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Case Report

Mediastinal Mass: A Diagnostic Odyssey from Iron Deficiency Anaemia to Thymoma

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Abstract: Thymic epithelial tumours represent a heterogeneous group of rare thoracic cancers. In adults, thymomas are the most common neoplasms arising in the thymus which is located in the anterior mediastinum. Mediastinal mass can be incidental findings on chest x-ray or present with systemic symptoms and/or direct effect of the mediastinal mass. The authors present the case of a 65-year woman with iron deficiency anaemia, hepatosplenomegaly, paravertebral node and mediastinal mass. Biopsy of the paravertebral node revealed extramedullary hematopoiesis (EMH). Biopsy of mediastinal mass revealed thymoma. She underwent video-assisted thoracoscopic surgery (VATS) thymectomy. The lesion was classified by the World Health Organization (WHO) system type B2 thymoma staging system of the tumor, node, metastasis (TNM) pT1a R0, Masaoka-Koga stage II. Three months later, thoracic computed tomography (CT) revealed a nodule inferior to the tumor site suspected of residual disease. The unexpected residual thymoma required treatment with radiotherapy. This case illustrates the difficulty of differentiating the etiology of anaemia. It highlights the current diagnostic approach to mediastinal mass.

Keywords: Mediastinal Mass; Thymus; Thymoma; Type B2; Iron Deficiency Anaemia; Video-Assisted Thoracoscopic Surgery; Thymectomy.

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1. Introduction

Extramedullary hematopoiesis (EMH) is a rare condition characterized by the production of blood cells outside the bone marrow as a compensatory response to inadequate marrow function. In disorders such as chronic anemia, the death of developing erythroid precursors within the bone marrow leads to ineffective erythropoiesis, which triggers the activation of hematopoietic sites outside the medulla of bone. Hematopoiesis is a lifelong process responsible for maintaining all blood cell lineages through hematopoietic stem cells (HSCs), which uniquely preserve their self-renewal and differentiation capacities. In adults, HSCs are primarily located in the bone marrow but can circulate in the peripheral blood through two main routes: direct circulation, in which HSCs leave the bone marrow, enter the peripheral blood, and later return; and lymphatic circulation, in which HSCs migrate into peripheral tissues, reach the lymph nodes, and eventually return to the blood via the thoracic duct, completing a migratory cycle before re-entering the marrow [1-6].

After birth, hematopoiesis outside the bone marrow is considered abnormal; however, many tissues retain stem cells capable of dedifferentiating into hematopoietic precursors under the influence of circulating factors. EMH can occur in almost any organ, although the spleen (splenomegaly), liver (hepatomegaly), and lymph nodes are the most

involved sites. Less frequently, it may affect the paravertebral regions, mediastinum, thymus, kidneys, adrenal glands, prostate, pleura, skin, peripheral nerves, or spinal canal [1-6].

Several mechanisms have been proposed to explain the occurrence of EMH. The filtration theory suggests that immature hematopoietic cells from the bone marrow are sequestered and proliferate in extramedullary sites such as the spleen. The compensatory theory proposes that EMH develops as a response to insufficient bone marrow hematopoiesis, with proliferation occurring in sites that offer adequate space and microenvironment. The myelostimulatory theory attributes EMH to unknown systemic factors that reactivate hematopoiesis in fetal sites. Finally, the redirected differentiation theory suggests that aberrantly secreted cytokines or other factors, often in the setting of chronic anemia, stimulate adult stem cells in peripheral tissues to differentiate into hematopoietic lineages. The presence of stem cells in several tissues with the ability to repair, proliferate, and differentiate into various cell types supports the plausibility of EMH occurring in multiple anatomical sites [1-6].

In adults, thymomas are the most common neoplasms arising in the thymus, which is located in the anterior mediastinum. They are more prevalent among individuals in their fifth and sixth decades of life. The sex distribution is approximately equal. There are no known risk factors. Thymomas can invade the surrounding mediastinal adipose tissue with or without invasion of the mediastinal pleura or extend into lungs, pericardium, heart, large vessels or phrenic nerves. Some patients present with pleural/pericardial effusions or with superior vena cava syndrome. The most common paraneoplastic syndrome associated with thymoma is myasthenia gravis. However, a wide range of other autoimmune paraneoplastic syndromes has been reported: pure red cell aplasia, hypogammaglobulinemia and pure white blood cell aplasia. Thymomas typically present in the following ways: as an incidental finding identified on imaging in an asymptomatic patient, due to local thoracic symptoms or due to symptoms from a paraneoplastic syndrome [7-15].

We present the case of a 65-year-old woman with iron deficiency anaemia, hepatosplenomegaly, paravertebral node and anterior mediastinal mass. Biopsy of the paravertebral node revealed EMH. Biopsy of mediastinal mass revealed thymoma. She underwent VATS thymectomy. The lesion was a type B2 thymoma TNM pT1a R0, Masaoka-Koga stage II. Three months later, thoracic CT revealed a nodule inferior to the tumor site. The residual thymoma required radiotherapy.

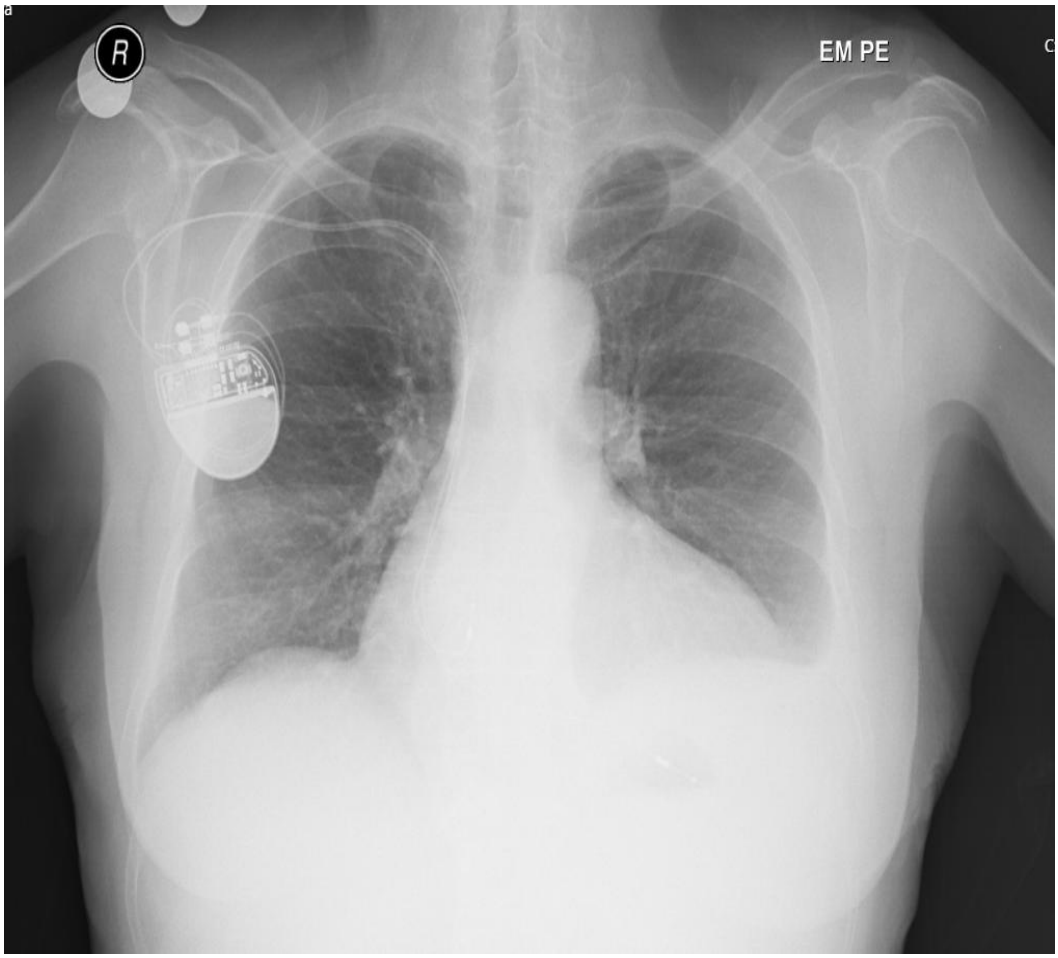
2. Case Report

A 65-year-old woman patient with previous history of pacemaker for sick sinus syndrome, thyroidectomy, dilated cardiomyopathy. She was medicated with levothyroxine 0.137 mg, spironolactone 25 mg, aspirin 100 mg. She was admitted to the emergency department hospital with asthenia for the previous 3 months. She lived in an urban area and no travel history was reported. On examination, she was alert and oriented, had fever (38,2ºC) and the blood pressure 119/94 mmHg, the pulse 50 beats per minute, oxygen saturation 98% while breathing ambient air, hepatosplenomegaly, weight 58 kg. The patient appeared pale. She had deafened heart sounds and decreased breath sounds in the left base to auscultation. The initial workup revealed iron deficiency microcytic anaemia (hemoglobin 11 g/dl), leukocytosis (23510), elevated RDW (20 %), DHL (320 U/L), c reactive protein (9 mg/dl). An electrocardiogram showed sinus rhythm. A chest radiograph showed superior mediastinal widening, increased cardiothoracic index and small volume left pleural effusion (Figure 1).

Thoracic CT with contrast revealed small volume left pleural effusion, small volume pericardial effusion, tissue densifications at the level of the posterior slope of the right base of nodular morphology, one of them with 34 x 14 mm located in the right paravertebral topography and other on the posterior slope of the aforementioned alteration with 34 x 11 mm. Abdominopelvic CT with contrast confirmed hepatosplenomegaly. Brain CT

was normal. The patient was admitted for diagnostic investigation and clinical monitoring. It was performed an extensive workup diagnosis. There was folate deficiency (2.46 ng/ml) and vitamin D deficiency (12 ng/ml). She was medicated with folic acid and vitamin D. Serum protein electrophoresis, thyroid function, vitamin B12, beta-human chorionic gonadotropin, alpha-fetoprotein, anti-acetylcholine receptor binding antibody, electromyography, Hb A2/HbF electrophoresis were normal.

Figure 1. Chest radiograph: superior mediastinal widening, increased cardiothoracic index, small volume left pleural effusion.

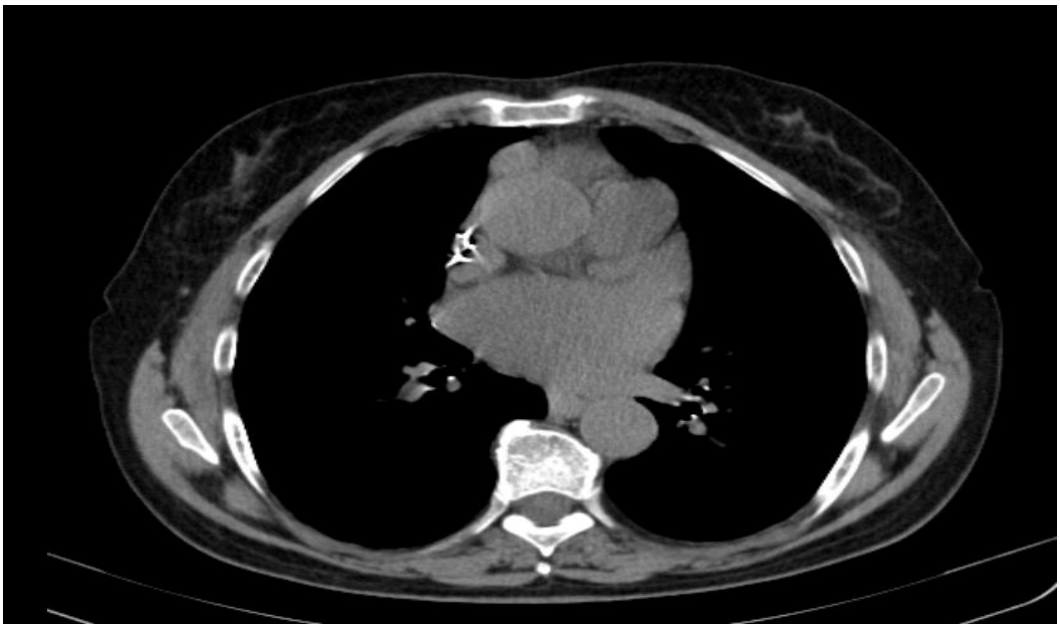


Myasthenia gravis was excluded. Viral hepatitis was excluded (HAV, HBV and HCV) together with HIV infection. Blood cultures, serology syphilis and CT excluded infection or neoplasia. Autoimmune screening was negative. Alpha-thalassemia study excluded deletions/duplications in the analyzed regions of the HBA1 and HBA2 genes. Transthoracic echocardiogram revealed small volume pericardial effusion, systolic function of both ventricles preserved, mild mitral and aortic regurgitation, moderate tricuspid regurgitation, mild pulmonary hypertension. Spirometry and colonoscopy were normal. Upper endoscopy revealed gastritis. After two weeks, additional thoracic CT revealed tissue densifications in the peripheral region of the posterior slope of the right base and in the paravertebral topography maintain the same morphostructural characteristics. Biopsy of the paravertebral node revealed EMH.

Positron emission tomography (PET–CT) revealed increased FDG-F18 uptake at right paracardiac adenomegaly 13x10 mm, intercavo-aortic, and along the left common iliac vessels, pericentimetric, exhibiting mild FDG uptake, most evident at D10-D11, right paravertebral nodular lesions exhibiting mild FDG-F18 uptake with no functional behavior suggestive of a high-grade malignant neoplastic lesion. She was discharged on the 11th

day of hospitalization. She was followed in an outpatient basis by Hematology and Oncology. After six months, a repeated thoracic CT revealed similar paravertebral nodules, densification of the anterior mediastinum with a 2 cm nodule, and nodular thickening of the posterior aspect of the right hemithorax, adjacent to the vertebral body, 40 x 14 mm, and in the posterior juxtapleural aspect 40 x 15 mm, overlapping with previous study (Figure 2).

Figure 2. Thoracic CT: densification of the anterior mediastinum with a 2 cm nodule and paravertebral nodules 40 x 14 mm and 40 x 15 mm.



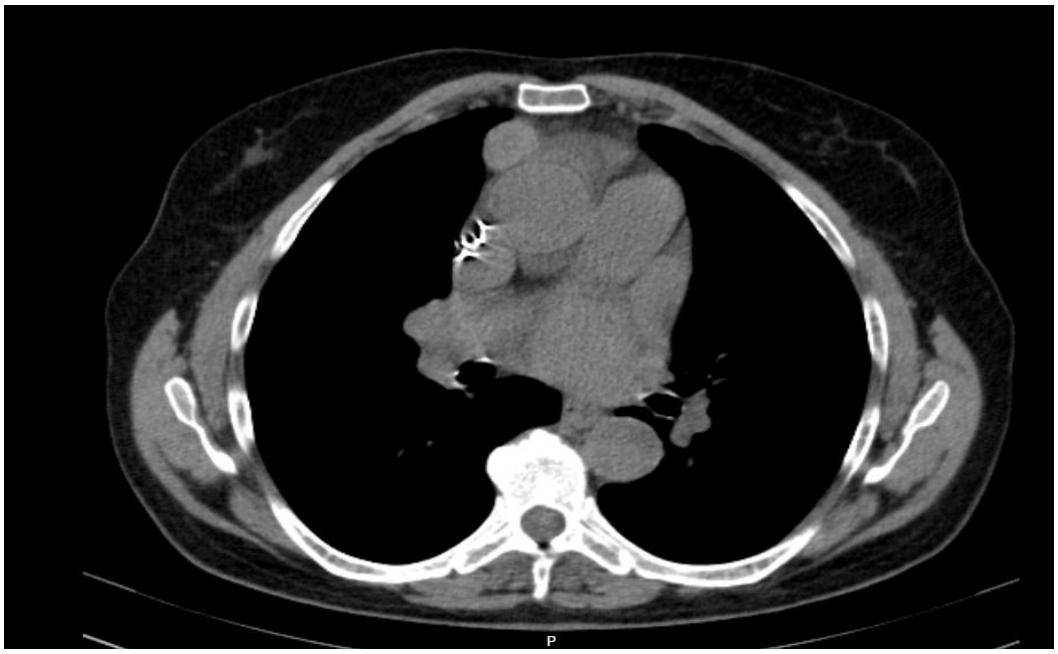
Bone marrow biopsy revealed hypercellular bone marrow with hyperplasia of the three hematopoietic lines, mainly the erythroid lineage, without signs of neoplastic involvement. Six months later, thoracic CT revealed densification in the anterior mediastinum, lateralized to the right, and a solid 24 mm nodule with a slight increase in size compared to the previous study, two posterior juxtapleural nodules persist in the right lower lobe, already diagnosed as foci of EMH (Figure 3).

A CT-guided biopsy of mediastinal nodule was performed and was suggestive of lymphoproliferative appearance (non-Hodgkin's lymphoma) but immunohistochemistry was suggestive of T lymphoblastic lymphoma. Patient had atypical and indolent clinical course against the hypothesis of lymphoproliferative disease. Review of slides by another doctor revealed the most likely diagnosis was thymoma. The B2 type of thymoma was defined as a tumor in which the neoplastic epithelial component appears as scattered plump cells with vesicular nuclei and distinct nucleoli among a heavy population of lymphocytes.

One month later, CT revealed hepatomegaly, splenomegaly and nodular densifications in the fat of the paravertebral and right posterior pleural region, the largest measuring 36 x 13 mm. Another PET-CT-FDG revealed moderate 18F-FDG metabolism in a nodular lesion in the right prevascular region, discrete radiotracer uptake is visualized in vaguely nodular tissue densifications in the paravertebral region, most evident in D9/D10 attributable to previously diagnosed EMH. As it was possible to resect the mass, patient underwent surgical approach VATS thymomectomy. Complete surgical resection of the thymic mass was achieved. Microscopically, the lesion represented a thymoma. Histology revealed microscopic transcapsular invasion into the perithymic adipose tissue, without mediastinal pleural involvement, tangential surgical margins without neoplastic involvement, one lymph node 0,6 cm with a reactive appearance, the neoplastic cells express

Cam5.2, CK19, p63, the thymocytes express TdT, CD5 and CD3, the reactive B cells express CD20. The lesion was classified as WHO type B2 thymoma TNM ninth version (AJCC): pT1a R0, Masaoka-Koga stage II. The surgical excision was considered adequate and curative for the thymoma and the patient was seen by the oncology department for follow-up. Her postoperative condition was satisfactory without serious complications. She was discharged on the 16th day of hospitalization.

Figure 3. Thoracic CT: densification in the anterior mediastinum, lateralized to the right and a solid 24 mm nodule with a slight increase in size compared to previous study.



A diagnosis of thymoma was made and the patient started surveillance. Six months later, thoracic CT revealed a nodule inferior to the tumor site suspected of residual disease. The unexpected residual thymoma required treatment with radiotherapy because the nodule was identified near the thymic loca had water density likely sequelae. The decision for postoperative radiotherapy was based on standard guidelines. Underwent adjuvant radiotherapy to the thymic loca (50 Gy/25 fractions). Recurrence of thymoma may not become apparent for years after initial treatment. After six months and one year, a revaluation thoracic CT showed no signs of local or distant recurrence. Now she is asymptomatic and maintains annual surveillance.

3. Discussion and Conclusion

In this patient 65-year-old woman, EMH was associated with iron deficiency anemia, hepatosplenomegaly, paraspinal masses. Intrathoracic EMH is rare, in this case, unexpected place such as the paravertebral region were found to have EMH activity. EMH was an incidental finding when patient with anemia was imaged. Although imaging was extremely useful in detecting EMH, imaging alone was non-diagnostic as no single mass shows all the typical findings. This case highlights the management of EMH. A judgement based on clinical background, combination of imaging findings and slow interval growth were appropriate in making the correct diagnosis. In this case, anemia-induced EMH.

Under normal conditions, erythrocytes are produced and eliminated periodically. Erythroblastic islands (EIs) are the essential structures of erythropoiesis in the bone marrow and spleen. Each EI is composed of a central macrophage and surrounding erythroblasts. These macrophages play an important role in erythropoiesis by providing iron for

hemoglobin production and enucleating and phagocytizing the nuclei of erythrocytes. Insufficient erythropoiesis can lead to anemia. EMH occurs when the bone marrow's capacity to produce blood cells is compromised or overwhelmed. This often happens in response to chronic anemia, where the body struggles to make enough red blood cells and trigger EMH. Anemia-induced EMH typically occurs in patients with thymoma and may result in clinical findings, such as hepatosplenomegaly and paravertebral mass like this case. Persistently proliferating erythroid progenitor cells fail to differentiate into mature erythrocytes. This vicious cycle results in EMH [1-6].

In this case, other causes of EMH were excluded: haemolytic anaemia, megaloblastic anaemia (vitamin B12 or folate deficiency), hemoglobinopathies (sickle cell disease, thalassemia, hereditary spherocytosis), thrombotic thrombocytopenic purpura, myeloproliferative disorders (polycythemia vera, essential thrombocythemia, myelofibrosis), bone marrow infiltration (leukemia, lymphoma, granulomatous diseases, metastasis, storage disorders), solid tumors (breast, lung, renal, colon, hepatocellular carcinoma, gastric, pancreatic, prostate and Kaposi's sarcoma), congenital disorders (Gaucher's disease), risk factor radiation or chemotherapy.

EMH is likely to be underreported because it does not produce distinguishing features on imaging and requires biopsy for confirmation. Clinicians are not often aware of the possibility of hematopoiesis occurring outside of the bone marrow and therefore may not be looking for it. A biopsy of a suspected EMH mass may be performed to confirm the diagnosis, but this procedure can carry risks depending on the mass's location. Most patients are asymptomatic and the lesions are discovered incidentally on imaging like this case. Symptoms occur according to location of EMH. EMH can occur in less common or ectopic sites. These include the thoracic vertebral column, leading to paraspinal masses that may cause neurological symptoms if they compress the spinal cord (posterior mediastinal). Paravertebral location causes pain. The presence of paravertebral masses may provide vital diagnostic clue in patients previously undiagnosed of their anaemia. EMH commonly develops within large soft tissue masses in the paravertebral thoracic regions. These rarely cause significant symptoms but may lead to pleural effusion like this case. CT chest demonstrated heterogeneous soft tissue paravertebral masses in the paraspinal regions. If clinical features of chronic anaemia are present, the diagnosis of EMH is easy to make.

In the absence of an underlying haematological condition or in uncertain cases, the diagnosis can be confirmed with CT-guided or thoracoscopic biopsy. Paravertebral EMH usually regresses after treatment with blood transfusions or radiation therapy. Diagnosis of EMH is usually made by the history of hematological disease in combination with CT of chest. If the diagnosis is not certain and controversial or if complications require surgical intervention, biopsy is mandatory. EMH is a rare cause of an intrathoracic mass and poses challenge in the differential diagnosis of mediastinal masses. The presence of any predisposing haematological condition is the most important factor, which raises the suspicion of EMH. EMH at atypical locations need to be monitored with follow-up imaging or correlated histologically to exclude other pathology and to ensure their stability. Tissue biopsy is appropriate to confirm the diagnosis and exclude other pathology (malignancy). Treatment is only required where symptoms are present [1-6].

Diagnosing EMH requires a combination of clinical evaluation, imaging and histopathological confirmation. While primarily used to assess bone marrow function, biopsies can help determine the presence of underlying disorders contributing to EMH. Biopsy of extramedullary masses may be necessary to confirm the diagnosis and rule out malignancy. Lesions are typically hypermetabolic hence FDG-18 PET avid. A definitive diagnosis can be obtained with histological examination of the fine-needle aspiration (FNAC), biopsy, or surgical specimen. Sampling of vascular EMH masses is not without risk, especially in the thorax where haemorrhage can occur. FNA tends to be safer than biopsy with lesser risk of haemorrhage. This stresses the importance of correctly diagnosing EMH on imaging, so that potentially catastrophic sampling may be avoided. Thoracic paraspinal

location below the D6 vertebral level is the commonest site for EMH imaging. The origin of EMH at this location has been postulated to be the extrusion of hyperplastic marrow through the thinned-out cortex of the vertebrae. Haematopoietic tissue from the vertebral bone marrow might be extruded through weakened trabecular bone into the epidural space and allowed to proliferate in this region. Alternatively, the hematopoietic elements may arise from nests of primitive hematopoietic stem cells, which later expand under the extreme demand present in patients with chronic anaemia like this patient [1-6].

Treatment of EMH is often guided by the underlying cause and severity of the condition. Managing the primary condition, such as controlling anemia is essential. Targeted radiation can reduce the size of extramedullary masses, alleviating symptoms. Hematopoietic tissue is radiosensitive. Radiotherapy relieves symptoms and causes regression of mass lesions. In cases where extramedullary masses cause significant symptoms or complications, surgical removal may be necessary. Blood transfusions may be necessary to manage symptoms and improve quality of life [1-6].

The authors present a case of a 65-year-old woman with iron deficiency anaemia, hepatosplenomegaly, small volume left pleural effusion, small volume pericardial effusion, paravertebral node with EMH and mediastinal mass whose biopsy revealed thymoma. Myasthenia gravis was excluded. She underwent VATS thymectomy. The lesion was classified as WHO type B2 thymoma TNM ninth version (AJCC): pT1a R0, Masaoka stage II. In literature, type B2 thymomas account for 25 % percent of all thymomas. Six months later, thoracic CT revealed a nodule inferior to the tumor site. The unexpected residual thymoma required radiotherapy. After six months and one year, a revaluation thoracic CT showed no signs of local or distant recurrence. Now she is being followed in an outpatient basis, asymptomatic, maintained annual surveillance.

This case highlights the current diagnostic approach to thymoma. It is necessary to obtain multidisciplinary evaluation at a center of excellence with expertise in the management of thymoma, with input from oncology, thoracic surgery and radiation oncology. The evaluation of an anterior mediastinal mass should include a contrast-enhanced CT of the chest. Obtaining a biopsy specimen can be a problem in the diagnosis of mediastinal tumors. As some mediastinal tumors are not treated surgically (lymphoma), diagnosis is often attempted with core needles or minimally invasive surgical biopsies. Biopsies may be diagnostic and assess resection margins and stage of the tumor, but it may be impossible to determine whether a thymoma is invasive based upon a biopsy alone [7-15].

The WHO system is used to classify thymic neoplasms based on their histologic appearance. For staging, all regional lymph nodes need to be sampled from the thymectomy specimen. Staging and degree of resection are stronger prognostic parameters for thymomas. Although staging is the most important prognostic factor, the prognosis is multifactorial with histologic features, staging, and completeness of resection contributing to the clinical behavior of these tumors. Systemic imaging to assess metastatic disease using a PET-CT-FDG is performed [7-15]. For those with early-stage localized resectable thymoma Masaoka-Koga stage II (AJCC) without myasthenia gravis, total thymectomy and lymph node resection is typically the standard of care like this case. VATS offers patients the best chance at curative therapy. The likelihood of long-term survival depends upon the completeness of surgical resection. Patients without high-risk features may be offered surveillance and do not require postoperative radiation [7-15].

Long-term posttreatment surveillance is necessary to monitor recurrent diseases and second cancers. For the cases of resected Masaoka stage II thymoma, perform a contrast-enhanced CT of the chest every 6 to 12 months for two years, then annually until 10 years for thymoma due to the risk of late recurrence [7-15]. In adults, the anterior mediastinum is the most common location where mediastinal masses occur. Thymoma is the first diagnosis to consider when facing a mediastinal mass. The age of this patient a 65-year-old woman was helpful because thymomas are more prevalent among individuals in their fifth and sixth decades of life. The differential diagnosis of an anterior mediastinal mass includes "the terrible Ts": thymoma, thymic carcinoma, mediastinal germ-cell tumours

(teratoma or seminoma/non-seminomatous tumours), (terrible) lymphoma and retrosternal thyroid. The mediastinum is the most common location for extragonadal germ cell tumors in adults. All patients with a mediastinal mass that could be a germ cell tumor should have alpha-fetoprotein (AFP) to malignant germ cell tumors, lactate dehydrogenase (LDH) to lymphoma and beta-human chorionic gonadotropin (beta-hCG) to seminoma measured prior to any therapy [7-15].

In this case Lymphoma was considered due to elevated lactate dehydrogenase but there were not rapid onset of B-signs or lymphadenopathy. Beta-hCG and AFP were normal and excluded germ-cell tumours. Reviewing the time course of the development of symptoms or the absence of specific symptoms helped narrow the list of potential diagnoses. Mediastinal masses can undergo slow growth over the course of years (thymoma) against rapid expansion (lymphoma). Patients who present with mediastinal lymphomas may present with systemic symptoms (fevers, weight loss, night sweats) but can also present with symptoms such as chest pain, dyspnea, wheezing, stridor, hoarseness, dysphagia or superior vena cava syndrome due to compression of mediastinal structures that in this case weren´t present.

The most common types of lymphoma presenting with disease in the mediastinum are nodular sclerosing Hodgkin lymphoma and primary mediastinal B-cell lymphoma that were excluded. Establishing the diagnosis of lymphoma required a core biopsy. Fine needle aspirates often do not provide sufficient tissue to determine structural composition to definitively diagnose all subtypes of lymphoma [7-15]. Although surgical resection is not typically considered part of the treatment regimen for lymphoma, surgeons may occasionally be asked to resect an isolated mediastinal mass proven to be lymphoma if the patient is thought to have prohibitive risks of complications with chemotherapy or radiation therapy or if the diagnosis remains in question based on a needle biopsy. Surgeons occasionally resect an isolated mediastinal mass that was clinically thought to be a lymphoma but, after resection, is confirmed to be thymoma like this case [7-15].

Thymomas typically present as an incidental finding identified on imaging in asymptomatics, due to local thoracic symptoms related to the size of the tumor or due to symptoms from a paraneoplastic syndrome [7-15]. A definitive diagnosis requires a tissue sample which can be obtained by biopsy prior to treatment or as part of a planned therapeutic resection of the entire mass. If the mass infiltrates surrounding structures or the patient has systemic symptoms or other findings that suggest an alternative diagnosis, biopsy should precede definitive resection as it may influence treatment significantly (preoperative chemotherapy, ability to participate in a clinical trial). Masses that appear to infiltrate surrounding structures are more likely to be malignant, which occurs in 15 percent of thymomas. Pre-resection biopsy is much more important in a situation where imaging suggests complete resection could either be difficult or not even possible based on local involvement and the diagnosis is not clearly suggested by the clinical presentation and imaging [7-15].

Prior to obtaining tissue, multidisciplinary input that includes evaluation by a surgeon is necessary. For patients with suspected thymoma amenable to complete resection (based on initial imaging studies), the diagnosis can be definitively established through surgical resection, which is also part of management. For patients with a suspected thymoma that is not considered amenable to complete resection or those who are ineligible for surgery (due to age or comorbidities), a tissue diagnosis can be established with a core needle biopsy or an open or thoracoscopic biopsy [7-15]. The decision to biopsy can be difficult when a patient clearly has a resectable anterior mediastinal mass, but the clinical scenario does not allow definitive distinction between lymphoma or thymoma. Confirming the diagnosis when lymphoma is suspected with biopsy is preferred. The risk of forgoing a biopsy and not obtaining a preresection diagnosis is the possibility that the surgeon will resect a lymphoma that could have been managed with nonsurgical treatment. On the other hand, a biopsy (percutaneous, endobronchial, surgical) of an encapsulated thymoma can cause tumor seeding. Although this situation is likely rare, multiple case

reports have demonstrated needle track and chest wall seeding after thymoma biopsy, and seeding of either the mediastinal space, the pleura, or the needle track can create a situation where surgery is no longer curative without adjuvant radiation [7-15].

Anterior mediastinal masses can often be biopsied under CT guidance. Core needle biopsy should be obtained whenever possible. Fine-needle aspiration (FNA) is generally not recommended as FNA often will not allow differentiation among the possible diagnoses because distinguishing a thymoma from lymphoma can be difficult histologically. This case highlights the difficulties in reaching a correct diagnosis, especially when biopsy results initially suggested lymphoma [7-15]. When percutaneous biopsy is not possible or cannot provide adequate tissue to definitively establish a diagnosis, surgical biopsy may be necessary. When lymphoma is considered, a possibility based on the clinical scenario, an excisional biopsy of a small mass, if possible, or an incisional biopsy of a large mass is preferred, although in select cases large core needle biopsies may be adequate [7-15].

The specific surgical approach (open or minimally invasive) depends upon the location and size of the lesion. Lesions that can be approached by thoracotomy can also be approached with VATS. The excellent anatomic view also allows biopsy of tissue anywhere in the mediastinum, even immediately adjacent structures such as the aorta, other great vessels or the heart [7-15]. The most appropriate surgical approach for resection of a mediastinal mass depends upon the patient, the location and size of the lesion, the presumptive diagnosis, and the preference and experience of the surgeon performing the resection. The enhanced field of view provided by the thoracoscope with a minimally invasive approach (VATS) allows this approach to be used for some anterior mediastinal masses that cross the midline, such as a thymoma. A minimally invasive approach is reserved for tumors less than 4 to 5 centimeters in size, although there are no definitive size criteria that preclude an attempt. The key to using a minimally invasive approach is to be able to provide a safe procedure that does not compromise the long-term oncologic effectiveness of the procedure [7-15].

The WHO system is widely used to classify thymic neoplasms based on their histologic appearance. Histologic classification may be difficult when classification is based on a biopsy with a relatively limited amount of tissue. It may be impossible to determine whether a thymoma is invasive based upon a biopsy alone. The clinical relevance of the WHO classification system has been validated by many studies. Thymomas are subdivided into types (A, AB, B1, B2, B3 and rare others) based upon the morphology of epithelial tumour cells, the relative proportion of the non-tumoural lymphocytic component (decreasing from type B1 to B3) and resemblance to normal thymic architecture. The prognostic significance may not apply to all subtypes, as some studies have shown a similar clinical outcome for type A and B1 and possibly B2 thymomas, while type B3 thymomas typically have a more adverse outcome. Staging and possibly degree of resection (complete versus partial) are stronger prognostic parameters for thymomas [7-15].

Type B2 thymomas contain more epithelial cells, often forming clusters of more than two epithelial cells. Although unusual, medullary islands may be present. The cytologic atypia of the tumor cells in B2 thymomas can be more pronounced and may even show anaplastic features. Although designed for surgical resection specimen, the WHO classification may be used for small biopsies. Immunohistochemistry is useful to establish the thymic primary nature. Thymoma subtyping on small biopsies is usually not needed for the therapeutically relevant distinction between lymphoma and solid tumour. Diagnostic discrepancies between core-needle and resection specimen histology can be anticipated, given the frequent occurrence of histological tumour heterogeneity that may be missed due to sampling error [7-15].

In thymoma, staging is the most critical step in patient management as it has been linked to prognosis. The Masaoka-Koga staging should remain the standard for the routine management of patients. Various studies in thymoma suggest that higher disease stages using the Masaoka staging system is associated with worsened prognosis. Masaoka-Koga staging system correlates with overall survival and is a surgical pathology

system that is assessable only after surgical resection of the tumour. A typical feature of thymic epithelial tumours is the correlation between the WHO classification and stage at diagnosis, which may explain its reported prognostic value. It is also used for treatment decisions. The thymoma is divided in four stages based on macroscopic and microscopic evaluation: stage I (macroscopically fully encapsulated with no capsular invasion), stage II (macroscopic invasion into surrounding fatty tissue or mediastinal pleura or microscopic invasion into the capsule, stage III (macroscopic invasion into the surrounding organs, such as the pericardium, great vessels, or lung), stage IV: pleural or pericardial dissemination or lymphoid or hematogenous metastasis. It is noted accurately in this amended staging system that a tumor cannot be categorized as invasive if it does not penetrate through the capsule. The modified Masaoka stage II tumors have either microscopic trans-capsular invasion or macroscopic invasion into the perithymic fatty tissue. Cases adhering to the pericardium or mediastinal plea but not rupturing them are also considered stage II. Masaoka stage affects disease-free survival and overall survival of patients with type B2 thymoma [7-15].

Staging according to proposed TNM system is optional. Thymomas are staged according to the ninth version American Joint Committee on Cancer (AJCC) staging system of the TNM. This version was updated to include tumor size in the T1 category (with tumors ≤5 cm classified as T1a and tumors >5 cm classified as T1b) and to reclassify tumor invasion of the lung or phrenic nerve as T2 disease (instead of T3). There are no changes to the regional lymph nodes (N) and distant metastases (M) categories, and all stage groups remain the same. The American Joint Committee on Cancer (AJCC) has updated its guidelines to include the new TNM proposal, which T is not based on the tumor size. It is related to the tumor capsule integrity and tumor invasion into the adjacent structure. Even though the TNM staging system is a useful method for thymoma staging, many studies view the modified Masaoka system as the gold standard. The Tumour–Node–Metastasis (TNM)-based staging system approach has the advantage of being more appropriate both for thymoma and thymic carcinomas, which present with a higher propensity toward nodal and distant metastatic invasion. Staging of thymomas is based upon the extent of the primary tumor and the presence of invasion into adjacent structures and/or dissemination. In approximately two-thirds of thymomas, preoperative chest CT can accurately predict the pathologic TNM stage [7-15].

The AJCC TNM staging system does not distinguish between encapsulated tumors and tumors that invade through the capsule into the surrounding adipose tissue. The presence of transcapsular spread should be noted when it is identified. Microscopic examination of possible invasion of adjacent organs and structures including the pericardium, mediastinal plea, phrenic nerves, lung, and large vessels, amongst others, should also always be mentioned. Pleural implants and metastases need to be microscopically confirmed. Thymomas may be adherent to adjacent structures without invasion. The surgeon should designate the site of adhesion on the specimen so that the pathologist can take sections from that area. An inflammatory fibrous reaction can also lead to the false impression of tumor invasion. The resection specimen should be oriented by the surgeon to identify the exact margins of the resection, which should then be inked. Lymph nodes need to be sampled from the resection specimen for microscopic evaluation, noting their location in the mediastinum (N1 [anterior [perithymic]] versus N2 [deep intrathoracic or cervical]) [7-15].

For precise staging, all regional lymph nodes need to be sampled from the thymectomy specimen. Separately submitted lymph nodes, appropriately site-identified, are also desirable. Histologic heterogeneity is common, with more than one histologic subtype frequently present in one tumor. Subtyping of thymomas is not performed on biopsies. Staging is the most important prognostic factor but the prognosis is probably multifactorial, with histologic features, staging and completeness of resection contributing to the clinical behavior of these tumors [7-15]. Because of the rarity of thymoma, there are few studies for the prognosis and treatment of type B2 thymoma. The B2 type thymoma has been

shown to have a worse prognosis than types A, AB and B1. Type B2 thymoma has a moderate aggressive nature compared with other subtypes. The Masaoka staging system has been shown to be an independent prognostic factor for type B2 thymoma [7-15].

In this patient, the extent of the tumor's invasiveness and its resectability were significant factors that were considered when determining if surgical resection was appropriate. The degree of invasion was directly related to the clinical prognosis. Surgical excision has been widely accepted as the preferred and most effective treatment modality for thymomas, regardless of their specific histological classification. This is evidenced by the high overall and disease-free survival rates it achieves in patients with stage II disease. The primary objective in managing these lesions is to achieve a complete resection, preferably with clear margins. Minimally invasive techniques have been documented in the literature, such as VATS. The assessment of resectability is mostly based on the surgeon's expertise; it is recommended to discuss indications for surgery in a multidisciplinary tumour board setting.

Preoperative CT findings reported to be associated with tumour invasiveness and/or completeness of resection include tumour size (>5/7/8 cm), lobulated or irregular contours, calcifications, infiltration of surrounding fat, lung infiltration, great vessel invasion or encirclement. The new TNM staging may even provide more help in formalising resectability: T1–3 level of invasion refers to structures amenable to surgical resection, while T4 level of invasion includes unresectable structures [7-15]. Prognostic assessment is challenging, as the impact of tumour stage and histology is superseded by the achievement of a complete resection. The treatment strategy is based on the resectability of the tumour. If complete resection is deemed to be achievable upfront, as is the case in Masaoka-Koga stage II, surgery represents the first step of the treatment. Minimally invasive surgery is an option for stage II tumours. It is necessary to obtain multidisciplinary evaluation at a center of excellence with expertise in the management of thymic epithelial malignancies, with input from surgical oncology, medical oncology, and radiation oncology [7-15].

For patients with localized thymoma who were treated with surgery, the approach to postoperative radiation therapy was based on the tumor stage. For patients with Masaoka stage II thymoma who are treated with surgery, the selection of postoperative therapy is also based on the presence or absence of high-risk features on postoperative pathology. For patients with Masaoka stage II thymoma and high-risk features for recurrence on postoperative pathology it is suggest postoperative RT rather than surveillance. High-risk features for recurrence are defined as invasion into the mediastinal fat or plea and microscopic or grossly positive surgical margins. Observational studies suggest that this approach reduces the risk of recurrence. Patients with Masaoka stage II thymoma and no high-risk features on postoperative pathology may be offered surveillance. Such patients do not require postoperative RT given the low risk of recurrence and lack of overall survival benefit with postoperative RT [7-15].

Potential RT-related toxicities include esophagitis, pneumonitis and pulmonary fibrosis, pericarditis, and, very rarely, radiation myelitis. Late radiation sequel includes radiation lung fibrosis in the lung included in the high-dose area and a small risk of constrictive pericarditis if a very large volume of heart was included in the RT field. Other potential late complications include acceleration of coronary artery disease, cardiac events such as myocardial infarcts and second cancers in the RT field [7-15]. Long-term posttreatment surveillance is necessary to monitor recurrent diseases and second cancers. For patients with recurrent disease detected on surveillance, early intervention may be more feasible and effective. Recurrence of thymoma may not become apparent for years (even decades) after initial treatment.

Even when a full resection was performed, thymoma often recurred, so it is important to plan for a long period of follow-up. Extrathymic haematopoietic cancers (non-Hodgkin lymphoma, diffuse large B-cell lymphoma and leukaemia), solid cancers (stomach, pancreas, colon, thyroid) and soft tissue sarcomas have been reported to occur more frequently in thymoma patients. This might be related to a shared unknown oncogenic

trigger, a thymoma-associated immune deficiency or less likely to adverse effects of treatments. Baseline thoracic CT scan should be carried out 3–4 months after surgery. For patients who have completed therapy for thymoma, the approach to posttreatment surveillance is consistent with guidelines from the National Comprehensive Cancer Network. For completely resected Masaoka stage II thymomas: a contrast-enhanced CT of the chest is performed every year for 5 years, then every 2 years. Follow-up may be continued for 10–15 years [7-15].

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References

1. Barisas DAG, Choi K. Extramedullary hematopoiesis in cancer. Exp Mol Med. 2024 Mar 5;56(3):549-558. doi:10.1038/s12276-024-01192-4.
2. Rivera-Torruco G, Muench MO, Valle-Rios R. Exploring extramedullary hematopoiesis: unraveling the hematopoietic microenvironments. Front Hematol. 2024 May 28;3:1371823. doi:10.3389/frhem.2024.1371823.
3. Aldapt MB, Haddad F, Abuasab T, et al. Extramedullary hematopoiesis and myelodysplastic syndrome. Blood. 2022;140(Suppl 1):12331-12332. doi:10.1182/blood-2022-163298.
4. Cenariu D, Iluta S, Zimta AA, Petrushev B, Qian L, et al. Extramedullary hematopoiesis of the liver and spleen. J Clin Med. 2021 Dec 13;10(24):5831. doi:10.3390/jcm10245831.
5. Georgakopoulou V, Damaskos C, Mantzouranis K, Melemeni D, et al. Invasive methods for the diagnosis and management of intrathoracic extramedullary hematopoiesis: a literature review. Respir Med Res. 2021 May;79:100815. doi:10.1016/j.resmer.2021.100815.
6. Yang X, Chen D, Long H, Zhu B. The mechanisms of pathological extramedullary hematopoiesis in diseases. Cell Mol Life Sci. 2020 Jul;77(14):2723-2738. doi:10.1007/s00018-020-03450-w.
7. Novais AG, Santos DP, Conceição M, Cunha S, Capelo J, et al. Thymoma and tubercoloma: unexpected coexistence. Eur J Case Rep Intern Med. 2021;8:2744. doi:10.12890/2021_002744.
8. Gomes A, Nascimento G, Barcelos N, Castro H, Assunção J. Thymoma: clinical features, diagnosis, and emerging therapies. Rev Iberoam Humanid Cienc Educ. 2025;11(7):20077. doi:10.51891/rease.v11i7.20077.
9. Sousa B, Araújo A, Teresina A, Azevedo I, Soares M, Sousa O. Malignant thymomas. Rev Port Pneumol. 2007;13(4):553-585.
10. Azevedo P, Magriço R, Luiz H, Judas T, Sanches F, Namora J. Dysphagia: an uncommon manifestation of thymoma. Rev Soc Port Med Interna. 2014;21(1):1-3.
11. Kallas E, Hueb A, et al. Middle mediastinal thymoma: case report. Braz J Cardiovasc Surg. 2005;20(2):189-191.
12. Alqaidy D. Thymoma: an overview. Diagnostics (Basel). 2023 Sep 18;13(18):2982. doi:10.3390/diagnostics13182982.
13. Terra RM, Milanez-de-Campos JR, Haddad R, Trindade JRM, et al. Cirurgia torácica robótica para resseção de timoma e tumores tímicos: desenvolvimento técnico e experiência inicial. J Bras Pneumol. 2020;46(1):e20180315.
14. Song Z, Jin X, Zhang Y. Treatment and prognosis of type B2 thymoma. World J Surg Oncol. 2014 Sep 20;12:291. doi:10.1186/1477-7819-12-291.
15. Girard N, Ruffini E, Marx A, Faivre-Finn C, Peters S. Thymic epithelial tumours: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015 Sep;26 Suppl 5:v40-55. doi:10.1093/annonc/mdv277.