



On the staging of thymic epithelial neoplasms

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The recent article by White *et al.* in the *European Journal of Cardiothoracic Surgery* on the efficacy of chest computed tomography prediction of the pathological TNM stage of thymic epithelial tumors (1) underscores an issue that has impacted the field of thymoma studies, namely what is the proper way for staging such tumors. The study by White *et al.* (1) shows that preoperative chest CT is able to accurately predict p-TNM stage in only two thirds of surgically resected thymic epithelial tumors. Thus, one third of patients will have false positives or false negatives that may adversely affect the management options for those patients, including decisions of whether to offer preoperative radiation that may lead to incomplete surgical resections or overtreatment of the lesions with added morbidity.

The study compares the effect of CT staging with pathologic staging using both the recently introduced TNM staging scheme of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) (2) and the more traditional modified Masaoka staging by Koga *et al.* (3). Unfortunately, neither of these two staging systems completely addresses the issues in the staging of thymoma. The TNM staging recently introduced in the 8th edition of the AJCC lends itself well for assessing some of the more aggressive variants of thymic epithelial neoplasms, such as thymic carcinoma and neuroendocrine carcinomas of the thymus, which often present in more advanced stages and with metastatic spread, but for the majority of the more conventional thymic epithelial neoplasms (i.e., thymomas), the N and M categories will be of little value given that regional lymph node and distant metastases are rather rare in such tumors (4).

The original Masaoka (5) scheme and its modified Koga staging system (3), which has stood the test of time and has been favored as the standard method for staging of thymoma for nearly 40 years, has also suffered from several limitations. Various studies have called attention to the fact that the distinction between infiltration into the capsule and invasion through the capsule do not result in significantly different outcomes (6). The study by Koga and colleagues (3) introduced changes to the original Masaoka staging that simplified the system and divided these tumors into two broad categories: invasive (for modified stages III and IV) and non-invasive (for modified stages I and II). The problem with the modified Masaoka staging is that it continues to rely on gross evaluation at the time of surgery for stages IIb and III (“Macroscopic invasion into thymic or surrounding fat...” for IIb and “Macroscopic invasion of neighboring organs...” for stage III).

Experience has repeatedly shown us that gross evaluation by the surgeon of invasion at the time of surgery can sometimes be inaccurate and misleading. Both thymomas and benign processes affecting the thymus can often lead to firm adhesions of the tumor to the pleura, pericardium and other structures, which can be grossly mistaken for invasion but that upon histopathologic examination are demonstrated to represent fibrous adhesions secondary to inflammation (7). Moreover, the current staging criteria take out of the hands of the pathologist the capability for rendering a reliable and definitive pathologic staging of the lesion, as communication between the surgeon and the pathologist is not always optimal. The ideal way to establish invasion in such instances is for the surgeon to biopsy

the grossly suspicious area and submit it separately with a specific site designation and with the specific query of “rule out invasion”. Unfortunately, this is not a common practice as evidenced by the numerous surgical pathology reports from a wide number of sources reviewed in our consultative practice.

What has emerged over time as a much more reliable feature for assessing prognosis in these tumors is the completeness of resection. Previous studies addressing this parameter have demonstrated that incomplete resection in thymoma, even for the low-grade organotypic tumors, is associated with increased incidence of recurrence and a more protracted clinical course (8,9). More recently, the same has been shown for thymic carcinoma, in which tumors that were completely resected with clear margins observed a much better prognosis than tumors with positive margins independent of the histology (10). Proper assessment of the status of the margins in thymoma thus represents a critical component in the evaluation of these tumors.

Unfortunately, there is no standard protocol or grossing guidelines that have yet been universally adopted for the handling of these specimens in pathology laboratories. Since a large proportion of these tumors are operated on in small, private community hospitals in the United States, the majority of cases submitted in consultation to experts in academic medical centers do not have adequate orientation or properly designated margins. Most pathologists have taken the approach of inking the entire outer surface of the specimen sent to pathology and of designating it as the “margins”. Technically speaking, however, a true margin is only represented by tissues that have been transected by the surgeon and separated from adjoining structures. Since thymomas are located in the anterior mediastinum, a virtual cavity, the areas of the tumor that were not adhered or attached to other structures do not represent true margins but simply constitute the “outer surface” of the specimen. It would thus be misleading to indicate that the margins are positive if the tumor reaches up to the inked outer surface of what is not really a margin.

A few years ago, several members of ITMIG (International Thymic Malignancies Interest Group) published a consensus guideline for the grossing of thymomas (11). The guidelines were developed by a panel of surgical pathologists with special interest/expertise in mediastinal pathology in collaboration with thoracic surgeons. The guidelines called for separate and specific inking or marking of the more relevant areas of the surgical specimen so the pathologist

could provide a more accurate rendering of the true margins. Adoption of such guidelines could go a long way in helping improve the accuracy of staging in these tumors and may improve our ability to establish prognosis for these patients.

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