Case Report

Retrobulbar secondary plasmacytoma: a case report and systematic review of the literature

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ABSTRACT
Multiple myeloma is described by the proliferation of malignant plasma cells, in which orbital involvement is rare. In this report, we collected all cases with **orbital** multiple myeloma from 2009 to 2018 and investigated the characteristics such as sex, age, common orbital symptoms, unilateral or bilateral and different therapeutic options. Also, we reported an uncommon case of multiple myeloma that has been developed into plasmacytoma. Our patient had been initially diagnosed with multiple myeloma, but after a few months, the disease had progressed to secondary extramedullary plasmacytoma in the retrobulbar. Therapeutic measures, such as surgery to prevent its development in the patient's eye, were successful.
Key words: Extramedullary plasmacytoma, Multiple myeloma, Orbital involvement, Retrobulbar

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History
- Received: 17 August 2018
- Accepted: 10 September 2018
- Published: 29 September 2018

DOI :

https://doi.org/10.15419/bmrat.v5i9.482

INTRODUCTION

Multiple myeloma is a tumor of malignant plasma cells that consider as the second most common hematologic malignancy[1]. This disease has an age-adjusted incidence of 4.7 cases per 100,000 populations[2]. It often occurs in adults, and the mean age at diagnosis is 70 years[3]. One of the most prominent features of this disorder is the presence of more than 10% clonal plasma cells in the bone marrow or biopsy associated with end-organ damage[2]. Also, in 1846, Dalrymple and Bence Jones discovered an uncommon plasma cell tumor known as plasmacytoma[4]. The etiology of plasmacytoma remains largely unknown, but factors such as viral pathogenesis have been identified and genetic factors may also be involved[5]. The purpose of this paper is to report a 62-year-old man with a clinical and pathological history of multiple myeloma, who presented evidence of a mass in the retrobulbar area of the eye.

CASE PRESENTATION

In January 2018, a 62-year-old man was referred to our Clinic of Hematology and oncology, with one week of back pain history, and loss of consciousness in the neurological examination. Further analysis revealed the symptom of kidney failure. In primary laboratory investigations, he had normocytic normochromic anemia with Hb: 9.6g/dL, normal WBC and a decrease in platelet count (WBC: 8,300/mm^3; Platelet count: 79,000/mm^3). Also, renal function tests (RFT) and serum electrolytes were usually performed in multiple myeloma. The results of these tests showed hypergammaglobulinemia (5g/dL) and an increase in blood urea nitrogen (BUN) and serum creatinine (Cr) levels (BUN 64 mg/dL, Cr 8.1 mg /dL). Magnetic resonance imaging of the lumbar spine indicated vertebral collapse at T12 and L2. Examination of thebone marrow aspiration (BMA) and bone marrow biopsy revealed that a high percentage of plasma cells (>20% plasma cells) were negative for CD19, and positive for CD38, CD138 (**Figure 1**).

Our diagnosis was multiple myeloma and immediately started treatment with bortezomib, cyclophosphamide, and dexamethasone (the approved VCD is preferable as induction therapy for newly diagnosed multiple myeloma especially with renal failure). Also, zoledronic acid was used to reduce bone pain.

After 6 cycles, the initial response to treatment was relatively good. Five months later, the patient referred to an ophthalmologist with symptoms such as swelling of the right eyelid with ptosis, diplopia and blurred vision. In fundus examination, few scattered hemorrhages were seen in the left eye and the results of Visual Acuity for this eye were as follows: OD: 6/10, OS: 4/10. Also, the results of orbit computed tomography (CT) demonstrated a soft tissue mass (26 × 12 mm) in the retrobulbar of the left eye (**Figure 2**). In fine needle aspiration cytology (FNAC) of the mass, mature and immature plasma cells were observed, which led to the diagnosis of secondary extramedullary plasmacytoma. Thus, the patient underwent surgical debulking, the lesion was removed

Cite this article : Payandeh M, Karami N, Enayati S, Karami A, Aeinfar M, Yari F. **Retrobulbar secondary plasmacytoma: a case report and systematic review of the literature**. *Biomed. Res. Ther.;* 5(9):2703-2707.

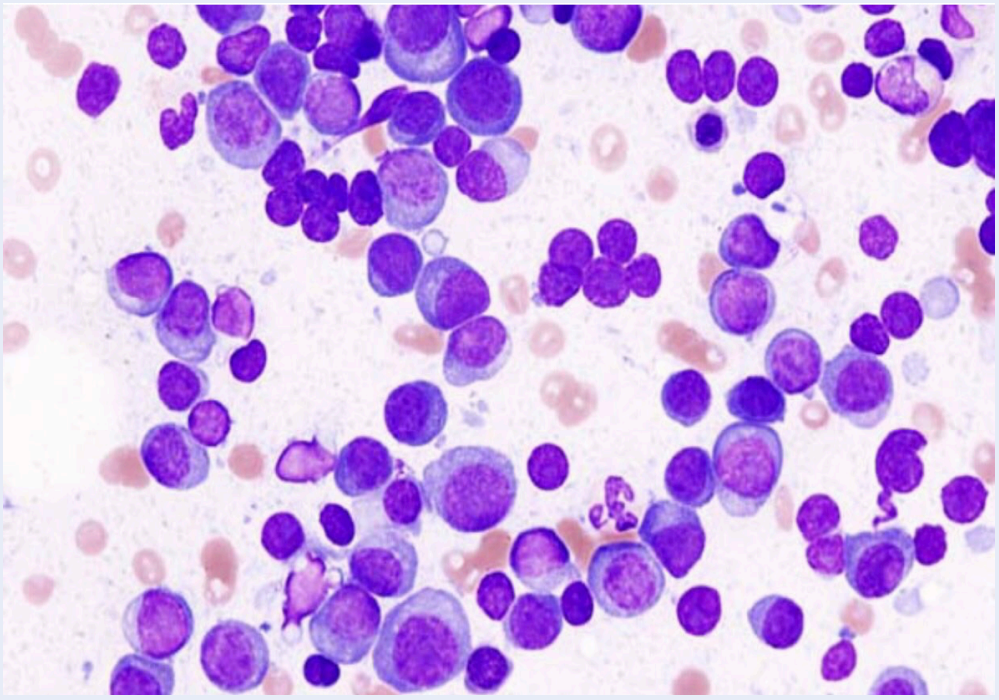

Figure 1: **Bone marrow aspirate showed plasmacytosis.**

from the retrobulbar area and the result was successful. Currently, the patient's condition is good, and he is continuing chemotherapy cycles with bortezomib and dexamethasone.

DISCUSSION

Plasmacytoma, as an unusual tumor of malignant plasma cells, indicates 5-10% of all plasma cell neoplasms[6] and plasmacytoma can occur as a primary or secondary tumor, based on the presence or absence of systemic disease[7]. Also, these neoplasms are divided into four different types: solitary plasmacytoma of bone (SPB), extramedullary plasmacytoma (EMP), multiple myeloma (MM) and plasma cell leukemia[8]. The organs involved in the SPB are mainly axial skeletal bones, such as vertebra and skull, while in EMP, the head and neck, nasal cavity and nasopharyngeal are commonly involved[6]. It has been reported that the rate of relapse after treatment for extramedullary plasmacytoma is 6-10%[9].

Also, MM is characterized by the proliferation of abnormal plasma cells and is usually limited to bone marrow[10]. Extramedullary plasmacytoma has been reported in 3% of patients with MM[11]. In these patients, orbital involvement is rare. According to the study performed by Burkat and colleagues[12], from 1972 to 2009, 52 cases of orbital multiple myeloma with a mean age of 56.5 have been reported and in 81% of them, the most common symptom was proptosis. Based on our reviews, from 2010 to 2018, about 20 cases have been described, which are listed in **Table 1**.

The mean age of these patients was 63.8 and in the many cases, orbital symptom has been unilateral (85%). The proptosis and diplopia were the most abundant orbital clinical symptoms involved, while ptosis, retrobulbar lesion, and low vision were less common (**Table 2**). Also, systemic chemotherapy and radiotherapy are good therapeutic options that in the most reports, the positive response to treatment has been reported[13]. We reported a multiple myeloma patient with extramedullary plasmacytoma that was unique because of the unilateral retrobulbar lesion and its successful orbital surgery.

CONCLUSION

According to studies conducted to date, in patients with multiple myeloma, orbital symptoms often occur in adulthood and unilaterally. Additionally, the important point in these cases is that during differential diagnosis between the types of plasmacytomas, initially multiple myeloma should be considered.

LIST OF ABBREVIATIONS

BMA: bone marrow aspiration

Table 1: Cases with orbital multiple myeloma from 2009-2018

Author (yr)	# Cases	Age (yr)	Sex	Orbital Symptoms	Unilateral *vs.* Bilateral	Typical management	Ref.
Burkat (2009)	1	65	M	decreased vision and eyelid pain	Unilateral	Orbital surgery and chemotherapy	12
Yumori (2010)	1	33	M	Vascularized conjunctival lesion	Bilateral	Ophthalmic solution and prednisolone acetate	7
Fernandez (2011)	1	53	M	Moderate ptosis and hypotropia	Unilateral	Chemotherapy treatment and autologous bone marrow transplantation	14
Chin (2011)	3	82, 76, 76	1F, 2M	Epibulbar lesion and proptosis	Unilateral	Palliative radiotherapy and chemotherapy (melphalan and prednisone)	15
Liao (2011)	1	53	F	Left globe proptosis	Unilateral	Ocular surface lubrication	16
Pan (2011)	1	57	F	Right eye proptosis	Unilateral	Pamidronate chemotherapy and orbital radiotherapy	17
Terenzi (2012)	1	50	M	Retro-orbital lesion	Unilateral	Intensity-modulated radiotherapy technique (IMRT)	3
Hassan (2012)	1	62	F	Proptosis, chemosis, diplopia and decreased vision	Unilateral	Radiotherapy	13
Felici (2013)	1	73	M	Retro-orbital localization	Bilateral	Combination chemotherapy (lenalidomide, dexamethasone, and cyclophosphamide)	18
Varım (2015)	1	64	M	Peri-orbital ecchymosis lesion (raccoon eye)	Unilateral	Combination chemotherapy (VAD and VCD)	19
Galea (2015)	1	58	F	Diplopia and variable Ptosis	Bilateral	Combination chemotherapy (Cyclophosphamide , Thalidomide, and Dexamethasone)	20
Vatansever (2016)	1	68	F	Right eye proptosis	Unilateral	Palliative radiotherapy	21
Nambiar (2017)	1	63	F	Ptosis and diplopia	Unilateral	Chemotherapy (bortezomib, lenalidomide, and dexamethasone)	22
Wang (2018)	5	68, 73, 51, 77, 75	3F, 2M	The retrobulbar lesion, diplopia, and proptosis	Unilateral	Orbital surgery in conjunction with radiotherapy and chemotherapy	11

M: male, F: female

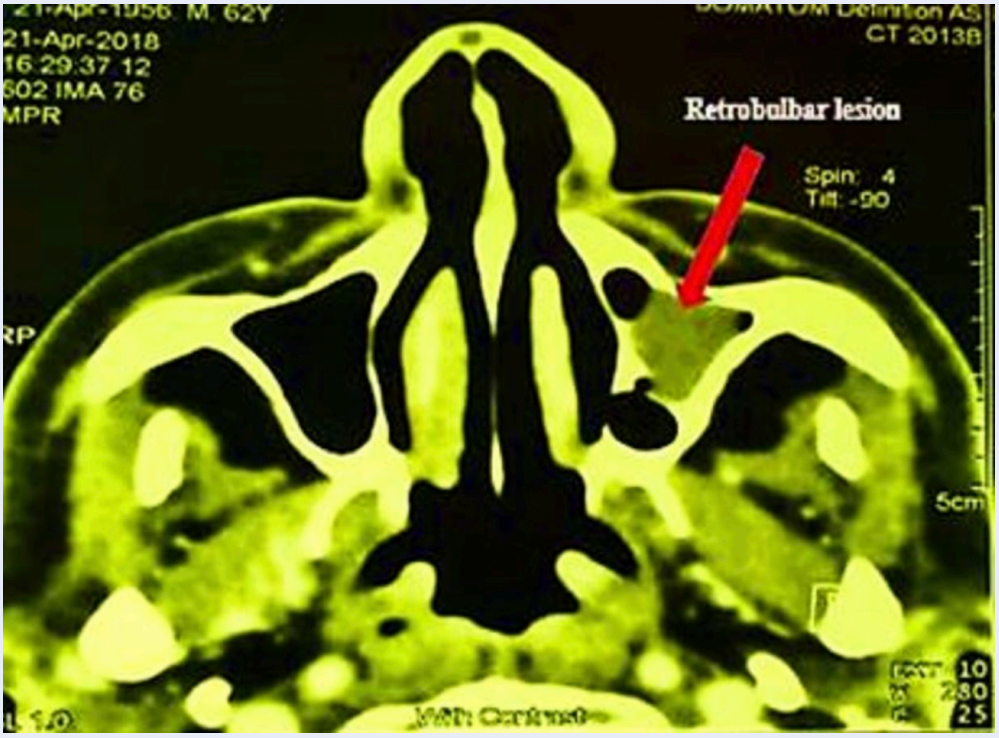

Figure 2: **CT of the orbital showed a soft tissue mass in the retrobulbar.**

Table 2: **Characteristics of cases with orbital multiple myeloma**

Characteristics	N: 20
Age	63.8
Sex	10 M (50%), 10 F (50%)
Unilateral *vs.* Bilateral	3 Bil (15%), 17 Uni (85%)
Common orbital symptoms	Proptosis: 12 (60%) Diplopia: 11 (55%) Ptosis: 3 (15%) Retro-bulbar (-orbital) lesion: 3 (15%)

Bil: bilateral, Uni: unilateral

BUN: blood urea nitrogen
CBC: complete blood count
Cr: creatinine
CT: computed tomography
EMP: extramedullary plasmacytoma
FNAC: fine needle aspiration cytology
MM: multiple myeloma
RFT: renal function tests
SPB: solitary plasmacytoma of bone
VCD: velcade (bortezomib), cyclophosphamide, and dexamethasone

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Yes

COMPETING INTERESTS

The authors declare that they have no financial or other conflicts of interest.

FUNDING

None.

AUTHORS' CONTRIBUTIONS

Mehrdad Payandeh & Noorodin Karami: Literature search, Clinical studies, Data acquisition, Data analysis; Noorodin Karami: Manuscript preparation, Manuscript review, Guarantor; Afshin Karami: Concepts, Design, Definition of intellectual content, Literature search, Manuscript editing; Soode Enayati, Fatemeh Yari & Mehrnoush Aeinfar: Manuscript editing, Literature search.

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