Solitary presumed choroidal tuberculomas masquerading as choroidal tumors

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ABSTRACT

إن إصابة العين بالدرن ليست من الإصابات غير المألوفة ولها أوجه مختلفة. ومن النادر أن يظهر هذا المرض بعلامات تتشابه مع أورام داخل مقلة العين الخبيثة. تصف هذه المقالة 3 مرضى أصيبوا بأورام درنية منعزلة لعنبية العين ومتنكرة على هيئة أورام داخل مقلة العين. إثنان من المرضى لم يكن لديهم أي من مؤشرات الإصابة بالدرن المجموعي، ولكن كانت هنالك ردة فعل جلدية موجبة وشديدة لإختبار مشتق البروتين المصفى (PPD). أما المريض الثالث فكان لديه إستجابة جلدية موجبة لمشتق البروتين المصفى بالإضافة إلى علامات إصابة قديمة وغير نشطة بإلتهاب الدرن الرئوي وذلك ما تبين بتصوير الصدر الطبقي. تم علاج جميع المرضى بمجموعة من مضادات الدرن وهذه تشمل كلا من آيزونيازيد 5ملغ/كغ/اليوم، ريفامبسين 600 ملغ/كغ/اليوم، إيثامبوتول 15 ملغ/كغ/اليوم، بيرازيناميد 30 ملغ/كغ/اليوم لمدة تسعة أشهر. بالإضافة إلى جرعة 1 ملغ/كغ/اليوم من الكورتيزون الفموي. إستجاب جميع المرضى للعلاج وشفوا بدون مضاعفات. تبين هذه المقالة أن تشخيص الدرن العيني قد يشكل تحدياً كبيراً، حيث أن التشخيص والعلاج المناسب قد ينقذ أعين المرضى بل وحياتهم.

The ocular involvement of tuberculosis is not uncommon but diverse. Rarely, patients initially present with ocular signs that simulate intraocular malignancy. We report 3 cases of isolated presumed choroidal tuberculoma masquerading as intraocular tumor. Two patients had no systemic evidence of tuberculosis with strongly positive purified protein derivative skin test and one patient had evidence of inactive old pulmonary tuberculosis demonstrated by chest computed tomography. Antituberculous regimen including isoniazid 5 mg/kg/day, rifampicin 600 mg/day, ethambutol 15 mg/kg/day, and pyrazinamide 30 mg/kg/day were employed in all cases for 9 months. In addition, oral prednisone 1 mg/kg/day has been given until clinical response was seen, then slowly tapered over 4 months until discontinued. All cases responded well to treatment without complications. Ocular tuberculosis may show challenging clinical presentations, and proper diagnosis and treatment can save the patient's eye and even life.

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Tuberculosis is re-emerging as global health problem. It is a chronic and slowly progressive granulomatous infectious disease caused by *Mycobacterium tuberculosis (M. tuberculosis)*.[1,2] Tuberculosis generally affects the lungs, but any organ can be affected. Ocular manifestations can occur in only 1-2% of patients known to have systemic tuberculosis.[2] The ophthalmic presentation of ocular tuberculosis might be caused by direct infection or indirect immune-mediated hypersensitivity.[1,3] Previous history of pulmonary or systemic tuberculosis is usually absent in most of the patients with ocular involvement.[4] Ocular tuberculosis can show a variety of different clinical presentations ranging from an amelanotic solitary choroidal mass to panophthalmitis.[1,2] Ocular tuberculosis can be diagnosed microbiologically or histopathologically by isolating *M. tuberculosis* from ocular fluid. However, the process is prolonged as it may take several weeks before culture results become available for starting specific therapy. Moreover, it is difficult and potentially risky to obtain biopsy specimens from the intraocular tissues for making a confirmatory histopathological diagnosis.

On the other hand, ocular tuberculosis can be diagnosed as presumed ocular disease suggestive of TB, with proven active systemic TB; or without evidence of

active systemic TB, and the diagnosis of ocular TB in these situation remains largely presumptive. Because of the potential risks and possible morbidity in obtaining microbiologic evidence, the diagnosis of most reported cases of intraocular TB were only presumptive.[1-3] In the literature, the diagnostic criteria for presumed tuberculous uveitis were: First, ocular findings consistent with possible intraocular TB with no other cause of uveitis suggested by history of symptoms, or ancillary testing. Second, strongly positive tuberculin skin test results (≥15 mm area of induration/necrosis). Thirdly, response to antituberculous therapy with absence of recurrences. Solitary choroidal tuberculoma is an amelanotic choroidal mass with indistinct margins, which is usually seen in the posterior pole, and can simulate a choroidal tumor.[2] There may be an overlying exudative retinal detachment. The active choroidal granuloma can be associated with concomitant uveitis or the inflammatory signs might be absent.[3] In this study, we report 3 cases of solitary presumed choroidal tuberculoma initially suspected to be choroidal tumor.

Case Report. *Case 1.* A 37-year-old male presented with a 2-day history of decreased vision and seeing black spots in the left eye. He had no significant medical history, and had not been exposed to tuberculosis. His visual acuity was 20/20 in the right eye and 20/100 in the left eye. In both eyes, the evaluation of anterior segment was within normal limits. Fundus examination of the right eye was unremarkable. Left eye fundus examination showed a yellow choroidal mass about 2 optic disc diameters bisecting the fovea with exudative retinal detachment (**Figure 1A**), which has been confirmed using Optical coherence tomography (**Figure 1B**). No inflammatory reaction was detected in the vitreous. Fundus fluorescein angiography (FFA) demonstrated early blockage (**Figure 1C**) and late staining (**Figure 1D**) of the lesion. Indocyanine green angiography (ICG) study illustrated a hypofluorescence of the lesion in all phases (**Figures 1E & 1F**). B-scan ultrasonography evaluation revealed a thick, dome-shaped choroidal lesion with a 3.0-mm of low to medium internal reflectivity. At this point, our differential diagnosis included infectious or inflammatory granuloma (tuberculosis versus sarcoidosis), choroidal melanoma, and metastatic choroidal tumor. Medical evaluation and detailed physical examination by our internist including CT chest was unremarkable. Blood tests for uveitis screening were negative. Serology of Human Immunodeficiency Virus (HIV) was negative. Purified protein derivative (PPD) skin test was strongly positive (18 mm induration). The clinical diagnosis of presumed solitary choroidal tuberculoma was made, and the patient started on 4-drug antituberculous therapy (isoniazid 5 mg/kg/day, rifampicin 600 mg/day, ethambutol 15 mg/kg/day, and pyrazinamide 30 mg/kg/day initially for 2 months. Thereafter, isoniazid and rifampicin were continued for 7 months). Oral prednisone 1 mg/kg/day was instituted until clinical response was seen, then slowly tapered over 4 months before moving toward discontinuation. Eventually, the choroidal granuloma decreased in the size over the following 2 months. In the last follow-up (18 months later), the visual acuity improved to 20/20 in the left eye and the choroidal granuloma ended with a flat chorioretinal scar (**Figure 1G**) without evidences of recurrence of the inflammation and complete resolution of subretinal fluid (**Figure 1H**).

Case 2. A 26-year-old healthy female presented with a 2-week history of decreased vision in her left eye. She had a family history of tuberculosis. The visual acuity was 20/20 in the right eye and counting fingers at 2 feet in the left eye. Anterior segment examination was unremarkable in both eyes. Vitreous was clear in both eyes. Fundus was normal in the right eye. Fundus examination of the left eye showed an amelanotic choroidal lesion with exudative retinal detachment in the macular area (**Figure 2A**). Fundus fluorescein angiography demonstrated early blockage and late staining of the lesion (**Figure 2B**). Indocyanine green angiography demonstrated that the lesion was hypofluorescent during the early and the late phases of ICG. Subsequent systemic, laboratory and radiologic evaluation showed a strongly positive PPD skin test (25 mm induration) and apical lung fibrotic lesion seen on CT chest suggestive of old pulmonary tuberculosis. A diagnosis of presumed choroidal granuloma secondary to tuberculosis was made. The patient was started on 4-drug antituberculous therapy (isoniazid 5 mg/kg/day, rifampicin 600 mg/day, ethambutol 15 mg/kg/day, and pyrazinamide 30 mg/kg/day) initially for 2 months. Thereafter, isoniazid and rifampicin were continued for 7 months. Oral prednisone 1 mg/kg/day was instituted until clinical response was seen then slowly tapered over 4 months before moving toward discontinuation. At 24-months follow-up, visual acuity improved to 20/30 in the left eye with complete regression of choroidal lesion leaving a flat chorioretinal scar (**Figure 2B**).

Case 3. A 30-year-old healthy female presented with a 3-week history of deceased vision and micropsia in her left eye referred to rule out metastatic choroidal tumor. She had unremarkable systemic review apart from family history of pulmonary tuberculosis.

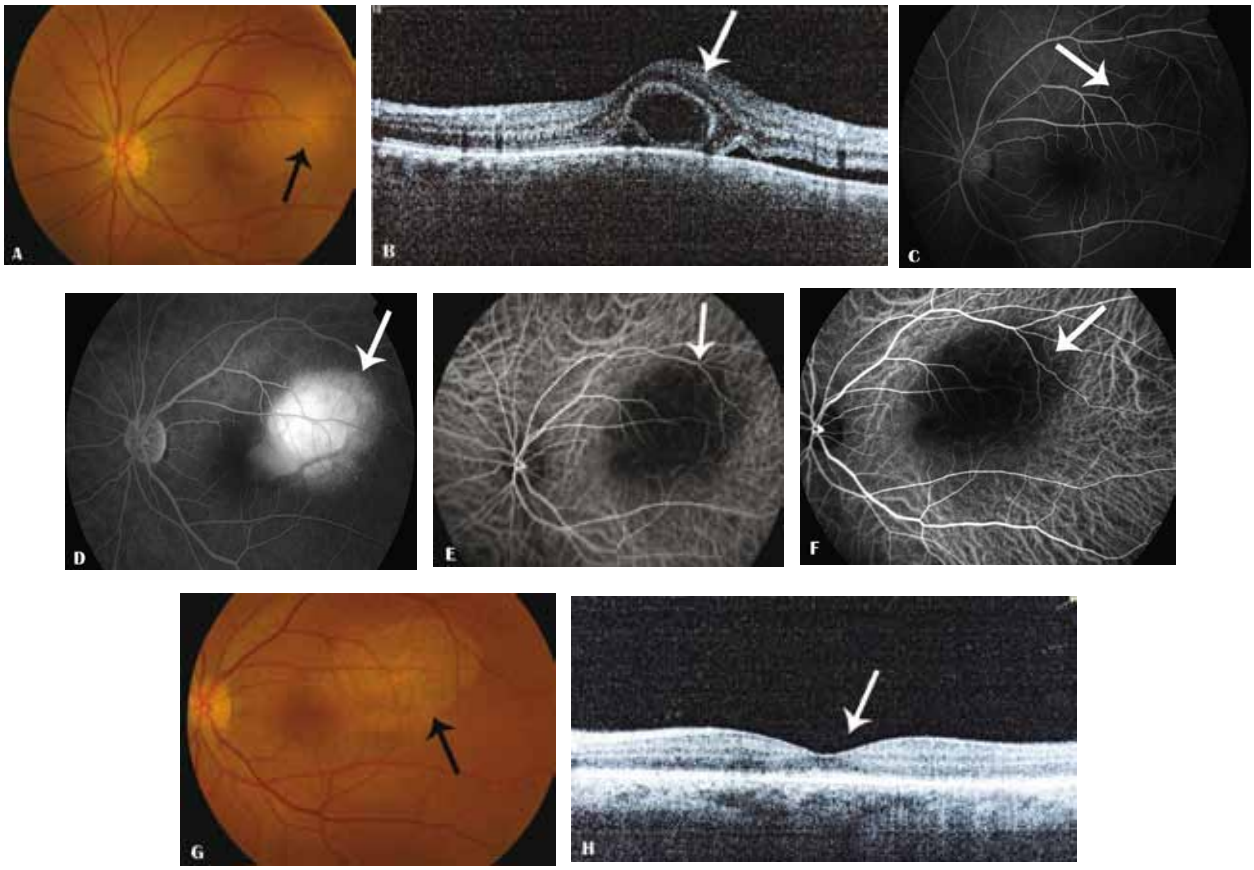

Figure 1 - Photograph showing **A**) fundus of left eye showing yellow choroidal mass bisecting the fovea with exudative retinal detachment. **B**) Optical coherence tomography showing exudative retinal detachment. Fundus fluorescein angiography demonstrated early **C**) early blockage and **D**) late staining of the lesion. Indocyanine green angiography demonstrated that the lesion is hypofluorescent during **E**) the early, and **F**) the late phases. **G**) The choroidal granuloma decreased in size and finally forms a flat chorioretinal scar. **H**) Optical coherence tomography showing complete resolution of subretinal fluid.

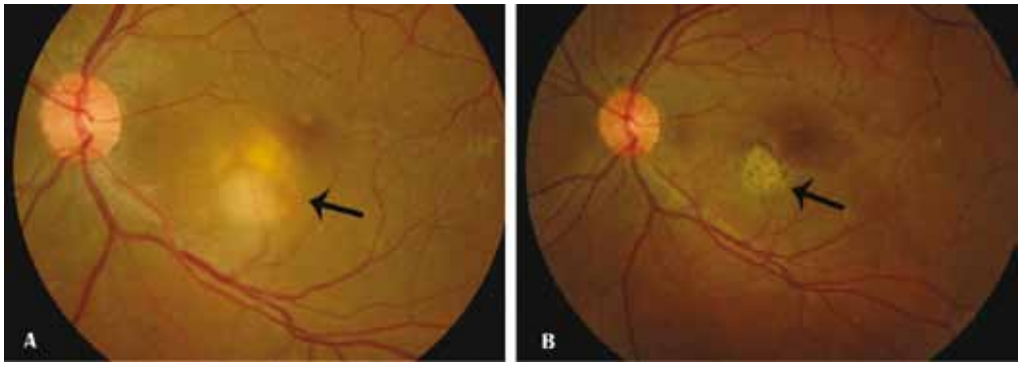

Figure 2 - Fundus photograph of left eye showing **A**) choroidal lesion with exudative retinal detachment in the macular area. **B**) The choroidal lesion decreases in size and finally forms a flat chorioretinal scar.

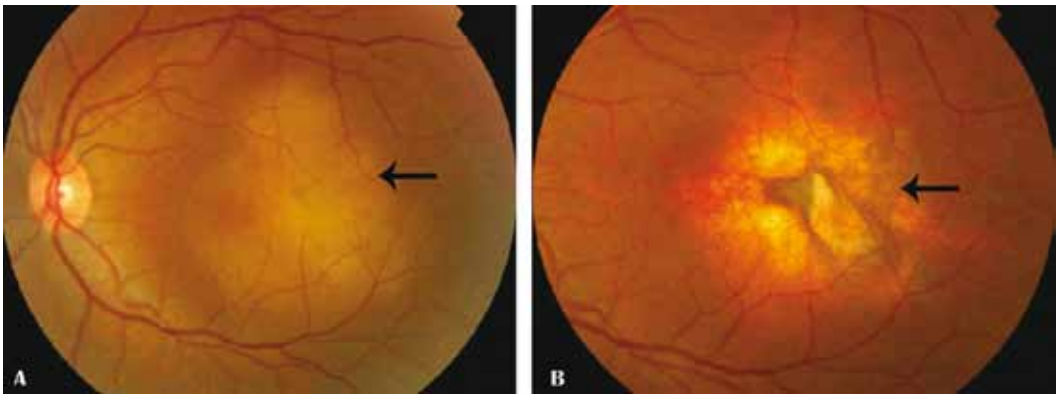

Figure 3 - Fundus photograph of left eye showing **A)** amelanotic choroidal lesion with exudative retinal detachment. **B)** The choroidal lesion decreased in size and finally formed a flat chorioretinal scar.

The visual acuity was 20/20 in the right eye and 20/300 in the left eye. The biomicroscopic examination of the anterior segment in both eyes was unremarkable. Vitreous was clear in both eyes. Fundus was normal in the right eye. Fundus examination of the left eye showed an amelanotic choroidal lesion with exudative retinal detachment (**Figure 3A**). Fundus examination demonstrated early blockage and late staining of the lesion. Indocyanine green angiography demonstrated that the lesion was hypofluorescent during the early and the late phases of ICG. Systemic workup revealed only a strongly positive PPD skin test (18 mm induration). The CT chest was normal. A clinical diagnosis of presumed solitary choroidal tuberculoma was made without systemic evidence of tuberculosis. The patient was started on 4-drug antituberculosis therapy (isoniazid 5 mg/kg/day, rifampicin 600 mg/day, ethambutol 15 mg/kg/day, and pyrazinamide 30 mg/kg/day) initially for 4 months. Thereafter, isoniazid and rifampicin were continued for 7 months. Oral prednisone 1 mg/kg/day was instituted until clinical response was seen then slowly tapered over 4 months months before moving toward discontinuation. Patient showed improvement on regular follow-up. Six months after starting treatment, visual acuity improved to 20/40 in the left eye with complete regression of choroidal lesion leaving only a flat chorioretinal scar (**Figure 3B**).

Discussion. Granulomatous inflammatory diseases can cause a localized fundus mass. Amelanotic choroidal granuloma could be of infectious or inflammatory origin such as tuberculosis and sarcoidosis. It may mimic choroidal melanoma or metastasis.[1-3] In English literature, we found only few similar cases of presumed choroidal tuberculoma without systemic evidence of tuberculosis and normal chest radiograph findings with only positive PPD skin test similar to Cases 1 and 3.[2,4-7] Few cases were also reported without systemic tuberculosis, normal chest radiograph and negative PPD skin test diagnosed to have ocular tuberculosis after histopathological examination of enucleated eyes and some by polymerase chain reaction of *M. tuberculosis* DNA amplification.[4-7] Most of these patients were initially suspected to have ocular malignancy.[2,4-7] Ocular diagnosis is generally presumptive and is based primarily on clinical findings suggestive of presumed TB, strongly positive PPD skin test or response to antituberculous agents without recurrence.[1,2,4] Obtaining ocular tissues for histopathological confirmation is difficult and potentially risky. Polymerase chain reaction has been recently utilized to diagnosis ocular tuberculosis after obtaining aqueous or vitreous samples.[4,7] Imaging studies are helpful to confirm the diagnosis. Choroidal tuberculoma lesions show early hypofluorescence and late hyperfluorescence on FFA. On ICG, the lesion is hypofluorescent during the early and the late phases. Ultrasonography displays a lesion with low internal reflectivity on A-scan and with solid elevated mass with absence of scleral echo on B-scan.[1,2] Failure of diagnosing choroidal tuberculoma early can lead to devastating complications. Some of these cases with delayed diagnosis ended up with being enucleated as reported by Demirci et al[2] and Biswas et al.[5]

In conclusion, ocular tuberculosis may show challenging clinical presentations which can simulate neoplasm. It cannot be overemphasized that keeping a high degree of clinical suspicion is important in

diagnosing tuberculosis. Delay in detecting this treatable condition can have serious consequences on the patient's eyes or even their life.

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