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Case Report

Superior Oblique Muscle Extramedullary Plasmacytoma in a Patient with Multiple Myeloma and a Review of Literature

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Keywords
Extramedullary plasmacytoma · Superior oblique muscle

Abstract

Introduction: Multiple myeloma (MM), a plasma cell malignancy, is a systemic disease affecting various body organs. Plasmacytoma of bone and extramedullary disease (EMD) are presentations of MM. EMD is usually the sign of a more aggressive form of the disease. Herein, we report a patient with refractory MM presenting with extramedullary plasmacytoma in the superior oblique (SO) muscle. ***Case Presentation:*** A 51-year-old female presented complaining of gradual protrusion of the left eye and ocular pain from 20 days prior. She received bone marrow transplantation 1 year prior and was on a chemotherapy regimen for MM for the past 1 year. Ocular examination revealed proptosis of the left eye and mild limitations of adduction and elevation. Orbital magnetic resonance imaging demonstrated remarkable enlargement of the left SO muscle with focal contrast enhancement. The patient underwent a biopsy and mass debulking. The histopathologic exam revealed fibromuscular tissue containing a neoplasm composed of sheets of plasmacytoid cells in a varying degree of differentiation with intervening scantly vascularized stromal components. The plasmacytoid cells were diffusely positive for a cluster of differentiation 138 (CD138), leading to a diagnosis of EMD involving the EOM and soft tissue of the orbit. The patient underwent palliative radiotherapy and a systemic workup. The PET-CT scan revealed involvement of the pelvic bone and left calf. Accordingly, the chemotherapy regimen was upgraded to reflect the aggressive nature of the disease. In the last follow-up, there was no sign of tumor reactivation in the orbital soft tissues. Unfortunately,

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the patient succumbed to her illness 7 months following her most recent presentation. ***Conclusion:*** Early recognition of disease recurrence is lifesaving in MM patients; ophthalmic manifestations should be seriously considered as a sign of MM activity.

Introduction

Multiple myeloma (MM), a plasma cell malignancy, accounts for 1% of all cancers and 10% of hematologic neoplasms. It includes a range of diseases from monoclonal gammopathy of unknown significance (MGUS), extramedullary disease (EMD), and plasma cell leukemia [1]. MM is a multisystem disease affecting more commonly the bones as bone-related plasmacytoma (BP) or less frequently the soft tissues outside the bone as extramedullary plasmacytoma.

Extramedullary involvement worsens the prognosis of MM and is a sign of a more aggressive disease. The incidence of EMD varies among different studies and differs based on the MM phase. In newly diagnosed MM, the incidence is 0.5–4.8%, while in relapse/refractory MM, the incidence ranges from 3.4 to 14% [2]. While the orbit can also be a site of both bone-related plasmacytoma and extramedullary involvement, the EMD in the orbital cavity is relatively rare [3].

Herein, we present a 51-year-old woman with EMD in the superior oblique (SO) muscle secondary to a refractory MM. To our knowledge, extramedullary involvement of SO muscle has not been reported yet. We also performed a literature review of MM involving orbital EOMs. The CARE Checklist, describing the multiple parts of the case report, has been completed by the authors for this case report and is attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000538120).

Case Presentation

A 51-year-old female presented to the oculoplastic clinic with a 20-day history of gradual protrusion of the left eye, which was accompanied by ocular pain. The patient had been diagnosed with MM 2 years previously but was otherwise systemically well apart from hypertension and controlled on medication. The patient had been undergoing chemotherapy for 8 months since the diagnosis of the disease until the bone marrow transplant. The patient was in remission 1 year after the transplant, until she presented with left eye protrusion. Because of previous amblyopia, her best corrected visual acuity was 1/10 in the right eye and 7/10 in the left eye. Ocular examination showed proptosis and a moderate fullness of the left eye with no dystopia or ptosis (Fig. 1a, b). Limitation in adduction and limitation in inferonasal gaze (−1) were detected. Pupils were equal and reactive with no relative afferent pupillary defect. The slit-lamp examination and dilated fundoscopy were normal. The corneal sensation was normal in both eyes. Optic nerves were normal in both eyes. A computed tomography (CT) scan of the orbits showed no evidence of bone involvement. Magnetic resonance imaging (MRI) of the brain and orbits (Fig. 1d–f) demonstrated a mass in the left superior oblique muscle belly with relatively homogenous contrast enhancement.

In order to obtain a definitive diagnosis, an anterior superonasal orbitotomy was performed through an extended incision at the medial end of the upper lid crease. After tissue dissection, we realized that the mass was within the superior oblique muscle belly. For this

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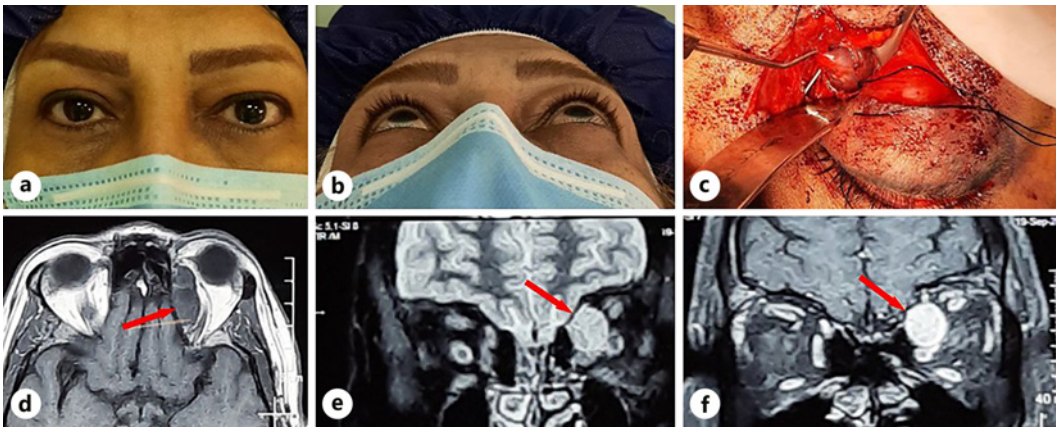

Fig. 1. External photo demonstrating proptosis and fullness in the superonasal aspect of the left orbit from the front view (**a**) and worm's eye view (**b**). Intraoperative photo demonstrating superior oblique (SO) muscle with a mass (**c**), T1-weighted magnetic resonance imaging without fat suppression, axial view demonstrating enlarged SO muscle (**d**), T2-weighted image, and post-contrast T1-weighted image, coronal view revealing a mass within the SO with contrast enhancement (**e**, **f**) pushing medial rectus muscle to the inferior. Red arrows demonstrate the SO in MRI images.

reason, it was not possible to completely excise the mass, and the mass was subjected to debulking and biopsy. After controlling the bleeding and placing a drain, the wound was sutured with nylon 6-0 (Fig. 1c).

Histopathologic examination revealed fibromuscular tissue containing a neoplasm composed of sheets of plasmacytoid cells in a varying degree of differentiation with intervening scantly vascularized stromal components. Immunohistochemistry (IHC) revealed that the plasmacytoid cells were diffusely positive for a cluster of differentiation 138(CD138). Thus, histopathology and IHC confirmed the diagnosis of plasma cell myeloma involving extraocular muscle and soft tissue of orbit (Fig. 2a–d).

The patient underwent palliative external beam radiotherapy. On systemic workup, positron emission tomography-computed tomography scan (PET-CT) revealed evidence of extramedullary disease (soft tissue density) on the left side of the pelvic cavity and left calf, compatible with active MM. The patient underwent an intensive chemotherapy regimen. The patient's ocular symptoms resolved over a follow-up period of 6 months, with no sign of tumor activity in the orbit. Seven months after presentation, despite augmented chemotherapy, recurrence of plasmacytoma in the pelvic region and subsequent pressure on the pelvic veins resulted in progressive edema of the left lower limb and secondary thrombosis in Doppler ultrasound reports. Although the patient underwent intensive antibiotic and anticoagulant therapy, she succumbed to her illness due to severe sepsis and cardiogenic shock.

Discussion

This report has documented extramedullary plasmacytoma in the SO muscle in a patient with MM. Despite treatment for 2 years before presentation, the disease was still active in our patient. To the best of our knowledge, EMD in SO muscle is being reported for the first time. In our patient, systemic workup confirmed the involvement of other organs which meant systemic activity of the disease.

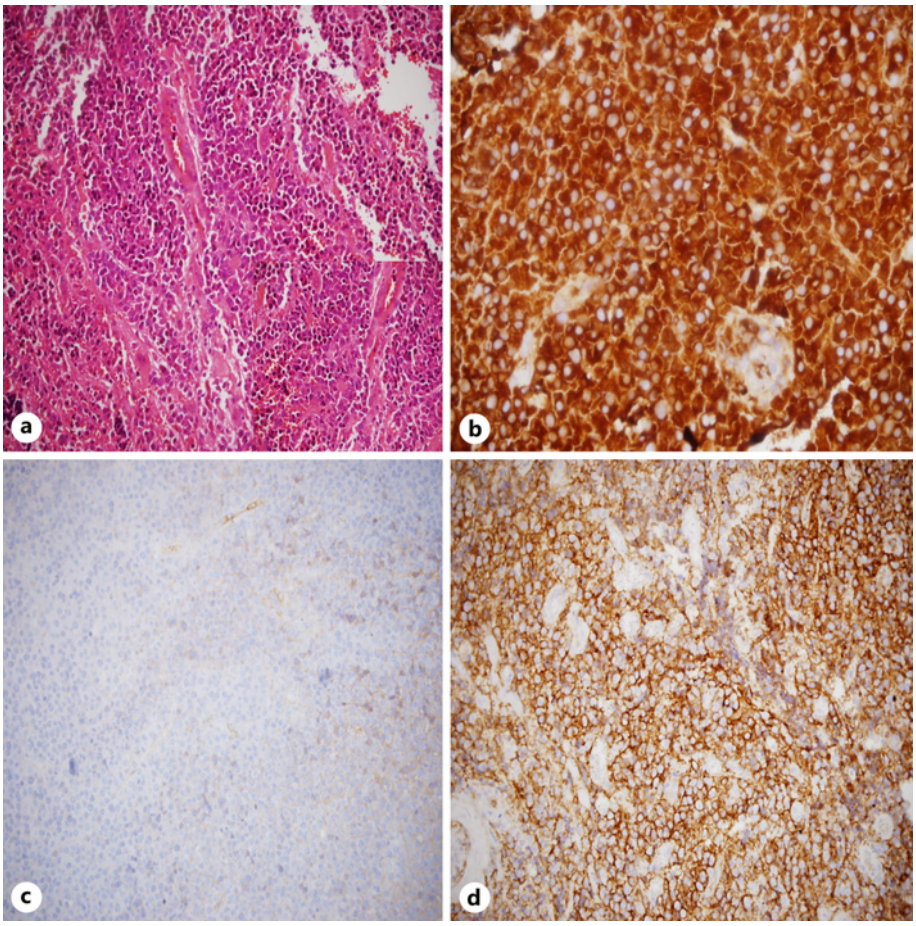

Fig. 2. a Sheets of plasma cells with the presence of atypical and anaplastic forms, H&E, *200. **b** Positive immunoreactivity for CD138. **c** Negative immunoreactivity for the kappa light chain. **d** Positive immunoreactivity for the lambda light chain.

The ophthalmic manifestations of MM can appear in many ocular structures. These include crystalline corneal deposits, chorioretinopathies, retinal hemorrhage, extraocular muscle paresis, and papilledema [4, 5].

Similar to other organs, orbital manifestations in MM are mainly caused by plasma cell infiltration into the bone (solitary plasmacytoma of bone) or extraocular soft tissue (EMD). Most plasmacytomas occur in the superotemporal quadrant due to the rich blood supply in the lacrimal gland and the sphenoid bone [6]. EMD affecting EOM is a relatively rare phenomenon. Studies reporting EOM involvement in MM are summarized in Table 1 [7–14]. EOMs are usually affected in combination with adjacent soft tissue or bone. To date, isolated involvement of EOM has been reported in 3 patients [7, 15, 16]. Whether isolated or in combination with other tissues, the hematogenous spread of neoplastic plasma cells could result in extramedullary involvement of EOM [2].

The mechanism explaining the development of EMD in MM has not yet been clarified. Both extramedullary and bone relapses have been reported in MM. However, the cell morphology and CD expressions might have differences between SPB and EMD. The presence of Ki 67 on extramedullary plasma cells is also a sign of mitotic activity in these escaping cells. The extramedullary plasmacytoma cells are considered to be more aggressive [17].

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Table 1. Summary of reported case reports of ocular muscle involvement secondary to multiple myeloma

Study	Age	Sex	Orbital location	First symptoms	MM, Y/N	Histopathologic findings	IHC stains expression	Treatment	f/u duration	Outcome
Rodman et al. (1972) [13]	37	M	Lateral rectus involvement	proptosis	YES	Poorly differentiated plasma cell		Irradiation, steroid, blood transfusion	4 months	The patient died
Kwartz et al. (1993) [12]	65	M	Intraconal and extraconal involving left lateral rectus	Blurred vision and proptosis			IgG kappa paraproteinemia	Radiotherapy, steroid, chemotherapy	Rapid response	Relapse after 6 months
Adkins et al. (1997) [14]	84	M	Orbital mass involving left medial rectus	proptosis	NO	Atypical plasma cells	Lambda light chains	–	–	–
Thoumazet et al. (2006) [8]	48	F	2 large masses in each lacrimal gland and lateral recti muscles	Chemosis, palpable fixed painless mass	Yes	Atypical monomorphic lymphoid plasma cells with	N/D	No treatment		The patient died 2 months later
Malik et al. (2009) [9]	58	M	Multiple soft tissue masses within the muscles	bilateral proptosis	No	Cellular sheets of mature and immature plasma cells	N/D	Chemotherapy	3 weeks	Remission
Chin et al. (2011) [4]	76	M	Two intraconal plasmacytomas	Red epibulbar mass	Yes	A soft tissue mass of plasma cells	Monoclonality consistent with multiple myeloma	Chemotherapy followed by EBRT	3 months	Patient died after 5 months
Pan et al. (2011) [10]	57	F	Lobulated soft tissue mass in the extraconal area of the right orbit	proptosis	Yes	Plasma cells in variable stages	N/D	Radiotherapy	1 month	Improvement of proptosis

(Continued on following page)

Table 1 (continued)

Study	Age	Sex	Orbital location	First symptoms	MM, Y/N	Histopathologic findings	IHC stains expression	Treatment	f/u duration	Outcome
Painter et al. (2015) [15]	74	M	Right medial rectus muscle	Proptosis	Yes	Extensive infiltration of plasma cells	CD20−CD79+VS38c^{+} Lambda light chain restricted	Intramuscular dexamethasone and chemotherapy	1 month	Ophthalmic manifestations resolved
Saffra et al. (2019) [7]	67	F	Lateral rectus muscle	Diplopia	Yes	N/D	N/D	Chemotherapy	1 month	Complete resolution
Barmas-Alamdari et al. (2020) [11]	45	M	Bilateral intraorbital masses	Bilateral proptosis	Yes	Diffuse plasma cell infiltration	CD38, CD138 and CD56	Anterior orbitotomy and lateral canthotomy		The patient expired
Mani et al. (2021) [6]	50	F	Enhancing lesions in the left superotemporal quadrant	Progressive proptosis	Yes	Numerous mature plasma cells with eccentric nuclei	Positive for CD38 and CD138	Chemotherapy	ND	Improvement
Vempuluru et al. (2022) [16]	51	M	Both medial recti and right lateral rectus muscle	Proptosis	Yes	ND	ND	External beam radiotherapy	ND	Controlled the disease process

Determining whether EMD is a local relapse or a manifestation of MM activity or relapse requires systemic workup including immunoelectrophoresis of serum and urine, skeletal survey, CT scan, and, in some cases, bone marrow aspiration. We think the tumor in our patient is a sign of MM activity, as a result of insufficient treatment. Based on the current literature, orbital metastasis is an unfavorable prognostic factor leading to a reduced survival rate [18, 19].

There are various treatments for EMD, depending on whether it is local or systemic. Solitary bone lesions are often treated with radiotherapy alone and extramedullary plasmacytomas are more likely to undergo surgery or in combination with radiotherapy [20]. Since MM is a systemic disease, treatment of MM typically involves chemotherapy, and in younger patients, hematopoietic stem cell transplantation is considered in combination with chemotherapy [1]. Our patient was under a chemotherapy regimen with bortezomib and dexamethasone and zoledronic acid at the time ophthalmic signs arose, but the pelvic cavity involvement suggested that the chemotherapy regimen was not adequate. Therefore, the chemotherapy regimen was changed to a more robust form.

In conclusion, a patient with MM may encounter extramedullary disease in the orbital cavity even under chemotherapy. Since early recognition of disease recurrence and insufficiency of treatment is lifesaving in MM patients, ophthalmic manifestations should be seriously considered as a sign of MM activity.

Statement of Ethics

Written informed consent was obtained from the patient's husband for the publication of the details of the medical case and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Author Contribution

A.V. and M.N. made the diagnosis, performed the surgery, and supervised the draft. S.H., K.D., and K.H. gathered the data and drafted the manuscript. P.M.T. confirmed the pathological diagnosis, prepared the pathology figures, and confirmed the final manuscript. All authors approved the final version.

Data Availability Statement

All data generated and analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Kazandjian D, editor. Multiple myeloma epidemiology and survival: a unique malignancy. Seminars in oncology Elsevier; 2016.
2 Bladé J, Beksac M, Caers J, Jurczyszyn A, von Lilienfeld-Toal M, Moreau P, et al. Extramedullary disease in multiple myeloma: a systematic literature review. Blood Cancer J. 2022;12(3):45–10.
3 Burkat CN, Van Buren JJ, Lucarelli MJ. Characteristics of orbital multiple myeloma: a case report and literature review. Surv Ophthalmol. 2009;54(6):697–704.
4 Chin KJ, Kempin S, Milman T, Finger PT. Ocular manifestations of multiple myeloma: three cases and a review of the literature. Optometry. 2011;82(4):224–30.
5 Vatansever M, Bozkurt FM, Dinç E, Yılmaz EB, Nayir E, Sarı AA, et al. Orbital metastasis of multiple myeloma: case report. Turk J Ophthalmol. 2016;46(3):148–50.
6 Mani M, Kasturi N, Sravya R, Kaliaperumal S, Gochhait D. Orbital plasmacytoma as the presenting feature in multiple myeloma. Eur J Ophthalmol. 2021;31(6):NP1–NP4.
7 Saffra N, Gorgani F, Panasci D, Kirsch D. Diplopia and proptosis due to isolated lateral rectus plasmacytoma in a patient with multiple myeloma. BMJ Case Rep. 2019;12(7):e229178.
8 Thoumazet F, Donnio A, Ayeboua L, Brebion A, Diedhou A, Merle H. Orbital and muscle involvement in multiple myeloma. Can J Ophthalmol. 2006;41(6):733–6.
9 Malik A, Narang S, Handa U, Sood S. Multiple myeloma presenting as bilateral orbital proptosis. Indian J Ophthalmol. 2009;57(5):393–5.
10 Pan SW, Wan Hitam WH, Mohd Noor RA, Bhavaraju V. Recurrence of multiple myeloma with soft tissue plasmacytoma presenting as unilateral proptosis. Orbit. 2011;30(2):105–7.
11 Barmas-Alamdari D, Sodhi GS, Shenouda TA. Bilateral proptosis in a case of recurring multiple myeloma: uncommon orbital presentation of plasmacytoma. Int Med Case Rep J. 2020;13:297–301.
12 Kwartz J, Jackson A, Noble J. Bilateral proptosis and corneal crystals in multiple myeloma. Eye. 1993;7 (Pt 1)(1):191–3.
13 Rodman HI, Font RL. Orbital involvement in multiple myeloma: review of the literature and report of three cases. Arch Ophthalmol. 1972;87(1):30–5.
14 Adkins JW, Shields JA, Shields CL, Eagle RC, Flanagan JC, Campanella PC. Plasmacytoma of the eye and orbit. Int Ophthalmol. 1997;20(6):339–43.
15 Painter SL, Dickens E, Elston JS. Isolated extraocular muscle infiltration with plasmacytoma treated with localized injection of dexamethasone. J Neuro Ophthalmol. 2015;35(2):168–70.
16 Kapoor A, Vempuluru V, Mishra DK, Kaliki S. Bilateral plasmacytoma of extraocular muscles presenting with orbital inflammation. Indian J Ophthalmol Case Rep. 2022;2(1):298.
17 Firsova MV, Mendeleeva LP, Kovrigina AM, Solovev MV, Savchenko VG. Plasmacytoma in patients with multiple myeloma: morphology and immunohistochemistry. BMC Cancer. 2020;20(1):346–8.
18 Holland D, Maune S, Kovács G, Behrendt S. Metastatic tumors of the orbit: a retrospective study. Orbit. 2003;22(1):15–24.
19 Uceda-Montañés A, Blanco G, Saornil M, Gonzalez C, Sarasa J, Cuevas J. Extramedullary plasmacytoma of the orbit. Acta Ophthalmol Scand. 2000;78(5):601–3.
20 Goyal G, Bartley AC, Funni S, Inselman J, Shah ND, Marshall AL, et al. Treatment approaches and outcomes in plasmacytomas: analysis using a national dataset. Leukemia. 2018;32(6):1414–20.