A cornerstone is laid on the great wall of thymoma knowledge

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Central Message

Fang et al have performed a seminal, prospective study, determining the incidence of as well as predictive factors for nodal metastasis from thymic tumors, with important implications for patient care.

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Thymic epithelial tumors (TETs) are rare tumors; the most common TET, thymoma, has an incidence of only 0.15 per 100,000 person-years.¹ As a rare group of tumors, our knowledge has been limited to either single-institution studies or large database studies. One area particularly lacking has been assessment of the incidence of nodal metastases in patients with TETs, and previous studies yielded relatively low-level evidence. Kondo and Monden² performed a retrospective study and reported an incidence of nodal metastases of 1.8% in patients with thymoma, 26.8% in patients with thymic carcinoma, and 27.5% in patients with thymic neuroendocrine tumors (NETT). In subsequent, retrospective studies using the Surveillance, Epidemiology, and End Results registry, the incidence of nodal metastases was 13.3% in thymoma, 33.5% in thymic carcinoma, and 62.3% in NETT,^{3,4} but the Surveillance, Epidemiology, and End Results data likely overestimated the number of nodal metastases. In a recent retrospective study the Chinese Alliance for Research in Thymomas (ChART) reported that the incidence of nodal metastases was 1.3% in thymoma, 7.9% in thymic carcinoma, and 16.7% in NETT.⁵

In the current issue of *The Journal of Thoracic and Cardiovascular Surgery*, Fang and colleagues⁶ provide much better evidence by prospectively studying the incidence of nodal metastases in patients with TET from 15 tertiary referral centers participating in ChART. All patients (n = 275) underwent resection and dissection of N1 nodes (anterior mediastinal nodes)—243 patients with thymoma (84.4%), 24 patients with thymic carcinoma (8.7%), and 8 with NETT (2.9%). The mean number of nodes harvested per patient was 4.9, and mean number of stations sampled was 3.1. The incidence of metastasis was 2.1% in patients with thymoma, 25% in patients with thymic carcinoma, and 50% in patients with NETT. In multivariable analysis, World Health Organization (WHO) type B3 thymoma, thymic carcinoma, or NETT; tumor category T3 or T4; and dissection of N2 nodes (deep mediastinal nodes) were significantly associated with nodal metastases. The authors

then predicted nodal metastases in patients with thymic malignancies and identified low risk (T1-2, WHO A/AB/B1/B2) and high-risk (T3 or above; type B3 thymoma, thymic carcinoma, or NETT) groups. Additionally, in patients with advanced tumors leaning toward one side of the chest, N2 nodes were seen only in the ipsilateral side, and patients with NETT had a high likelihood of bilateral nodal disease.

This prospective study has long been missing from the thymoma literature. It was well executed and very pragmatic, allowing the participating surgeons to follow their typical practice patterns. Although there was a lack of standardization in the nodal stations sampled, this study is still a leap forward compared with previous studies of nodal metastases in thymoma. The risk stratification devised in the report is helpful, but the information needed for risk stratification can only be obtained after pathologic review of the surgical specimen and will not help surgeons decide how much nodal sampling is required. How clinicians should decide on their approach for node dissection and sampling remains an important question. Most procedures done today are minimally invasive and usually performed unilaterally. One option is to routinely sample all accessible lymph nodes during surgery in patients with TET. However, this might be an overkill for T1/T2 thymomas classified as WHO type A or B1. However, patients with NETT might need a more aggressive bilateral nodal sampling/dissection.

Also, the increased likelihood of detection of nodal metastases in patients who had N2 dissection suggests that most patients who received surgery for TET should have sampling of N2 nodes. The current study appears to suggest that some patients with anterior mediastinal masses suggestive of TET should have a preoperative biopsy. An option is to assess patients radiologically for tumor status,⁷ and biopsy those that have a more invasive profile.

The study by Fang and the ChART investigators will become one of the seminal reports in the thymoma literature. Surgeons will need to gain familiarity with the nodal stations in the anterior mediastinum to properly treat patients with TETs.⁸ There are some immediate changes to current practice that should be made in response to this study including dissection of N2 nodes in all patients with a TET higher than category T1a. I suspect that surgeons will also become more aggressive in determining the histology of anterior mediastinal masses preoperatively to properly plan for surgery.

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