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Mediastinal Mass Posting Etiological Diagnostic Problem.

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Abstract:
Epithelial tumours of thymus are rare tumors occurring frequently after the age of 50 years. They are classified histologically according to the World Health Organization (WHO), and staged according to the Masaoka-Koga classification and the TNM classification. We report a case of WHO type B1 thymoma in a young 17 years old, presenting a very aggressive character contrary to the presentation usually encountered in this type of thymomas. Surgery is challenged and chemotherapy is the first-line treatment.
Key Words: *Thymoma- young- WHO- type B1- stage-treatment.*

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I. Introduction:

Thymic epithelial tumors are rare tumors, representing 0.5% of all cancers [1]. In France, between 250 and 300 new cases are diagnosed each year. They account for 20% of mediastinal tumors and more than half of anterior mediastinal tumors, and are preferentially associated with autoimmune diseases [2]. We report a case of type B1 thymoma in a 17-year-old boy, with highly invasive characteristics inconsistent with the presentation usually seen in this type of thymoma.

II. Case Report:

Mr. K.M., 17 years old, with no significant past medical history, was admitted to the pulmonology department for chest pain and general malaise. The onset of symptoms dates back 3 months with the development of exertional dyspnea, which progressively worsened from stage 1 to stage 3 on the dyspnea scale mMRC, associated with anterior and interscapular chest pains of the side stitch type which worsen with exertion, and a spontaneous dry cough, without hemoptysis , myalgia or swallowing difficulties, all the symptomatology evolved in a context of unquantified weight loss and fever.

The general examination revealed pallor, a performance status (PS) of 2, and a normal temperature of 37.2°C. The pleuropulmonary examination revealed tachypnea at 20 breaths per minute, a pulse oximetry saturation of 96% on room air, and consolidation in the upper half of the anterior chest wall without superior vena cava syndrome. Neurological examination showed no motor or sensory deficits, and cranial nerve examination was normal. Lymph nodes were not enlarged. Examination of other systems was unremarkable. A standard chest X-ray revealed superior and middle mediastinal widening with heterogeneous mediastinal opacity, the left contours of which were polycyclic with tracheal displacement to the right (Figure. 1). A chest CT scan shows a multilobulated tissue mass in the anterior and middle mediastinum, measuring 112 × 72 × 110 mm, with uneven enhancement after contrast injection. In the anterior mediastinum, this mass projects onto the thymic region with invasion of the perithymic fat. It encompasses and compresses the supra-aortic vessels and is in close contact with the aorta and cardiac chambers, displacing the lung parenchyma without invading it (Figure. 2). Given this radioclinical presentation, the following diagnoses were considered: lymphoma, thymoma, and germ cell tumors. As part of the etiological workup, a bronchoscopy was performed, which did not reveal any lesions or other abnormalities suitable for biopsy. A CT-guided transthoracic biopsy of the mediastinal mass was performed without complications. Histopathological examination of the biopsies revealed tumor tissue with a lobulated architecture rich in lymphocytes expressing CD3, CD5, and Tdt, with regular monomorphic nuclei without atypia, and poor in CD20-negative epithelial cells, which formed a low-density network as shown by immunostaining with cytokeratins AE1/AE3. Furthermore, perivascular spaces were rare. This is therefore a type B1 thymoma (Figures. 3 and 4). As part of the impact assessment, the patient underwent spirometry, which was normal, and a transthoracic echocardiogram showing minimal pericardial effusion. To investigate for an autoimmune disease that may be associated with thymoma, serum protein electrophoresis was performed, which showed no abnormalities, particularly hypogammaglobulinemia. Immunological testing was

negative, especially for antinuclear antibodies (ANA) and anti-acetylcholine receptor antibodies. A complete blood count was normal, with a normal hemoglobin level of 13.5 g/dL and normal lymphocytes of 1500 cells/mm³.

Electromyography and positron emission tomography were not performed.

This is a type B1 invasive thymoma without signs of associated autoimmune disease.

Surgery was ruled out due to the presentation of the mass and its close proximity to vascular structures. The treatment recommended by the multidisciplinary tumor board is chemotherapy with cisplatin, doxorubicin, and cyclophosphamide in three cycles, followed by reassessment to determine the role of surgery and radiotherapy in subsequent treatment.

III. Discussion:

Thymic tumors frequently occur between the ages of 50 and 60 but can be observed at any age [3]. For the diagnosis of these tumors, if the tumor is immediately resectable, first-line surgery is recommended and will allow for a conclusive diagnosis through histopathological analysis of the surgical specimen [4]. When the mass is of doubtful resectable quality, when the clinical and radiological context suggests other causes such as lymphoma, germ cell or connective tissue tumors, or when the patient is not a surgical candidate, surgery may be indicated. Transcutaneous fine-needle aspiration guided by ultrasound or CT scan is of limited use because the biopsies are generally single or few in number and rarely followed by intraoperative histological examination to verify their contribution. Percutaneous trocar biopsies, on the other hand, appear to be more informative [5]. The histological classification of thymic epithelial tumors developed by the World Health Organization (WHO) is based on the morphology of the tumor cells, the relative proportion of the associated lymphoid component, and the resemblance of the tumor tissue to the different anatomical zones of the normal thymus. Thymomas represent the majority of thymic tumors and are composed of epithelial cells, which constitute the tumor component, and mature or immature T lymphocytes. They are thus distinguished as: spindle cell thymomas or medullary thymomas (thymomas A), mixed thymomas (thymomas AB), lymphocortical thymomas (thymomas B1, B2, and B3). Thymic carcinomas are purely epithelial tumors with an invasive character and must first be distinguished from metastasis and lung carcinoma. Non-epithelial thymic tumors include neuroendocrine tumors, germ cell tumors, lymphomas, stromal tumors, cystic tumors, and metastases [2]. Indeed, the 2004 WHO histological classification is currently recommended and used; it employs a system of letters and numbers. The letters are based on the appearance of the epithelial cells: In type A, the cells resemble those of the subcapsular zone of adult thymic remnants; in type B, the cells resemble those of the cortical zone of an active thymus. The numbers 1, 2, and 3 are related to the increasing degree of atypia of the tumor cells and the number of these cells relative to the non-tumor lymphocytic component [6]. For type B1 thymomas, they have an organoid architecture combining dark areas resembling the normal cortex, where epithelial cells are sparse, oval, with a pale, rounded nucleus and a small nucleolus, surrounded by non-tumor lymphocytes, and minor light areas resembling the medulla with possible Hassall's corpuscles. The differential diagnosis may include thymic hyperplasia, type B2 thymoma, or lymphoblastic lymphoma. This classification, which is consensual and relatively reproducible, generally has prognostic value; types A and AB were generally considered benign, B1 low-grade malignancy, while types B2 and B3 had a poorer prognosis [7]. In our case, the thymic mass exhibits a significant degree of locoregional invasion; however, the majority of B1 thymomas are characterized by a low degree of invasion. Thymoma staging is based on the Masaoka classification revised by Koga [8] and the TNM classification developed by the International Thymic Malignancy Interest Group (ITMIG) and the International Association for the Study of Lung Cancer (IASLC) [9]. According to these classifications, invasive thymomas correspond to stages II to IV. The WHO histological types A, AB, and B1 frequently correspond to Masaoka-Koga stages I and II, for which surgical treatment is feasible and desirable. Recurrence after surgical resection of a B1 thymoma varies between 0 and 9%, with a good prognosis [10]. Our patient presents with a large thymoma invading the perithymic fat, encompassing and compressing the large vessels with the presence of a pericardial effusion, even in the absence of first-line surgery, we can conclude at least a Masaoka Koga stage III and the intimate contact with the large vessels makes the tumor unresectable from the outset as a first-line treatment. In practice, the Masaoka clinicopathological classification and the WHO histological classification determine therapeutic strategies and allow for an understanding of the prognosis. At diagnosis, approximately 50% of thymic epithelial tumors are discovered at Masaoka stage I, 40% at stages II and III, and 10% at stage IV. The vast majority (approximately 80%) of Masaoka stage III and IV tumors correspond to histologically aggressive types: B3, thymic carcinoma, and neuroendocrine tumors. Similarly, 80% of epithelial tumors of these histological types are diagnosed at advanced stages [11]. Myasthenia gravis is the most frequently reported autoimmune disease associated with thymomas (approximately 44% of patients with a thymoma), but other autoimmune diseases have been described in association with these tumors, among the most common being systemic lupus erythematosus, autoimmune pure red cell aplasia, Isaacs syndrome, polymyositis, and Good's syndrome [3]. Clinical examination and paraclinical

investigations performed on our patient revealed an isolated thymoma without signs suggestive of autoimmune diseases.

Patients with Masaoka stage III thymomas require management based on operability at diagnosis. For operable patients, the quality of the resection and the histological type are the main prognostic factors [12-13]. The RYTHMIC guidelines recommend:

If the tumor is resectable from the outset: surgery and postoperative radiotherapy at 50 Gy, even in cases of complete resection of the entire initial volume, plus 10 to 15 Gy to any residual tumor identified intraoperatively.

If the tumor is not resectable from the outset (as in our patient's case): neoadjuvant chemotherapy with 3 cycles of cisplatin, adriamycin, and cyclophosphamide (CAP protocol), representing the best protocol used and yielding the highest response rates. Surgery will be decided based on the tumor's response to this chemotherapy.

IV. Conclusion:

Thymomas are rare tumors that frequently occur after the age of 50. The prognosis for these tumors depends on the WHO histological type and the stage according to the Masaoka-Koga classification; these two classifications determine the therapeutic approach. Type B1 thymoma is a low-grade tumor in the majority of cases, but can present as a highly invasive tumor, resulting in a very poor prognosis, as in the case of our patient.

Declarations Of Interest:

The authors declare that they have no conflicts of interest related to this article.

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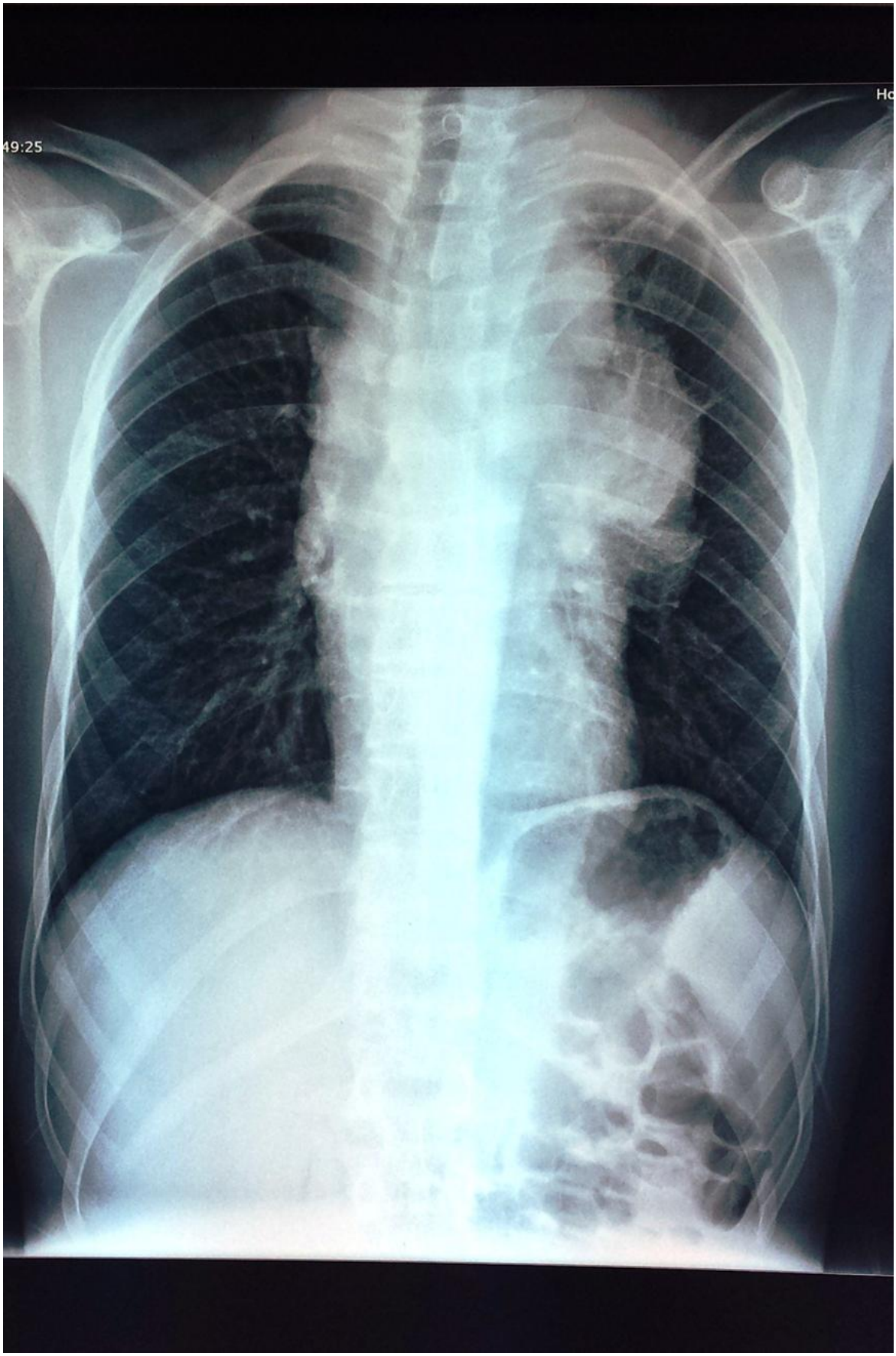

Figure 1: Standard chest X-ray showing a mediastinal opacity with polycyclic contours and displacement of the trachea towards the right side.

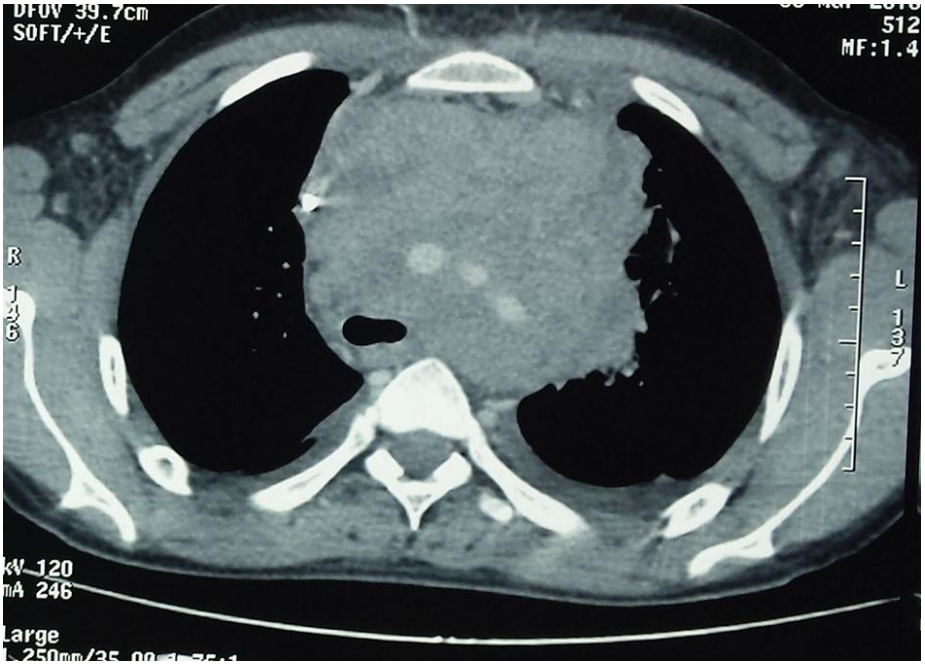

Figure 2: Chest CT scan with contrast injection, showing the mass in the anterior and middle mediastinum.

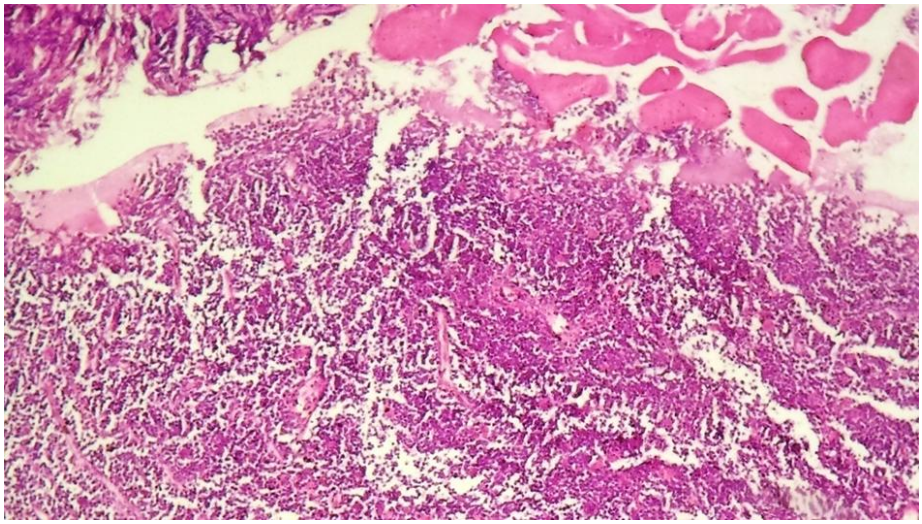

Figure 3: H&E staining showing a lobulated architecture with medullary areas resembling a normal thymus (×1000).

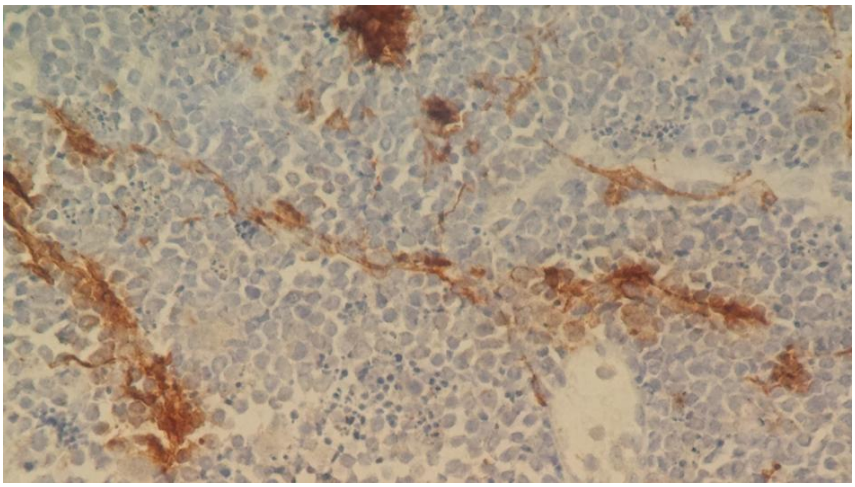

Figure 4: Immunostaining with cytokeratins AE1/AE3 marking the epithelial network proliferation (×400).