Bad thymic tumors often exhibit wanderlust

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CT scan demonstrating a centrally necrotic thymic cancer with enlarged subaortic nodes.

Central Message

Locally advanced thymomas, thymic cancers, and thymic neuroendocrine tumors are often associated with lymph node metastases. Deliberate node dissection should be considered when resecting these tumors.

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Fang and colleagues¹ report a prospective multicenter observational study over 2 years on 275 patients with thymic tumors. Lymph node sampling of at least 1 lymph node station was mandated, but surgeons were encouraged to remove as many nodes as possible. Lymph node metastases were found in 15 of 275 patients (5.5%). As expected, thymic tumors that had an advanced T category (20% incidence of nodal metastasis) and World Health Organization (WHO) histology (18% incidence of nodal metastasis) were associated with more lymph node metastases. A remarkable aspect of this study is the accrual of 275 patients with thymic tumors in a prospective study over just 2 years. Our Chinese colleagues have a large population to serve and regional centers of excellence in thoracic surgery, which allow them to report studies with numbers of patients never matched in Western reports. They are leading the way forward in uncommon diseases as their studies accrue large numbers of patients that then allow more accurate conclusions on treatments. With careful study design, accurate data collection, and careful analysis, Chinese surgeons will be leading the way with “big data.”

As noted by Fang and colleagues,¹ there are several limitations to this study. These include the limited number of thymic cancers and neuroendocrine tumors, the lack of mandating routine sampling of all relevant nodal stations, the varied surgical approaches, and the fact that neither of these 2 important variables (T category and WHO histology) are usually known before resection in the typical patient.

How are we to use this study in the care of our patients? The low incidence of lymph node metastases in typical patients with thymoma and the high disease-free survival with standard surgery suggest lymph node dissection is unnecessary in smaller tumors that appear to be T1 or T2. The standard practice pattern is to resect anterior mediastinal tumors that clinically appear to be a readily resectable thymoma without a preoperative biopsy. Anterior mediastinal tumors that are clinically invasive are often biopsied first and offered induction therapy. Needle biopsies are usually accurate for thymic cancers and neuroendocrine tumors,

whereas thymomas are more challenging to assign an accurate WHO histology. Computed tomography (CT) characteristics that suggest a locally advanced thymic tumor include large size, areas of necrosis, edge characteristics that suggest invasion, vascular invasion, elevated diaphragm, pleural nodule, heterogeneous internal density, and lymphadenopathy. Locally advanced thymomas, thymic cancers, and thymic neuroendocrine tumors require aggressive resection to achieve an R0 resection. Given the results of this study and others,^{2,3} it seems prudent to perform a lymph node dissection when resecting these more advanced thymic tumors to better stage the patient and to achieve an R0 resection.

Weksler and colleagues² reported on lymph node metastases using the Surveillance, Epidemiology, and End Results database in 176 patients with thymic carcinoma (62%) and thymic neuroendocrine tumors (34%). In a multivariable analysis, nodal metastases were more likely in patients with thymic neuroendocrine tumors and with more advanced tumors. Nodal metastases had a significant independent adverse impact on survival (hazard ratio, 2.9; $P = .001$). Median survival was 47 months in patients with nodal metastases and 124 months in patients without nodal metastases ($P < .001$). Hwang and colleagues³ reported on 131 patients who underwent lymph node dissection who had a thymoma or thymic carcinoma. Lymph node metastases were more common in patients with thymic carcinoma (25%) than in patients with thymoma (5%). Nodal

metastases were associated with advanced WHO histology and advanced T category. Patients with nodal metastases had a significantly worse freedom from recurrence rate compared with those with pN0 (39% vs 89%, $P < .001$).

Locally advanced thymic tumors should ideally undergo integrated fluorodeoxyglucose positron emission tomography (FDG PET) imaging. A recent study reported on accuracy of staging thymic tumors with whole-body magnetic resonance imaging (MRI), FDG PET/MRI, integrated FDG PET/CT, and conventional imaging examinations. Diagnostic accuracy of the N category was higher with PET/MRI (94%) and MRI (94%) compared with conventional CT imaging (81%).⁴ Clearly, thymic tumors with nodal metastases have a worse prognosis, which suggests the need for systemic therapy. Induction therapy may be given first if nodal metastases are identified or the tumor is clearly T3 or T4. Systemic adjuvant therapy also may be given for patients who are found to be node positive after resection. Which strategy is better is unknown. Girard and Merveilleux du Vignaux⁵ recently reviewed the role of systemic treatment for thymic malignancies, highlighting newer promising drugs. Adjuvant radiation is typically administered to patients after resection of a thymic

carcinoma. Lim and colleagues⁶ recently reported a propensity-matched SEER database study of 312 patients with thymic carcinoma, of whom 184 had postoperative radiation.⁶ The receipt of postoperative radiation was associated with an improved 5-year survival ($P = .007$).

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