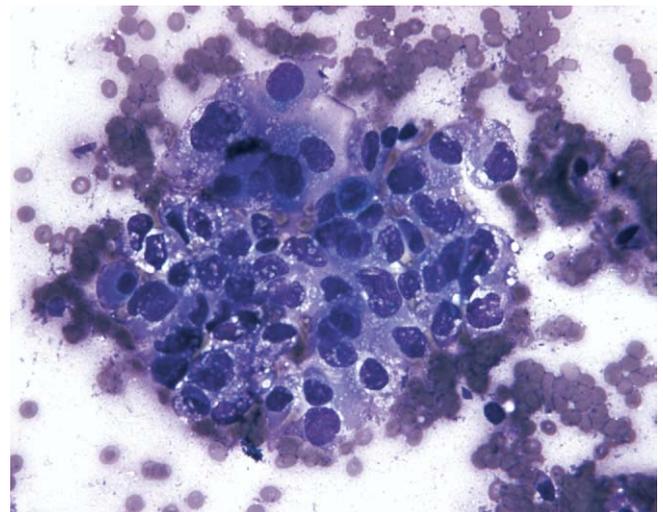


Figure 18 Clear cell adenocarcinoma. Malignant cells are grouped in a ball-like cluster, and no lymphocytes are seen. Markedly enlarged cells exhibit nucleomegaly and nuclear pleomorphism. Nucleoli are difficult to see with this stain. The moderate amount of cytoplasm is coarsely vacuolated. Romanowsky stain.

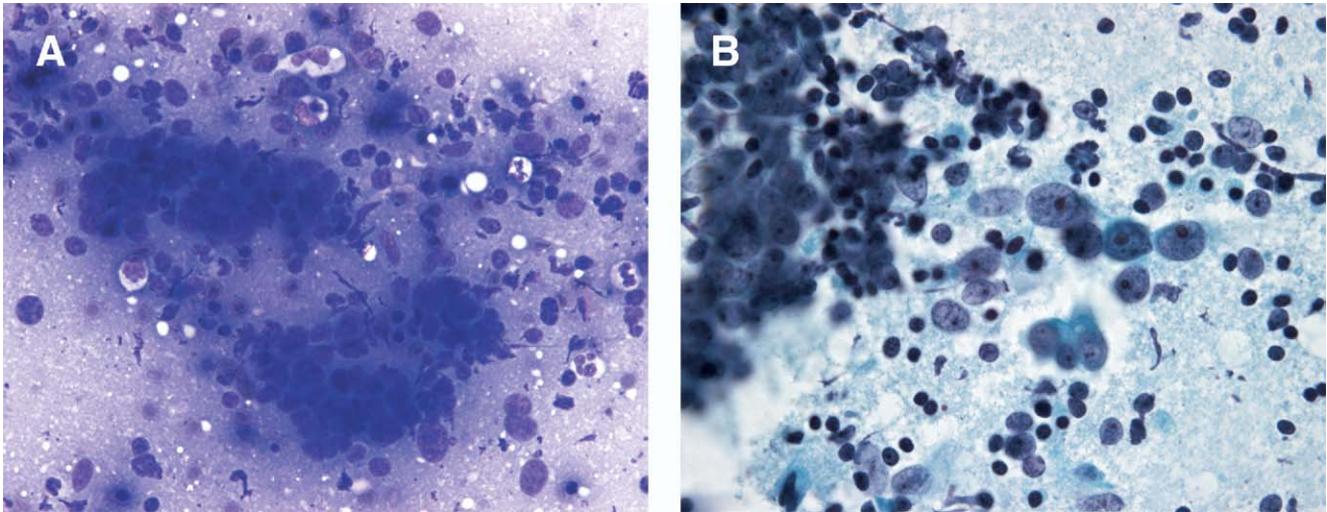


Figure 19 Lymphoepithelioma-like thymic carcinoma. Cell aggregates contain large malignant nuclei set in a cytoplasmic syncytium. Many lymphocytes and a few neutrophils are scattered throughout and mixed with the malignant cells. Macronucleoli are better seen in the Papanicolaou stained slide. (A) Romanowsky stain. (B) Papanicolaou stain.

cells, nucleoli are markedly enlarged—a feature that is better appreciated in Papanicolaou-stained slides (Figure 19).

Thymic neuroendocrine carcinomas

The histologic criteria used to separate neuroendocrine carcinomas (NEC) of the thymus into 4 subtypes are identical to those used in the lung. These include well-differentiated NEC [Carcinoid Tumor], moderately differentiated NEC [Atypical Carcinoid Tumor], small cell NEC, and large cell NEC. Little if any cytomorphologic dissimilarity exists between the various types of NEC of the lung and those of the thymus. Unlike their pulmonary counterpart, NECs of the thymus as a group are much more aggressive biologically.

The vast majority of thymic NEC are subtyped as moderately differentiated NEC.^{1,9} However, few reports of the cytopathology of thymic moderately differentiated NEC (atypical carcinoid) exist.¹⁰ Most reports and my own experience with a small number of histologically proven “atypical carcinoid” tumors of both lung and thymus show a cytopathology that is difficult if not impossible to distinguish from small cell NEC. Smears are highly cellular and composed of a two-cell population of larger intact cells, and smaller apoptotic malignant cells. These are dispersed in loose or tightly aggregated clusters, and as single cells. Nuclei are about three times the diameter of a small lymphocyte, and are round, oval, or fusiform with coarse or smudged chromatin, indistinct or absent nucleoli and minimal visible cytoplasm (Figure 20). Seemingly bare nuclei “molding” against each other, and streaking of nuclear chromatin are common features. The slide background characteristically has a diathesis of cellular debris.

One cannot use mitotic counts in smears (a fruitless exercise without validated correlation to tissue mitotic counts) as is done in tissue specimens to separate moderately differentiated NEC from small cell NEC. Neither can scattered punctate foci of necrosis or presence of vascular invasion (50% in one series),⁹ features of moderately differentiated NEC in tissue, be appreciated in cytologic slides. Thus, two of the most critical criteria necessary to separate moderately differentiated NEC from small cell NEC and well-differentiated NEC are not measurable in FNA material. Additionally, conflicting published descriptions of “atypical carcinoid” exist in the

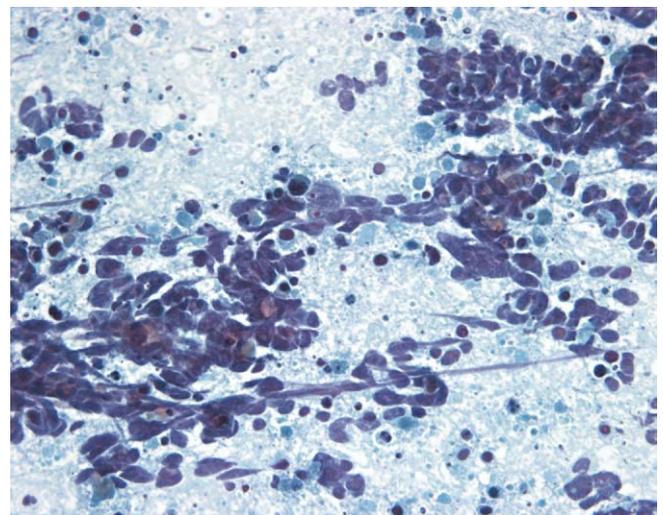


Figure 20 Moderately differentiated neuroendocrine carcinoma. This slide from a histologically proven “atypical carcinoid” is cytologically indistinguishable from small cell neuroendocrine carcinoma. Small to intermediate sized cells in clusters and single forms exist in a necrotic background. Hyperchromatic nuclei are oval, fusiform, or rounded with nuclear streaking, molding of nuclei with each other, and absent nucleoli. Papanicolaou stain.

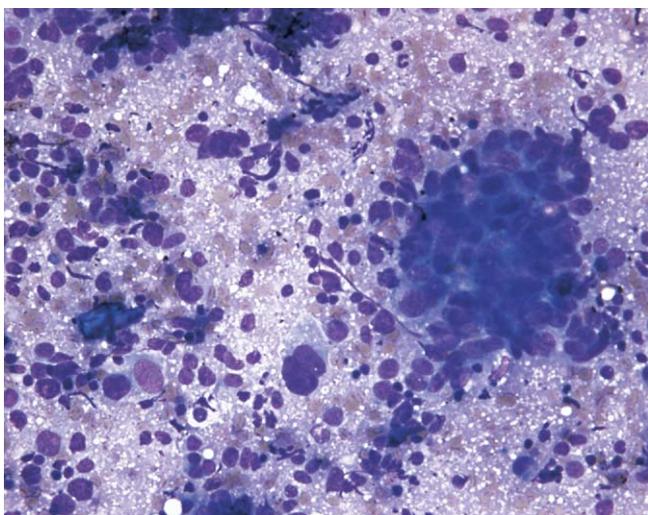


Figure 21 Poorly differentiated large cell neuroendocrine carcinoma. Large cells have the nuclear features of neuroendocrine carcinoma, but also display a moderate to abundant amount of cytoplasm. Individually necrobiotic cells litter the slide. Romanowsky stain.

cytology literature. Some reports and textbooks state that nuclear molding and cell necrosis are absent, while others document its presence. Thus, a *specific* cytopathologic of moderately differentiated NEC (atypical carcinoid) is probably not possible.

Since large cell NEC is often a difficult diagnosis to reproduce in tissue sections, one can imagine that the same dilemma easily takes place in cytologic specimens. Most of the morphologic overlap exists with small cell NEC. In a study of pulmonary large cell NECs, Wiatrowska and coworkers found subtle cytologic differ-

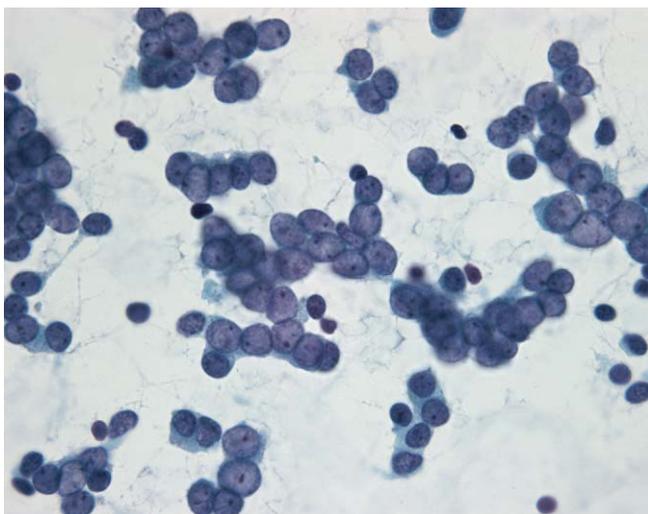


Figure 22 Well-differentiated neuroendocrine carcinoma (carcinoid tumor). Uniformly sized cells with round-oval nuclei, very small nucleoli, and minimal cytoplasm are positioned in short linear chains. Note the absence of nuclear molding and the clean background. Papanicolaou stain.

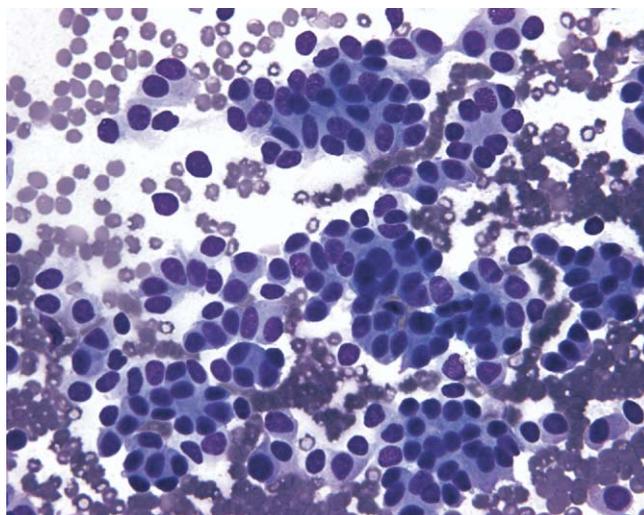


Figure 23 Well-differentiated neuroendocrine carcinoma (carcinoid tumor). Cells arrayed in trabecular rows and acinar groups show marked uniformity with rounded nuclei and an intermediate amount of cytoplasm. Romanowsky stain.

ences in this group depending on whether aspirates were air-dried or alcohol fixed.¹¹ In general, cells were described as large with oval/rounded nuclear shapes, thickened nuclear borders, and visible nucleoli in the majority of cases with scant to moderate cytoplasm. Nuclear molding was described as rare in their series, but my experience is that it can be present (Figure 21). A necrotic background typical of a high grade NEC is common.

The least common thymic NEC is well-differentiated NEC [carcinoid tumor]. Analogous to its appearance in the lung smears contain a high cellular content with a nonnecrotic background. Cells are dispersed in loose groups and singly, and do not exhibit the marked hyperchromasia or nuclear molding seen in moderately differentiated NEC or small cell NEC.^{5,12} Some cell groups are aligned in linear or acinar profiles (Figure 22). Most have uniform round to oval nuclei with finely granular chromatin, indistinct nucleoli, and a small-moderate amount of finely granular cytoplasm (Figure 23). In some cases cells will display a predominantly spindle shape.¹³ Analogous to thymoma, it should be remembered that thymic NECs have the potential to contain a histologic spectrum with the same mass. Areas of well-differentiated NEC converting to foci of moderately differentiated NEC or poorly differentiated NEC may be seen.¹⁴ This is extremely important for any biopsy procedure (core needle or FNA biopsy) where the entire tumor is not available for complete microscopic examination.

Conclusion

FNA biopsy of thymic epithelial neoplasms remains an underutilized method of sampling mediastinal masses compared with its application in other body sites. A

specific cytologic diagnosis of thymoma is possible when the aspirate contains a dual population of proven epithelial cells and lymphocytes in the correct clinical-radiologic context. Nonetheless, the cytologic morphology of thymoma is insufficiently discriminative to categorize it into various histologic subtypes, nor can capsular invasion be determined using this technique. Thymic carcinomas, including neuroendocrine carcinomas mimic their appearance in extra-thymic sites, and display easily recognizable features of malignancy. Separation of moderately differentiated NEC from poorly differentiated small cell NEC is generally not possible due to the inability to judge mitotic activity, and potential sampling error.

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