

Primary mediastinal pure seminoma presenting with cervical lymphadenopathy and dyspnea in a young adult male: A Case Report

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Abstract

Background: Primary mediastinal seminoma is a rare extragonadal germ cell tumor accounting for a small proportion of mediastinal neoplasms. It predominantly affects young adult males and commonly arises within the anterior mediastinum. Because its clinical and radiological manifestations overlap with those of other mediastinal tumors, diagnosis may be challenging.

Case Presentation: We report the case of a 27-year-old man with no significant medical history who presented with progressive dyspnea, constitutional symptoms, and left cervical lymphadenopathy. Chest radiography demonstrated mediastinal widening, and contrast-enhanced computed tomography revealed a bulky anterior mediastinal mass measuring approximately 12.7 × 12 × 10.4 cm. Histopathological examination of a cervical lymph node biopsy demonstrated features consistent with pure seminoma. Immunohistochemistry showed strong positivity for CD117 and OCT3/4. Serum alpha-fetoprotein and beta-human chorionic gonadotropin levels were within normal ranges, and scrotal ultrasonography excluded a gonadal primary tumor. The patient received first-line cisplatin-based chemotherapy using the BEP regimen (bleomycin, etoposide, and cisplatin), resulting in significant tumor regression and clinical improvement.

Conclusion: Primary mediastinal seminoma should be considered in the differential diagnosis of anterior mediastinal masses in young men, particularly when associated with cervical lymphadenopathy. Histopathological confirmation with immunohistochemical characterization remains essential for diagnosis. Cisplatin-based chemotherapy continues to provide excellent outcomes, even in patients presenting with bulky disease.

Keywords: Primary mediastinal seminoma; Extragonadal germ cell tumor; Anterior mediastinal mass; BEP chemotherapy; Cervical lymphadenopathy; Case report

1. Introduction

Extragonadal germ cell tumors (EGGCTs) are uncommon neoplasms arising outside the gonads and account for approximately 2–5% of all germ cell tumors. The mediastinum represents the most frequent extragonadal location in adults, followed by the retroperitoneum, pineal gland, and sacrococcygeal region. Primary mediastinal germ cell tumors (PMGCTs) constitute only 1–4% of all mediastinal tumors and approximately 15–20% of anterior mediastinal masses in young men [1–3]. PMGCTs are classified into seminomatous and non-seminomatous subtypes. Seminomas account for approximately 30–40% of malignant mediastinal germ cell tumors and generally exhibit a more favorable prognosis than non-seminomatous tumors [4,5]. These tumors predominantly affect males between 20 and 40 years of age and are believed to arise from primordial germ cells that fail to migrate appropriately during embryogenesis [6,7].

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Clinically, mediastinal seminomas often present as large anterior mediastinal masses because of their slow growth and indolent biological behavior. Symptoms are usually related to local compression of mediastinal structures and may include chest pain, dyspnea, cough, superior vena cava syndrome, or constitutional manifestations such as fever and weight loss. In some cases, the disease is discovered incidentally on imaging studies performed for unrelated reasons [8,9]. Radiologically, mediastinal seminomas appear as bulky, lobulated, homogeneous or mildly heterogeneous anterior mediastinal masses. However, imaging findings are not pathognomonic and may overlap with those of lymphoma, thymoma, thymic carcinoma, and metastatic malignancies, making histological confirmation mandatory [10,11]. Histopathology combined with immunohistochemistry remains the cornerstone of diagnosis. Typical seminoma cells express placental alkaline phosphatase (PLAP), OCT3/4, SALL4, D2-40, and CD117 (c-KIT), while alpha-fetoprotein levels are generally normal, helping distinguish seminoma from non-seminomatous germ cell tumors [12,13]. The prognosis of primary mediastinal seminoma has improved considerably with the introduction of cisplatin-based chemotherapy. Current treatment strategies rely mainly on platinum-containing regimens such as bleomycin, etoposide, and cisplatin (BEP), with radiotherapy or surgery reserved for selected residual masses. Long-term survival rates exceeding 85–90% have been reported in contemporary series [14–16].

Herein, we describe a case of primary mediastinal pure seminoma presenting with cervical lymphadenopathy and progressive dyspnea in a young adult male. The case highlights the diagnostic challenges associated with anterior mediastinal tumors and underscores the favorable response of seminomatous mediastinal germ cell tumors to platinum-based chemotherapy.

2. Case Presentation

A 27-year-old male police officer with no significant past medical history and no history of tobacco use presented with a one-month history of progressive left cervical swelling associated with exertional dyspnea, intermittent fever, and night sweats.



Figure 1 Posteroanterior chest radiograph demonstrating marked mediastinal widening caused by a large anterior mediastinal mass at initial presentation

He denied chest pain, hemoptysis, weight loss, or previous malignancy. Physical examination revealed multiple firm, non-tender, fixed left cervical lymph nodes. The remainder of the examination was unremarkable, with no evidence of gynecomastia or palpable testicular abnormalities. Vital signs were stable, and no signs of superior vena cava syndrome

were observed. A chest radiograph performed as part of the initial evaluation demonstrated widening of the mediastinum, prompting further radiological investigations (figure 1).

Contrast-enhanced thoracic computed tomography (CT) revealed a large anterior mediastinal mass measuring approximately $12.7 \times 12 \times 10.4$ cm (figure 2), occupying the anterior and middle mediastinum and exerting a mass effect on adjacent structures. Given the patient's age and the radiological findings, a malignant mediastinal tumor was suspected, and tissue diagnosis was pursued.



Figure 2 Contrast-enhanced thoracic computed tomography (CT) showing a large heterogeneous anterior mediastinal mass measuring $12.7 \times 12 \times 10.4$ cm, extending into the middle mediastinum and exerting mass effect on adjacent mediastinal structures. Axial (A) and sagittal (B) views are shown

2.1. Investigations

Initial laboratory investigations, including complete blood count, renal function tests, and liver function tests, were within normal limits. Chest radiography demonstrated marked mediastinal widening suggestive of a mediastinal mass. Subsequent contrast-enhanced thoracic CT confirmed the presence of a bulky anterior mediastinal tumor measuring approximately $12.7 \times 12 \times 10.4$ cm with heterogeneous enhancement. No pulmonary parenchymal lesions were identified. Thoracic magnetic resonance imaging (MRI) further characterized the lesion and demonstrated close contact with adjacent mediastinal vascular structures without clear evidence of vascular invasion (figure 3).

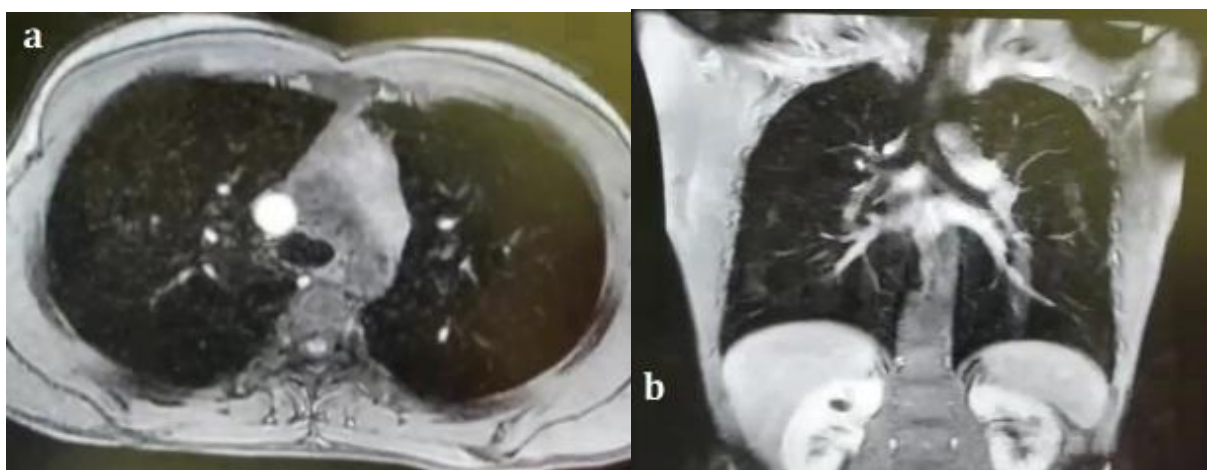


Figure 3 Thoracic magnetic resonance imaging (MRI) demonstrating a large anterior mediastinal mass with irregular margins and close proximity to major mediastinal vascular structures. Axial (A) and coronal (B) views are shown

An excisional biopsy of a cervical lymph node was performed. Histopathological examination revealed sheets of large polygonal cells with abundant clear cytoplasm, distinct cell membranes, and centrally located nuclei associated with a lymphocytic infiltrate. Immunohistochemical analysis showed strong positivity for CD117 (c-KIT) and OCT3/4, supporting the diagnosis of seminoma.

Serum tumor markers were evaluated and showed normal alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β -hCG) levels. Lactate dehydrogenase (LDH) was mildly elevated. Scrotal ultrasonography revealed no testicular mass or suspicious lesion, excluding a gonadal primary tumor. A staging thoraco-abdomino-pelvic CT scan showed no evidence of distant metastatic disease.

2.2. Diagnosis

Based on the clinical presentation, imaging findings, histopathological examination, and immunohistochemical profile, the patient was diagnosed with a primary mediastinal pure seminoma. The diagnosis was supported by the presence of a bulky anterior mediastinal mass in a young adult male, typical seminomatous morphology on histopathology, positive immunohistochemical staining for CD117 and OCT3/4, normal AFP levels, and the absence of a testicular primary lesion on ultrasonography. Differential diagnoses initially considered included lymphoma, thymoma, thymic carcinoma, and non-seminomatous germ cell tumor. These were excluded following pathological and immunohistochemical evaluation. According to the International Germ Cell Cancer Collaborative Group (IGCCCG) classification, the patient was classified as having a good-prognosis extragonadal seminomatous germ cell tumor.

2.3. Treatment

The patient was discussed at a multidisciplinary tumor board meeting. Given the diagnosis of primary mediastinal pure seminoma and the absence of distant metastases, first-line systemic chemotherapy with the BEP regimen (bleomycin, etoposide, and cisplatin) was initiated. Treatment consisted of cisplatin ($20 \text{ mg/m}^2/\text{day}$) and etoposide ($100 \text{ mg/m}^2/\text{day}$) administered on days 1–5, together with bleomycin (30 IU) administered on days 1, 8, and 15 of each 21-day cycle. The patient completed chemotherapy without major complications.

Clinical assessment and post-treatment imaging demonstrated a marked reduction in tumor volume with the development of intratumoral necrotic and calcified areas, consistent with a favorable therapeutic response. Follow-up contrast-enhanced thoracic CT demonstrated regression of the mediastinal mass from $12.7 \times 12 \times 10.4 \text{ cm}$ to approximately $69 \times 36 \text{ mm}$ (Figure 4).



Figure 4 Follow-up contrast-enhanced thoracic CT demonstrating marked regression of the mediastinal seminoma after BEP chemotherapy, with residual necrotic and calcified components measuring $69 \times 36 \text{ mm}$

2.4. Outcome and Follow-up

The patient tolerated cisplatin-based chemotherapy well, with no major treatment-related adverse events requiring dose reduction or treatment interruption. Progressive clinical improvement was observed after the first cycles of chemotherapy, with resolution of dyspnea and complete regression of cervical lymphadenopathy. Response assessment by contrast-enhanced thoracic CT demonstrated a marked decrease in tumor size from an initial diameter of approximately $12.7 \times 12 \times 10.4 \text{ cm}$ to $69 \times 36 \text{ mm}$. The residual lesion exhibited areas of necrosis and calcification, findings consistent with a favorable response to treatment. Small bilateral pleural effusions were noted during follow-up but remained asymptomatic and did not require intervention. At the most recent follow-up evaluation, the patient remained clinically stable with no evidence of disease progression. Tumor markers remained within normal limits, and

ongoing surveillance was planned with periodic clinical examinations, serum tumor marker assessment, and cross-sectional imaging according to current germ cell tumor follow-up recommendations.

3. Discussion

Primary mediastinal seminoma is a rare extragonadal germ cell tumor (EGGCT) arising within the anterior mediastinum and accounts for approximately 1–4% of all mediastinal tumors and nearly one-third of malignant mediastinal germ cell tumors [1,2]. In contrast to testicular seminoma, primary mediastinal seminoma develops in the absence of a gonadal primary lesion and predominantly affects young adult males between 20 and 40 years of age [2,3]. The pathogenesis of mediastinal germ cell tumors remains incompletely understood. The most widely accepted theory proposes that these tumors originate from primordial germ cells that fail to complete their migration from the yolk sac to the developing gonads during embryogenesis, resulting in ectopic germ cell rests within midline structures such as the mediastinum [4,5]. This embryological hypothesis explains the preferential occurrence of extragonadal germ cell tumors along the body's midline.

Clinical manifestations are highly variable and largely depend on tumor size and local invasion. Because mediastinal seminomas often exhibit slow growth, they may attain considerable dimensions before diagnosis. Common presenting symptoms include chest pain, dyspnea, cough, and superior vena cava syndrome secondary to compression of adjacent mediastinal structures [2,8]. Constitutional symptoms such as fever, weight loss, and night sweats may also occur and can mimic lymphoma. In the present case, the initial presentation with cervical lymphadenopathy and progressive dyspnea was unusual and contributed to a broad differential diagnosis that included lymphoma, thymic neoplasms, and metastatic disease.

Radiological evaluation is essential for defining the extent of disease and guiding diagnostic procedures. Computed tomography typically demonstrates a large, lobulated anterior mediastinal mass with homogeneous or mildly heterogeneous enhancement, while magnetic resonance imaging may provide additional information regarding vascular invasion and local extension [10,11]. Nevertheless, imaging findings are not specific, and tissue diagnosis remains mandatory.

Histopathological examination combined with immunohistochemistry is the cornerstone of diagnosis. Seminoma is characterized by sheets or nests of large polygonal cells with clear cytoplasm, distinct cell membranes, and prominent nucleoli accompanied by a lymphocytic infiltrate [12,13]. Immunohistochemical markers such as OCT3/4, PLAP, SALL4, and CD117 (c-KIT) are typically expressed and help distinguish seminoma from other mediastinal malignancies [12,13]. In our patient, strong positivity for OCT3/4 and CD117, together with normal AFP levels and the absence of a testicular lesion on ultrasonography, confirmed the diagnosis of primary mediastinal pure seminoma.

The treatment of mediastinal seminoma has evolved considerably over recent decades. Owing to its remarkable sensitivity to platinum-based chemotherapy, cisplatin-containing regimens remain the standard of care [11]. Current international guidelines recommend three cycles of BEP (bleomycin, etoposide, and cisplatin) or four cycles of EP (etoposide and cisplatin) for patients with good-risk seminomatous germ cell tumors [15,16]. Surgery plays a limited role compared with non-seminomatous mediastinal germ cell tumors and is generally reserved for selected residual masses or cases with diagnostic uncertainty. Similarly, radiotherapy may be considered in specific situations but is no longer routinely employed as first-line treatment in the era of highly effective systemic therapy [14,16].

The prognosis of primary mediastinal seminoma is substantially better than that of mediastinal non-seminomatous germ cell tumors. Large international series have reported long-term overall survival rates exceeding 85–90%, reflecting the excellent responsiveness of seminoma to cisplatin-based chemotherapy [11,14]. The updated International Germ Cell Cancer Collaborative Group (IGCCCG) classification continues to classify seminomatous mediastinal germ cell tumors as good- or intermediate-risk disease, with outcomes that have improved significantly over time owing to advances in multidisciplinary management [14]. Consistent with these observations, our patient achieved a marked clinical and radiological response following BEP chemotherapy, with substantial tumor regression and no evidence of disease progression during follow-up.

In conclusion, this case illustrates the diagnostic challenges posed by primary mediastinal seminoma, particularly when presenting with atypical manifestations such as cervical lymphadenopathy. It further emphasizes the importance of histopathological confirmation, exclusion of a gonadal primary tumor, and prompt initiation of platinum-based chemotherapy, which remains associated with excellent clinical outcomes.

4. Conclusion

Primary mediastinal seminoma is a rare extragonadal germ cell tumor that predominantly affects young adult males and should be considered in the differential diagnosis of anterior mediastinal masses, particularly when associated with atypical manifestations such as cervical lymphadenopathy. Because clinical and radiological findings are often non-specific, definitive diagnosis relies on histopathological examination and immunohistochemical characterization, together with exclusion of a gonadal primary tumor. Consistent with previous reports, our case demonstrates the excellent chemosensitivity of mediastinal seminoma and the favorable outcomes achievable with cisplatin-based chemotherapy. Early recognition, accurate pathological diagnosis, and multidisciplinary management are essential to optimize prognosis, which currently exceeds 85–90% in most contemporary series. This case further contributes to the limited literature on primary mediastinal seminoma and highlights the importance of considering germ cell tumors in young patients presenting with bulky mediastinal masses.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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