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CASE REPORT

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Pericardial ectopic thymoma

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Abstract Primary intrapericardial thymoma is an unusual localization. We report a case of a patient with an isolated and primary pericardial thymoma. This 72-year-old woman presented with dyspnea, dysphony and myalgia. The radiological evaluation revealed an intrapericardial mass. Surgical exploration showed a hemorrhagic and infiltrative tumor in the pericardial sac, while the mediastinum was free of tumor. Surgical biopsies and, later, an ablation of pericardial mass were done. The tumor was a thymoma, composed of large epithelial cells and immature T lymphocytes and was classified B2 according to the World Health Organization classification (1999). Clinically, a myasthenia gravis was revealed. We discuss the few cases reported in the literature.

Keywords Thymoma · Pericardium · Ectopic thymoma · Myasthenia gravis

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Introduction

Thymomas, as tumors originating from the epithelial elements of the thymus, are more often located in the anterior mediastinum, sometimes extending to the superior compartment. However, some thymomas can occur in an unusual location, secondary to a probable failure in embryological thymic displacement. Among ectopic locations, authors have reported cases occurring in the neck, the inferior or posterior mediastinum, the bronchial tract and the diaphragm [3, 8, 12]. Rarely, isolated and solitary pericardial thymomas, without another tumor site, have been described [11]. We report a case of primary intrapericardial thymoma, revealing a myasthenia gravis. The clinicopathological and immunohistochemical features of this tumor are presented, along with a literature review of ectopic presentation.

Clinical history

A 72-year-old woman presented with dyspnea, dysphony and myalgia. She had a long personal history, with endometriosis, depression, polymyostis, nephrotic syndrome and Parkinson's disease. She had polymyositis with finger retraction and muscular weakness 20 years prior to presentation, treated by corticotherapy. On a recent chest-X-ray, there was a slight enlargement of the heart. The superior aerodigestive endoscopy found a left recurrent nerve deficit. A 5-cm solid mass, located in the pericardium, was observed on computed tomography scan, while the mediastinum was free of tumor. On surgical exploration, a solitary mass was identified, precisely in the aorta–pulmonary sinus, between the left superior pulmonary vein and the left pulmonary artery. It was large, infiltrative and extremely hemorrhagic, and its base of implantation could not be noted. Multiple biopsies were performed. Later, on surgical exploration, the mediastinum was free of tumor. The pericardial mass was completely excised, as well as a proximal bronchial enlarged lymph node.

Materials and methods

Tumor tissues from biopsies and surgical excision were routinely fixed in formalin (10%), embedded in paraffin and subsequently stained with hematoxylin–eosin–saffron. A panel of antibodies

(provider, dilution) was also applied to paraffin sections, using automated immunohistochemical technique (Dako), CD3 (Dako, 1/100), CD5 (Tebu Novocastra, 1/25), CD20 (Dako, 1/250), AE1/AE3 (Biogenex, 1/50), CD1A010 (Beckman-Coulter, prediluted) and TTF1 (Dako, 1/50).

Results

Macroscopically, the tumor was in the pericardium and measured approximately 6×4×3 cm. The cut surface revealed a white solid mass, with a 4-cm hemorrhagic and cystic area (Fig. 1). Its base of implantation was exactly in the pericardium and measured 2 cm. Microscopically, biopsies and tumor tissues had similar profiles. Low-power view of tumor sections showed lobulated architecture with two different cell types. At higher magnification, a medium-sized mesh of epithelial cells intermixed with abundant lymphocytes (Fig. 2). The epithelial cells were ovoid with eosinophilic cytoplasm and oval nuclei with fine chromatin, regular outline and prominent nucleoli. These cells were connected to each other by enlarged eosinophilic cytoplasmic processes. There was no atypia and no mitotic figure. The lymphocytes were small and round, with a scant cytoplasm. Another histopathological hallmark was the formation of perivascular clear spaces, bordered by palisading epithelial cells and sometimes containing serous fluid and lymphocytes. On the surgical mass, the tumor invades the pericardium, while the bronchial lymph node was metastatic with extracapsular extension.

Immunohistochemical studies showed that cells expressed cytokeratin (AE1/AE3), confirming their epithelial nature and highlighting their connected network (Fig. 3). The lymphocytes expressed CD3, CD5 and CD1a, and were recognized as immature T lymphocytes, i.e. thymocytes (Fig. 4). Very few lymphocytes were CD20 positive, while TTF1 did not mark any tumor cell. Putting together the clinical, the morphological and the immunohistochemical findings, this tumor was classified as a thymoma located in the pericardium. The tumor was malignant according to Levine and Rosai's classification [4] because it invaded the pericardium and because of the presence of metastatic lymph node. Pathologically, it was classified B2 according to the World Health Organization (WHO) classification (1999) or mixed lymphocytic and polygonal epithelial cell type, as known as cortical thymoma in Muller–Hermelink classification [6]. Morphological description of thymic tumors and concordances among classifications are summarized in Table 1 [9].

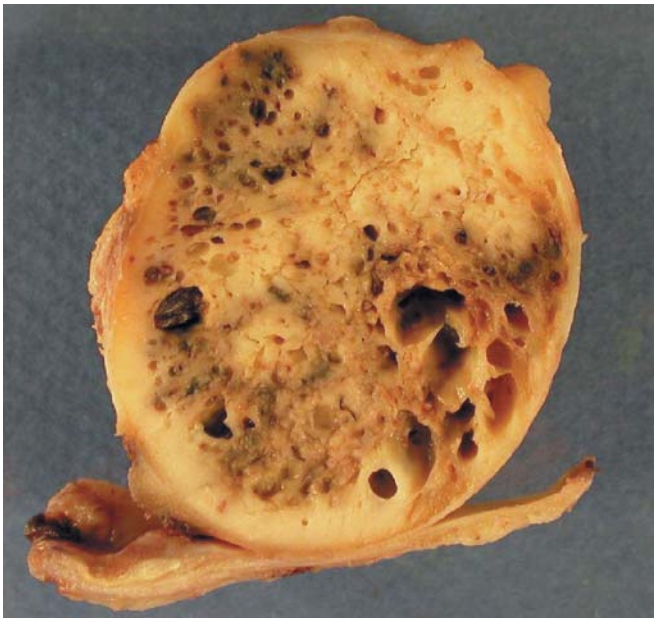

Fig. 1 Cut surface of the resected pericardial tumor showing the intrapericardial development of the lesion

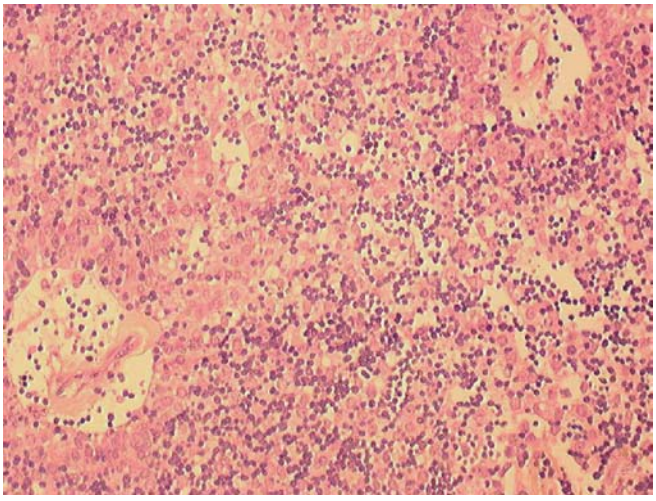

Fig. 2 Photomicrograph emphasizing the two cells populations, and the perivascular empty spaces (×400)

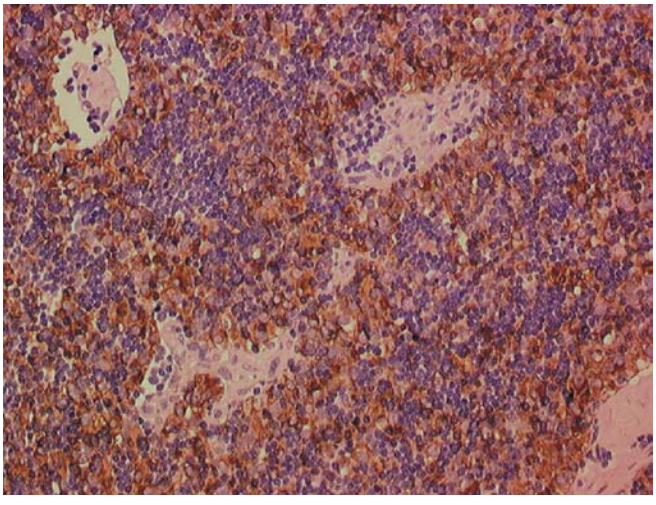

Fig. 3 Immunohistochemistry using AE1/AE3 antibody highlighting the large epithelial cells and their connected network (×400)

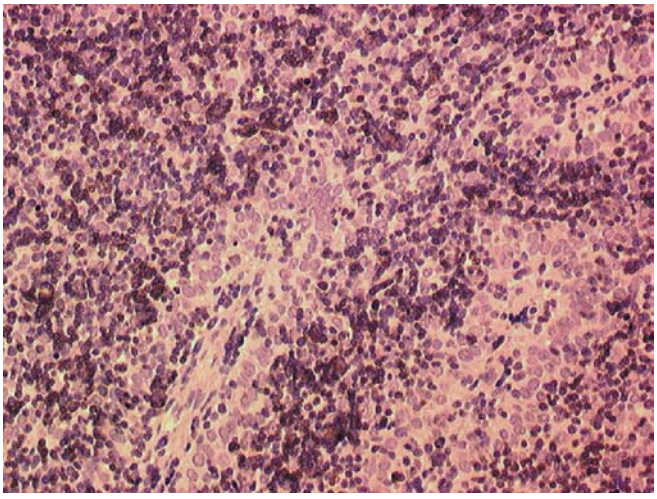

Fig. 4 Immunohistochemistry using the CD1a antibody highlighting the immature T-lymphocytes (×400)

Upon the discovery of a thymoma, complementary exams were done and revealed the existence of myasthenia gravis. Our hypothesis is that some of her symptoms, such as muscular weakness and dysphony, could be explained by the myasthenia gravis. The patient died of post-operative complications, and there was no autopsy performed.

Discussion

Primary intrapericardial thymomas are unusual neoplasms that have been rarely reported in the literature [1, 11]. To our knowledge, there are only three reported cases in this location, one surgical case and two autopsy cases, but with no associated myasthenia gravis (reviewed in Table 2). In 1996, Ben Hami et al. reported the case of a primary pericardial thymoma, revealed by pericardic effusion [1]. This report concerns a 54-year-old man, without history or sign of myasthenia gravis, who presented with thoracic pain and fever. On surgical explorations, hemorrhagic fluid in the pericardial sac was sampled, and a mass, infiltrating the heart, was biopsied. In this case, the mediastinum was also free of tumor. The tumor was composed of spindle cells, small lymphocytes and focally large polygonal cells. It was, therefore, classified as mixed thymoma (Muller–Hermelink) or AB (WHO) (Table 1). The patient was treated by chemotherapy and radiation therapy. In 1997, Maurizio Mirra et al. reported a retrospective evaluation of autopsy cases (between 1980 and 1995 in an Italian general hospital) [7]. Approximately 31,000 postmortem investigations were encoded, 57 thymomas were on record and only 2 cases of thymomas showing an exclusive intrapericardial growth were retrieved. The patients were 61 years and 82 years of age; both were women. They died of chronic diseases. There was no history or sign of myasthenia gravis. At autopsy, both tumors were in the pericardium, attached to the lateral or posterior wall of the parietal pericardium with a broad base and measuring 6–10 cm in largest dimension. There was no infiltration of myocar-

Table 1 Morphological description and concordances between classifications

Description	Muller–Hermelink	World Health Organization
Spindle cells accompanied by few lymphocytes (immature)	Medullary thymoma	A
Mixed spindle and round cells, with foci rich in lymphocytes (immature)	Mixed thymoma	AB
Round cells and abundant lymphocytes (immature)	Predominantly cortical thymoma	B1
	Cortical thymoma	B2
Round cells, with mild atypia and rare lymphocytes (immature)	Well-differentiated thymic carcinoma	B3
Atypic cells accompanied by few lymphocytes (mature)	Thymic carcinoma	C

Table 2 Literature review of pericardial thymomas

Authors, years	Sex, age (years)	Presentation	Myasthenia gravis	Pathology	Classification (World Health Organzation)	Treatment
Ben Hami, 1996 [1]	Male, 54	Thoracic pain, fever	Absent	Spindle and large polygonal cells, lymphocytes	AB	Chemotherapy Radiation therapy
Mirra, 1997 [7]	Female, 61	Autopsy	Absent	Spindle cells, lymphocytes	A	-
	Female, 82	Autopsy	Absent	Spindle cells, lymphocytes	A	-
Current case	Female, 72	Dyspnea, dysphony, myalgia	Present	Large polygonal cells, lymphocytes	B2	Surgery

dium in both tumors. Histologically, both were spindle cell thymomas or medullary type (Muller–Hermelink) or A (WHO) (Table 1). In all four cases, including our case, thymomas were only located in the pericardium, without any other tumor site. That eliminates pericardial invasion by mediastinal malignant thymoma. The alternative possibility of a solitary metastasis from a small undetected primary tumor in the thymus can not be totally eliminated, especially knowing that myasthenia gravis can reveal microscopic thymoma [10]. However, in our review, we did not find any such reported case. Thus, the diagnosis of ectopic pericardial primary thymoma was kept. The thymus is embryologically derived from the third pair of pharyngeal pouches, and during the development it descends into the anterior mediastinum. Ectopic locations of the thymus usually result from failure of the organ to descend or from an excessive descent. Classically, reported ectopic sites were cervical, middle or inferior mediastinum, as well as diaphragmatic sites [3, 12]. More rarely, other ectopic thymomas arose in the supraclavicular region, in the pleura and intrapulmonary regions [2, 8]. All these unusual sites of thymomas may pose a serious diagnostic challenge for pathologists. Differential diagnoses could be malignant lymphoma, particularly of the lymphoblastic type, and carcinoma (primary or metastatic), especially small cell lung carcinoma [5]. The large epithelial cells scattered in the background aid in distinguishing thymoma from lymphoblastic lymphoma. Immunohistochemical stains, particularly cytokeratin, may be very supportive in difficult cases, by highlighting the presence of an epithelial cell component drawing a connected network. The identification of an immature lymphoid cell component expressing CD1a should distinguish thymoma from carcinoma. Moreover, unlike thymoma, cells of small cell lung tumor have high mitotic count, and a specific marker can be useful in this context, such as TTF1, expressed in 80% of small cell lung carcinoma. Another histological sign that should alert the pathologist to the possibility of thymoma is the identification of perivascular clear spaces.

We have reported that thymoma may occur in the pericardium as a lesion independent from a mediastinal tumor. It can be, therefore, considered as an ectopic location of thymoma accompanied with clinical manifestation. The presence of myasthenia gravis in a patient with no mediastinal tumor should encourage the clinician to pursue investigations looking at ectopic sites for thymoma.

References

1. Ben Hami B, Caulet-Maugendre S, Valla J, Heresbach-Le Berre N, Kernec J, Laurent M, Ramee MP (1996) Primary pericardial thymoma: an unusual etiology of neoplastic pericarditis. Ann Pathol 16:445–448
2. Fushimi H, Tanio Y, Kotoh K (1998) Ectopic thymoma mimicking diffuse pleural mesothelioma: a case report. Hum Pathol 29:409–410
3. Jansen JD, Johnson FE (1990) Fatal ectopic thymoma. Ann Thorac Surg 50:469–470
4. Levine GD, Rosai J (1978) Thymic hyperplasia and neoplasia: a review of current concepts. Hum Pathol 9:495–515
5. Loire R, Hellal H (1993) Neoplastic pericarditis. Study by thoracotomy and biopsy in 80 cases. Presse Med 22:244–248
6. Marino M, Muller-Hermelink HK (1985) Thymoma and thymic carcinoma. Relation of thymoma epithelial cells to the cortical and medullary differentiation of thymus. Virchows Arch 407:119–149
7. Mirra M, Zanella M, Bussani R, Falconieri G (1997) Intrapericardial thymoma: report of two incidental autopsy cases and review of the literature. Arch Pathol Lab Med 121:59–63
8. Moran CA, Suster S, Fishback NF, Koss MN (1995) Primary intrapulmonary thymoma. A clinicopathologic and immunohistochemical study of eight cases. Am J Surg Pathol 19:304–312
9. Okumura M, Miyoshi S, Fujii Y, Takeuchi Y, Shiono H, Inoue M, Fukuhara K, Kadota Y, Tateyama H, Eimoto T, Matsuda H (2001) Clinical and functional significance of WHO classification on human thymic epithelial neoplasms: a study of 146 consecutive tumors. Am J Surg Pathol 25:103–110
10. Poulard G, Mosnier JF, Dumollard JM, Prades JM, Convers P, Boucheron S (1994) Microscopic thymoma and myasthenia gravis. Ann Pathol 14:203–204
11. Salih Deveci M, Ceyhan K, Deveci G, Finci R (2001) Pericardial rhabdomyomatous spindle cell thymoma with mucinous cystic degeneration. Histopathology 38:479–481
12. Salyer WR, Eggleston JC (1976) Thymoma: a clinical and pathological study of 65 cases. Cancer 37:229–249