Approaching the Patient with an Anterior Mediastinal Mass: A Guide for Clinicians

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Abstract: Anterior mediastinal masses are relatively uncommon, include a wide variety of entities, and often pose a diagnostic challenge for clinicians. In this article, available data is assembled in a clinically oriented manner to develop a structured approach to evaluation of these patients. Attention to age and gender, combined with identification of certain radiographic and clinical characteristics, allows a presumptive diagnosis to be established in most patients. This structure efficiently guides what additional workup is needed.

Key Words: Mediastinum, Anterior, CT, MRI, PET.

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Mediastinal masses are relatively uncommon. Most occur in the anterior compartment and include a variety of different entities demonstrating a spectrum of clinical and pathologic features. A simple, uniform "standard" approach to these patients is not appropriate given the heterogeneity and variety of different features that can be characteristic of particular entities. Whether to pursue specific laboratory tests, look for specific associated conditions, obtain additional imaging or biopsy depends on which entities are realistic possibilities.

Particularly because most clinicians encounter such patients only occasionally, there is a need for some structure in how to proceed with evaluating them. Unfortunately, most reports do not provide information that lends itself to clinical application; these series start with a specific known diagnosis and describe the cohort, whereas the clinician is faced with a patient with certain characteristics (such as age and appearance of the lesion) and is struggling to arrive at a diagnosis.

A structured, clinically oriented approach increases the efficiency of the investigation and eliminates unnecessary studies. In this article, we review key features of anterior mediastinal lesions and propose a clinical approach to the evaluation of these masses. The approach taken is to begin with features that are readily available (e.g., age, sex) and then to consider aspects of the clinical presentation to develop an initial presumptive diagnosis. The lesion under consideration and the degree of certainty about the presumptive diagnosis guide the next steps in an efficient manner. Some tumors are immediately and reliably recognizable; however, because these are more rare entities, in general it is best to focus first on the more common entities and to consider uncommon lesions primarily when the common ones have been deemed unlikely. This review is intended to serve as a general structure to the approach that we hope can guide management; it is important to note that these are general statements and that there will always be exceptions.

METHODS

A core workgroup (F.C.D., E.M.M., and B.W.C.) reviewed the existing literature on the evaluation of patients presenting with an anterior mediastinal mass. This group drafted the proposed approach to the patient presenting with an anterior mediastinal mass. The document was then reviewed by an extended workgroup (Motoki Yano, Ricardo Beyruti, In Kyu Park, Alper Toker, Marinus A. Paul, Ehab Bishay, and Stephen D. Cassivi).

In the generation of this review, series from 1950 to 2010 that included age- and gender-specific data on the incidence of mediastinal tumors were analyzed.[1] Additional studies that reviewed data on the relative proportions of mediastinal tumors were also included. Some older series were excluded which included lesions that could not be accurately translated into modern classification schemes and diagnostic categories. The data regarding the incidence of anterior mediastinal masses is an approximation and does not represent a precise quantitative incidence.

NOMENCLATURE

Although the nomenclature that is typically used for classification of anterior mediastinal masses is fairly straightforward, several specific entities and circumstances necessitate discussion. For instance, although thymic malignancies such as thymic carcinoma and thymic carcinoid are distinct and separate entities from thymoma, these tumors were included under the term "thymoma" in some series. In order to be consistent, we have considered these entities as one group (thymic malignancy) in this article. Numerous classification schemes have been devised for lymphomas. As many series included in this review employed the Revised European-American Lymphoma system, this scheme is used in this article. The most common lymphomas resulting in anterior mediastinal

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masses include Hodgkin disease (HD), mediastinal large cell (MLC) non-Hodgkin lymphoma (NHL), and lymphoblastic (LB)-NHL.

The term teratoma in this article refers to benign primary mediastinal teratomas, which may also be referred to as mature teratomas or dermoid cysts. We did not follow the policy of some series which included such benign teratomas in the category of germ cell tumors along with primary mediastinal seminoma and non-seminomatous tumors (NSGCTs). Furthermore, the term teratoma in this review does not encompass secondary mediastinal teratomas, which represent residual neoplasms following treatment of NSGCTs with chemotherapy, or malignant teratomas that appear secondarily in this setting as well. Such secondary tumors are excluded entirely from this article, because they are not part of the differential diagnosis of primary anterior mediastinal tumors.

The data presented in this review is based on papers that have defined the anterior mediastinal compartment according to various schemes (based on the lateral chest radiograph). Nevertheless, the approach outlined here is applicable to the more well-defined computed tomography (CT)-based definition of anterior mediastinal compartment described elsewhere in this issue.[2]

INCIDENCE

The true incidence of anterior mediastinal masses is difficult to ascertain from the medical literature for several reasons. For one, different clinical and/or radiologic classification schemes may be used to define mediastinal compartments. Additionally, the inclusion of nonneoplastic lesions such as thymic and pericardial cysts is variable between different series. Finally, there is variability in the inclusion of lymphomas in different series. Whereas 50% of HD and 20% of NHL involve the mediastinum,[3] only approximately 3% of HD and 6% of NHL arise as primary mediastinal malignancies.[4–6] Inclusion of the latter group as mediastinal tumors is warranted because they are located primarily in the mediastinum and are clearly a consideration in a patient with an anterior mediastinal mass. However, inclusion of lymphomas that present as obvious extrathoracic tumors seems inappropriate; pathologically enlarged extrathoracic lymph nodes (e.g., neck, groin, or axilla) can be easily sampled by percutaneous biopsy and these patients are not viewed as presenting with an anterior mediastinal mass.[1]

Despite these challenges in determining an exact incidence, several studies have demonstrated that the most common anterior mediastinal masses include the following entities: thymic malignancy in approximately 35%, lymphoma in approximately 25% (HD, 13% and NHL, 12%), thyroid and other endocrine tumors in approximately 15%, benign teratoma in approximately 10%, malignant germ cell tumors in approximately 10% (seminoma, 4% and NSGCT, 7%), and benign thymic lesions in approximately 5%.[7–9]

CLINICAL APPROACH TO AN ANTERIOR MEDIASTINAL MASS

This review article approaches evaluation of an anterior mediastinal mass from a clinical perspective, which typically begins with a detailed patient history and focused physical examination. Age and gender are the two most important initial features to consider in the evaluation of patients with an anterior mediastinal mass, as specific lesions tend to be more common in certain demographic groups (Table 1). The presence of particular clinical symptoms, the severity and duration of these symptoms, and the presence of additional signs and symptoms can provide important clues to the diagnosis. Additional tests such as laboratory studies, the most common of which include α-fetoprotein (α-FP), β-human chorionic gonadotropin (β-HCG), and lactate dehydrogenase (LDH), play an important adjunctive role. Features of anterior mediastinal masses in imaging studies can sometimes be essentially pathognomonic, but are more often only suggestive of a particular diagnosis by themselves; details are discussed in *Approaching the Patient with an Anterior Mediastinal Mass: A Guide for Radiologists*.[10] CT is the recommended imaging modality for the evaluation of most anterior mediastinal masses. However, magnetic resonance imaging (MRI) is superior to CT in distinguishing cystic from solid masses, can be performed without contrast in patients who cannot receive intravenous contrast as part of a CT examination (due to renal failure or allergy), and can be used to differentiate thymic hyperplasia from thymoma through the use of chemical shift techniques. 18F-FDG PET/CT is not routinely performed to evaluate or characterize an anterior mediastinal mass, but is typically used to stage lymphomas and monitor response to therapy. In most patients, a combination of demographic information, clinical presentation, and imaging features allows a presumptive diagnosis to be made with a fair amount of confidence.

Women And Men Older Than 40 Years

The proportion of anterior mediastinal lesions by decade in women and men greater than 40 years of age is demonstrated in Figure 1. In this patient population, thyroid goiter and thymic malignancies account for more than two-thirds of anterior mediastinal masses. Most substernal thyroid goiters manifest as a hyperdense mediastinal mass in continuity with the thyroid gland and extending posterior to the great vessels on CT.[11]

The majority of anterior mediastinal lesions in the remainder of patients in this group represent thymic malignancy. Clinical evaluation of these patients is paramount, as approximately 30% to 50% of patients with thymoma will exhibit paraneoplastic syndromes. The most common paraneoplastic syndrome associated with thymoma is myasthenia gravis, followed by hypogammaglobulinemia and pure red cell aplasia.[12,13] Autoimmune disorders such as systemic lupus erythematosis, polymyositis, and myocarditis may also be associated with thymoma.[14] CT is typically the initial imaging modality used to evaluate for thymoma, and a homogeneous or slightly heterogeneous soft tissue mass in the anterior mediastinum with smooth or lobular margins is the usual finding. However, when paraneoplastic syndromes are present, such as myasthenia gravis, an increasing number

