Case Report

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Optic nerve head plasmacytoma as a manifestation of multiple myeloma

Kaitlin P. Sandor[1]*, Jonathan A. Micieli[2], Jason H. Peragallo[1,3]

Abstract:

Extramedullary disease in multiple myeloma is uncommon and associated with a poorer prognosis. Extramedullary disease involving the orbit is even more unusual, with optic nerve involvement being rare. We describe an optic nerve head plasmacytoma in a 45-year-old female in the setting of systemic relapsed, refractory IgA kappa multiple myeloma. The case highlights the importance of keeping extramedullary disease spread in the differential for vision loss in a patient with a history of multiple myeloma. In addition, it describes an unusual location for presentation of extramedullary disease, the optic nerve head, which has rarely been described.

Keywords:

Multiple myeloma, optic nerve head, optic neuropathy, plasmacytoma

Introduction

Multiple myeloma is a neoplastic proliferation of plasma cells in the bone marrow, classically presenting with lytic bone lesions, hypercalcemia, increased total serum protein, or monoclonal protein in the serum or urine. It has a worldwide incidence rate of approximately two cases per 100,000 people.[1] Systemic manifestations, such as renal or neurologic disease, can be present. Neurologic complications can include compression of nerves or the spinal cord due to plasmacytomas or bone fractures, hyperviscosity symptoms such as mucosal bleeding and visual changes, and neurologic manifestations, or more rarely, peripheral neuropathies.[2] Ophthalmic manifestations of multiple myeloma have been reported in varying forms in the literature from copper and crystalline deposits of immunoglobulin in the cornea and conjunctiva to the orbit and optic nerve involvement.[3] Involvement of the cranial nerves is uncommon and usually occurs most frequently in the cases of advanced disease.[2] Here, we describe an optic nerve head plasmacytoma in the setting of systemic relapsed, refractory immunoglobulin A kappa multiple myeloma, which is a very rare manifestation of the disease.

Case Report

A 45-year-old woman presented with gradual, progressive blurred vision for 1 month after being diagnosed with optic neuritis at an outside clinic. Her past medical history was significant for relapsed, refractory immunoglobulin (Ig) A kappa multiple myeloma diagnosed 2 years prior. At the time of her initial multiple myeloma diagnosis, she was initiated on lenalidomide, bortezomib, and dexamethasone (RVd) therapy but experienced disease progression and was switched to carfilzomib, lenalidomide, and dexamethasone (KRd). She then received tandem autologous stem cell transplants at 9 and 12 months after diagnosis but relapsed shortly after with malignant plasma cell pleural effusions. She was started on daratumumab, pomalidomide, and dexamethasone but developed a humoral pathologic fracture and breast mass positivity for plasma cells. She

[1]Department of Ophthalmology, Emory University, Atlanta, GA, USA, [2]Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada, [3]Department of Pediatrics, Emory University, Atlanta, GA, USA

***Address for correspondence:**
Kaitlin P. Sandor, Emory Eye Center, 1365-B Clifton Road, NE, Atlanta, GA 30322, USA.
E-mail: kaitlin.sandor@emory.edu

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was then started on bortezomib, dexamethasone, cyclophosphamide, etoposide, and cisplatin (V-DCEP) salvage therapy approximately 22 months after the initial diagnosis. A few weeks later, she was found to have spinal extraosseous soft-tissue masses and was treated with radiation, but treatment was interrupted due to a pathologic femur fracture requiring repair.

Shortly thereafter, she developed progressive vision loss in her left eye with superior and temporal visual field loss. She was seen by an ophthalmologist who diagnosed her with optic neuritis. At a follow-up with her oncologist, there was concern that the vision loss was related to central nervous system involvement of her multiple myeloma, and she was referred for neuro-ophthalmology evaluation. On initial presentation to our clinic, the patient's best-corrected visual acuity was 20/20 OD and hand motion OS with a left relative afferent pupillary defect. She denied diplopia or pain with eye movement but endorsed bilateral frontal headaches. She had 2-mm ptosis of the left eyelid, which she stated was chronic. Extraocular movements were full. Confrontation visual fields were intact OD but were unable to be performed OS. Red desaturation test was 100% normal in the right eye and 30% normal in the left eye. Dilated fundus examination was normal OD but revealed disc edema and hyperemia with splinter hemorrhages superiorly OS. In addition, there was a small area of lobulated elevation on the nasal optic nerve head with blurring of disc margin and obscuration of small vessels, felt to represent a plasmacytoma of the optic nerve head [Figure 1].

A lumbar puncture showed malignant plasma cells in the cerebrospinal fluid. Hemoglobin was 7 g/dL, platelet count was 84 × 10^3/L, and serum IgA was elevated at 1712 mg/dL. Magnetic resonance imaging (MRI) of the brain and orbits demonstrated multifocal areas of nodular leptomeningeal enhancement with associated abnormal enhancement of the posterior left optic nerve sheath that also involved the left orbital apex and anterior clinoid process [Figure 2]. There was an additional extracranial large soft-tissue mass in the left paraspinal muscles adjacent to the left C2–C5 facets and left C1–2 and C2–3 involvement of the neural foramina. An MRI of the complete spine revealed extensive spinal and paraspinal tumor infiltration throughout the cervical, thoracic, and lumbar spine with severe tumor involvement of the bilateral sacral ala.

The patient was treated with palliative radiotherapy to the orbits, intrathecal methotrexate, and intravenous dexamethasone for 2 days. Visual acuity improved to 20/20 OD and 20/400 OS with a left relative afferent pupillary defect. Confrontational fields were full OU. Red saturation remained decreased OS and normal OD. Humphrey automated perimetry performed with the 24-2 SITA-Fast protocol was unreliable with nonspecific nasal depressions OD. She was unable to perform automated perimetry in the left eye, and Goldmann visual field OS revealed an island of inferonasal vision [Figure 3]. Optical coherence tomography (OCT) of the retinal nerve fiber layer was normal OD with increased thickness OS. OCT of the ganglion cell layer was normal OU.

The patient elected to pursue follow-up treatment at a center closer to home, entered hospice care, and died 3 months later.

Discussion

Extramedullary disease in multiple myeloma is estimated to be present in approximately 7%–18% of cases at diagnosis and up to 20% of recurrent cases. It is associated with poorer overall and progression-free survival.[4,5] The incidence of extramedullary disease has increased in recent years, potentially due to more frequent identification with improved imaging modalities and longer length of survival with newer treatments. Extramedullary disease in the orbit is rare

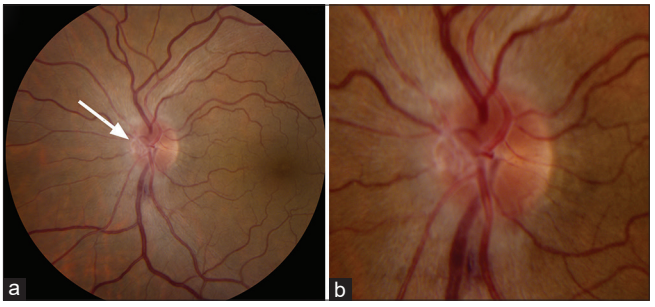

Figure 1: (a) Fundus photograph revealing a small area of nasal lobulated elevation on the optic nerve head with blurring of disc margin and obscuration of small vessels in the left eye, felt to represent a plasmacytoma of the optic nerve head (arrow). (b) Magnified fundus photograph of the optic nerve head shown in a

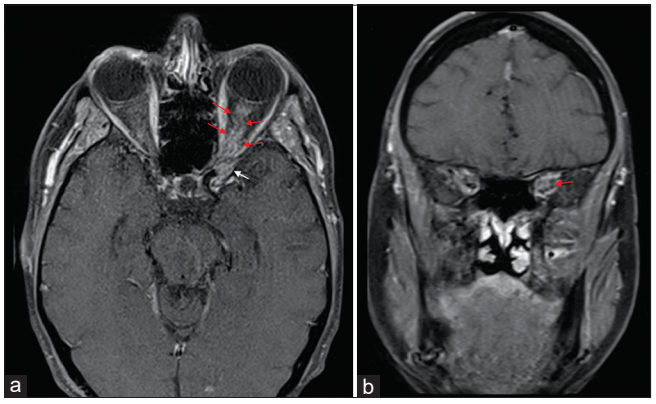

Figure 2: Axial (a) and coronal (b) T1-weighted postcontrast magnetic resonance imaging of the orbits with fat suppression demonstrating multifocal abnormal enhancement of the posterior left optic nerve sheath (red arrows) and anterior clinoid process (white arrow)

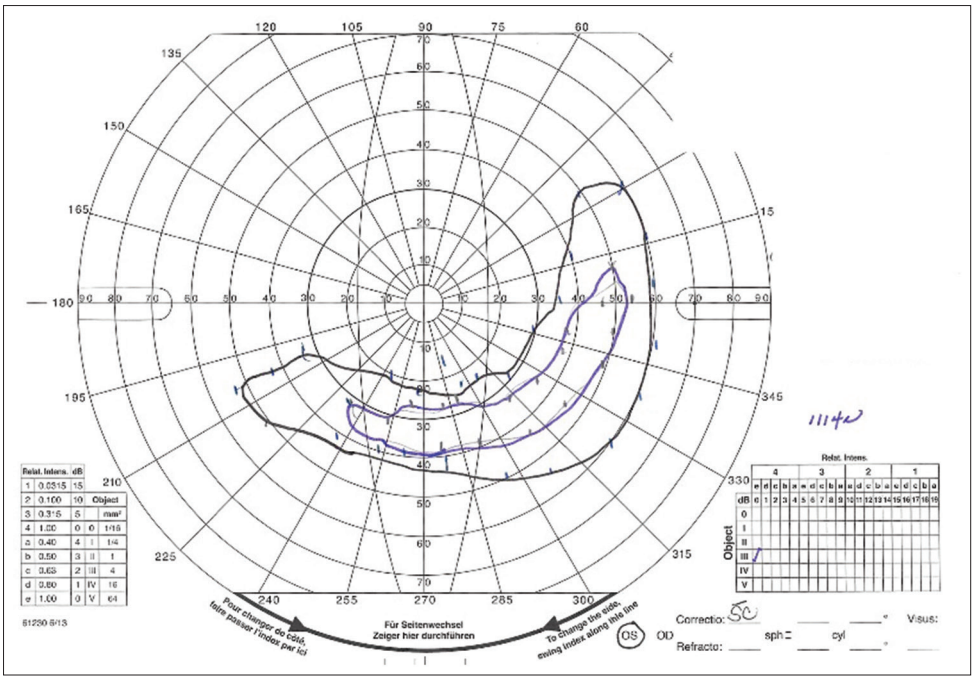

Figure 3: Goldmann manual perimetry of the left eye demonstrating an inferonasal island of vision at III4e isopters

and has been described only in case reports and case series, and the exact incidence has not been described. A review in 1972 described thirty cases in the literature, and a more recent review in 2011 described an additional 41 cases.[6,7] Orbital involvement is most commonly seen in patients with known active disease or as an initial presentation of disease.[6] However, it is important to keep orbital involvement in the differential of possible diagnoses for a patient with a history of multiple myeloma as it can also be the first manifestation of disease recurrence.[8,9] The most common presenting signs and symptoms of orbital involvement include proptosis, decreased vision, diplopia, edema, and ptosis, with the majority presenting as unilateral lesion.[6,10] The majority of extramedullary plasmacytomas arise from the walls of the upper respiratory tract, where they can spread directly to the orbits from the sinuses.[6,11] Intraorbital disease tends to indicate a more aggressive course in comparison to extraorbital plasmacytomas.[6]

Intraocular involvement is less common than orbital involvement, and involvement of the optic nerve is extremely rare.[9,10] Multiple myeloma involving the optic nerve can be thought of in three broad categories, as follows: ischemic optic neuropathy due to hyperviscosity syndrome, direct infiltration of the optic nerve, or compression of the optic nerve from a plasmacytoma.[9,12] Hyperviscosity syndrome created by excess monoclonal immunoglobulins can impair microvascular circulation, leading to downstream ischemia and optic neuropathy.[9,13,14] The optic nerve can also be infiltrated directly by malignant plasma cells.[9] Lastly, extramedullary plasmacytomas are soft-tissue plasma cell tumors that can occur as primary or secondary processes which can cause direct mass effect on the optic nerve.[15] As seen in our case as well as others, plasmacytomas resulting in optic nerve compression can initially be confused for retrobulbar neuritis by presenting with the similar clinical symptoms of monocular vision loss and pain.[8,16-19] However, further workup for optic neuropathy with fundus examination, OCT, MRI, and laboratory investigation will enable identification of the cause of vision loss.[19]

Isolated involvement of the optic nerve head itself is even more unusual than optic nerve involvement, and has been described in only a handful of cases.[8] Similar to our case, Salazar-Diez *et al*. described a case in which a 70-year-old male in remission for multiple myeloma presented with a 1-month history of unilateral decreased visual acuity.[7] A smooth, vascularized growth was found on the optic nerve head without retrobulbar extension, and further workup diagnosed recurrence of his multiple myeloma. In the case described by Salazar-Diez *et al*., their patient's optic nerve involvement was contained to the optic nerve head without retrobulbar extension, whereas our case demonstrated retrobulbar involvement as well.[8] As mentioned previously, involvement of the orbit usually indicates an aggressive course of disease, and the prognosis is poor. Treatment involves treating the underlying disease, radiation, or surgical excision.

Our case highlights the importance of keeping extramedullary disease spread in the differential for vision loss in a patient with a history of multiple

myeloma. In addition, it describes a rare location, the optic nerve head, for presentation of extramedullary disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient gave consent for de-identified images and other clinical information to be used for teaching and research purposes. The patient understood that their name and initials would not be published, and due efforts would be made to conceal their identity, but anonymity could not be guaranteed.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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