

A Rare Case of POEMS-Associated Multicentric Castleman Disease with an Atypical Osteolytic Presentation

Atipik Osteolitik Bulgularla Seyreden POEMS ile İlişkili Multisentrik Castleman Hastalığı: Nadir Bir Olgu

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To the Editor,

Castleman disease (CD) is a rare heterogeneous lymphoproliferative disorder characterized by distinctive lymph node histopathology and clinical manifestations ranging from localized lymphadenopathy to severe systemic inflammatory disease. It is classified as unicentric Castleman disease (UCD) or multicentric Castleman disease (MCD). UCD involves a single lymph node region, whereas MCD usually presents with generalized lymphadenopathy and multiorgan involvement. MCD is further categorized as human herpesvirus-8-associated MCD or idiopathic multicentric Castleman disease (iMCD) [1]. Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes (POEMS) syndrome is a rare paraneoplastic multisystem disorder associated with an underlying plasma cell dyscrasia. Additional manifestations may include extravascular volume overload, papilledema, thrombocytosis, and sclerotic bone lesions [2]. A rare but clinically significant variant is POEMS-associated MCD. The diagnostic criteria require polyradiculoneuropathy and monoclonal gammopathy with at least one major feature such as elevated vascular endothelial growth factor (VEGF), osteosclerotic bone lesions, or lymph node histopathology consistent with CD. Recognizing this entity is crucial because its management generally requires plasma cell-directed therapy rather than the cytokine-targeted therapy used for idiopathic MCD [3]. CD is identified in approximately 11%-30% of patients with POEMS syndrome, most commonly as the multicentric plasma cell variant [2,3]. The pathogenesis of this association is not completely understood but is thought to involve dysregulated cytokine signaling, particularly overproduction of interleukin-6 and VEGF, leading to systemic inflammation, angiogenesis, lymphoid proliferation, and increased vascular permeability. These overlapping inflammatory and plasma cell-driven mechanisms contribute to the shared clinicopathological features observed in POEMS-MCD [1,2]. However, atypical presentations with unusual skeletal lesions or

incomplete features may occur, causing diagnostic difficulty and misdiagnosis as plasma cell disorders.

A 43-year-old man presented with progressive shortness of breath, abdominal fullness, a tingling sensation in both lower limbs, and swelling in both sides of the neck that had gradually enlarged over the course of 1 year. Examination revealed cervical lymphadenopathy with hepatosplenomegaly and ascites; neurological evaluation showed distal muscle wasting with reduced power, absent lower limb reflexes, and reduced vibration and proprioception below the knees. Laboratory evaluation showed hemoglobin of 11.2 g/dL, leukocyte count of $8 \times 10^9/L$, and thrombocytosis ($5.5 \times 10^5/\mu L$). Serum protein electrophoresis revealed a monoclonal band (1.3 g/dL), and immunofixation confirmed immunoglobulin G lambda monoclonal gammopathy with elevated lambda free light chains (228 mg/L). Serum β 2-microglobulin (11.01 mg/L) and VEGF (500 pg/mL) were elevated. Nerve conduction studies revealed demyelinating sensorimotor polyneuropathy involving both lower extremities. Positron emission tomography revealed fluorodeoxyglucose (FDG)-avid cervical lymphadenopathy, hepatosplenomegaly, bilateral pleural effusion, ascites, and multiple FDG-avid vertebral lytic lesions involving C3, D8, D11, and L4 with partial collapse of D11 (Figures 1A and 1B). Excisional lymph node biopsy showed features of CD with atretic germinal centers, onion-skin mantle zones, and marked plasmacytosis (Figures 1C and 1D). Immunohistochemistry showed CD20-positive follicles and CD38/CD138-positive plasma cells with lambda light chain restriction; HHV-8 staining was negative. Bone marrow examination revealed normocellular marrow with 6% plasma cells. The constellation of monoclonal gammopathy, polyneuropathy, CD histology, organomegaly, lymphadenopathy, and extravascular fluid overload suggested POEMS-MCD. The patient was treated with bortezomib, cyclophosphamide, and dexamethasone, with significant clinical and laboratory improvement after four cycles.

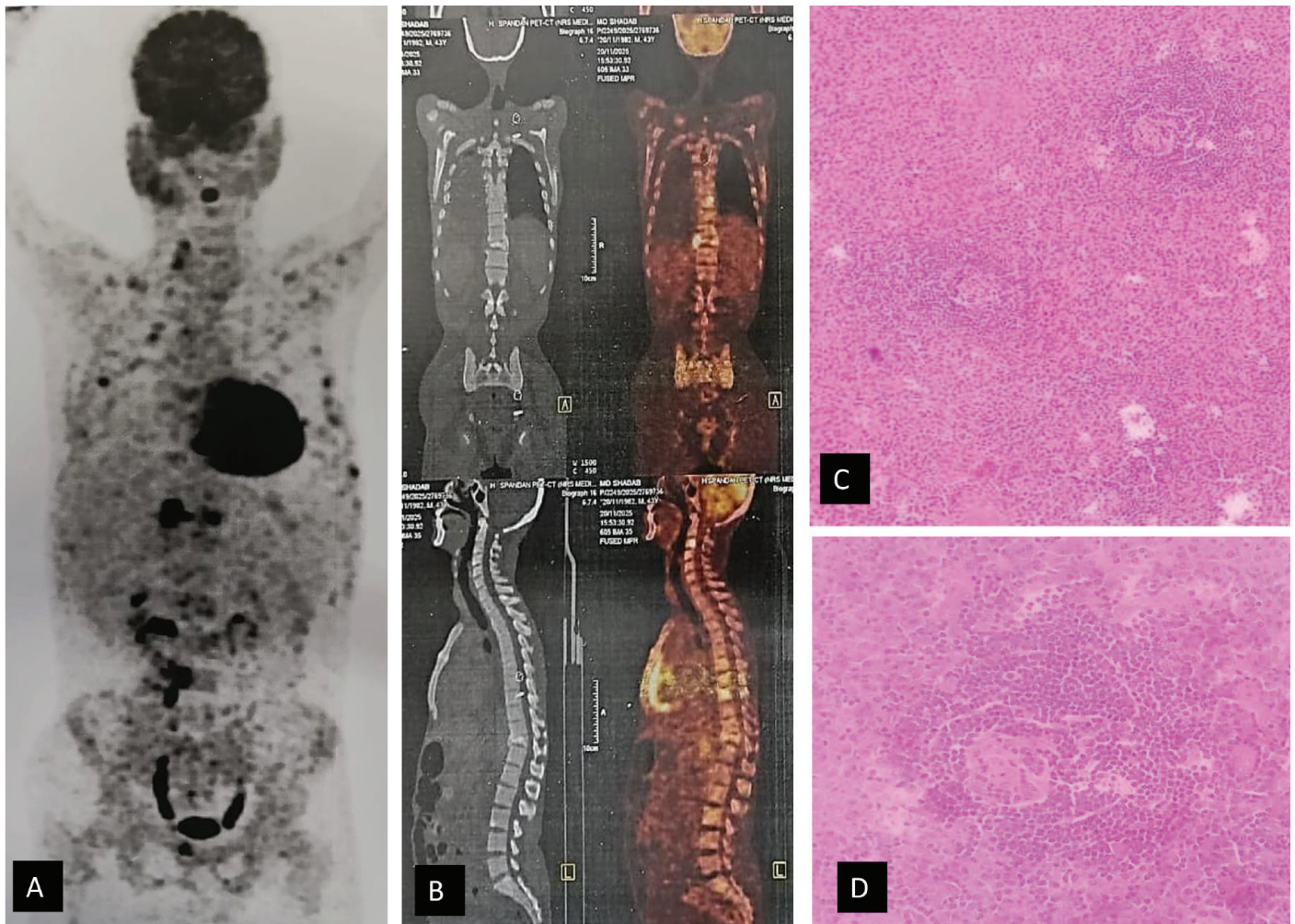


Figure 1. A) Maximum intensity projection fluorodeoxyglucose positron emission tomography image showing metabolically active cervical lymphadenopathy with hepatosplenomegaly, bilateral pleural effusion, and ascites. B) Fused positron emission tomography/computed tomography and sagittal computed tomography images demonstrating multiple fluorodeoxyglucose-avid vertebral lytic lesions involving C3, D8, D11, and L4 with partial collapse of D11. C) Low-power photomicrograph (hematoxylin and eosin, 40 $\times$) showing diffuse lymphoplasmacytic infiltration with regressed/atrophic germinal centers and expanded interfollicular zones, consistent with features of Castleman disease. D) Higher-power photomicrograph (hematoxylin and eosin, 100 $\times$) demonstrating a hyalinized blood vessel penetrating the germinal center ("lollipop" appearance) with onion-skin mantle zone, characteristic of Castleman disease.

Polyclonal hypergammaglobulinemia is typical of iMCD; however, small monoclonal spikes (<3 g/dL) may occasionally occur, creating diagnostic overlap with plasma cell disorders, particularly POEMS syndrome [1]. Patients with POEMS syndrome frequently exhibit systemic manifestations such as progressive demyelinating neuropathy, organomegaly, thrombocytosis, volume overload, and elevated VEGF levels, while bone marrow plasma cell infiltration is often limited compared to overt multiple myeloma [2,3]. Skeletal involvement in POEMS syndrome is usually osteosclerotic; however, uncommon osteolytic variants have also been reported and may radiologically resemble multiple myeloma, metastatic malignancy, or lymphoma-associated lytic lesions [4,5]. This case highlights the diagnostic challenges of osteolytic

lesions in POEMS syndrome-associated MCD mimicking multiple myeloma; early recognition enables effective plasma cell-directed therapy.

Keywords: Castleman disease, Multicentric Castleman disease, Polyneuropathy, Monoclonal gammopathy, Osteolytic lesions

Anahtar Sözcükler: Castleman hastalığı, Multisentrik Castleman hastalığı, Polinöropati, Monoklonal gamopati, Osteolitik lezyonlar

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Concept: T.K.D.; Design: T.K.D.; Data Collection and Processing: T.K.D., S.R., K.G.; Analysis or Interpretation: T.K.D., S.R., K.G.; Literature Search: S.R., K.G.; Writing: K.G.

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