

Thymoma

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Introduction

Tumors developing in the thymus are termed thymic tumors. The term thymoma is used to describe histologically benign neoplastic tumors even though they may exhibit clinically invasive behavior. Those with apparent atypia and histological features no longer specific to the thymus are known as thymic carcinomas. Various tumors, such as germ cell tumors, lymphomas, cysts, and neuroendocrine carcinomas may also be found in the thymus.

Thymoma has an indolent growth pattern and shows rare metastasis; however, there are more locally aggressive tumors, and some are frankly malignant, invading into surrounding structures and disseminating into pleural cavity. A thymoma is treated as a malignant tumor clinically, when capsular or vascular invasion occurs. There are many pathological subtypes of thymoma, and many classifications exist.

Approximately 30% of patients with thymomas are asymptomatic at the time of diagnosis.¹⁾ In other cases, the presenting clinical signs be local or systemic symptoms, or a combination of both. Constitutional symptoms associated with thymoma may include weight loss, fever, fatigue, or more severe symptoms, such as superior vena cava syndrome, phrenic nerve paralysis, hoarseness, and pleural or pericardial effusions.

Etiology

According to the Annual report by the Japanese Association for Thoracic Surgery, there were 1,205 (39.5%) thymomas among 3,053 mediastinal tumors.²⁾ The operative rate of thymoma is increasing.

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Classification

The classification of thymoma is based on the histological cellular classification and the staging description.

Thymoma features a distinct infiltration of immature nonneoplastic lymphocytes,³⁾ in variable numbers depending on the histological subtype with predominance of lymphocytic or epithelial tumor cells, or mixed type. Bernatz classified four types which applied predominance of spindle cell type to above mentioned three,⁴⁾ because the prognosis for thymoma that has a spindle/oval shaped predominance of epithelial cell is comparatively good. Further classification is into noninvasive and invasive thymoma according to the degree of invasion. This classification is of prognostic significance for overall survival but not for disease free survival when postoperative radiotherapy is employed.⁵⁾ The mixture ratio of lymphocytes varies with medical treatment aiming toward lymphocyte reduction. The Bernatz classification could be reflecting the natural history of medical treatment, with the lymphocyte infiltration decreasing with disease progress.

There have been many cellular classifications developed according to the shape of the tumor cells. These remain controversial in diagnosis, because cellular classifications do not allow for two or more intermingling subtypes, nor placement of unclassified subtypes.

In the World Health Organization (WHO) classification,⁶⁾ several types of thymoma are distinguished based on histological criteria, and the histological subtypes have independent prognostic significance:^{7,8)} 1) type A thymomas (also called medullary or spindle-cell thymoma); 2) type AB thymomas (also called mixed thymoma); 3) type B thymomas which are sub classified as type B1 thymomas (also called lymphocyte-rich thymoma, lymphocytic thymoma, predominantly cortical thymoma, or organoid thymoma); type B2 thymomas (also called cortical thymoma) and type B3 thymomas (also called epithelial, atypical, or squamoid thymoma or well-differentiated thymic carcinoma, respectively) and; 4) type C thymomas (thymic carcinomas) which exhibit morphological

similarities to corresponding neoplasms in organs other than the thymus. Consensus on the degree of malignancy in WHO classification is now divided, but at least type A and type AB thymomas frequently follow a benign clinical course, types B1-3 need to be considered as low to moderate level malignant neoplasms.⁹⁾ In a retrospective study, type A, AB, and B1 thymomas, and type B2 and B3 thymomas formed the base of malignant tumors due to great vessel involvement found more frequently with type B2 and B3 tumors than in type A, AB, and B1 tumors.¹⁰⁾ In a further report, there was no recurrence in patients with type A, AB, or B2 thymoma.¹¹⁾

The WHO classification summarizes various previous classifications. It is also becoming clear that there is a type which may complicate myasthenia gravis (MG), and a type which does not do so. It may be necessary to medical treatment because biological response may be different to that suggested by the WHO classification.

Staging

The tumor stage and Karnofsky performance status have been shown to be most important prognostic indicators in thymoma.⁵⁾ Among the staging systems, the most widely used is that devised by Masaoka et al.¹²⁾ The modification of Bergh's proposal¹³⁾ by Masaoka staging has gained widespread acceptance.⁵⁾ Neither the recent proposal for a similar TNM classification nor the extension of Masaoka's stage for surgical extent¹⁴⁾ has replaced the traditional staging system. However, recent data suggest that the staging system of the French Study Group on Thymic Tumors (GETT system), which is based on the surgical and pathologic features of the tumor, may be superior to the Masaoka system.¹⁵⁾ Although Masaoka staging may predict disease-free survival⁵⁾ and is useful in staging patients with thymoma, it does not appear to predict outcome for patients with thymic carcinoma.¹⁶⁾

Diagnosis

The diagnostic work-up of a patient with thymoma patients begins with an interview and an abnormal shadow found in a routine chest X-ray. Occult thymoma is found as an incidental tumor lacking X-ray abnormalities but revealed by other imaging modalities.

Computed tomography (CT) is of limited value in differentiating histologic subtypes according to the WHO classification,¹⁷⁾ but is helpful in clinical staging of thymoma, especially for capsulated or highly invasive le-

sions. Particular attention is given to the evaluating of tumor relationship to adjacent mediastinal structures, and predicting the feasibility of biopsy or radical surgical procedures.¹⁸⁾ In MG patients CT is a sensitive, specific and efficient modality for detecting thymoma, but is less so for detecting thymic hyperplasia. MR was shown to be accurate in detecting invasive thymoma both preoperatively and in postoperative follow-up.¹⁹⁾ Appearance of the tumor on CT may be related to the WHO histologic type;²⁰⁾ indicating that smooth contours and a round shape are most suggestive of type A; whereas irregular contours are higher prevalence of type C. Calcification is frequent in type B. However, CT is of limited value in differentiating type AB, B1, B2, and B3 tumors.²¹⁾

Surgery

Although a preoperative biopsy of an anterior mediastinal mass may aid in its diagnosis, a planned resection of an anterior mediastinal mass may be appropriate without a preoperative biopsy in some cases when a thorough clinical and radiographic evaluation of peripheral lymph nodes is negative.²²⁾ Surgery is the mainstay treatment of thymomas. Affecting the prognosis includes resectability, postoperative irradiation or chemotherapy, MG, and tumor staging.²³⁾ In thymoma MG patients, the factors that influence outcome are the presence of ryanodine receptor (RyR) antibodies in thymoma MG. Titin/RyR in non-thymoma MG may indicate a less favorable prognosis.²⁴⁾ Postoperative radiotherapy does not seem necessary after removal of encapsulated thymomas, but it is advisable in case of invasive thymomas, regardless of the extent of the resection.²⁵⁾

The long-term outcome of thymoma patients is related to completeness of surgical resection, and to tumor stage, WHO histologic type, and type of treatment.²⁶⁾ In locally advanced unresectable malignant thymomas, debulking surgery followed by postoperative chemo-radiation therapy should be considered. A combined multidisciplinary approach may prolong life and may be curative.²⁷⁾

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