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Case report: clinical manifestation of a rare myeloma associated retinopathy

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Abstract

Aim: Multiple myeloma is a cancerous disease caused by plasma cell proliferation and mainly affects people in their adulthood. Ophthalmic presentation of multiple myeloma is not typical and appropriate tactics of treatment rely on clinical variations. In this case, we discuss retinal involvement in multiple myeloma which was treated with systemic chemotherapy, plasmapheresis and intravitreal injections of anti-VEGF.

Results: A 59-year-old woman with recently diagnosed multiple myeloma underwent ophthalmological examination due to decreased visual acuity. Edema of the optic nerve disc, multiple retinal hemorrhages, cotton-wool spots and Roth spots were seen in both eyes on fundus examination and OCT revealed macular edema in both eyes. Systemic treatment with chemotherapy and two plasmapheresis reduced retinopathy symptoms, although macular edema remained clinically significant. To reduce macular edema by preventing angiogenesis and further hemorrhage formation intravitreal anti-vascular endothelial growth factor bevacizumab was decided to be used.

Conclusions: Evaluation of multiple myeloma patients should be comprehensive in regard to their symptoms and complaints. Despite the rare ocular manifestations, multiple myeloma patients with decreased visual acuity have to be frequently examined by an ophthalmologist and eligible treatment should be selected to control ocular symptoms.

Keywords: multiple myeloma, ocular manifestation, retinopathy, Roth spots.

Introduction

Multiple myeloma (MM) is a rare proliferative disease that accounts for approximately 1% of neoplasms and 12 – 15% of all hematological malignancies [1]. The risk of getting MM grows with age, therefore, it mostly affects adults over 65 years old. Treatment of MM is developing fast and now the 5-year survival rates are 52.2% [2,3]. Ocular manifestations of this cancerous disease is not common and it usually shows as plasmacytoma of the soft tissues or infiltration of anterior segment of the orbit [4,5].

We present a case of a patient who has demonstrated typical clinical symptoms of a rare myeloma related retinopathy, which was treated with systemic chemotherapy, two plasmapheresis and intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections.

Case Report

A 59-year-old female presented for ophthalmological examination complaining of worsening vision during the last month. The patient has been recently diagnosed with MM after elevated rates of IgM and serum protein was found. MM was confirmed with trepan biopsy. The prevailing symptoms were dizziness, general fatigue and weakness, decreased visual acuity. Other test results showed anemia, renal dysfunction and lesions in spinal vertebrae. She underwent chemotherapy with Velcade (bortezomib), thalidomide and dexamethasone (VTD) immediately. Two plasmapheresis were administered later due to hyperviscosity symptoms.

Ophthalmological examination was performed and best corrected visual acuity was 0,15 in the right eye (OD) and 0,8 in the left eye (OS). The intraocular pressure (IOP) was 18,9 mmHg and 17,3 mmHg respectively.

During slit-lamp biomicroscopy there were no significant changes of anterior segment observed, although fundus examination revealed edema of the optic nerve disc (OND),multiple retinal hemorrhages of various size, cotton-wool spots and few white centered hemorrhages similar to Roth spots in both eyes. One preretinal hemorrhage was noted in the OD below OND [Figure 1]. Optical coherence tomography (OCT) showed macular edema in both eyes, significantly larger in OD together with preretinal hemorrhage[Figure 2].No treatment additional to chemotherapy was added at that time and patient was left for monitoring.

Three weeks later patient came back to the clinic and has complained of complete vision loss in the right eye. She was examined repeatedly and haemophthalmus without retinal detachment in OD was found on ocular ultrasound. Intravitreal surgeon recommended observation and follow-up to evaluate the dynamics of the intravitreal hemorrhage. Blood in the vitreous body reabsorbed and during the later follow-ups positive dynamics of the retinal and preretinal hemorrhage were observed on fundus examination [Figure 3].

However, macular edema in OD was still significant and caused decrease in visual acuity. Consequently, to reduce macular edema further retinal hemorrhages treatment with intravitreal bevacizumab injections was decided.

After two injections, macular edema decreased, but still remained and patient indicated that her vision has improved. Best corrected visual acuity was 0,1 in OD and 1,0 in OS. According to the positive response, intravitreal bevacizumab was continued

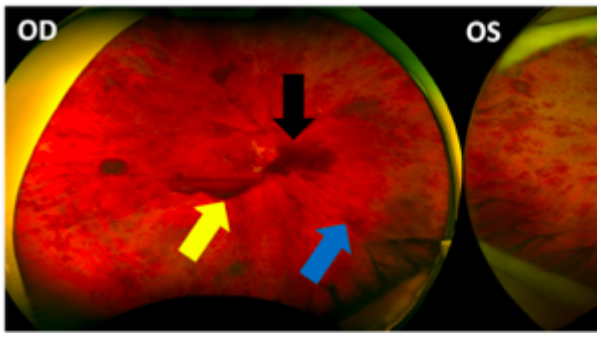

Figure 1. Fundus photography: OD – right eye, OS – left eye, preretinal hemorrhage (yellow arrowhead), intraretinal hemorrhage (black arrowhead), Roth spot (blue arrowhead) and cotton-wool spot (white arrowhead).

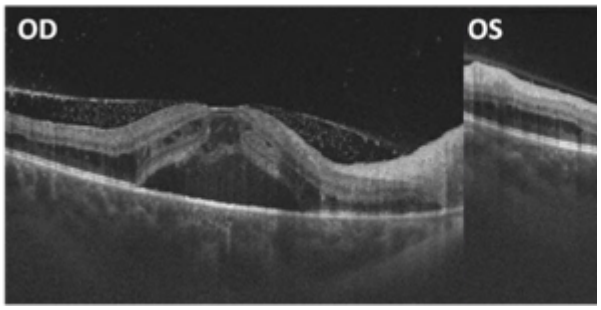

Figure 2. Optical coherence tomography: OD – right eye, OS – left eye, macular edema significantly larger in OD, preretinal hemorrhage in OD.

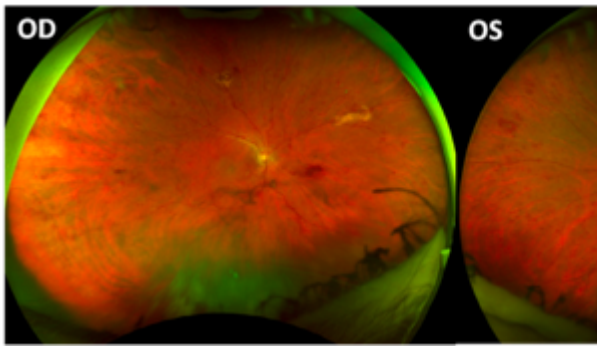

Figure 3. Fundus photography: OD – right eye, OS – left eye, reabsorbed intravitreal hemorrhage, preretinal hemorrhage. Fewer intraretinal hemorrhages compared to Figure 1 findings.

Discussion

Multiple myeloma is a type of cancer that causes plasma cells to proliferate and accumulate in the bone marrow, causing reduction of healthy antibodies [6]. IgG (52 %) and IgA (21 %) are the most common types of abnormal immunoglobulins that MM produces. [7]. In our case IgM protein was present, which, according to studies, accommodates only for 0,5 % of all MM cases [8].

Multiple myeloma is diagnosed when there is at least 10 % of plasma cells in the bone marrow, monoclonal protein and evidence of end-stage organ damage [7]. End-stage organ damage is defined by findings of: hypercalcemia, renal failure, anemia and bone lesions (CRAB) [9]. Patients with MM usually present with bone pain, fatigue and recurrent infections [10].

Ophthalmic manifestations of MM tend to be rare and variable. Due to its complex pathophysiology, MM can involve almost all structures of the eye including orbit, conjunctiva, uvea, lacrimal glands [11]. The main pathophysiological mechanism of disease in the eye is due to infiltration of plasma cells to the eye tissue and hematological abnormalities [10]. Orbital involvement is very rare, but it is most commonly described manifestation of ocular MM in the literature. Orbital MM involves unilateral proptosis, decreased vision, diplopia, ptosis [11]. These symptoms usually develop over several weeks or months and might be the first sign of the disease at all [11]. Corneal and conjunctival deposits are much rarer manifestation of ocular involvement in MM. Corneal crystals or copper depositions, in MM patients, usually are asymptomatic, but if distributed in the center of the cornea, might affect the vision [12,13]. Neuro-opthalmic manifestation of the disease is either due to hematological abnormalities or due to plasma cell infiltration of the optic nerve [10].

In our case, patient presented to the opthalmologist due to hyperviscosity induced retinopathy. In MM patients, hyperviscosity syndrome occurs due to an overproduction of monoclonal immunoglobulin in the bone marrow [14]. This increases the plasma viscosity which impairs the microcirculation [14,15]. Hyperviscosity in the eye manifests as dilated retinal veins, superficial and deep retinal hemorrhages, vitreous and subhyaloid bleedings [16]. Roth spots and cotton-wool spots might also be present in MM patients, as it was in our case [17]. All of this retinopathy manifestations also might be present in other systemic diseases, such as hypertension or diabetes mellitus, so an ophthalmologist should be alert if these signs are present [18].

Our patients ocular manifestation of MM, was treated with intravitreal injections of anti-VEGF – bevacizumab (Avastin). Bevacizumab, when used systemically, regresses the vascularisation of tumours and inhibits the formation of new tumor vasculature, thereby inhibiting tumor growth [19]. In this case it was used to control macular edema and prevent from further intravitreal hemorrhages, that might result in total loss of vision for the patient [20]. Patient underwent 2 injections of bevacizumab which helped to control ocular hemorrhages, but macular edema was still present consequently, additional injections will be performed. In other studies intraocular bevacizumab was used to control secondary glaucoma and binocular metastasis caused by MM and the most remarkable effects included the rapid decline in IOP to normal levels and the resolution of iris neovascularization [21].

To control the systemic manifestation of multiple myeloma patient was treated with 2 courses of chemotherapy using VTD and two plasmapheresis to control hyperviscosity syndrome. Patient responded well to chemotherapy – levels of IgM dropped significantly.

All in all, ocular manifestations of plasma cell neoplasms are rare, but can present in a variety of signs and symptoms. It is important that all eye care practitioners follow up with patients frequently, since MM can affect all ocular tissues. With new treatments emerging MM patients are now living longer with their disease and will require constant monitoring of their visual system.

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