Treatment of Choroidal Neovascular Membrane Secondary to Tuberculoma in a Case of Miliary Tuberculosis

Miliyer Tüberkülozlu Hastada Tüberküloma Sekonder Koroid Neovasküler Membran Gelişimi ve Tedavisi

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ABSTRACT

Twenty year-old female patient was consulted to our clinic from infectious diseases clinic. Ophthalmoscopic examination revealed presence of vitritis. There were multiple foci of choroiditis in both eyes and a chorioretinitis scar at temporal area of macula on the left eye.CNVM (Choroidal neovascular membrane) was detected over the scar tissue. Lung high-resolution CT (HRCT) revealed signs consistent with tuberculosis (TB). PPD test result was 16 mm, therefore, she was diagnosed with miliary TB, and systemic antituberculosis treatment was initiated. Optic coherence tomography (OCT) showed as an active type III CNVM /RAP (Retinal Angiomatous Proliferation). It was considered as an active CNVM as there was hemorrhage on the membrane and since it had an extrafoveal localization and the patient was pregnant argon laser photocoagulation (ALP) was applied.

: Ocular tuberculosis, retinal angiomatous proliferation, tuberculoma, choroidal neovascular membrane, uveitis.

ÖZ

Yirmi yaşında bayan hasta kliniğimize enfeksiyon hastalıkları kliniğinden konsulte edildi.Oftalmoskopik incelemesinde vitritis varlığı saptandı. Her iki gözde multipl koroidit odakları ve sol gözde fovea temporalinde koryoretinit skarı mevcuttu. Skar dokusu üzerinde KNVM (koroidal neovasküler membran) tespit edildi. Akciğerin yüksek çözünürlüklü BT'sinde (HRCT) tüberküloz (TB) ile uyumlu bulgular saptandı.. PPD testi sonucu 16 mm idi. Hastaya miliyer TB tanısı kondu ve sistemik antitüberküloz tedaviye başlandı. Optik koherens tomografisi'nde (OKT) lezyon üzerinde aktif tip III KNVM / RAP (Retinal Anjiyomatöz Proliferasyon) saptandı. Membran üzerinde hemoraji olduğu için aktif bir KNVM olarak düşünüldü ve hasta hamile olduğu için ekstrafoveal lokalizasyonlu lezyona argon lazer fotokoagulasyon (ALP) uygulandı.

Anahtar Kelimeler: Oküler tüberküloz, retinal anjiyomatöz proliferasyon, tüberkülom, koroidal neovasküler membran, üveit.

INTRODUCTION

Ocular tuberculosis (OTB) is a form of TB. Diagnosis of OTB can be with clinical evaluation and laboratory investigations. Our study describes a case where the diagnosis of OTB which was confirmed with microbiological and radiological evaluation. Multifocal choroiditis is the most clinical presentation of OTB with deep, multiple, discrete, yellowish lesions.[1] Choroidal granulomas are the widespread dissemination of mycobacterium tuberculosis via hematogenous spread and the choroiditis is likely to be due to hypersensitivity reactions to the bacterial protein.[2] History of tuberculosis exposure, clinical examination, positive tuberculin test, HRCT had been used evaluating patients of retinitis for systemic tuberculosis. Posterior uveitis including choroidal tubercules is the most common ocular clinical presentation of OTB.[3] In an immunocompromised patient, it is generally a self-limited infection; but severe compli-

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Geliş Tarihi - Received: 01.06.2017
Kabul Tarihi - Accepted: 23.08.2017
Ret-Vit 2018; 27: 288-291

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cations, such as retinochoroidal involvement, have been known to occur. Our study describes a case where the diagnosis of OTB which was confirmed with microbiological and radiological evaluation.

CASE REPORT

Infectious diseases clinic consulted a 20 year-old female patient to our clinic for her complaints of seeing flying spots and blurred vision in both eyes. One week ago, she was presented to emergency service with fever. Because of presence of neck stiffness and positive Kernig sign, she was admitted to infectious diseases clinic with an initial diagnosis of meningitis. In her cranial computed tomography (CT) and magnetic resonance imaging (MRI) examinations, there were lesions affecting white matter in brain stem and cerebellum, some of which showed contrast uptake. Tuberculous meningitis was considered in the patient.

Lumbar puncture was planned for the patient and in the fundus examination, grade 2 papilledema and multiple retinitis were observed. High-resolution computed tomography (HRCT) revealed signs consistent with TB. Lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis showed increased protein and reduced glucose levels, and CSF PCR analysis was reported as positive for mycobacterium. PPD test result was 16 mm, therefore, she was diagnosed with miliary TB, and systemic antituberculosis treatment was initiated. Laboratory results were negative for infectious markers except for Toxoplasma IgG positivity. The patient's laboratory results were negative for infectious markers but Toxoplasma IgG was positive . white blood cell count was (WBC):18,000/mcL . There were no pathological results in routine clinical chemistry and urinalysis tests.

Complete ophthalmological examination performed. Visual acuity was 20/20 bilaterally , anterior chambers of both eyes were free from inflammation, intraocular pressures were normal. Fundus examination revealed 1+ vitreous haze and cell in both eyes. There were multiple foci of choroiditis at upper nasal segment of the right eye (Figure 1A) and on the left eye, there were multiple foci of choroiditis around the macula, chorioretinitis scar and associated choroidal neovascular membrane (CNVM) over the scar tissue temporal to the macula. (Figure 1B)

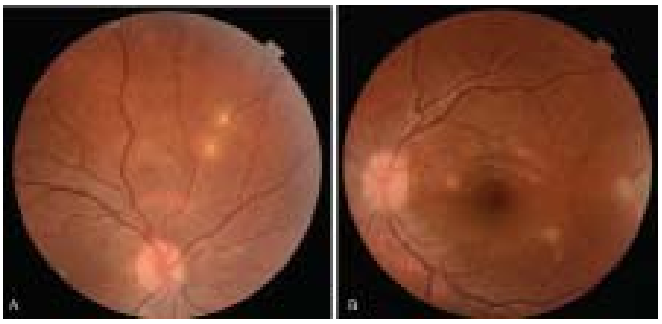

Figure 1. A) *Multiple foci of choroiditis at upper nasal segment of the right eye.* **B)** *Multiple foci of choroiditis around the macula, chorioretinitis scar and CNVM over the scar tissue temporal to the macula.*

A detailed anamnesis from the patient revealed that she had applied to ophthalmology clinic with complaints of blurred vision and redness at her left eye 3 months before her presentation to emergency service. She was treated for ocular toxoplasmosis and the clinical response to a combination trimethoprim sulfamethoxazole and clindamycin tablets .

Fundus fluorescein angiography (FFA) revealed two foci of hyperfluorescence superior to the optic nerve on the right eye and hyperfluorescent foci of multiple choroiditis at the posterior pole of the left eye. (Figure 2A) At the temporal region of posterior pole of the left eye, there was hyperflu-

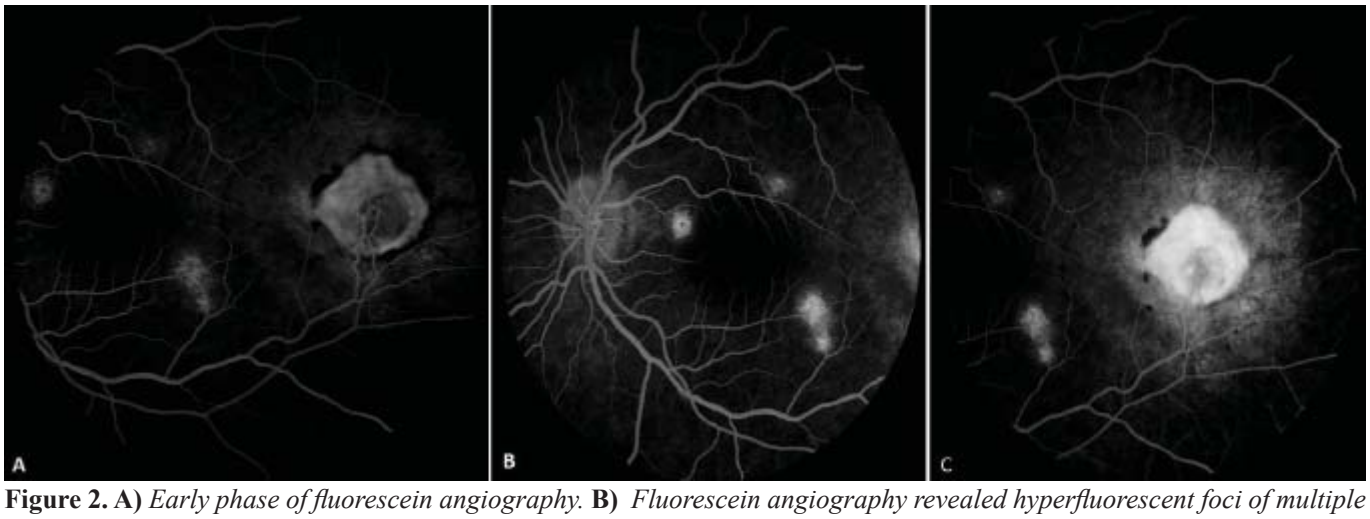

Figure 2. A) *Early phase of fluorescein angiography.* **B)** *Fluorescein angiography revealed hyperfluorescent foci of multiple choroiditis at the posterior pole of the left eye.* **C.** *Fluorescein angiography revealed hyperfluorescence at an area corresponding to chorioretinitis scar , at the temporal region of posterior pole of the left eye.*

orescence at an area corresponding to chorioretinitis scar. (Figure 2B) OCT revealed hypereflectance of CNVM both under the retina and the retinal pigment epithelium over the scar tissue and hyporeflectance column due to the blood vessels at the center of the lesion. (Figure 3A) The lesion was considered as an active type III CNVM so called retinal angiomatous proliferation (RAP) which may be seen commonly in TB granuloma and since it had an extrafoveal localization and the patient was pregnant , Argon laser photocoagulation (ALP) was applied to the lesion (52 pulses, 200um, 320mW, 0.2s). (Figure 4A-B)

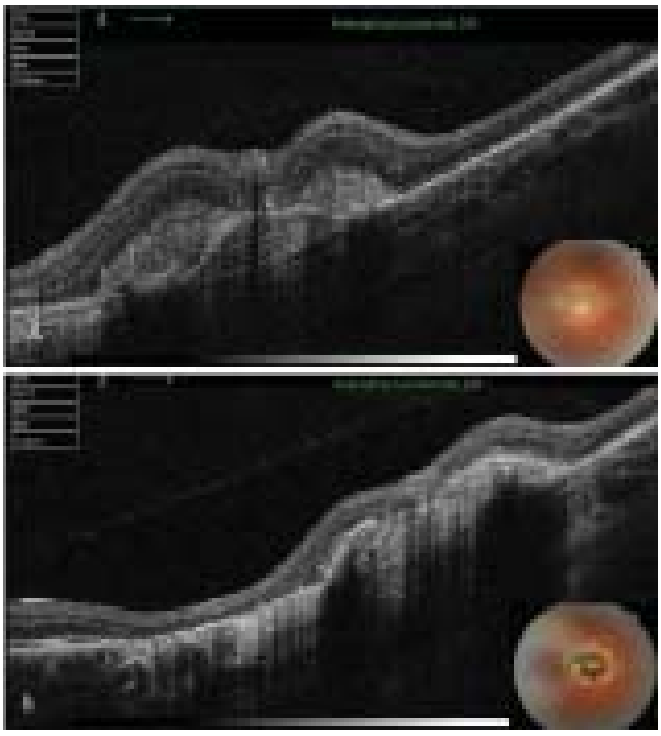

Figure 3. A) *OCT shows hypereflectance of CNVM both under the retina and the retinal pigment epithelium over the scar tissue and hyporeflectance column due to the blood vessels at the center of the lesion. Presence of new intraretinal capillaries that grow toward the subretinal space and choroid described as RAP.* **B)** *OCT shows shrinkage in scar tissue, decrease in fluid decline in CNVM was detected in OCT controls.*

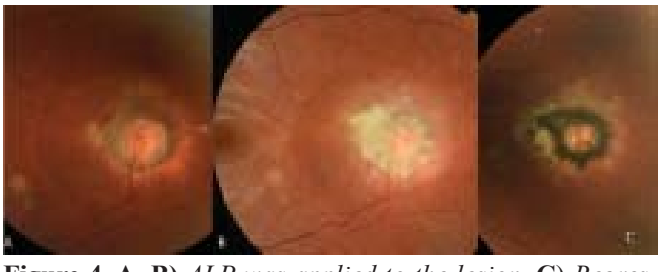

Figure 4. A, B) *ALP was applied to the lesion.* **C**) *Regression of CNVM and pigmentation over the lesion.*

As patient was receiving anti-TB therapy, no additional treatment was planned. She had regression of CNVM and pigmentation over the lesion at her control examinations. (Figure 4C) Shrinkage in scar tissue, decrease in fluid decline in CNVM was detected in OCT controls. (Figure 3B)

DISCUSSION

Patients with systemic TB may manifest signs of ocular inflammation. CNVM may develop secondary to retinochoroidal inflammation. Bansal R et al. retrospectively examined 73 eyes of 60 patients with inflammatory CNVM.[4] Most frequently overlooked early CNVM signs were determined as small subretinal hemorrhage, peripapillary halo/fluid/scar, and subfoveal scar. Most frequent causes detected in this series were; Vogt-Koyanagi-Harada disease, tuberculous uveitis, idiopathic uveitis and sympathetic ophthalmia .

Multifocal choroiditis (MFC) should be noted in the differential diagnosis of tuberculosis ocular involvement. MFC is a chronic, bilateral disease that affects young, healthy individuals. The choroid, RPE, and retina are involved. The etiology of MFC is unknown. The classic lesions of multifocal choroiditis are 50–100 micron punched out chorioretinal scars with pigmented borders in the posterior pole. Characteristically the lesions are hypofluorescent in FFA. MFC can present with an uncommon pattern of zonal, multizonal, or diffuse outer retinal or chorioretinal atrophy as part of its clinical spectrum.[5]

RAP, has been described as a variant of exudative age-related macular degeneration (AMD), caused by the intraretinal capillaries that grow from the subretinal space and choroid. Three stages of the disease are distinguished: stage I, presence of intraretinal neovascularization; stage II, new capillaries in the subretinal space , stage III CNVM with retinochoroidal anastomosis.[6] Different approaches have been used in RAP treatment, such as surgery, ALP, transpupillary thermotherapy, photodynamic therapy (PDT) with verteporfin, and the intravitreous injection of triamcinolone. Recent studies have been published for the efficacy of antiangiogenic drugs intreatment .[7] RAP is frequently associated with the development of retinal pigment epithelial tears. Although indocyanine green angiography is the gold-standard for diagnosis , RAP lesions can be diagnosed with OCT .[8]

Imaging techniques, such as FFA and B-scan, can be used for differantial diagnosis to exclude other diagnoses for ocular TB. TB uveitis most affects the choroid. Liquefaction necrosis in the tuberculomas results in yellow-coloured subretinal lesions. In angiography, tubercules produce hypofluorescence at the early phase and hyperfluorescence at the late phase, whereas tuberculomas yield hyperfluorescence at the early phase and stain ponding sign at the late phase .

Retinochoroidal anastomoses display a connection between retinal and choroidal circulation, and they have been de-

scribed in CNVM due to age related macular degeneration. Pilli S et al. treated type 3 CVNM developing in a case with retinal angiomatous proliferation using ranibizumab.[9] OCT sections revealed that retinal arteriole in this region entered in the scar tissue, and this was thought to be a retinochoroidal anastomosis.

Ischemic and inflammatory processes are the most important reason to the development and progression of RAP. Anti-VEGF therapy is the most important choice in the treatment of lesions of RAP. Long-term results indicate that anti-VEGF therapy alone will not be sufficient.[10]

Retinochoroidal vascular anastomoses are rare in chorioretinitis, they are most common in toxoplasmosis, and the observed ones are venous anastomoses. The authors thought that there was destruction in Bruch membrane and choriocapilllaris due to chorioretinitis, and that the generalized impedance in retinal venous outward flow was exaggerated in capillaries and veins near the inflammatory focus.

Many studies proposed the treatment options to find the best result for treating RAP lesions. Treatment with anti-VEGF, PDT and triamcinolone treatment regimens are among the options.[11]

Treatment and diagnosis of RAP in patients with age-related macular degeneration (AMD) could be with the help of OCT. Increased foveal thickness, macular edema ,large central cysts and smaller cystoid spaces at the outer retinal layers, serous retinal detachment and elevated retinal pigment epithelium (RPE) can be determined with OCT.[12]

This was one of the rare cases of choroidal tuberculoma complicated with type 3 CNVM and RAP. With the reason that the patient was pregnant the lesion was treated with ALP.

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