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(CASE REPORT)

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A rare presentation of biclonal gammopathy in primary mediastinal lymph node plasmacytoma: A case report

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Abstract

Primary plasmacytomas are localized proliferations of clonal plasma cells occurring in the absence of a systemic plasma cell dyscrasia, such as multiple myeloma. They most commonly manifest as solitary lesions in the bone or in the upper aerodigestive tract. Presentation in a lymph node is quite rare, especially when it involves the mediastinum. We report the case of a 32-year-old woman presenting with worsening dyspnea, cough, and chest discomfort, with radiologic evidence of mediastinal enlargement. An excisional biopsy of a large mediastinal mass revealed a plasma cell infiltrate, while protein electrophoresis analysis showed a biclonal gammopathy of the IgG kappa and IgA lambda type. She was treated with a myeloma-like regimen consisting of four cycles of bortezomib/dexamethasone followed by two cycles of thalidomide/prednisone, resulting in improvement of symptoms and complete resolution of lymphadenopathy. She remained in remission over 18 months following completion of therapy. This case report illustrates an unusual instance of biclonal gammopathy in primary mediastinal lymph node plasmacytoma, emphasizing its unique presentation and successful treatment through systemic therapy.

Keywords: Primary plasmacytoma; Mediastinal lymph node; Biclonal gammopathy; Plasma cell; Paraproteinemia

1. Introduction

Plasma cell neoplasms are characterized by the proliferation of malignant plasma cell clones, with multiple myeloma being the most prevalent form. This condition is marked by a significant presence of clonal plasma cells (>10%) in the bone marrow, alongside the detection of monoclonal proteins in serum and/or urine, and systemic symptoms CRAB (hypercalcemia, renal insufficiency, anemia, and bone lesions) [1, 2]. Notably, metastasis to lymph nodes occurs in approximately 40% of advanced-stage multiple myeloma cases [3]. In contrast, plasmacytomas represent local clonal proliferations of plasma cells without systemic involvement or bone marrow infiltration [4]. The most common presentation of primary plasmacytoma is solitary osseous plasmacytoma, where a singular bone lesion is observed [2]. Extramedullary plasmacytomas, occurring outside the bone, account for only 1.6% to 4% of all plasma cell tumors [5-7]. These extramedullary manifestations can arise in various organs but predominantly affect the upper respiratory tract, including the nasal cavity, sinuses, oropharynx, salivary glands, and larynx, which collectively represent 80% of reported cases. Other affected areas include the gastrointestinal tract, urogenital tract, skin, and lungs [5, 6]. Among these, primary lymph node plasmacytoma is exceptionally rare, representing only 2% of all extramedullary plasmacytomas [7], 0.5% of all malignant lymph node neoplasms [8], and a mere 0.08% of all plasma cell malignant neoplasms [7, 9]. At diagnosis, approximately 25% of patients with extramedullary plasmacytomas present monoclonal gammopathy [10]. The monoclonal protein is detected by serum protein electrophoresis as a single M-band most often in the gamma globulin region. In rare instances, 2-6% of cases may present with two distinct bands, which can result from either a single clone producing different types of immunoglobulins or the existence of two separate malignant

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clones [11]. We present a unique case of primary extensive mediastinal lymph node plasmacytoma characterized by the presence of double M-bands, suggestive of true biclonality. Given the extensive nature of the mass, systemic therapy was necessary. The success of this treatment approach demonstrates that diffuse primary plasmacytomas can be effectively managed using myeloma-like therapeutic regimens.

2. Case Presentation

Our patient is a 32-year-old south Moroccan woman, married and mother of 2 children, she had neither any remarkable past medical history, nor a family history. She presented with a chronic dry cough of 2 months duration, associated with dyspnea and chest discomfort without fever or hemoptysis, all evolving in a context of progressive fatigue. Her vital signs were within normal limits with a temperature of 36.5 °C, blood pressure of 120/85 mmHg, and a heart rate of 75 beats per minute. On physical examination, no palpable lymph nodes or masses in any other area of the body were noted. The plain chest X-ray revealed mediastinal area enlargement and abundant left pleurisy. Chest computerized tomographic (CT) studies, performed after the intravenous administration of a contrast agent, revealed a 12.8×11×16 cm sized, well defined, heterogeneously enhancing mass lesion in the left anterior mediastinum with pleural effusion causing collapse of the left lung and deviating the elements of the right mediastinum. No definite evidence of bony erosion of the thoracic vertebrae was observed. Initial laboratory values revealed anemia (Hb 9.8 g/dL), but normal leukocyte and platelet counts. Blood urea nitrogen, creatinine, calcium, inorganic phosphate, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum electrolyte levels were found to be normal. Serum albumin was 39.44 g/L, and total protein was 116 g/L. Therefore, a left lateral mediastinotomy with biopsy was performed for a confirmatory diagnosis. Histologically, the tumor was infiltrated by a monomorphic population of plasma cells. Immunohistochemical staining of neoplastic plasma cells was positive for CD79a (a pan-B cell marker) and CD138, while negative for CD3 (a pan-T cell marker), CD20, PAX5, and cytokeratin, which was consistent with plasma cell differentiation. Based on these findings, the tumor was diagnosed as a plasmacytoma.

Serum protein electrophoresis revealed two monoclonal spikes in the beta (17.98 g/L) and gamma (19.60 g/L) regions (Fig. 1). Serum immunoelectrophoresis confirmed the presence of two monoclonal bands (M-band), one in the beta globulin region identified as IgA Lambda and the other one in the gamma globulin region identified as IgG Kappa type (Fig. 2).

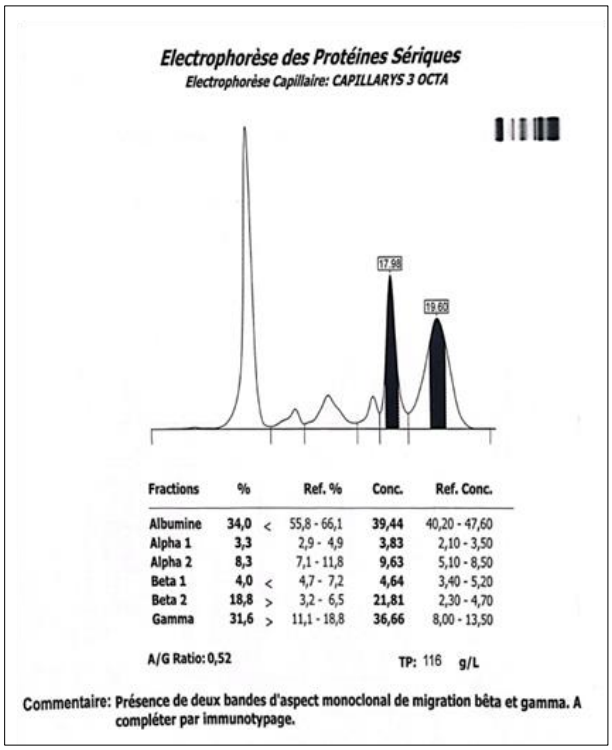

Figure 1 Serum protein electrophoresis revealed two monoclonal spikes in the beta (17.98 g/L) and gamma (19.60 g/L) regions

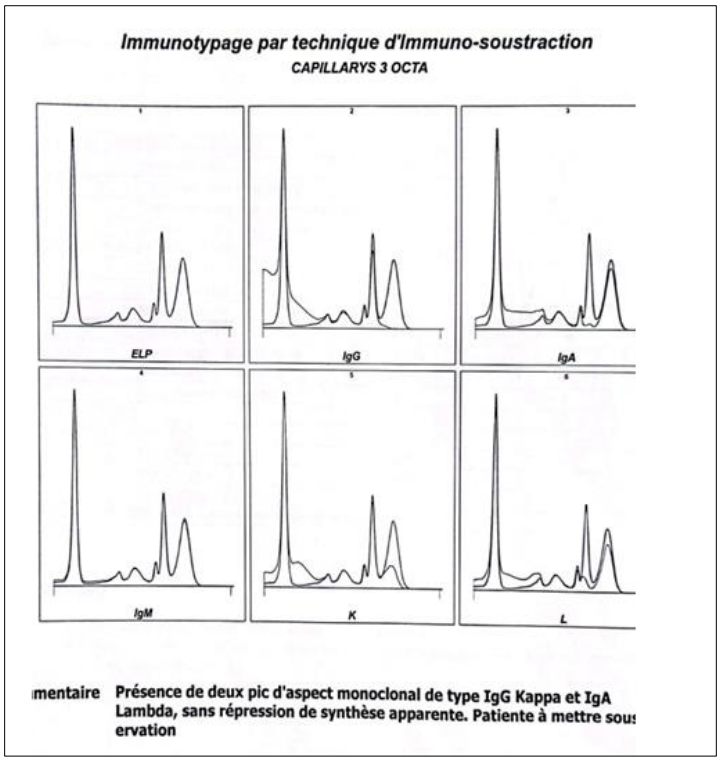

Figure 2 Serum immunoelectrophoresis confirmed the presence of two monoclonal bands identified as IgA/Lambda and IgG/Kappa

A bone marrow biopsy performed shortly afterward demonstrated largely unremarkable trilineage hematopoiesis with 8% of plasma cells detected. Treatment was promptly initiated with subcutaneously administered bortezomib at a dose of 1.5 mg/m^2 and orally administered dexamethasone at 40 mg weekly for three weeks, followed by a one-week break. Following the initiation of this treatment, the patient experienced considerable improvement in platelet count and anemia, which allowed for the addition of thalidomide to her regimen. She completed four cycles of bortezomib/dexamethasone, after which she transitioned to two continuous 28-day cycles of thalidomide at a dose of 100 mg orally, administered alongside prednisone. The patient has maintained sustained remission for over 18 months following the completion of therapy, indicating a favorable response to treatment.

3. Discussion

Primary plasmacytomas can be categorized into two main types: medullary plasmacytoma, which originates in the bone marrow, and extramedullary plasmacytoma, typically found in soft tissues across various organs. These solid tumors predominantly occur in the upper respiratory tract, affecting areas such as the nasal cavity, sinuses, oropharynx, salivary glands, and larynx, accounting for about 80% of reported cases. They can also be found in the gastrointestinal and urogenital regions, as well as in the skin and lungs. [12]. Most plasmacytomas in lymph nodes are considered metastatic, stemming from multiple myeloma or other extramedullary plasmacytomas. Primary lymph node plasmacytomas are quite uncommon, representing only 2% of all extramedullary cases [7] and a mere 0.08% of all malignant plasma cell tumors [7, 9]. The current case is noteworthy due to its substantial size, involvement of the mediastinum, pleural effusion, and the presence of biclonal gammopathy. The exact reason for the pleural effusion remains uncertain, but it may be due to the tumor obstructing normal pulmonary lymphatic flow [13].

Primary plasmacytomas are defined as localized tumors without systemic manifestations of plasma cell malignancy. For a diagnosis of primary plasmacytoma of the lymph nodes, it is crucial to demonstrate the absence of plasma cell proliferation in other sites and to rule out any associated malignant lymphoma components [14].

Biclonal gammopathies are a vanishingly rare group characterized by the production of two distinct monoclonal proteins. This rare presentation can result from either a proliferation of two clones of plasma cells with each producing an unrelated monoclonal spike or from the production of two monoclonal spikes by a single clone of plasma cells. Approximately 1.5% of multiple myeloma cases present biclonal paraproteinemia [15]. Mullikin et al. [16] reported that

23 out of 393 patients with biclonal gammopathy of unknown significance in their study had progression to either multiple myeloma, smoldering myeloma, light chain amyloidosis or Waldenstrom macroglobulinemia with the dominant clone being the principal player through the course of the disease in 21 patients [16]. Several cases of isotype switching have been reported in myeloma patients with biclonal spikes. A case exhibited a shift from primarily IgG with a minor IgD component to a predominant IgD immunoglobulin production after chemotherapy with findings revealing neoplastic origin from a single clone of B-cells [17]. Franck et al. [18] reported another case with shift from a single paraprotein IgG Kappa to a biclonal paraprotein IgG kappa and IgD kappa. Pragnan et al. [10] reported the first case with biclonal gammopathy in multiple myeloma with simultaneous extramedullary involvement showing a presentation with lambda restricted IgG predominant cells from cervical lymph node and kappa restricted IgA cells from the bone marrow simultaneously. [10]

Because primary plasmacytomas are local phenomena, they may be treated and cured with local interventions. The mainstay of treatment is surgery and has a good prognosis. Extramedullary plasmacytoma is radiosensitive and is treated with radiotherapy [19]. In contrast, because multiple myeloma is a systemic disorder, it requires systemic treatments such as chemotherapy and/or immune therapy or autologous hematopoietic stem cell transplantation. Due to the extreme paucity of data describing systemic therapy for primary plasmacytoma, treatment had to be planned largely without well-established precedent. Given the anatomically diffuse nature of the disease, it was deemed prudent to pursue a myeloma-like regimen. [20] In our case, the massive mediastinal lymph node was diffused enough to make radiotherapy not feasible. Therefore, systemic therapy was deployed and the patient was treated with myeloma specific regimen VTD. Kyle et al. [15] reported no difference in prognosis between biclonal and monoclonal gammopathy. However, recognition of this existence increases the credibility and helps in assessing treatment response during follow-up.

4. Conclusion

This case report and accompanying literature review highlight the easily misclassified entity of primary extensive lymph-node plasmacytomas involving the mediastinum, potentially mistaken as lymphoid malignancy, and the exceedingly rare biclonal gammopathy that can have its origin from either a single clone or two clones of plasma cells. The recognizing and understanding of biclonal gammopathy in the context of plasmacytomas enables a precise diagnosis, an adequate treatment and an adjusted follow up response that takes into account the risk of future progression to systemic myeloma, particularly in cases with evidence of marrow involvement. Further research into the implications of biclonality in plasma cell neoplasms could provide valuable insights into patient management and therapeutic outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

We declare that the present research work does not contain any studies performed on animals/humans subjects by any of the authors. This case report is based on clinical observations and does not involve experimental interventions. It adheres to the ethical principles outlined in the Declaration of Helsinki.

Statement of informed consent

We affirm that this case report complies with ethical standards for medical and academic publishing. The patient, an adult, provided written informed consent for the publication of the case details. All identifiable personal information has been anonymized to protect confidentiality.

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