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Primary Mediastinal Sarcoma: A Case Report

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Abstract **Case Report**

We report the case of a 78-year-old patient with hypertension and underlying heart disease (bearing a mechanical valve), who presented to the pneumology department at Rodez Hospital with progressive dyspnea and thoracic pain. Thoracic-abdominal-pelvic computed tomography (TAP CT) and positron emission tomography (PET-CT) revealed a mediastinal mass, and a CT-guided biopsy confirmed the presence of a grade III mediastinal sarcoma. Consequently, we decided to initiate chemotherapy.

Keywords: Mediastinal sarcoma, Histological diagnosis, Chemotherapy, Prognosis.

INTRODUCTION

Primary mediastinal sarcomas are rare malignant mesenchymal tumors, accounting for between 2 to 8% of all malignant mediastinal tumors and 1.4% of adult soft tissue sarcomas [1, 2]. These sarcomas are often aggressive, large, and closely located to vital structures, necessitating a multidisciplinary approach to management. They pose specific challenges regarding histological diagnosis, confirmation of primary nature, and therapeutic management. Primarily affecting young adults, with a slight male predominance [2], these sarcomas typically present with nonspecific respiratory symptoms or symptoms due to compression of adjacent structures. Imaging studies, though nonspecific, often reveal a large heterogeneous mass predominantly located in the posterior mediastinum [2, 3]. However, distinguishing between different histological types can be difficult. Histological examination is complex; thus, immunohistochemical studies are essential for classification. Malignant tumors of peripheral nerve sheaths are the most common. Treatment is based on as complete surgical resection as possible, which is often challenging due to the large size of these tumors and their proximity to vital structures [4]. The role of adjuvant treatments is controversial and poorly understood. However, chemotherapy appears to be effective in metastatic forms, potentially reducing tumor size for subsequent surgery. Radiotherapy is indicated for inoperable tumors or cases of incomplete resection to eradicate residual tumor tissue. Local recurrences and deaths characterize the clinical course of mediastinal sarcomas. The prognosis is poor, with a five-year survival rate estimated at 33%, primarily depending on histological grade and the quality of surgical resection [2, 4].

OBSERVATION

This is Mr. C.G., a 78-year-old man with a history of uncomplicated asthma, hypertension, and aortic valve insufficiency (with a mechanical valve). He progressively developed resting dyspnea (NYHA class IV) accompanied by thoracic pain. He presented to the emergency department where he underwent an angio-CT scan revealing a large right pleural effusion without significant evolving pulmonary parenchymal lesions. Subsequently, a thoraco-abdomino-pelvic and cerebral CT scan was performed, revealing a large right anterior and paramedian mediastinal mass extending from the aortic arch to the right diaphragmatic dome over approximately 16 cm craniocaudally, measuring 8 cm in the largest axial transverse axis by 9 cm in the largest anteroposterior axis. The lower part of the mass is globular and hypodense with multiple intralesional septa enhanced by contrast injection, while the upper part in the lower right lateral-tracheal position presents mainly a intensely and heterogeneously enhanced fleshy component. The mass causes compression of the right atrium, which appears flattened, and compression of the superior vena cava without signs of thrombosis. There are two heterogeneously enhanced pleural nodules in the right lower paramedian parietal pleura, both measuring several centimeters. Additionally, a 30 mm heterogeneously enhanced pleural nodule in the right posterior cul-de-sac was noted. There were no secondary

lesions. A PET-CT scan was performed after pleural drainage, showing intense and heterogeneous hypermetabolism in the anterior mediastinal mass and ipsilateral mediastinal lymph nodes. Pleural biopsy specimens returned negative. A biopsy was performed under CT guidance, revealing spindle cell lesions with a difficult diagnosis, showing a non-characteristic phenotype, cytonuclear atypia, and areas of necrosis, prompting classification as an undifferentiated sarcoma. It was classified as a grade 3 sarcoma according to the FNCLCC classification, despite a low proliferation index. The case was discussed at a multidisciplinary sarcoma meeting at Oncopôle de Toulouse, where it was decided to initiate anthracycline-based chemotherapy (EC100), along with pleural talcage to prevent pleural effusion recurrence. The patient received one cycle of chemotherapy after cardiac evaluation and was then lost to follow-up.

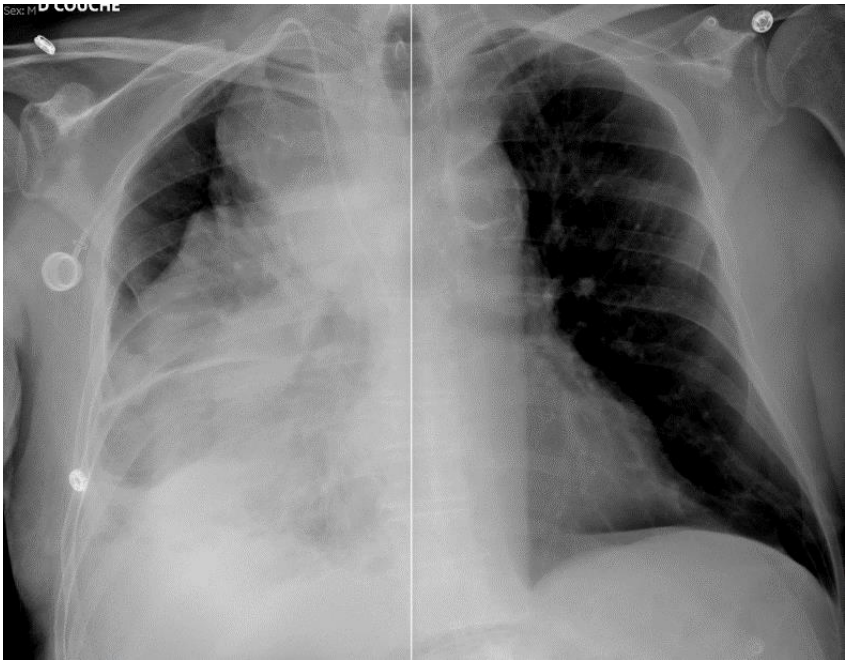

Figure 1: Chest X-ray (malignant anterior mediastinal tumor): Homogeneous opacity in the anterior mediastinum with leftward mediastinal deviation and widening of the intercostal spaces, accompanied by pleural effusion

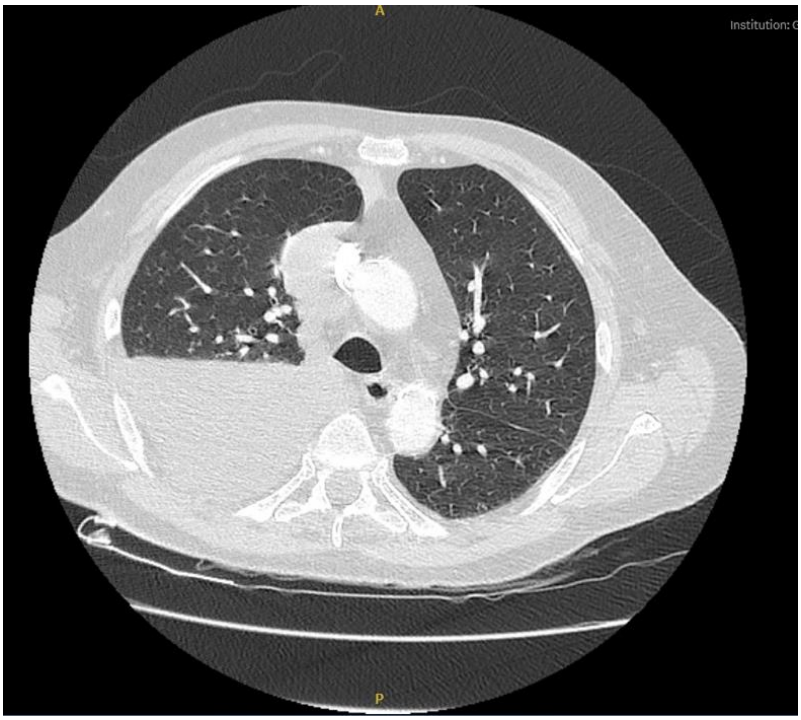

Figure 2: Thoracic computed tomography (CT) scan in lung window: Moderate pleural effusion with passive atelectasis of the underlying lung parenchyma

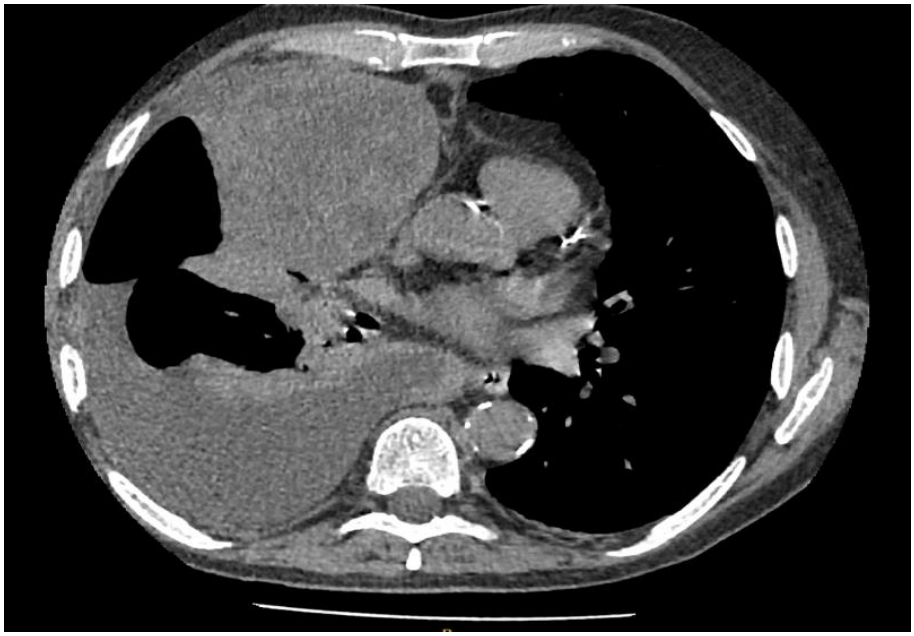

Figure 3: Thoracic computed tomography (CT) scan in mediastinal window: Large right anterior and paramedian mediastinal mass. The mass compresses the right atrium, which appears flattened, and compresses the superior vena cava without signs of thrombosis

DISCUSSION

Primary mediastinal sarcomas are rare, representing 2 to 8% of all malignant primary mediastinal tumors [1]. In Burt *et al*.,'s series, comprising 47 primary mediastinal sarcomas, thymoma-associated myasthenia gravis neuropathy (TMGNP) was the most common histological type, while other sarcomas were less common [2]. These tumors have a predilection for the posterior mediastinum (49%), with approximately 41% occurring in the anterior mediastinum [5, 6]. Our patient presented with a right anterior mediastinal mass and ipsilateral mediastinal lymph nodes. The middle mediastinum is affected in 10% of cases. The mean age at diagnosis is 39 years, ranging from two to 69 years, with a slight male predominance reported by most authors [2, 7]. Most patients are symptomatic with a variable clinical presentation. Clinical signs are nonspecific or secondary to compression or invasion of neighboring organs [5], with incidental discovery reported in 11% of cases [2]. In our case, the patient presented with purely respiratory symptoms: NYHA class IV dyspnea accompanied by thoracic pain. These tumors most often arise de novo but can develop in irradiated fields (13% of cases) [8, 9]. Radiation-induced sarcomas are mainly represented by malignant histiocytoma and fibrosarcoma [2, 4, 8, 10], being classically less sensitive to radiotherapy and chemotherapy [8]; however, our patient had no history of radiation exposure. Associated genetic conditions are described in 1 to 10% of these sarcomas, notably von Recklinghausen's disease or neurofibromatosis type 1 (NF1), less commonly familial retinoblastoma, or Li-Fraumeni syndrome [2, 4]. The diagnosis of primary mediastinal sarcoma is not always considered preoperatively. Imaging findings are non-pathognomonic as these tumors have highly variable characteristics [2, 14], although they may reveal malignant features or assess resectability. Typically, they appear as large, heterogeneous mediastinal masses, sometimes well-defined, which can be confused with chondrosarcoma, osteogenic sarcoma, teratoma, or thymoma [2, 15, 16]. The average size is 10 cm; however, in our case, it was 10 cm in diameter and extended over 17 cm vertically. Thoracic computed tomography (CT) is the first-line investigation for exploring a mediastinal mass, providing precise localization, assessment of relationships with adjacent structures, and identification of pulmonary metastases. There are no definitive malignancy criteria apart from indirect signs such as invasion of neighboring structures, bone lysis, or distant metastases [12]. In our case, CT revealed a moderate right pleural effusion associated with passive atelectasis of the right lower and middle lobes, and a large hypo-dense mass with heterogeneous contrast enhancement measuring approximately 10 cm in diameter in its axial plane. It was located adjacent to the right atrium, extending paramedian to the superior vena cava, causing significant extrinsic compression. Its vertical dimension was about 17 cm. Magnetic resonance imaging (MRI) is useful both for initial evaluation and follow-up, providing better delineation of tumor relationships with adjacent structures, particularly large vessels, and assessment of intracanal extension [3, 18]. However, it presents similar uncertainties regarding malignancy criteria as observed on CT. In our patient, we performed additional positron emission tomography (PET) scan, which revealed intense and heterogeneous hypermetabolism in the right anterior mediastinal mass and ipsilateral mediastinal lymph nodes. Intense focal hypermetabolism was also noted in the right parietal pleural wall and two other metabolic activity foci,

seemingly pleural in origin, within the right pleural effusion, specifically in the paravertebral and postero-basal positions. The diagnosis of primary mediastinal sarcoma is always histopathological. It is established by histological examination of surgical specimens or, less commonly, imaging-guided biopsy. Biopsy should obtain a sufficiently representative tumor fragment for precise histological typing. Immunohistochemical studies are essential for confirmation [19]. For our patient, given the medical history and general condition, we opted for a CT-guided biopsy, revealing spindle cell lesions. However, the diagnosis was complicated due to the small size of the viable area. This lesion had a non-characteristic phenotype, with cytonuclear atypia and necrotic areas, leading to classification as an undifferentiated sarcoma. According to the FNCLCC classification, it was a grade 3 sarcoma, despite a low proliferation index. Therapeutically, these tumors require an aggressive approach. Surgical resection should be as complete as possible, which is often challenging due to their large size and proximity to vital structures. Resection of mediastinal sarcomas is possible in only about two-thirds of cases [2]. The quality of resection is judged by the absence of tumor involvement of the margins [18]. This resection serves both histopathological diagnostic purposes and therapeutic aims. Some authors emphasize the importance of multidisciplinary management, particularly involving radiotherapy for extensive tumors [12]. It is indicated for inoperable tumors or incomplete resection to eradicate residual tumor tissue and reduce the risk of local recurrence. The role of chemotherapy is poorly understood. It appears effective in metastatic forms and may reduce tumor size for subsequent surgery [12]. In our case, we submitted the case to a multidisciplinary sarcoma meeting at the Oncopole de Toulouse. During this meeting, two options were proposed. The first option is supportive care due to the patient's general condition classified as WHO 3. The second option considered is anthracycline-based chemotherapy (EC100 = Epirubicin + Cyclophosphamide), but it would be implemented after improvement in his general condition, evaluated using the WHO index. The prognosis of these tumors is poor. The five-year survival rate averages 32%, 66% for low-grade tumors but drops to 27% for high-grade tumors. For inoperable patients or those with incomplete resection, the three-year survival rate is 18%. It depends on surgical resection and histological grade [12, 20]. The presence of von Recklinghausen's disease is a worsening factor [12]. Local recurrences are reported in 64% of cases, while metastases are only reported in 43% of cases [2]. Metastases occur in the lungs, liver, or bones [2]. The survival of patients with well-differentiated liposarcomas is longer than that observed in undifferentiated forms [6]. For our patient, he was lost to follow-up after one session of chemotherapy. The main risk factor for metastatic relapse for all soft tissue sarcomas is grade [21].

CONCLUSION

In summary, primary mediastinal sarcomas are rare tumors, usually large and aggressive, requiring a multidisciplinary approach for management. Imaging results are nonspecific, and the diagnosis of mediastinal sarcoma is rarely made before surgery. The prognosis of these tumors is poor and largely depends on the quality of surgical resection and histological grade. Our study highlights the aggressive nature of these tumors and emphasizes the importance of as complete surgical resection as possible. We also underscore the need for careful evaluation of the histological grade of the tumor mass to assess significant prognostic implications. However, it is essential to recognize the limitations of our study. It is based on a single case, involving a patient whose general condition and medical history restricted the feasibility of certain complementary exams and the possibility of complete surgical management. For a deeper understanding, future studies, particularly prospective ones involving a larger number of patients, will be necessary. These studies will allow for a more detailed evaluation of the role of imaging and its correlation with histopathological results, while further specifying management approaches, especially for extensive forms of these sarcomas. These research efforts will also more accurately analyze prognostic factors associated with these tumors.

Conflict of Interest: The authors have declared that they have no potential conflicts of interest related to the theme of the article.

Authors' Contributions: All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

Abbreviations:
OMS: Eastern Cooperative Oncology Group (ECOG) Performance Status TMGNP: Malignant Peripheral Nerve Sheath Tumor FNCLCC: French National Federation of Cancer Centers IUCT Oncopole: University Cancer Institute of Toulouse Oncopole

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