



Case presentations and recommendations from the October 2017 ITMIG tumor board: an international multidisciplinary team

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Abstract: The International Thymic Malignancy Interest Group (ITMIG) has periodic tumor board meetings to discuss perplexing cases. Two of these cases from the October 2017 meeting are discussed in this article. The diagnoses of a simple thymic cyst and a thymoma are confirmed. Radiology imaging from both cases and pathology slides from the thymoma are reviewed. Treatment and surveillance recommendations are discussed for both cases, as well as lessons learned from group discussion.

Keywords: Mediastinal mass; thymic cyst; thymoma; case presentations; tumor board; international multidisciplinary team (iMDT)

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Introduction

The International Thymic Malignancy Interest Group (ITMIG) is an academic society that has periodic virtual tumor board meetings to discuss challenging cases. The tumor board is composed of a moderator and at least one of the following clinicians; thoracic surgeon, medical oncologist, radiation oncologist (RO), diagnostic radiologist, and thoracic pathologist. Challenging cases and clinical questions are submitted by treating clinicians to get an expert opinion from multiple specialists, all with significant interest and experience in thymic malignancies. Following the case discussion, the tumor board summarizes its conclusions in writing for the treating clinician to help guide them in their treatment plan. We present two cases discussed at our virtual tumor board meeting that was conducted in October 2017. This group attempts to meet once a month with representation from multiple specialties, on this occasion the following were present: surgical oncology, medical oncology, radiation oncology, pathology, and radiology.

Case presentation 1

A 72-year-old woman presented to the Emergency Department after a fall complaining of bilateral leg weakness. She had polio as a child, but no other contributing history. On physical examination her vital signs were normal as well as her neurological examination. She had normal reflexes, no neurological deficits, and no leg weakness.

As part of the routine investigation, a chest radiograph was obtained which demonstrated a prevascular mass abutting and inseparable from the right heart border (*Figure 1A*). To further investigate this mass, a contrast-enhanced chest CT scan (*Figure 1B*) was obtained followed by a chest MRI (*Figure 1C,D*). Upon review of the images the tumor board radiologist described the mass as a homogenous fluid density prevascular mass, most suggestive of a benign cyst. Although radiologists and clinicians are more comfortable interpreting chest CT scans, MRI is superior to chest CT when investigating cystic lesions (1). This is due to MRI's superior contrast resolution, which enables better differentiation between soft tissue tumors

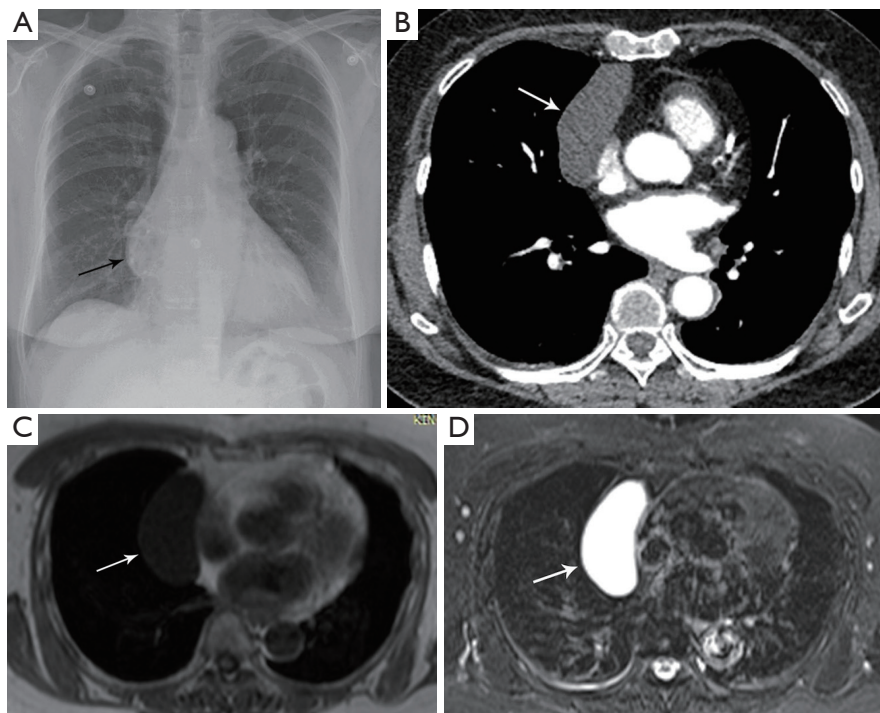


Figure 1 Incidental mediastinal cyst in a 72-year-old woman. (A) Frontal chest radiograph demonstrates a mediastinal mass (arrow) abutting and inseparable from the right heart border. Because it silhouettes out the right heart border, it abuts it and is thus located anteriorly in the mediastinum, in the prevascular mediastinum; (B) contrast enhanced chest CT at the level of the left atrium shows a homogeneous low attenuation mass (arrow) in the prevascular mediastinum, measuring 15 HU; (C,D) MRI axial slices at the level of the left atrium show the prevascular mass (arrows) a low attenuation on the T1-weighted image (C) whereas high attenuation on the T2-weighted image (D) consisting of fluid density and shows no enhancement after contrast injection. These features are consistent with a simple cyst.

and fluid, and enables one to detect soft tissue within cysts. When dealing with prevascular mediastinal masses this is important, as benign cysts typically have imperceptible walls and no nodularity within them, whereas cystic thymomas, which may at first seem to mimic a simple cyst, actually have soft tissue nodularity and/or a thickened septum or wall, which enhance after contrast injection (2). The MRI was reviewed and showed that indeed the tumor was of fluid density, low on T1-weighted images, and high on T2-weighted images with no thickened septa and no nodularity (Figure 1C,D). Thus, the prevascular mass had the typical imaging features of a benign cyst, which may have arisen from the thymic bed as a thymic cyst, or the pericardium as a pericardial cyst.

The initial reviewing radiologists had come to the same conclusion that this was a simple thymic cyst and therefore a biopsy was not recommended, and the patient was told the diagnosis by her RO. She was reassured that no intervention was required for this benign condition.

Questions for ITMIG tumor board

Three months after the diagnosis the patient's daughter called the attending RO to report the patient had been having intermittent chest pain. She had never had chest pain previously and the patient was very concerned that this was related to the mass. The RO presented her case to the ITMIG group with the following questions: (I) would anyone in the group suggest surgical resection, and (II) if not how frequently should the mass be imaged and with what modality for observation?

ITMIG expert opinions

In the groups expert opinion there was adequate imaging that was consistent with a simple thymic cyst. Therefore, the mass is not contributing to her symptoms and there may be a component of psychological overlay if other causes of chest pain are unlikely or ruled out. In this case she should be reassured that surgery is not required. Additionally,

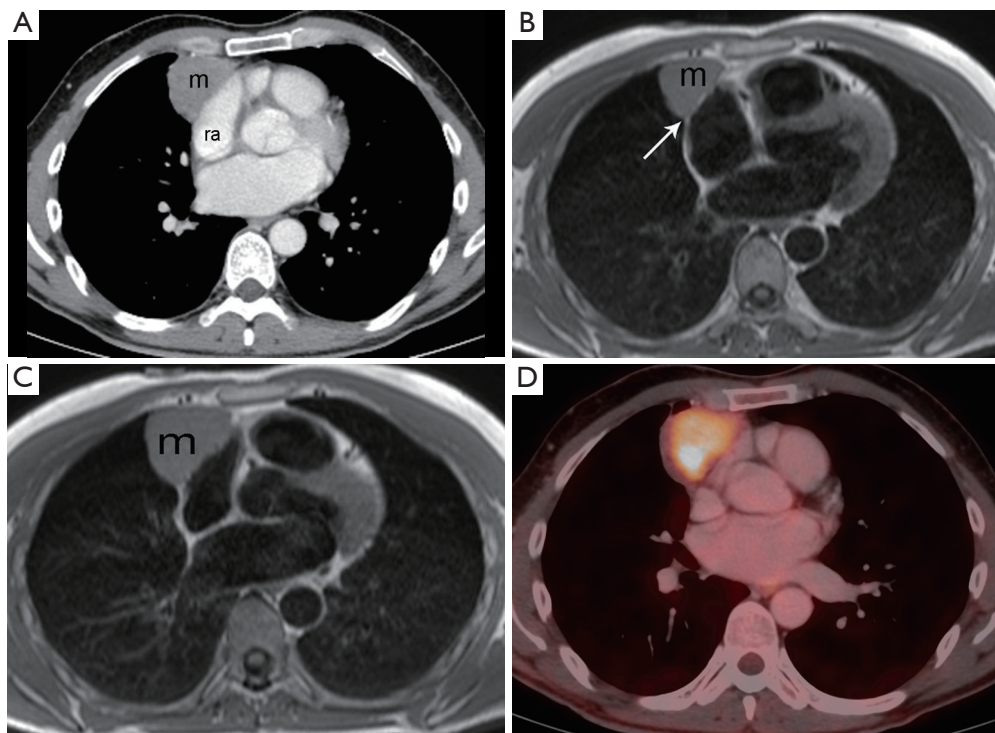


Figure 2 Incidental thymoma in a 51-year-old man. (A) Contrast enhanced chest CT at the level of the left atrium demonstrates a prevascular smooth homogeneous soft tissue mass, which abuts the right atrium; (B) T1-weighted MRI image at the level of the left atrium shows the mass with fat separating it from the right atrium (arrow). Although the mass abuts the pericardium, the mass does not extend through it into the epicardial fat; (C) T1-weighted MRI image superior to image 2B, at the level of the aortic root shows that at this level, the mass abuts and is inseparable from the right atrium and even indents it anteriorly. Because there is no fat separation, it is difficult to know if the mass simply pushes the right atrium or actually involves its wall; (D) FDG PET-CT at the level of the left atrium shows the prevascular mass is FDG avid. m, mass; ra, right atrium.

the group does not recommend ongoing observation with imaging. If the managing RO believes further imaging is necessary for patient reassurance an annual MRI would be the frequency and modality of choice.

Discussion

If a man or woman over the age of 40 presents with a prevascular mediastinal mass that on CT imaging is well-circumscribed, round/oval/saccular, and homogeneous located near the thymic area, this is a highly characteristic lesion for a thymic cyst and requires evaluation with an MRI (3). If purely cystic this is determined to be a unilocular thymic cyst with a very high level of confidence that can be diagnosed with imaging alone and does not require tissue diagnosis (3). It is thought to be a relatively rare diagnosis which makes up <5% of prevascular mediastinal masses, though this is based on surgical series and not on

the prevalence of incidentally detected cysts which are often not resected. In fact, benign thymic cysts are often mistaken for thymomas and excised when MRI is not used for their investigation, as sometimes CT may not be able to distinguish them from solid masses (4). Such cysts do not require resection, as they are benign. Common practice is to follow these cysts with MRI for about 2 years (3).

Case presentation 2

As part of his routine medical check-up, a 51-year-old asymptomatic marathon runner had a chest radiograph, which revealed a mediastinal mass. His physical examination was normal. Four years before that he had had pericarditis which was diagnosed by clinical symptomatology and echocardiography, presumed to be of viral etiology, and the patient recovered with non-steroidal anti-inflammatory medication.

Following the chest radiograph, the patient had a chest CT, chest MRI, and whole body FDG PET-CT that were reviewed by the diagnostic radiologist on the tumor board. The chest CT demonstrates a prevascular soft tissue mass (*Figure 2A*) which abuts the right atrium. Taking into account the patient being asymptomatic and his age, this solitary prevascular smooth soft tissue mass most likely represents a thymoma. Since no definite fat separates the tumor from the right atrium, it is difficult to know if the tumor simply abuts and does not involve the pericardium and right atrium, or if the tumor involves them. The MRI demonstrates that at certain levels (*Figure 2B*) there is a fat plane separating the tumor from the right atrium, and thus no right atrial involvement, but at other levels (*Figure 2C*), there is no such separation and the tumor even indents the right atrium. It is impossible from these images alone to know if the right atrium is involved or only abuts but is separable from the tumor. MRI cine images, in motion (not shown), showed that the mass does not move with the cardiac contractions, demonstrating that it is not attached to the right atrium. As for the pericardium, it is impossible to say if it only abuts the tumor or is actually involved by it, which will have to be determined by a pathologist. The tumor is FDG avid (*Figure 2D*) and no distant FDG avid metastases were identified. The use of FDG PET-CT is not routine with thymomas as not all are FDG avid. When the FDG uptake is very high, this often goes with more aggressive thymic tumors such as thymic carcinoma and type B3 disease.

The patient had unremarkable complete blood count (CBC), coagulation, urine test, echocardiogram, and spirometry. The echocardiograph (ECG) demonstrated complete right bundle branch block that was not present 2 years prior. Tumor markers were done to rule out a germ cell tumor and alpha-fetoprotein (AFP), beta human chorionic gonadotropin (hCG), carcinoembryonic antigen (CEA), and lactate dehydrogenase (LDH) were all within the normal range.

The patient was diagnosed with a thymoma and underwent surgical resection 3 weeks after the initial finding. The surgery protocol was for complete resection of the thymoma (R0 resection). The presenting ITMIG member was the surgeon and he reported the mass was resected easily, was not attached to the pleura, and capsule of the tumor was completely preserved with the specimen.

The available images (*Figure 3*) show a circumscribed neoplasm that focally invades into the surrounding adipose tissue (*Figure 3A,B*). The neoplasm is comprised of a

mixture of small lymphocytes and large epithelial cells (*Figure 3C,D*), some of which are clustering (*Figure 3E,F*). The morphologic features are consistent with a minimally invasive WHO type B2 thymoma. This is supported by multiple keratin immunostains, including pancytokeratin and high molecular weight cytokeratin that highlight a meshwork of epithelial tumor cells (*Figure 3H,I*). CD5 marks T cells (*Figure 3J*). A large fragment of thymoma is identified within a vessel outside of the tumor (*Figure 3G*). However, this fragment shows no definite attachment to the vessel wall and therefore it might not present true angiolymphatic invasion. The pathologic tumor stage is pT1a, stage I (TNM staging) or Masaoka-Koga stage IIa.

Questions for ITMIG tumor board

The questions for the tumor board were: (I) is the final diagnosis Thymoma B2, Masaoka stage IIa? (II) the patient was advised he did not require post-operative radiotherapy but would undergo close surveillance, would the group advise differently? (III) what are the chances of recurrence? (IV) what is the implication of the “microscopic foci of lymphatic vascular invasion” described in the pathology report? and finally (V) what are the follow up recommendations?

ITMIG expert opinions

The group agrees with the stage IIa tumor diagnosis as per the Masaoka-Koga staging system since pathology demonstrated microscopic transcapsular invasion (5). The tumor is type B2 (intermediate increasing epithelial/lymphocyte ratio and emergence of atypia) by the World Health Organization Histopathological Classification of Thymomas (6). With regards to indication for post-operative radiotherapy the ITMIG RO indicated there are no clear guidelines, however with an R0 resection and no concerns since the margin is 5 mm there would likely be no benefit of adjuvant radiotherapy for the patient, however if there was invasion of other structures upstaging the tumor to stage III then this is less clear. As noted by the ITMIG pathologist, a large fragment of thymoma is identified within a vessel outside of the tumor, however it demonstrates no definite attachment to the vessel wall and therefore it might not present true angiolymphatic invasion. Therefore, the group recommended no additional treatment since there is no concern that the patient is at increased risk of recurrence since there is a clear margin and confirmed stage IIa disease, however, the patient

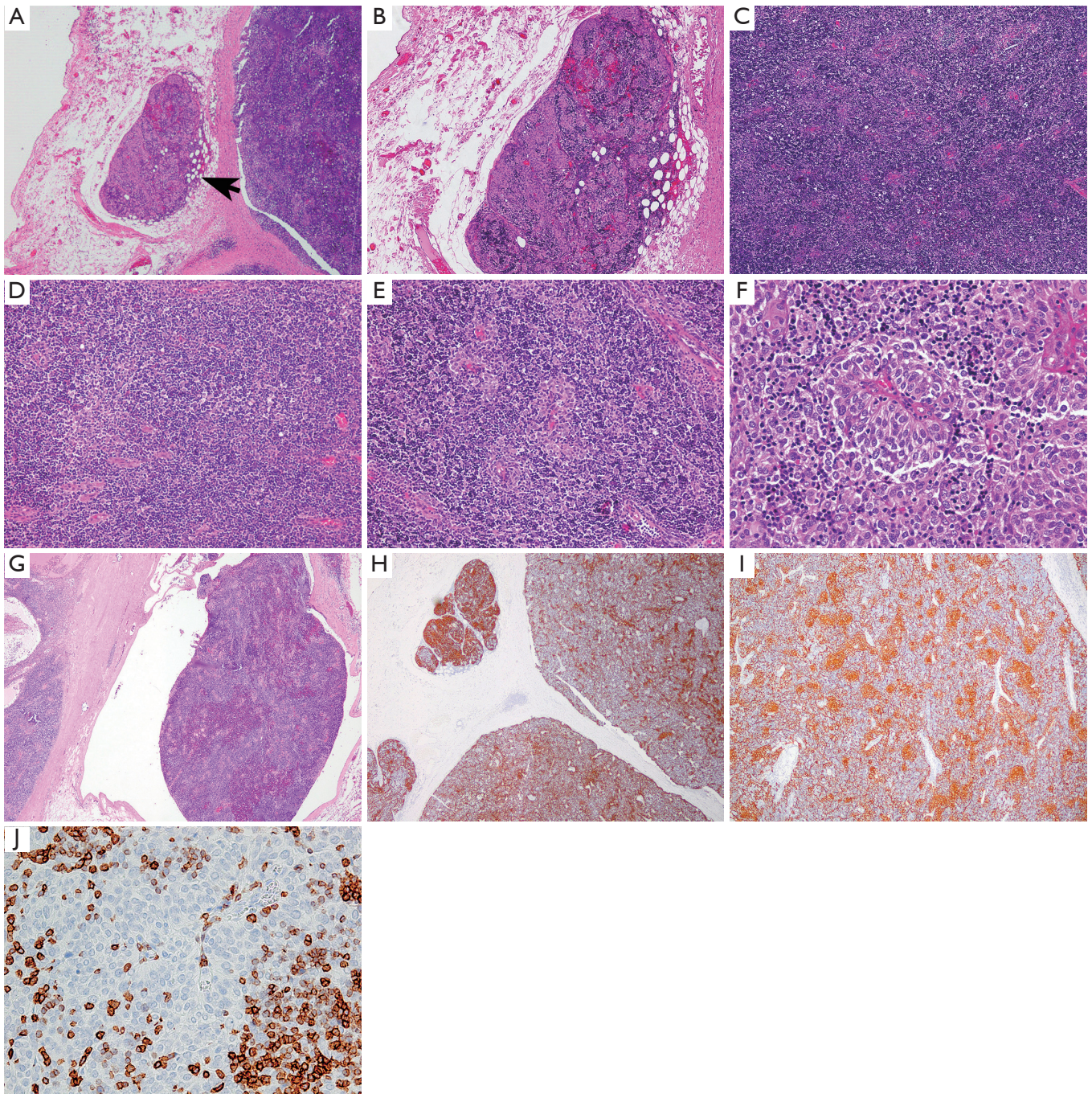


Figure 3 Incidental thymoma in a 51-year-old man. (A,B) Low magnification shows a well-circumscribed cellular neoplasm that is partially encapsulated but invades into the surrounding adipose tissue (arrow) (A, 4×; B, 10×); (C,D) at medium power view this is a hypercellular neoplasm comprised of small lymphocytes and scattered epithelial cells (C, 20×; D, 20×); (E,F) focally, the epithelial cells are forming clusters and palisade around small vessels (F). These morphologic features are consistent with a WHO type B2 thymoma (E, 20×; F, 40×); (G) a rather large fragment of thymoma is located within a vessel, however, no definite attachment to the vessel wall is apparent (4×); (H,I) pan-cytokeratin (H) and high molecular weight cytokeratin (34betaE12, I) reveal large meshworks of epithelial tumor cells (H, 4×; I, 4×); (J) CD5 marks the thymocytes. This immunoprofile supports a thymoma (40×). A-G, HE staining; H-J, immunohistochemical staining. Courtesy by Dr. Antonio Piottante, Clínica Las Condes.

should be advised that adjuvant radiotherapy could reduce the local recurrence rate but would not impact his overall survival. As per the ESMO surveillance protocol published in 2015 the patient will require serial imaging, specifically the group proposed thoracic imaging annually for 5 years, then decrease the frequency to every 2 years for 5 years (7). In regards to whether to follow the patient with serial CT scans or MRI scans, the sternotomy wires may produce some artifacts in the retrosternal region but these are quite limited to that area. It is thus recommended that the patient has a baseline postoperative chest CT scan, with later follow-ups, which could be performed with either CT or MRI to decrease cumulative radiation dose.

Discussion

Many patients with Masaoka-Koga stage I or II tumors die of causes other than thymoma, and patients can also live for many years despite a recurrence due to the indolent behaviour of this disease (8). Patients with stage IIa disease who have a complete resection have a 10-year overall survival of 75–85%, and type B2 patients have a 10-year disease-free survival of 85% (9). The mean time to recurrence of a completely resected thymoma, which is a major prognostic factor, is approximately 5 years, however for stages II–IV it is 3 years (8). After tumor stage, complete resection is the most significant prognostic factor for progression free and overall survival (9). Postoperative radiotherapy is recommended in incompletely resected thymomas, and completely resected stage II and III thymomas may also benefit from adjuvant radiotherapy to reduce local recurrence rates but there has been no impact on survival demonstrated (9). At a minimum, follow-up imaging should include CT scans of the thorax annually for 5 years after surgical resection, then alternating annually with a chest radiograph until year 11, and then annual chest radiographs alone (8). Obtaining a new baseline examination 4–12 weeks postoperatively is recommended (8). MRI may be useful instead of CT either for better visualization or to minimize exposure to radiation, especially in younger patients (8).

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Footnote

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