Bratisl Lek Listy 2010; 111 (12)
670 – 672

CASE REPORT

Successful treatment of early relapse of ocular myeloma with bortezomib and steroid after autologous stem cell transplantation

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Abstract: Autologous stem cell transplantation (ASCT) can prolong remission duration, overall and progression free-survival in multiple myeloma (MM). Ocular relapse is rare in MM. Here we present a patient with only ocular relaps and without evidence of bone marrow progression after ASCT.
Ig A kappa myeloma, stage IIIA was diagnosed in a 53-year-old man, according to Kyle-Greipp and Durie Salmon. He was treated with three courses of VAD therapy. Then he received high dose melphalan (200 mg/m^2), followed by the ASCT. After two months from ASCT, he had bilateral blurry vision, pain, redness in both eyes and diplopia. We detected 5 mm of right-sided proptosis by Hertel exophthalmometry (base 110, 20 mm right eye, 15 mm left eye). Ocular motility of oculus dexter (OD) was restricted in up and lateral gaze. He has diplopia in up gaze. His color vision was 7 of 12 in the right eye and 10 of 12 in the left eye with Ishihara plates. Best corrected visual acuity was 6/10 in the right eye and 7/10 in the left eye. Intraocular pressures were 19 mmHg for OD and 18 mmHg for oculus sinister (OS). Slit lamp biomicroscopy revealed subconjunctival hemorrhages superiorly and temporally in the right eye and bilateral conjunctival hyperemia with chemosis. Fundus examinations of both eyes were unremarkable. Computed tomography and magnetic resonance imaging of orbita revealed a right intraorbital extraconal soft tissue density mass that involved the lacrimal gland and lateral rectus muscle. Prednisolon 1mg/kg/day and bortezomib 1.3 mg/m^2 were started (1, 4, 8, 11 days). Eye findings were recovered after one month. Ocular relapse should be considered if there are ocular findings after ASCT for MM. Bortezomib and steroid may be useful for ocular extramedullary relapse of MM *(Fig. 2, Ref. 8)*. Full Text in free PDF *www.bmj.sk.*
Key words: ocular myeloma, bortezomib.

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by anemia, monoclonal gammopathy in serum and/or urine, bone pain, hypercalcemia, osteolytic lesions, hyperviscosity, renal failure (1). High dose chemotherapy and autologous transplantation (ASCT) can prolong remission duration, progression free-survival and overall survival in a significant proportion of patients with myeloma (2). Extramedullary plasmacytomas (EP) are rare plasma cell tumours. EP are rare plasma cell tumors originating mostly from the upper respiratory tract and oropharynx and rarely eye (3, 4). Ocular involvement as plasmacytoma is rare in multiple myeloma. It is also seldom after ASCT (5). Here we present a patient with only ocular relaps and without evidence of bone marrow progression after ASCT and successful treatment with bortezomib- steroid combination.

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Case report

A 53-year-old man, presented with 2-month history of progressive tiredness. Physical examination revealed pallor with a grade 2/6 systolic ejection murmur in the pulmonary area. Laboratory results were as follows: hemoglobin was 8.2 g/dl, hematocrit was 27 %, white blood cell count was 9300/mm^3, platelet count was 516000/mm^3. Lactate dehydrogenase (LDH), calcium, total urine count, and kidney function test levels were normal. The total protein and globulin values were 13.2 g/dl and 9 g/dl, respectively. Serum IgA was 7.8 g/dl and electrophoresis demonstrated a monoclonal spike. Immune electrophoresis revealed monoclonal IgA kappa paraprotein. Beta 2-microglobulin level was 9.5 mg/l and bone marrow aspirate and biopsy showed 88 % plasma cells.

Radiography revealed no osteolytic lesions in bones. He was diagnosed with stage III-A Ig A Kappa MM according to The International Myeloma Working Group criteria, and international prognostic index was 3. For induction regimen he received vincristine, doxorubicin, and dexamethasone (VAD regimen). This regimen was administered every 4 weeks. After third course, peripheral stem cell collection was performed following cyclophos-

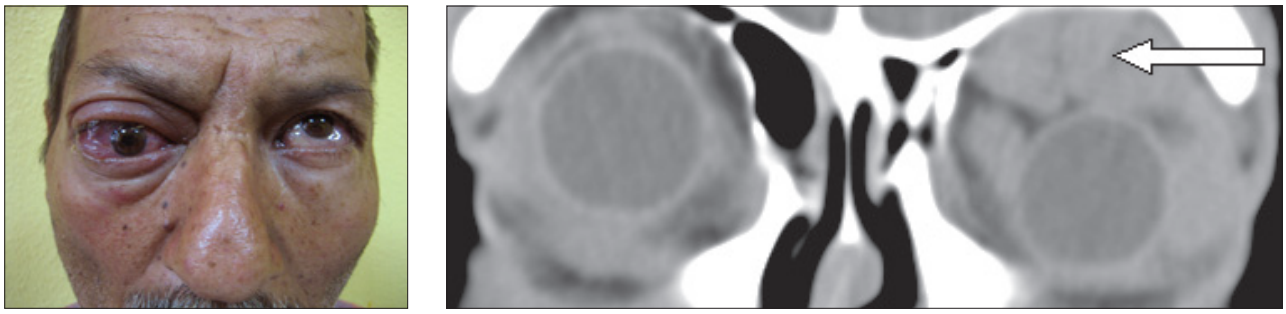

Fig. 1. Pretreatment imaging.

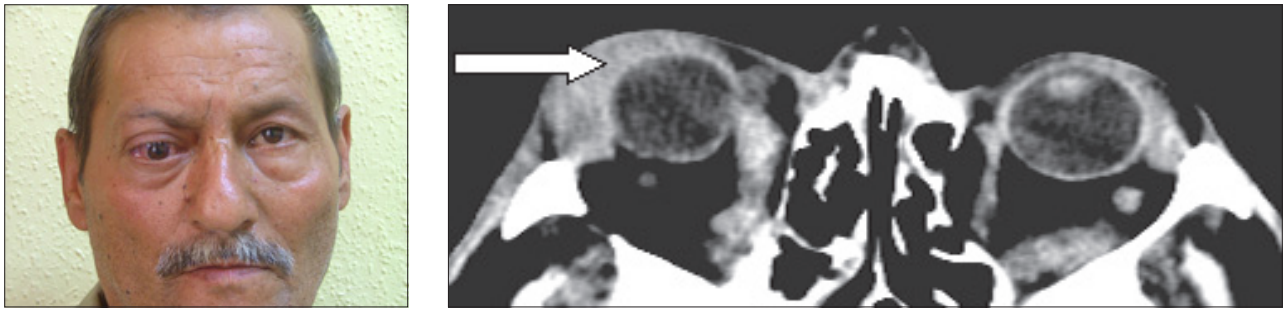

Fig. 2. Posttreatment imaging.

phamide 4 g/m^2 and filgrastim 10 ěg/kg. Finally, the treatment was followed by high-dose melphalan (200 mg/m^2) i.v. in combination with peripheral blood stem cell infusion containing 35x10^6/kg CD 34 + cells. Neutrophil and platelet engraftments were observed on 14th and 18th days respectively.

He underwent ASCT in MM a month ago, consulted from emergency service for a 2-week history of bilateral blurry vision, pain, redness and diplopia in June 2006. He presented with 5 mm of right-sided proptosis by Hertel exophthalmometry (base 110, 20 mm right eye, 15 mm left eye). Ocular motility of OD was restricted in up and lateral gaze. He had diplopia in upgaze. His color vision scorewas 7 of 12 in the right eye and 10 of 12 in the left eye with Ishihara plates. Best corrected visual acuity was 6/10 in the right eye and 7/10 in the left eye. Intraocular pressures were 19 mmHg for OD and 18 mmHg for OS. Slit lamp biomicroscopy revealed subconjunctival hemorrhages superiorly and temporally in the right eye and bilateral conjunctial hyperemia with chemosis. Fundus examination of both eyes was unremarkable. Computed tomography and magnetic resonance imaging of orbita revealed a right intraorbital extraconal soft tissue density mass that involved the lacrimal gland and lateral rectus muscle (Fig. 1). This patient was found to have a localized malignant plasma cell tumour arising from the orbital soft tissues without bone involvement and no evidence of systemic disease. Monoclonality for light Kappa chains was demonstrated with no paraproteins in serum or urine, associated with 4 % plasma cells in the bone marrow trephine. Prednisolon 1 mg/kg/day and bortezomib 1.3 mg/m^2 were started on days 1, 4, 8, and 11.

On follow up, one day later, in the cornea clinic, he was found to have corneal epithelial defect that stained with fluorescein and started on carboxymethylcellulose sodium 0.5 % lubricant eye drops 6 times a day and 0.2 % carbomer gel lubricating gel 4 times a day and a lubricating ointment at bedtime in the right eye. Since the IOP increased to 28 mmHg in the right eye, while left eye's pressure was 16 mmHg. Fixed combination of 0.5 % timolol and 2.0 % dorzolamide twice daily was started.

Over the next 10 days, his best corrected vision had improved to 9/10 OD and 10/10 OS. Intraocular pressures were 17 mmHg for OD and 16 mmHg for OS. Corneal fluorescein staining was negative in the right eye appearance with subconjunctival hemorrhages superiorly and temporally. Color vision was tested with Ishihara plates were 19/21 OD and 19/21 OS. External view demonstrating the clinical appearance with reduction of the right-sided proptosis, Hertel exophthalmometry at a base of 110 mm showed 16 mm right eye and 14 mm left eye, but he continued to have double vision on extremes of up and lateral gaze. These findings recovered after one month (Fig. 2).

Discussion

Malignant plasma cell tumours are divided according to site of origin. They can be multicentric, such as multiple myeloma, or localized, originating from bone (solitary plasmacytoma of bone) or from soft tissue (EP). EP represents a minority (3 %) among all malignant plasma cell tumors. The vast majority arises from the walls of the upper respiratory tract, including the paranasal sinuses, the orbit being an extremely rare primary location for them to originate. The ocular area is a seldom site for plasmacytoma. Cysts of the ciliary body have been reported in 33–50 % of myeloma patients, and retinal vascular lesions have

been reported in up to 66 %. Corneal and orbital involvement is less common. Males are affected more frequently than females in a 3 to 1 ratio (3, 4).

ASCT is the first-line treatment for patients with myeloma. After ASCT, relapses may be seen. Second autologous transplant, allogenic transplant and medications such as bortezomib, thalidomide are used for the treatment of relapsed or refractory myeloma. The clinical presentation of relapse after ASCT of myeloma is very heterogeneous. Isolated ocular relapse is very rare after ASCT. Terpos et al. reported that 14 of 147 patients who underwent ASCT relapsed with plasmacytomas, without marrow involvement. Median time reported was 24 months (range: 2–72 months) from transplant to relapse without any ocular findings in those patients (5). Whereas, ocular relapse occurred in second month in our patient. The optimal treatment strategy for isolated EP relapse remains unclear. EP and MM show significant immunophenotypic differences, some of which may be of both diagnostic utility and biological relevance. In contrast to primary EP, secondary extramedullary spread of MM frequently indicates aggressive disease and often heralds a poor prognosis (6).

The treatment of choice is external beam radiation at low doses (40–60 Gy) with good results in almost all cases. Irradiation of regional lymph nodes is not done routinely. Surgery and chemotherapy are used when radiotherapy fails to control the process or is not indicated (7).

Patriarca et al. has described the first case in the literature in which bortezomib was very effective in producing a partial remission (PR) in a patient who had relapsed post-ASCT and mini allo transplant with multiple bone plasmacytomas and central nervous system involvement, without any evidence of marrow recurrence. Patient continues to be in PR for 10 months post-bortezomib administration. Therefore, bortezomib may be another valuable agent for these cases. However, this has to be proven in large trials (5, 8).

In conclusion, ocular relapse should be considered if there are ocular findings. Bortezomib and steroid may be useful for ocular extramedullary relapse.

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Received December 2, 2008.
Accepted September 20, 2010.