Isolated Abducens Nerve Palsy: A Rare Manifestation of Recurrent Extramedullary Myeloma

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ABSTRACT

Multiple myeloma is a plasma cell neoplasm, which may present as a solitary plasmacytoma and, uncommonly, as an extramedullary plasmacytoma. Intracranial plasmacytomas may manifest in central nervous system involvement as cranial nerve palsies. Cranial nerve six palsy is the most common in cases of malignancy. However, isolated abducens palsy presenting as multiple myeloma recurrence is very uncommon. Here, we detail two cases in which intracranial plasmacytoma lesions were present within the region of the Dorello canal, resulting in acute isolated unilateral diplopia from disease recurrence in the absence of systemic marrow involvement.

CASE REPORT

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CASE 1

A 72-year-old male presented to the emergency room with three to four days of new onset diplopia. He had a mild headache the day prior to onset and awoke to see double images on the left side. He denied any weakness. Physical exam was notable for reduced left eye abduction compared to the right eye, consistent with cranial nerve six palsy. A review of systems was positive for two weeks of a dry cough for which he was taking prednisone for presumed bronchitis, weight loss, and chronic diarrhea. No fevers or chills. The patient also had a history of hypertension and chronic back pain.

Imaging findings

Magnetic resonance imaging (MRI) of his orbits showed a small eight-millimeter enhancing focus along the petroclinoid ligament in the region of the Dorello canal and an additional T2 hyperintense focus with enhancement at the left petrous apex (Figure 1). A computed tomography (CT, not shown) scan was recommended to evaluate for osseous changes which revealed no associated findings at the petrous apex. Given the patient's cough at presentation, a chest radiograph revealed right upper lobe collapse (not shown) with otherwise clear lungs. Cross-sectional imaging was recommended. A CT chest with contrast image demonstrated multiple enlarged mediastinal lymph nodes, with the largest located in the right paratracheal region, causing leftward deviation of the trachea and esophagus with severe narrowing of the trachea (not shown). These imaging findings were highly suggestive of lymphoma.

The following history was only available after all imaging was complete. Over eight years prior, the patient was diagnosed with IgA kappa multiple myeloma, manifesting with serum monoclonal protein, bone marrow plasmacytosis, and lytic bone lesions. The bone marrow biopsy at that time showed CD138+ plasma cells accounting for 50% of the cellularity and were kappa-restricted with a ratio of >100:1 by FISH. Flow cytometry identified an IgA+ kappa-restricted CD56+ and C117- plasma cell population of 8.5%. He started high-dose chemotherapy with subcutaneous bortezomib, oral lenalidomide, and oral dexamethasone. Six months after diagnosis and chemotherapy, he underwent an autologous stem cell transplant after high-dose cytoxan and G-CSF stimulated stem cell harvest. Following this, the patient was in remission and on maintenance oral lenalidomide and oral dexamethasone until this presentation.

Management/follow up

The mediastinal lymph node was subsequently biopsied, showing an atypical infiltration of plasma cells in sheets. Multiple abnormal populations of cells, along with intranuclear pseudoinclusions (Dutcher bodies) were appreciated. Immunohistochemistry was positive for CD138+ plasma cells. FISH analysis showed kappa restriction. Flow cytometry for leukemia/lymphoma did not detect monoclonal B-cell populations or T-cells with loss of aberrant expression of PAN T-cell antigens. Collectively, these findings were consistent with the recurrence of plasma cell myeloma and not leukemia or lymphoma. The patient received five days of radiation therapy to the base of the skull, equivalent to 20 Gy, with high-dose

dexamethasone treatment with plans for close oncologic follow-up.

CASE 2

A 66-year-old male with hypertension, a remote smoking history, a previously provoked pulmonary embolism in a postoperative period on apixaban, and multiple myeloma in remission presented with two to three days of sudden onset binocular diplopia, worst in left lateral gaze. Upon evaluation by an ophthalmologist, his physical exam was notable for a disconjugate gaze and poor left eye abduction, consistent with a sixth cranial nerve palsy. Due to his prior medical history, the cause of his cranial nerve deficit was thought to be due to a vascular cause likely.

Imaging findings

However, MRI of his orbits showed a small nodular enhancing lesion centered at the posterior cavernous sinus/petroclinoid ligament, in the region of the left Dorello canal (Figure 2). Given the patient's history of multiple myeloma, these findings were suspicious for an extramedullary myeloma.

Management/follow up

The patient was diagnosed with multiple myeloma over ten years ago being found to have multiple pathologic fractures of his thoracic spine. A T11 bone biopsy demonstrated plasmacytic infiltration at that time. The patient was started on oral lenalidomide and oral dexamethasone. One year later, he underwent autologous stem cell rescue using high-dose melphalan and completed an HLA-matched autologous stem cell transplant a few months later. Following this, he was in remission for six years. Upon a repeat bone marrow biopsy, the patient was diagnosed with recurrent plasma cell myeloma with 26% plasma cells and CD138+ enriched cells. Throughout the next few years up until a few months before this presentation, the patient had times of chemotherapy non-compliance and disease relapse. Given these findings, the patient received five fractions of palliative radiation therapy to his skull and high-dose dexamethasone treatment with plans for close oncologic follow-up.

DISCUSSION

Etiology & Demographics

Multiple myeloma/plasma cell myeloma involves the monoclonal proliferation of plasma cells from red bone marrow. The four recognized multiple myeloma patterns include well-defined "punched out" lytic lesions, diffuse skeletal osteopenia, solitary plasmacytoma, and osteosclerosing myeloma. Distribution varies, from vertebral bodies being the most common to extraosseous, which is uncommon [1]. For solitary plasmacytomas, there is minimal to no systemic bone marrow involvement. Based on an epidemiological study, overall incidence rates in adults for solitary plasmacytoma were 0.45, for extramedullary plasmacytoma 0.09, and 8.47 for multiple myeloma per 100,000 persons [2]. Rarely, central nervous system involvement accounts for 0.7% of plasma cell neoplasm cases [3]. This may manifest as a nerve palsy from an intracranial plasmacytoma.

The most common causes of ocular motor nerve palsies (OMNP) include inflammation (32.7%), space-occupying lesions like aneurysms or neoplasms (17.3%), diabetes mellitus (13.3%), and brainstem infarctions (11%) [4]. In isolation, the most common OMNP is abducens nerve palsy [5]. The abducens nerve is a purely motor nerve carrying somatic efferent nerve axons to innervate the lateral rectus muscle, which abducts the ipsilateral eye. It secondarily innervates the contralateral medial rectus by medial longitudinal fasciculus to coordinate lateral conjugate gaze [6]. The abducens nerve has the second longest intracranial course of all the cranial nerves: originating from the caudal dorsal pontine, it exits at the pontomedullary groove, courses through the prepontine cistern, enters the clival dura and just below the level of the petrous ridge, enters Dorello canal, a point below the posterior clinoid and the anteromedial portion of the petrous ridge. Abducens nerve palsy presents as an inability to abduct ipsilaterally and adduct contralaterally, resulting in diplopia due to unopposed medial rectus action with esotropia on primary gaze with the inability to abduct past midline [7]. Here, we describe two cases of patients presenting with isolated abducens nerve palsy, found to have intracranial plasmacytoma in the Dorello canal, a very rare demonstration of multiple myeloma recurrence.

Clinical & Imaging Findings

Although abducens nerve palsy is the most common palsy presenting in cases of malignancy, multiple myeloma recurrence presenting as an isolated abducens palsy is very uncommon. Extramedullary recurrence can be from a dural, meningeal, or parenchymal origin and as an extension of an intraosseous lesion. Here, we presented two cases for which recurrence was within the Dorello canal, concordant with their clinical presentations of acute isolated diplopia. Our first case was most peculiar in the sense that the patient had mediastinal adenopathy, which was biopsied and showed extramedullary plasmacytoma, thus allowing more confidently to interpret results from the MRI orbits which showed an enhancing focus in the region of the Dorello canal.

Compared to existing cases in the literature, these examples highlight unique features for which extramedullary plasmacytoma can occur in the Dorello canal, causing sixth nerve palsy as a presenting symptom of recurrence. There are multiple locations for which abducens palsy can occur but is not limited to multiple myeloma, including the petroclival region [8], the sphenoid sinus [9], petrous segment of the temporal bone [10], lesser wing of the sphenoid bone, [11] and the cavernous sinus [12]. Erosion of bone, leptomeningeal, or pachymeningeal enhancement/thickening in these regions must also be assessed. Abducens nerve palsy may not only

be isolated; Meckel's cave is near the course of the nerve, and lesions can also involve the trigeminal nerve. Diffuse diseases may manifest bilaterally with multiple cranial nerve palsies, such as leptomeningeal carcinomatosis. MR anatomy of the abducens nerve includes exiting the brainstem at the pontomedullary sulcus anterolaterally within the subarachnoid space to its dural opening (cisternal segment). The nerve then passes the basilar plexus between two dural leaves (petroclival segment) through the inferior petrosal sinus and below the petrosphenoidal ligament (Gruber's ligament) into the upper posterior region of the cavernous sinus. The Dorello canal is thought to start when the abducens nerve pierces the dura until the cavernous sinus [13].

Differential Diagnoses

The differentials to consider in the region of the petrous apex and the Dorello canal is meningioma and lymphoma, both of which would enhance more avidly compared to a plasmacytoma. Lymphoma would exhibit greater restricted diffusion due to an increased nuclear/cytoplasmic ratio. Metastatic lesions to the bone, meninges, or parenchyma are also important for consideration. Enhancement of the nerve is an important finding since it may indicate perineural spread, and other differentials could be considered. Additional differential diagnoses include but are not limited to schwannomas, solitary fibrous tumors, chordomas, chondrosarcomas, carcinomas, sarcoidosis, and granulomatosis with polyangiitis [14]. Granulomatous diseases, much like multiple myeloma, can have various clinical presentations and regions of involvement. Neuro-ophthalmologic manifestations of sarcoidosis, a multisystem disease affecting any organ, most commonly involve the uveal tract and the optic nerve [15]. It has been shown that granulomas in sarcoidosis can obstruct the Dorello canal and cause abducens palsy [16]. Granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis) can also present with multiple cranial nerve palsies secondary to pachymeningitis, including abducens palsy [17]. Knowledge of stroke and its mimics are also essential when patients present with diplopia. It is important to note that plasmacytoma can occur in the absence of systemic involvement. Pathology involving the cavernous sinus and orbital apex can include syndromes involving abducens palsy, but isolated palsy may be uncommon. Whole-body PET-CT could help determine any soft tissue components to suggest a plasmacytoma, which could then be biopsied if there is no marrow involvement. This could potentially avoid a skull-based biopsy, depending on its location. These two unique cases where isolated sixth nerve palsy was secondary to multiple myeloma recurrence provide valuable insight so as not to delay diagnosis and treatment.

TEACHING POINT

Extramedullary intracranial plasmacytoma can present as an isolated cranial nerve six palsy as recurrence or initial presentation of multiple myeloma, with or without initial marrow involvement. Careful interrogation on contrast enhanced MRI is warranted, which can show an enhancing focus with variable T1, T2 and diffusion characteristics in the region of Dorello canal.

KEYWORDS

Multiple myeloma; plasmacytoma; cranial nerve palsy; Abducens nerve; Dorello canal

QUESTIONS

1. Lesions in these regions can cause abducens nerve palsy, except which one of the following?
   a. Petroclival region
   b. Sphenoid sinus
   c. Petrous segment of the temporal bone
   d. Cavernous sinus
   e. Mastoid process

   Answer e.

Explanation:

The abducens nerve runs through or near all the structures except the mastoid process.

Applies to article: McElveen JT Jr, Dorfman BE, Fukushima T. Petroclival tumors: a synthesis. Otolaryngol Clin North Am. 2001;34(6):1219-x. doi:10.1016/s0030-6665(05)70375-3

2. Which of the following are considered differential diagnoses for lesions in the region of the petrous apex and Dorello canal?
   a. Schwannoma
   b. Solitary fibrous tumor
   c. Chordoma
   d. Chondrosarcoma
   e. All the above

   Answer: e

   Explanation: All the above are in the differential diagnoses.

3. At what site does the Abducens nerve arise from in the brainstem?
   a. Midbrain
   b. Midbrain-pontine junction
   c. Pons
   d. Pontine-medullary junction
   e. Medulla oblongata

   Answer: d

   Explanation: the abducens nerve arises at the pontomedullary sulcus. Trochlear nerve arises from the midbrain, oculomotor from the midbrain-pontine junction, trigeminal from the pons, and glossopharyngeal, vagus, and accessory from the medulla.

4. What extraocular muscle does the abducens nerve innervate?
   a. Lateral rectus
   b. Superior oblique
   c. Medial rectus
   d. Inferior rectus
   e. Inferior oblique

Answer: a

Explanation: the abducens nerve is a general somatic efferent nerve that innervates the lateral rectus muscle and ipsilaterally abducts.

Applies to article: Hörner R, Kassubek J, Dreyhaupt J, Ludolph AC. The spectrum and differential diagnosis of acquired ocular motor nerve palsies: a clinical study of 502 patients. J Neurol. 2022 Apr;269(4):2140-2148. doi: 10.1007/s00415-021-10761-w. Epub 2021 Sep 19. PMID: 34537871; PMCID: PMC8940813.

5. What is the most common cause of ocular motor nerve palsies?

a. Space-occupying lesions
b. Diabetes mellitus
c. Brainstem infarctions
d. Inflammation
e. Trauma

Answer: d

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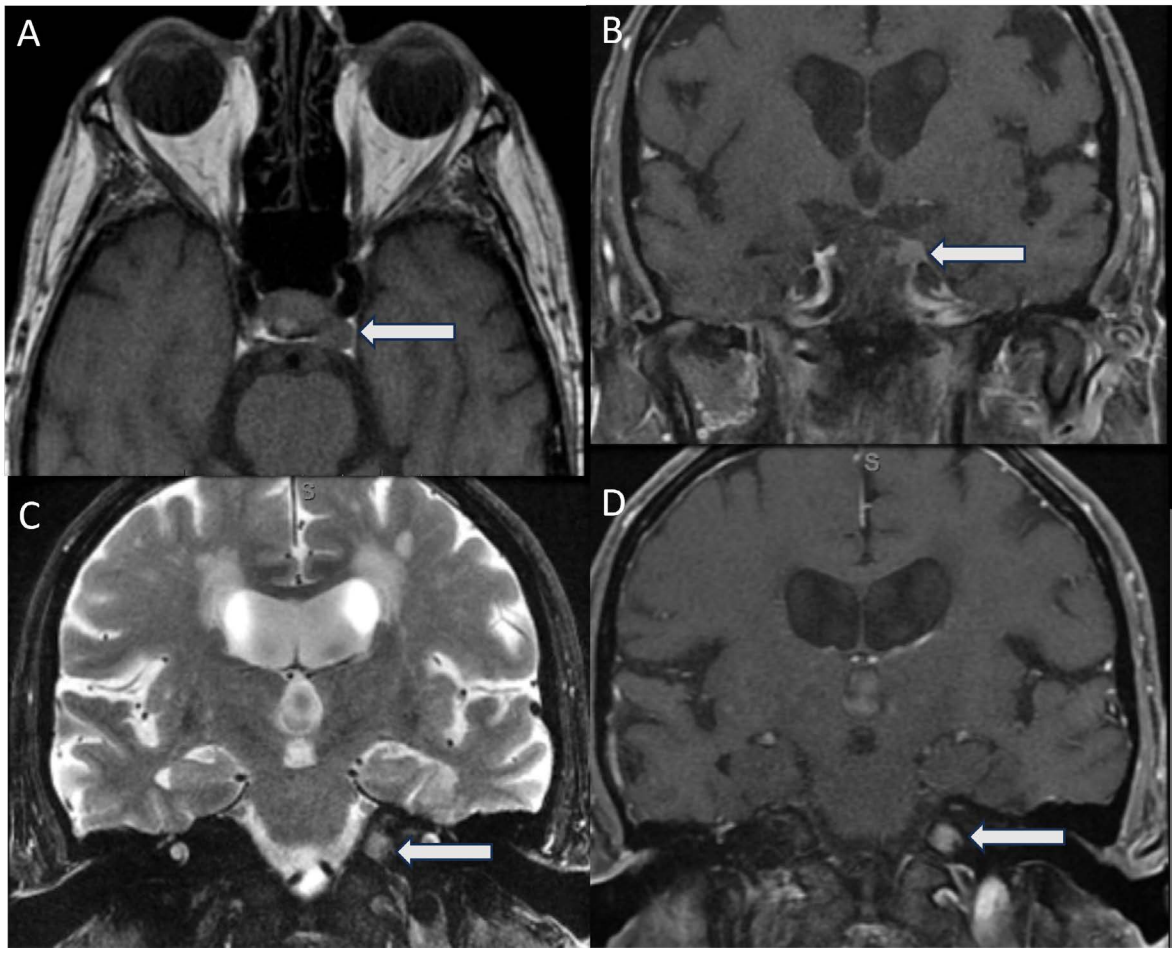
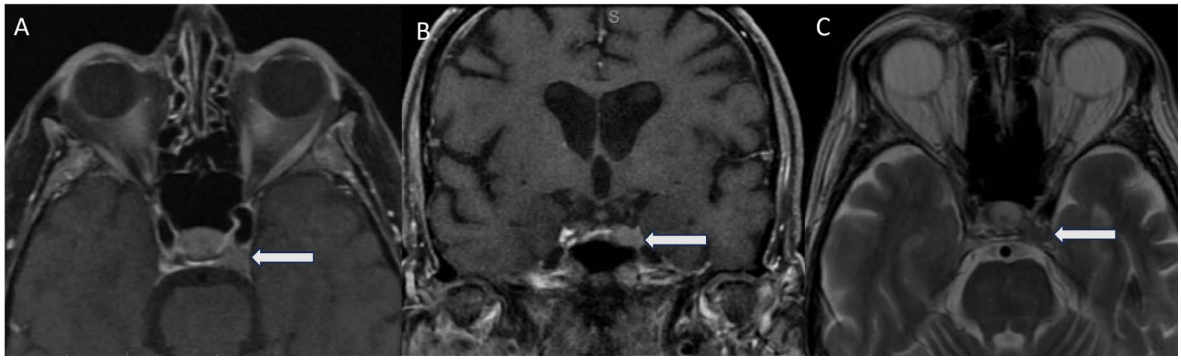
FIGURES



Patient 1: Figure 1. MRI orbits and without contrast, coronal T1-weighted with contrast (A-B), T2-weighted (C), and axial T1-weighted with contrast (D). There is a T1-weighted isointense (A), T1-weighted 8 mm enhancing lesion (B) along the left petroclinoid ligament in the region of Dorello canal (A-B, white arrows). There is an additional focal T2 hyperintense focus (C) and enhancement (D) at the left petrous apex with associated mild focal restricted diffusion (not shown).



Patient 2, Figure 2: Axial (A) and coronal (B) T1-weighted post-contrast images shows a focus of enhancement (white arrows) at the posterior left cavernous sinus/petroclinoid ligament in the region of the left Dorello canal. On T2-weighted, the lesion is isointense (B). There is no restricted diffusion (not shown).

KEYWORDS

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