Ocular lymphoma in two cases

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ABSTRACT

We are reporting primary ocular lymphoma in two male patients who are sixty seven and seventy years old. The first case was admitted to the hospital after an ophthalmologic examination that revealed a soft, pink homogenous vascular mass originating from the conjunctiva, and extending behind the bulbous oculi, completely covering the upper quadrant of the right eye. There was also right axial exophthalmy. Ocular adnexal and intraocular involvement was seen at physical examination and orbital imaging. Optic atrophy and retinal pigment epitheloid changes were seen at fundoscopic examination. Biopsy taken from the right eye revealed mucosa associated lymphoid tissue (MALT) lymphoma. The case was diagnosed as primary ocular adnexal and intraocular lymphoma. Left eye was normal. The cranial, thoracic and abdominal imaging examinations and other laboratory analysis were normal. He received six courses of CNOP (cyclophosphamide, mitoxantrone, vincristine, prednisolone) chemotherapy and full remission was achieved following radiotherapy. He is in full remission for two years. The second case came with proptosis and chemosis at the lower part of left eye. The cornea and anterior chamber were normal. At fundoscopy, there was superficial haemorrhage on temporal edge of discus, wide haemorrhage at the periphery of discus at the same level with parafoveal little haemorrhage focus. Orbital imaging revealed a retroorbital mass. A biopsy was done from the retroorbital mass by craniotomy. B-cell small lymphocytic lymphoma was diagnosed. Right eye was normal. He received radiotherapy.after a diagnosis of ocular adnexal lymphoma.

Key Words: Lymphoma, MALT, Ocular.

ÖZET

Oküler lenfomalı iki olgu

Primer oküler lenfomaların nadir görülmesi nedeni ile tarafımızdan tespit edilen altmışyedi ve yetmiş yaşında, iki erkek olgu sunulmuştur. İlk olguda göz muayenesinde sağ gözde konjunktivadan başlayan ve arkaya doğru uzanan yumuşak kıvamda ve üst kadranı tamamen kaplayan, pembe homojen vasküler kitle, sağ aksiyel ekzoftalmi tespit edildi. Fundoskopide optik atrofi ve makulada retinal pigment epitel değişiklikleri görüldü. Muayene bulguları ve orbital görüntüleme tetkiklerinde oküler adneksal ve intraoküler tutulum görüldü. Sağ göz konjunktivadan alınan biyopside MALT lenfoma rapor edildi. Bu nedenle hasta primer oküler adneksal ve intraoküler lenfoma kabul edildi. Sol göz normal olarak değerlendirildi. Hastanın kranial, toraks, tüm batın bilgisa-

yarlı tomografi ve diğer laboratuvar tetkikleri normal bulundu. Olgu evre 1E kabul edildi ve altı kür CNOP (cyclophosphamide, mitoxantrone, vincristine, prednisolone) kemoterapisi uygulandı. %50 remisyona girmesi nedeniyle takiben radyoterapi verildi, tam remisyona girdi ve takibe alındı. İkinci olguda göz muayenesinde sol gözde proptozis ve altta kemozis vardı. Kornea ve ön segment normaldi. Fundoskopide disk üzerinde temporal kenarda yüzeyel hemoraji diskin dışında 12 hizasında geniş hemoraji, parafoveal küçük hemoraji odağı vardı. Orbital görüntüleme tetkiklerinde retroorbital kitle tespit edildi. Sağ göz normal olarak değerlendirildi. Kraniotomi ile sol retroorbital kitleden biyopsi alındı. B tipi küçük hücreli lenfoma rapor edildi. Oküler adneksal lenfoma tanısı ile radyoterapi başlandı.

Anahtar Kelimeler: Lenfoma, MALT, Oküler.

INTRODUCTION

Ocular lymphoma is a rare type of lymphoma. Ocular adnexa is evaluated as an extra lymphatic region and composed of conjunctiva, eyelids, orbita and lacrymal glands. Ocular adnexal lymphoma may be primary or secondary. It is usually seen at sixth and seventh decades of life. They are usually diffuse low-grade lymphomas and show 10-15% follicular formation[1,2]. Such lymphomas are classified under mucosa associated lymphoid tissue (MALT) lymphomas. Primary diffuse large B-cell, peripheral T-cell subtypes and secondary involvement can also be seen[3-5]. Front part of the superior orbita is the most frequently involved localization, and 15% percent of the cases are bilateral[2,6]. Cases who have single or both eye involvement are accepted as stage IE[7]. Diplopia, proptosis, ptosis, pain, conjunctival congestion, soft tissue swelling, palpable mass and rarely glaucoma can be present. Patients have no visual problems, unless apex of the bulbous is involved[3,6,8]. Intraocular lymphoma is extremely rarely seen and uvea, retina, vitreous and central nerve system (CNS) are frequently involved. CNS involvement originates from cerebrum, spinal cord, leptomenings and eyes. Vitreous, retina, optic nerve involvement might be seen[9,10]. The definite diagnosis can be made by biopsy, and usually of B-cell type. Primary T-cell lymphomas are exceedingly rare. Ocular lymphomas can be localized at single or both of eyes without dissemination[7,11-13]. Orbital ultrasonography, computerized tomography and magnetic resonance imaging are helpful in diagnosis[14].

CASE REPORTS

Case 1

A 62-years-old male patient was admitted to our clinic with complaints of a gradually growing mass on the right eye and visual problems. Patient's history was unremarkable. In ophthalmologic examination, we found a soft, pink homogeneous vascular mass which originated from right limbal conjunctiva, extended towards the behind of bulbous, covered entirely right upper quadrant and with right axial exophthalmus (Figure 1). Right eye tension was 21 mmHg and left eye tension was 15 mmHg. In fundoscopy, optic atrophy and retinal pigment epitheloid changes were determined in right eye (Figure 2). Left eye was normal. The remaining physical examination was unremarkable.

Laboratory analysis revealed a sedimentation rate: 14 mm/hour, leukocyte: 6920/mm^3, Hb: 14.1 g, Hct: 42.4%, platelet: 245.000/mm^3, neutrophil: 72%, lymphocy-

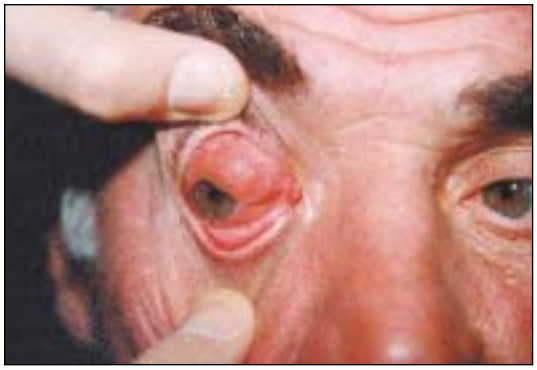

Figure 1. Pink homogeneous vascular mass in the right eye.

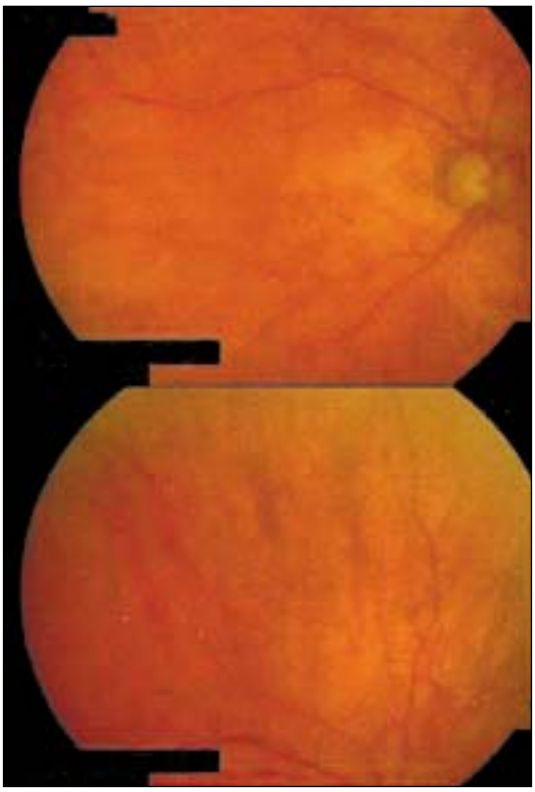

Figure 2. In fundoscopy, optic atrophy and retinal pigment epitheloid changes were determined in right eye.

te: 18%, monocyte: 8%, eosinophil: 1%, basophil: 1%. Biochemistry results were normal. Serologic tests for anti-HIV 1-2, HBs antigen, anti-HCV were negative, urine analysis was normal, EKG was normal. On whole abdomen ultrasonography, there was a 12 mm diameter calcification in anterior segment of the right lobe of the liver. In the middle pole of left kidney a 2 cm diameter simple cortical cyst was seen. Pulmonary X-ray and neck, thorax, abdomen computerized tomographies were normal. Two pieces of white-coloured biopsies were performed from the conjunctiva. In the cross-sections of tissue samples, lymphocytic proliferation which was composed of small, middle size, lymphocytes with round, hyper chromatic nucleus and scant cytoplasm were seen.

In immunohistochemical study, B-cell markers were positive, T-cell markers were negative on tumour cells (Figure 3). Conjunctival MALT lymphoma was diagnosed. Bone marrow aspiration and biopsy was normal. Orbital bones were normal, and there were no abnormality in retroorbital space and orbital muscles in orbital computerized tomography. Lacrymal glands were normal. A 12 mm size, disseminated nodular wall thickening was seen on behind upper of right bulbous oculi. There was no evident abnormality in muscles or in optic nerve. The solid mass, which surrounded medial and lateral posterior bulbous oculi, and intraconal part of optic nerve, extended to lateral rectus muscle and also extended to lacrymal gland on superior bulbous, approximately 25 x 16 x 10 cm, lobular contoured on posterior, was seen in right orbital magnetic resonance imaging. There was oedema in subcutan eous soft tissue of right periorbital region and proptosis because of the mass on right bulbous oculi (Figure 4). There was no evident thickening at retroocular muscles. Oedema was not seen at retroorbital fat tissue. Left orbital tissues were evaluated as normal. International Prognostic Index was evaluated as 2 (low middle) owing to old age and extra nodal involvement.

Case 2

A 70-years-old male patient was admitted to a health centre with complaints of a burning sensation in the left eye. There was

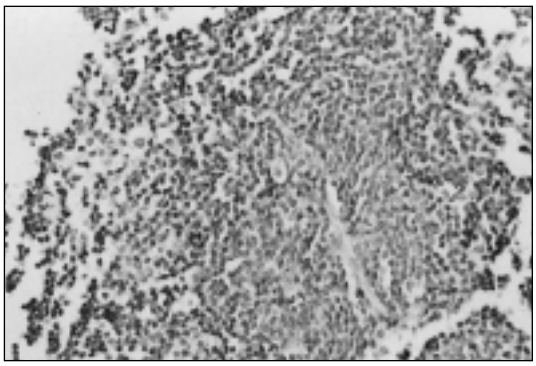

Figure 3. In the cross-sections of tissue samples, lymphocytic proliferation which was composed of small, middle size, lymphocytes with round, hyper chromatic nucleus and scant cytoplasm were seen.

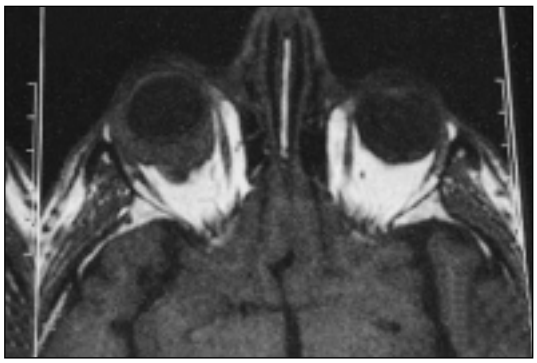

Figure 4. A 12 mm size, disseminated nodular wall thickening was seen on behind upper of right bulbous oculi in orbital computerized tomography.

hyperlacrimation, pain and feeling of being pushed to front. The complaints had begun six months ago, the left eye had been pushed to front gradually, there was little left eye pain. The left eye had become redden gradually. He had complaints of left face numbness, becoming matted and night sweating. He had no weakness, and loss of weight. At physical examination blood pressure was 120/80 mmHg, pulse: 60/min, fever: 37.5°C. In ophthalmologic examination right eye and fundoscopy was normal. Left eye vision was 0.6. There was proptosis and chemosis (Figure 5). Cornea and front segment were normal. At fundoscopy, oedema was not seen on optic discus. There was superficial haemorrhage on temporal edge of discus with prudential deep haemorrhage, with a diameter of 1.5-2 discus. There was haemorrhage at the same level at hour twelve and it was two discuses diameter distant to discus. There was a parafoveal little focus of haemorrhage. Upper and below movements of left eye were restricted, the patient described diplopia, because left eye had no exterior movement (to left side). Patient's other systemic examinations were normal. Laboratory analysis revealed; leukocyte: 11.200/mm^3, Hb: 16.1 g, Hct: 48.6%, platelet: 318.000/mm^3, on blood smear; neutrophil: 76%, lymphocyte: 14%, monocyte: 8%, eosinophil: 1%, basophil: 1%. Biochemical analysis and pulmonary X-ray were normal. Serologic tests for HBs antigen, anti HIV 1-2, anti HCV was negative, urine

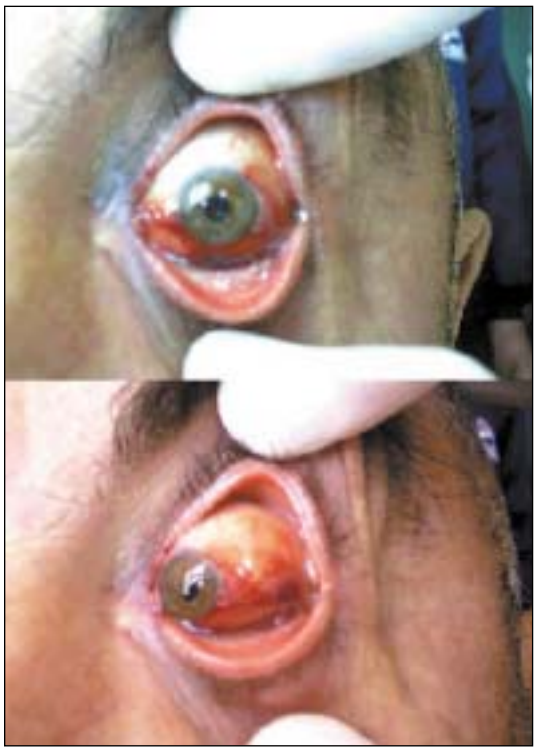

Figure 5. Proptosis and chemosis in the left eye.

analysis was normal and EKG was normal. Proptosis was seen in left bulbous oculi and there was an irregular bordered solid mass, which was seen on posterior and inferior part of interior left orbita, situated intraconally at retro orbital region, infiltrating lateral and inferior rectus muscles, extending to inferior and superior orbital fissures as far as the optic canal, surrounded the optic nerve and invading the optic nerve sheath, in leftorbital magnetic resonance imaging (Figure 6). Right bulbous ocular, retroocular muscles, retroocular distance, optic nerve, and, lachrymal gland were normal. Orbital computerized tomography showed a soft tissue lesion which oblitered infratemporal fossa at left and pterygopalatin fossa, infiltrating left lateral pterygoid muscle, filling up the orbital apex, surrounding extraoculer muscles and the left optic nerve. Left bulbous oculi was exophtalmic. Right bulbous ocular, retrobulber distance, extraoculer muscles and the optic nerve were normal. Cranial computerized tomography was normal. Punch biopsy was

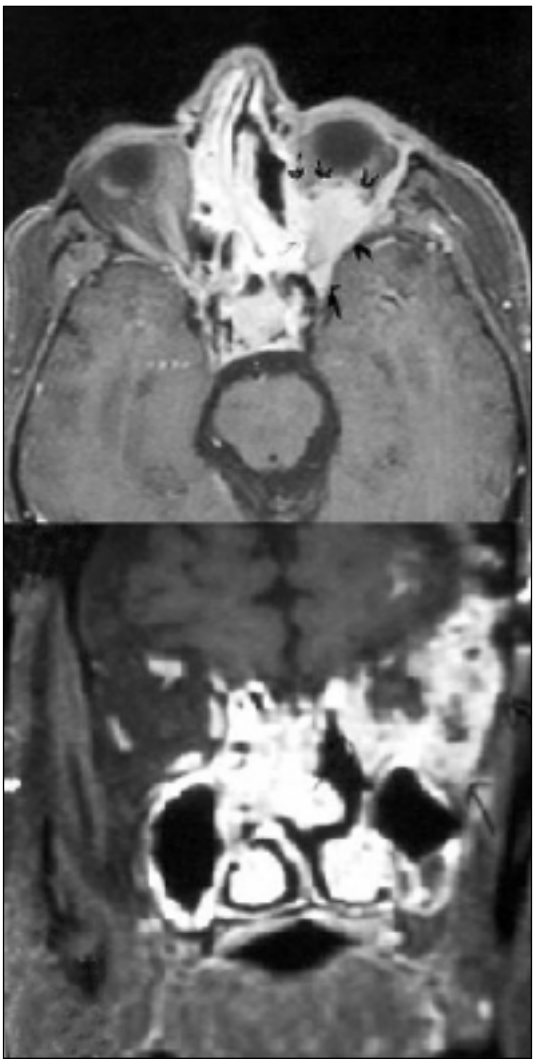

Figure 6. Left orbital magnetic resonance imaging.

done from the left eye retroorbital mass, and malignancy was not diagnosed. The patient later admitted to our hospital. Biopsy was done from the mass by craniotomy. It was reported as B-cell small cell lymphoma. Postoperative cranial magnetic resonance imaging was normal except the left orbital mass. Patient's neck, thorax, and abdominal computerized tomographies were normal. Bone marrow biopsy and aspiration were normal. The patient was diagnosed as primary, stage IE ocular adnexal lymphoma. International Prognostic Index was evaluated as 2 because of old age and extra nodal involvement.

DISCUSSION

The first case was diagnosed as primary adnexal and intraocular MALT lymphoma with orbital computerized tomography and magnetic resonance imaging findings. Lymphadenopathy was not found on patient's physical examination. Bone marrow aspiration and biopsy were normal. Patient was admitted stage IE. Patient's LDH was normal, performance status was evaluated zero. Six courses of CNOP (cyclophosphamide, mitoxantrone, vincristine, prednisolone) chemotherapy were given. The conjunctival lesion had regressed 50% at the end of chemotherapy and there was still intraocular involvement on fundoscopy. Radiotherapy was given. The conjunctival lesion and the intraocular involvement disappeared at the end of radiotherapy at fundoscopy. It was seen that the patient was still in remission at the end of two years on controls. The cause of giving chemotherapy is that the patient has both ocular adnexal and intraocular lymphoma. Long time remission was reported only with radiotherapy in adnexal lymphomas. But, early relapses was reported although recovery was obtained only with radiotherapy in intraocular lymphomas. Therefore, if the patient enters full remission, it would not last long. If the diagnosis is intraocular lymphoma, chemotherapy is the first choice. As the remission ratio is low, relapse ratio is high with only radiotherapy at intraocular lymphomas. The second patient was diagnosed as ocular adnexal B-cell small lymphocytic lymphoma with clinical findings and imaging tecniques. He had no peripheral lympadenopathy. Chemotherapy was not given because of only ocular adnexal lymphoma. Radiotherapy was started. Chemotherapy was approved only when the patient is refractory to radiotherapy or relapses.

The patients who were diagnosed as ocular adnexal low stage lymphoma are at stage IE or stage IIE. Local radiotherapy is the therapy preference in localized disease. Full remission was reported with radiotherapy. Disseminated disease is treated with chemothe-

rapy. CNOP, DHAP therapies initial choices in chemotherapy[1,2]. Baumann et al observed therapeutic levels in vitreus fluid after single high dose cytosine arabinoside (3 g/m^2) infusion in patient whose diagnosis was disseminated large cell lymphoma and characterized with ocular involvement and refractory to conventional chemotherapy of Ara-C with standard doses of methotrexate[15]. High dose Ara-C may alsobe useful as salvage therapy in relapsed cases[14]. Local ocular therapy also results in high drug concentration and was successful in animal experiments. Intraocular injections of methotrexate was used alone or with thiotepa. Antineoplastic drugs are limited for local ocular therapy, because they may be toxic to the retina and the optic nerve. Methotrexate is not toxic when 400 µg was injected to the human eye. Fluorouracil and corticosteroids are not toxic when they are injected to animal eye[16]. Physical examination and a blood examination at three months intervals, imaging examinations at six months must be done after ocular lymphoma cases entered remission. Prognosis is bad in patients who have not received therapy. Average survival is 1.8-3.3 months. It was 42.5 months with aggressive therapy. Relapse was usually seen within the first three years of diagnosis and five years survival is less than 5%[10]. Therapy recommendations are variable for primary intraocular lymphoma. Cases who have ocular and CNS involvement respond to CNS and ocular radiation well but they have a high relapse ratio, and average survival is 10-18 months. Combined radiotherapy and chemotherapy provide longer remission in these cases[6].

REFERENCES

1. Jakobiec FA, Knowles DM. An overview of ocular adnexal lymphoid tumors. Trans Am Ophthalmol Soc 1989;87:420-44.
2. Liesegang TJ. Ocular adnexal lymphoproliferative lesions. Mayo Clin Proc 1993;68:1003-10.
3. Kostas V. Vogiatzis, lymphoid tumors of the orbital and ocular adnexa: a long-term follow-up. Annals of Ophtalmology 1984;16:1045-55.
4. Cahill M, Barnes C, Moriarty P, Daly P, et al. Ocular adnexal lymphoma comparison of MALT lymphoma with other histological types. Br J Ophthalmol 1999;83:742-7.
5. Char DH, Ljung BM, Deschenes J, Miller TR. Intraocular lymphoma; immunological and cytological analysis. Br J Ophthalmol 1988;72:905-11.
6. Qualman SJ, Mendelsohn G, Mann RB, Green WR. Intraocular lymphomas. Natural history based on a clinicopathologic study of eight cases and review of the literature. Cancer 1983;52:878-86.
7. Bessell EM, Henk JM, Wright JE, Whitelocke RA. Orbital and conjunctival lymphoma treatment and prognosis. Radiother Oncol 1988;13:237-44.
8. Buettner H, Bolling JP. Intervitreal large-cell lymphoma C. Maya Clin Proc 1993;68:1011-5.
9. Velez G, Smet MD, Whitcup SM, Robinson M, et al. Iris involvement in primary intraocular lymphoma: report of two cases and review of the literature. Surv Ophtalmol 2000;44:518-26.
10. Gill MK, Jampol LM. Variations in the presentation of primary intraocular lymphoma: case reports and a review. Surv Ophtalmol 2001;45:463-71.
11. Char DH, Ljung BM, Miller T, Phillips T. Primary intraocular lymphoma (ocular reticulum cell sarcoma) diagnosis and management. Ophthalmology 1988;95:625-30.
12. Shibata K, Shimamoto Y, Nishimura T, Okinami S, et al. Ocular manifestations in adult T-cell leukemia/lymphoma. Ann Hematology 1997;74:163-8.
13. Peterson K, Gordon KB, Heinemann MH, DeAngelis LM. The clinical spectrum of ocular lymphoma. Cancer 1993;72:843-9.
14. Jakobiec FA, Iwamota T, Patell M, Knowles DM. Ocular adnexal monoclonal lymphoid tumors with a favorable prognosis. Ophtalmology 1996;103:631-5.
15. Baumann MA, Ritch PS, Hande KR, Williams GA, et al. Treatment of intraocular lymphoma with high-dose Ara-C. Cancer 1986;57:1273-5.
16. Velez G, Yuan P, Sung C, Tansey G, et al. Pharmacokinetics and toxicity of intravitreal chemotherapy for primary intraocular lymphoma. Arch Ophtalmol 2001;119:1518-24.

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