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Primary Mediastinal Seminoma: A Case Report

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Abstract:
Primary mediastinal seminoma is a rare and distinct form of malignant germ cell tumor that originates in the mediastinal region. While seminomas are more commonly found in the testes, their mediastinal occurrence accounts for approximately 5% of cases. This type of cancer, typically diagnosed in young adults, is characterized by its generally indolent course, although in some instances, it may present with symptoms related to the compression of adjacent organs or metastasis. The diagnosis is based on histological examination, and chemotherapy is the cornerstone of treatment, offering a generally favorable prognosis with a low risk of recurrence. We report the case of a 25-year-old male, with no history of toxic habits, who was admitted to our institution following the incidental radiological discovery of right mediastinal enlargement. The diagnosis was histologically confirmed via a CT-guided trans-thoracic biopsy, suggesting primary mediastinal seminoma. Therapeutic management consisted of chemotherapy. The patient's clinical course has been favorable, with no signs of recurrence observed to date.

Introduction:
Primary mediastinal seminomas are extremely rare germ cell tumors that develop within the mediastinal region. Germ cell tumors occurring outside the gonads are infrequent, comprising only 5 to 7% of all cases. In the absence of a primary testicular or ovarian mass, the tumor is classified as extragonadal. The mediastinum and retroperitoneum are the predominant sites for extragonadal germ cell tumors. Mediastinal seminomas are often asymptomatic and are frequently identified as incidental findings. These tumors typically exhibit a slow growth rate and demonstrate limited metastatic potential [12].

1. Patient and observation:

A 25-year-old patient, with no toxic habits, not known to be bronchitic or chronically dyspneic, who has never been treated for pulmonary tuberculosis, and with no known recent contact with tuberculosis in the family. He had been treated 45 days earlier for a metacarpophalangeal fracture of the second finger following an accidental trauma, by osteosynthesis. He was admitted to our institution following the incidental radiological discovery of mediastinal enlargement during a pre-anesthetic evaluation for the removal of fixation hardware. The patient presented no respiratory or extra-respiratory symptoms.

2. Clinical findings

Examination upon admission to the hospital:
The clinical examination revealed a patient in good general condition, with a performance status (PS) of 0, afebrile, hemodynamically and respiratorily stable, and with a scar from osteosynthesis over the

metacarpophalangeal joint of the second finger. The rest of the physical examination was unremarkable; notably, no testicular mass was found, and the thyroid was not palpable.

Radiological and biological assessment:

The chest X-ray (Figure 1) showed the presence of opacity with hilar projection, dense and inhomogeneous both above and below the hilum, with the internal boundary blending into the mediastinum and the external boundary being poly-lobed and roughly convex toward the lung parenchyma. Applying the convergence and overlapping sign, this opacity was not vascular. The thoracic CT scan (Figure 2) revealed a process occupying the anterior-superior and middle mediastinum, with an invasive appearance and areas of hypodensity within, measuring approximately 78 mm in diameter along the long axis.

A blood count, showed no abnormalities. The tumor markers (beta-human chorionic gonadotropin (β-HCG) and alpha-fetoprotein (AFP)) were urgently requested due to the patient's young age, male sex, and the presence of an anterior mediastinal mass. The β-HCG level was 11 IU/L (normal <2), slightly elevated but not significant. The AFP level was 2 ng/ml, within normal range, and the LDH level was elevated at 265 IU/L

Endoscopic assessment:

The flexible bronchoscopy showed no abnormalities.

Positive Diagnosis and Severity Assessment:

A CT-guided trans-thoracic biopsy of the mediastnal mass was performed. The microscopic examination revealed fibrous tissue infiltrated by a tumor proliferation with a carcinomatous appearance, forming fibrous septa with a lymphocytic infiltrate and epithelioid granulomas in sheets on a stromal background. The tumor cells were medium to large in size, with cytological atypia, including hyperchromasia and anisokaryosis.

The Immunohistochemical analysis showed diffuse and intense nuclear and cytoplasmic expression of anti-Oct-3/4, placental alkaline phosphatase, very focal and weak cytokeratin expression, and CD30 negativity, which was consistent with a germ cell tumor of the seminoma type. To confirm the primary mediastinal origin of the seminoma, a testicular ultrasound was performed, which showed no abnormalities.

After a minimal staging work-up, including a brain CT scan, abdominal-pelvic CT scan, and bone scan, we were able to establish the diagnosis of non-metastatic primary mediastinal seminoma.

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Therapeutic intervention :

The case was discussed at the multidisciplinary thoracic oncology meeting, and the decision was made to initiate combination chemotherapy based on the BEP protocol (3 to 4 cycles): Bleomycin 30 mg/day, Etoposide 100 mg/day, and Cisplatin 25 mg/day.

Follow-up and outcome:

The clinical progression was marked, three weeks after admission, by the rapid onset of progressive superior vena cava syndrome, which regressed with anticoagulant therapy, corticosteroids, and etiological treatment. After two cycles of chemotherapy, the patient developed fecal retention complicated by sepsis, requiring hospitalization in the intensive care unit with parenteral antibiotic therapy for 5 days, followed by oral antibiotics and strict monitoring, with significant improvement. After the fourth cycle of chemotherapy, a marked clinical improvement was noted, with complete resolution of the superior vena cava syndrome. Radiologically, a PET scan showed almost complete

regression of the process, with no detectable hypermetabolic mass. Monthly monitoring of β-HCG and AFP levels was initiated.

To date, our patient has shown a durable complete pathological response to neoadjuvant chemotherapy and has not required surgical intervention.

Discussion:

Germ cell tumors account for only 1 to 4% of all mediastinal tumors, which can be either benign or malignant, with mediastinal seminomas being the malignant type. These tumors were first identified in the late 1950s, and significant progress has been made in curing patients with this disease and extending their lives. The 5-year survival rate has increased from 87% to 100%, similar to the survival rates for testicular seminomas [2-3].

Primary mediastinal seminomas are predominantly found in young men in over 90% of cases, although cases involving female patients with seminomatous tumors have also been reported. The peak incidence occurs between the ages of 20 and 35 [4-5].

It is hypothesized that extragonadal germ cell tumors result either from abnormal migration of germ cells along the midline of the yolk sac to the embryonic gonadal ridge during embryogenesis or from germ cells that are normally distributed in the liver, bones, marrow, and brain to ensure regular functions or to transmit hematological or immunological information [6-7].

Mediastinal seminomas typically exhibit a very slow growth pattern and limited metastatic potential. Symptoms are nonspecific, and many patients are often asymptomatic, with incidental findings, as in the case of our patient. Respiratory symptoms primarily include chest pain (50% of cases) and cough (30% of cases). Superior vena cava syndrome can occur in 10 to 20% of cases [8]. These tumors are typically located in the anterior-superior mediastinum and, more specifically, tend to develop where the innominate vein meets the superior vena cava [1-8].

Tumor markers such as β-HCG and AFP can be used both for diagnosis and for monitoring recurrences. αFP is not secreted by primary mediastinal seminomas and would therefore suggest either a mixed germ cell tumor or a primary testicular tumor [9, 10]. β-HCG is secreted in only about one-third of primary mediastinal seminoma cases [10]. However, the diagnosis of seminoma remains histological, with immunohistochemical analysis showing tumor cell positivity for placental alkaline phosphatase (PAL), CD117, and focal, weak positivity for cytokeratins [11].

Mediastinal seminomas are highly sensitive to chemotherapy and radiotherapy. Surgical intervention can also be considered in the treatment of mediastinal seminomas, but achieving an R0 resection is challenging due to tumor invasion into adjacent mediastinal structures, with only 12.5% of patients undergoing this procedure in previous studies [11].

Complete remission after chemotherapy is achieved in more than 90% of cases, with a late recurrence risk of 1.4%, most often in the retroperitoneal area [12].

3. Conclusion

Primary mediastinal seminoma is a rare germ cell tumor in young adults, often asymptomatic. Tumor markers are typically normal. The diagnosis is histological, and treatment primarily involves preoperative chemotherapy with cisplatin, followed by aggressive surgical resection of residual masses. Thanks to advancements in therapy, particularly chemotherapy, the prognosis for patients has significantly improved over the past few decades, providing better chances of a cure. However, early

detection and appropriate management remain crucial to ensuring effective treatment and minimizing the risk of recurrence.

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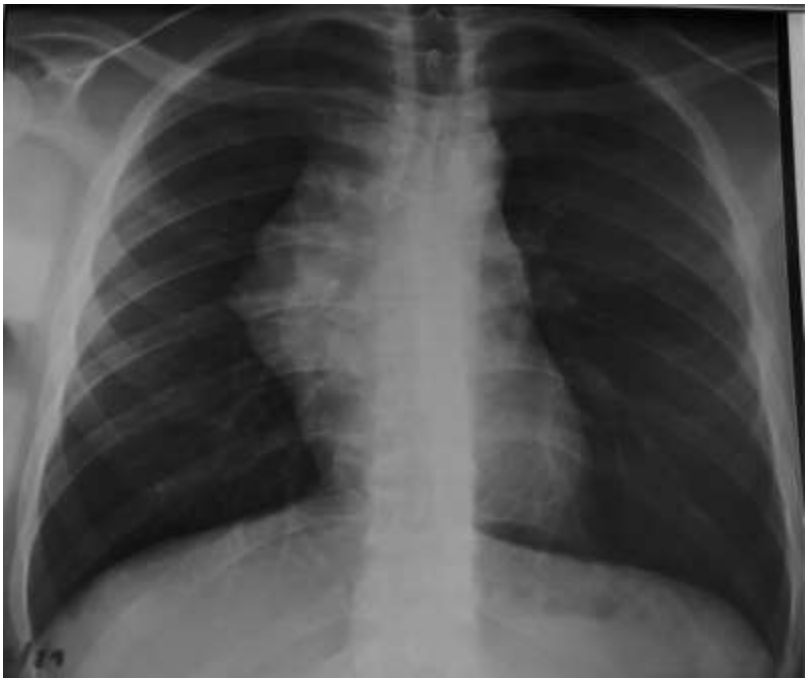

Figure 1: Radiographie thoracique de face objectivant une opacité dense homogène à projection hilaire, sus et sous hilaire dense inhomogène, la limite interne est noyée dans le médiastin, limite externe polylobée grossièrement convexe vers le parenchyme pulmonaire.

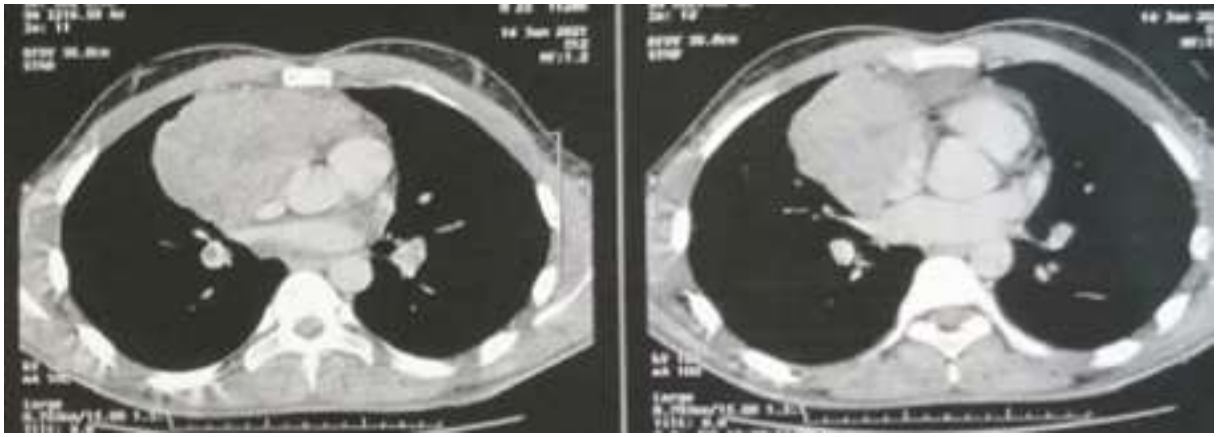

Figure 2: TDM thoracique, coupe axiale fenêtre médiastinale, objectivant un processus tissulaire occupant le médiastin antéro-supérieur et moyen d'allure invasif avec des plages d'hypodensité en son sein, mesurant environ 78 mm de diamètre de grand axe.