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CASE REPORT

Primary plasmacytoma involving mediastinal lymph nodes: A diagnostic mimicry of primary mediastinal lymphoma

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Abstract
Plasmacytomas could involve any organ, and at times might pose a diagnostic challenge when the site of involvement is unusual, or if the presentation is similar to other diseases. We describe a 48-year-old man presenting with worsening shortness of breath and chest discomfort with radiologic evidence of mediastinal enlargement, mimicking a lymphoma with mediastinal involvement. An excisional biopsy of a mediastinal lymph node showed a plasma-cell infiltrate strongly positive for CD138, with a flow-cytometry analysis showing a population of lambda-restricted neoplastic plasma cells. He failed to respond to 50 Gy involved-field radiotherapy, but achieved a partial response to combination chemotherapy. He underwent high-dose chemotherapy with melphalan (200 mg/m^2) followed by lenalidomide maintenance, and is in complete remission 18 months postautografting. This case illustrates a unique and rare presentation of primary lymph-node plasmacytomas involving the mediastinum potentially mistaken as lymphoid malignancy. Clinicians should be aware of the plasma-cell origin of the mediastinal neoplastic process.
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A plasmacytoma represents a neoplastic process comprised of clonal plasma cells [1]. Plasmacytomas can present as an isolated disease process, or might represent the first manifestation of multiple myeloma, or could signal evidence of disease relapse/progression after the treatment

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[1,2]. Plasmacytomas could involve any organ, and at times might pose a diagnostic challenge when the site of involvement is unusual or if the presentation is similar to other diseases [2]. We describe a case of multiple extramedullary plasmacytomas presenting as a symptomatic mediastinal mass mimicking a lymphoma with mediastinal involvement. This case illustrates diagnostic challenges that clinicians might face in daily practice.

Case report

A 48-year-old man presented with worsening shortness of breath and chest discomfort. He had no constitutional symptoms. A complete blood count showed mild anemia (hemoglobin: 11.2 g/dL) and reactive thrombocytosis (platelets: 616,000/μL). The serum lactate-dehydrogenase level was 152 (normal range: 94—250 U/L). The serum beta-2 microglobulin was 1.65 (normal range: 0.002—2.70 μg/mL). The serum calcium level was 9.7 (normal range: 8.4—10.6 mg/dL). A chest X-ray showed mediastinal enlargement. A positron emission tomography with computed tomography demonstrated diffuse hypermetabolic mediastinal adenopathy involving the paratracheal, precarinal, and subcarinal areas. An aortopulmonary-window lymph node measured 5.6 × 4.5 cm in size with a maximum standardized uptake value (SUV) of 14. There were two additional hypermetabolic skeletal lesions: a 0.9 cm lytic lesion in the posterior superior iliac bone (maximum SUV 4.7) and another 0.9 cm lytic lesion on the right side of the sternum (maximum SUV 8.2). A bone-marrow aspirate and biopsy showed normocellular marrow with maturing trilineage hematopoiesis and slightly hyperplastic megakaryopoiesis without evidence of monoclonal plasma cells. A serum protein electrophoresis with immunofixation identified an immunoglobulin-G-lambda monoclonal gammopathy (monoclonal spike [M-spike] 2.1 g/dL), as well as a free lambda protein band. The serum-lambda-free light chain was elevated at 1613.74 (normal range: 5.71—26.30 mg/L) with a serum-kappa-free light chain of 4.61 (normal range: 3.30—19.40 mg/L). A bone survey revealed a 1.3 cm lucent lesion overlying the parietal bone. An excisional biopsy of a mediastinal lymph node showed a plasma-cell infiltrate (Figure 1A), which was strongly positive for CD138 (Figure 1B) and negative for CD3, CD20, PAX-5, bcl-1 (cyclin D1), and human herpes virus-8. In-situ hybridization for EBER (EBV) was negative. A flow cytometric analysis showed a population of lambda-restricted neoplastic plasma cells positive for CD38, CD138, CD117, CD56, and CD16.

The patient received involved-field radiotherapy to the mediastinal lesions at a cumulative dose of 50 Gy (in 25 fractions) without significant evidence of response. He then received two cycles of infusional chemotherapy with bortezomib, thalidomide, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide (VTD-PACE). A repeat positron emission tomography with computed tomography showed no metabolic activity in the mediastinum. Subsequently, a third cycle of VTD-PACE was administered. Prior to autografting, his serum M-spike was 0.4 g/dL, and the serum-free lambda chain was 16.45 mg/L, consistent with a partial response. There were fewer than 5% plasma cells in the bone marrow. He then received high-dose melphalan at 200 mg/m [2], followed by autologous hematopoietic cell transplantation (HCT). At 3 months after transplantation, the serum M-spike remained stable at 0.4 g/dL. A posttransplant maintenance therapy with lenalidomide was prescribed. Six months after autografting, he developed axillary and infraclavicular fluorodeoxyglucose avid lesions (maximum SUV 7.8), as well as subcutaneous lesions (maximum SUV 7.9). A needle biopsy of the left axillary node and subcutaneous lesions demonstrated no evidence of plasmacytoma, but cultures grew methicillin-resistant *Staphylococcus aureus*. The patient was treated with sulfamethoxazole/trimethoprim, with complete resolution of symptoms. He is in complete remission with an undetectable serum M-spike and negative immunofixation at 18 months postautologous HCT.

Discussion

This case illustrates a rare presentation of a plasmacytoma predominantly involving the mediastinal lymph nodes with significant clinical symptomatology mimicking a mediastinal lymphoma. An extensive review of the literature (published in the English language) identified a limited number of cases with mediastinal involvement by extramedullary plasmacytomas [3—5]. Plasmacytomas primarily involving lymph nodes are even rarer [6,7]. Primary lymph-node plasmacytomas are estimated to represent only 2% of all extramedullary plasmacytomas [6]. Many primary lymph-node plasmacytomas are mostly described in case-reports [6,8], with a minority of cases described as arising in plasmacell-type Castleman's disease [7]. An extramedullary plasmacytoma in the mediastinum can also present with superior-vena-cava syndrome by its mediastinal location and possibly compressive nature, although deemed rare [9].

Menke et al. [6] reviewed 26 cases of primary lymph-node plasmacytomas reported in the literature that were not associated with Castleman's disease. There was a male predominance, and the average age of affected patients was 56 (range: 10—72 years) [6]. The most common presentation was neck swelling due to a localized mass. Otherwise, those plasmacytomas were asymptomatic, contrary to our case. The average size of the excised lymph node was 4.6 (range: 2—10 cm) [6]. In the review of additional 25 lymph-node plasmacytomas from Mayo Clinic, Menke et al. [6] described the distribution of these lymph nodes as follows: cervical 56%, abdominal 16%, mediastinal 12%, axillary 8%, and inguinal 8%. Only very few cases had disseminated lymphadenopathy on both sides of the diaphragm, and by definition there were no bone-marrow plasma-cell involvement, as in our case. Immunophenotypically, these lymph-node plasmacytomas may have distinct profiles compared with other extramedullary plasmacytomas or myeloma. They have increased CD30 expression and decreased MB2 (B-cell antigen) and CD45RO expression [6]. These plasmacytomas were frequently associated with serum monoclonal gammopathy (43%) of the immunoglobulin-G subtype [6].

Those patients who had a localized disease were treated with surgical excision alone or radiation therapy, and had reportedly excellent outcomes [6]. They described one case with a localized 5 cm unresectable mediastinal plasmacytoma treated with 50 Gy of radiation. There was

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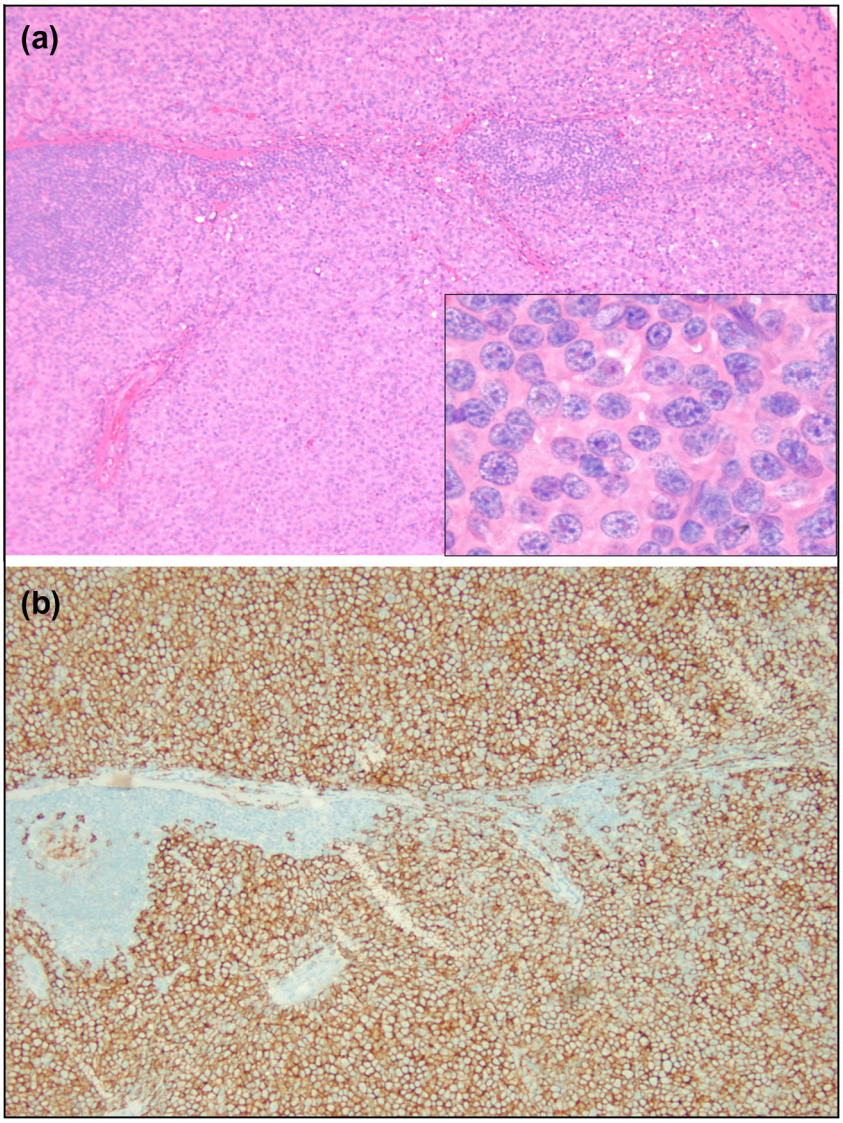

Figure 1 (A) The photomicrograph of mediastinal lymph node by hematoxylin-and-eosin stain shows extensive plasma cell infiltrate replacing the underlying lymph node structure. The image insert in the right lower corner demonstrates a higher magnification view of medium-size atypical plasma cells with condensed chromatin, conspicuous small nucleoli, round to irregular nuclear contours, eccentric nuclei, and moderate amounts of amphophilic cytoplasm. (B) Immunohistochemical staining with CD138 antibody demonstrates effacement of lymph node by numerous plasma cells consistent with a plasmacytoma.

a disappearance of the paraprotein; however, the tumor persisted on subsequent imaging [6]. Patients could develop a disseminated disease after failing surgical or radiation therapy. Disseminated lymph-node plasmacytomas were mostly treated with combination chemotherapy akin to treatment of multiple myeloma. The use of high-dose therapy followed by autologous HCT has not been specifically reported in lymph-node plasmacytomas, although it is conceivable that patients receiving systemic chemotherapy may have been offered autologous HCT as consolidation. Patients with a disseminated disease did not attain long disease control due to disease spreading to lymph nodes, and frequently succumbed to their disease [6].

Our patient initially presented with disseminated multiple mediastinal lymph-node plasmacytomas without bone-marrow involvement. The radiation therapy did not produce a significant disease response; however, the patient achieved an excellent disease control with combination chemotherapy with VTD-PACE. Whether radiation therapy should be included as the treatment of mediastinal lymph-node plasmacytoma remains unknown due to the rarity of this particular pattern of disease manifestation. Prior literature on solitary plasmacytoma suggested the elevated light chain and a hypermetabolic lesion on a positron emission tomography scan as predictors of evolution to myeloma, which were present in our case [10]. Once a disease response is achieved with initial systemic therapy, it appears reasonable to proceed with high-dose chemotherapy followed by autologous HCT for consolidation primarily based on the multiple-myeloma literature.

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A previous case of extramedullary mediastinal plasmacytoma treated with autologous HCT as intensification of therapy has been described in the literature [11]. We also initiated the patient on lenalidomide maintenance therapy and so far there is objective evidence of complete remission.

With regard to treatment outcomes of plasmacytomas in general, Suh et al. [12] described an impressive objective response rate of 100% (complete response of 82%) in a series of 38 patients with solitary plasmacytomas (extramedullary soft tissue [EMS] = 16 and solitary bone plasmacytoma [SBP] = 22) treated with radiation therapy either alone or in combination with chemotherapy and/or surgery. The Greek myeloma study group described the outcomes of 97 patients with solitary plasmacytomas (EMS = 32, SBP = 65) showing no difference in 10-year overall survival in solitary plasmacytomas (EMS = 89% vs. SBP = 69%, $p = .2$) [13]. Interestingly, their analysis showed that the addition of conventional chemotherapy or proteasome inhibitors/immunomodulatory agents resulted in increased toxicity without adding an apparent survival advantage over radiation therapy alone [13].

In summary, our case illustrates the unique and rare presentation of primary lymph-node plasmacytomas involving the mediastinum potentially mistaken as lymphoid malignancy. Clinicians should be aware of the plasma-cell origin of the mediastinal neoplastic process. When the disease involves the mediastinum, it is unclear whether radiation therapy has a significant role contrary to what is known in lymphoid malignancy. Systemic therapy extrapolating from the treatment strategy of multiple myeloma should be strongly considered. Disseminated primary lymph node plasmacytomas may be best consolidated with intensive high-dose therapy followed by autologous HCT and subsequent maintenance therapy.

Conflicts of interest

The authors declare no relevant conflicts of interests in relation to this paper.

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