



Revealing the mysteries of thymoma

Thymic tumors (TTs) are rare neoplasms arising from thymic epithelial cells. In adults thymomas, thymic carcinomas and thymic neuroendocrine cancers are the most common TTs usually located in the anterior mediastinum. Thymomas account for about 50% of anterior and 20% of all mediastinal tumors. There are no known risk factors for these tumors; however, there is a strong association with myasthenia gravis and other paraneoplastic syndromes (PNS) and autoimmune disorders (AID) (1).

Thymomas and other TTs typically present with one of the three major scenarios: as an incidental finding on imaging in an asymptomatic patient, with local (thoracic) symptoms, or with symptoms due to PNS or AID. The most common PNS associated with TTs is myasthenia gravis, but a wide range of other disorders with PNS and AID have been reported. Up to one-half of patients with thymoma have symptoms consistent with myasthenia gravis (1,2).

Key elements in the differential diagnosis of an anterior mediastinal mass include not only thymoma and thymic carcinoma, but also retrosternal thyroid, lymphoma, and mediastinal germ cell tumor. Optimal evaluation and diagnosis of mediastinal tumors generally require comprehensive clinical, radiologic and histologic investigations. The clinical approach includes consideration of several factors including detailed symptomatology and associated conditions of PNS and AID. CT is essential to determine the mediastinal location and intrathoracic extent of the tumor whereas MRI and PET-CT are used on a selective basis depending on the case. Histological confirmation before treatment is necessary in locally advanced or unresectable TTs (1-3).

Following imaging findings that suggest a tumor of thymic origin, the definitive diagnosis of a TT requires histologic confirmation. For a TT amenable to complete resection, the initial step in the management is surgical resection, which also enables the histologic diagnosis. For patients with unresectable tumor due to locally advanced or metastatic disease, or those who are inoperable due to old age or comorbidity, a histologic diagnosis by core needle biopsy, other minimally invasive procedure, or surgical biopsy is required prior to treatment decision (3-6).

The histologic classification of TTs is performed according to the WHO classification system (7). For staging which is based on the extent of the primary tumor and presence of invasion into adjacent structures and/or dissemination, generally the Masaoka staging system (1,4,6) or the new IASLC/ITMIG staging system (8th edition of the AJCC TNM classification) (8) is used.

Surgery is the standard of care for resectable TTs. For patients in whom a complete resection is not feasible as the initial step, multimodality treatment incorporating preoperative chemotherapy, postoperative chemotherapy, and/or postoperative radiotherapy may be indicated. If neoadjuvant chemotherapy allows for a partial or complete response, such disease is considered potentially resectable. For unresectable disease chemotherapy, radiotherapy, or chemoradiotherapy is considered (1,3,4,6). As for immunotherapy, further research and clinical experience in treatment with immune checkpoint inhibitors is needed to determine the definite role of immunotherapy in patients with advanced TTs (9).

Morbidity and mortality in TTs are determined by (I) advanced stage or oncologically uncontrolled disease, (II) serious conditions associated with AID or PNS, (III) impaired immunocompetence and AID or PNS resulting in infections or secondary malignancies, and (IV) therapy-related complications (3,4,10).

This special issue of the *Journal of Thoracic Disease* focused on thymoma presents up-to-date and extensive reviews spanning from the epidemiology to the genetics and biology and to the diagnostic and therapeutic modalities. Similarly to other rare tumors, thymoma has been largely understudied for years. However, in the last few years there has been significant research performed particularly in the field of molecular biology of these tumors. Several important and novel advancements in genetics and molecular biology are discussed in two chapters of this issue. Furthermore, the principles of current care including all novelties regarding diagnostic and treatment modalities are provided in several other chapters.

With the pleasure of being the editors, we thank all of our colleagues for their efforts in constituting this focused issue with their excellent reviews and anticipate that the readers will enjoy reading and benefit from them.

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Dragana Jovanovic



Semra Bilaceroglu

Dragana Jovanovic, MD, PhD¹

¹Professor of Pulmonology, Thoracic Oncology and Palliative Medicine, Internal Medicine Clinic “Akta Medica”, Belgrade, Serbia; (Email: draganajv@yahoo.com)

Semra Bilaceroglu, MD²

²Professor of Pulmonology, Dept. of Pulmonology, University of Health Sciences, Dr. Suat Seren Training and Research Hospital for Thoracic Medicine and Surgery, Izmir, Turkey. (Email: s.bilaceroglu@gmail.com)

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