

Case report

Retinal involvement of Paracoccidioidomycosis: A Case Report

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Received 22 October, 2012 Accepted 24 October, 2012 Published online 19 January, 2013

Abstract: Purpose: to describe the clinicopathologic features and treatment of a rare case of systemic paracoccidioidomycosis with choroidal and retinal involvement. Design: retrospective interventional case report. Participant: A 36-year-old young man with visual impairment in left eye with anterior uveitis and presence of whitish perimacular choroidal nodule, multiple underlying whitish spots and mid-periphery exudative retinal detachment. A primary extensive work-up for systemic infectious, autoimmune, neoplastic or inflammatory conditions was performed and high-resolution computer tomography scan demonstrated asymmetric parietal thickening of the trachea and bilateral diffuse multiple lobular opacities. Pulmonary bronchoscopy/biopsy of larynx, trachea and bronchial tube were also performed. Histopathological evaluation showed characteristic of Paracoccidioidomycosis. Intervention: Patient was treated with oral sulphadiazine (1.5 g/day). Main Outcome Measures: Anterior uveitis, retinal examination, histopathological evaluation and primary clinical outcome were observed during systemic treatment. Results: After 3 months of irregular treatment, choroidal lesions decreased in size forming atrophic scars and fibrotic spots; however visual acuity did not show any improvement. Conclusion: We report a rare case of systemic paracoccidioidomycosis with choroidal and retinal involvement treated with oral sulphadiazine.

Key words: Paracoccidioidomycosis, retina, eye

INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic mycosis infection caused by *Paracoccidioides brasiliensis*, first described in Brazil in 1908 by Adolpho Lutz [1]. It is endemic in South and Central America, and its incidence is very high in Brazil, Venezuela, Colombia and Argentina [1]. In Brazil, paracoccidioidomycosis is the most prevalent systemic mycosis among immunocompetent individuals.

Pulmonary involvement occurs in 70 to 90% of cases, but other organs can be affected such as skin/mucosa, adrenal glands, lymph nodes, gastrointestinal tract, musculoskeletal system and central nervous system [1–4]. Eye involvement of PCM is very rare and usually affects the eyelid and conjunctiva. There are few reports of PCM cases with retinal or choroidal involvement [5–8].

We present a rare case of a patient with systemic paracoccidioidomycosis in which ophthalmologic findings are limited to the choroid and retina. We also report a favorable response to systemic therapy with oral sulphadiazine.

CASE REPORT

A 36-year-old male Caucasian rural worker was referred to the ophthalmology emergency room in January 2009 (Department of Ophthalmology- Santa Casa de São Paulo), reporting a one-month history of gradual visual impairment of the left eye. The patient did not report any history of redness or pain in either eye. Further questioning and review of the clinical status revealed that he had also suffered asthenia, weight loss (4 kg in one month) and daily mild cough for the last five years. He had had no episodes of fever, night sweats, hemoptysis or allergic disease. He admitted to have been a heavy smoker (two packs/day) and drinker (five doses/day) for approximately 15 years.

On ocular examination, the best-corrected visual acuity (BCVA) was 20/35 in the right eye (−17.00 DE) and < 20/400 in the left eye (finger count 3 m). Ocular examination of the right eye was unremarkable, but the left eye showed fine-pigmented keratic precipitates inferiorly on the cornea with 2+ cells in the anterior chamber (AC) and mild-

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moderate (2+) vitreous cells in slit lamp examination. The retinal findings of the left eye showed the presence of a whitish perimacular choroidal nodule of approximately six disc diameters in size (suggesting granuloma). Multiple underlying whitish spots (smaller than one disc diameter) and mid-periphery exudative retinal detachment was also observed in the left fundus (Fig. 1).

Fluorescein angiography of the left eye revealed hyperfluorescence in the choroidal lesion area with late leakage (Fig. 2). Echography identified the presence of a choroidal nodule measuring 11.2 × 3.0 mm with adjacent serous retinal detachment (Fig. 3).

A primary extensive work-up for systemic infectious, autoimmune, neoplastic and inflammatory conditions was performed including complete blood profile, serologic tests

(toxoplasmosis, syphilis, HIV, hepatitis, cytomegalovirus), and other investigations for tuberculosis (purified protein derivative skin test and sputum analysis), fungi, BAAR and bacteria. No remarkable findings were observed.

Chest radiology analysis showed the presence of multiple bilateral peri-hiliary nodules with no cavitation or evident mass. High-resolution computer tomography (CT) scan demonstrated asymmetric parietal thickening of the trachea (irregular and worse on the right side) and bilateral diffuse multiple lobular opacities. Given the suggestive tracheal image on CT scan, pulmonary bronchoscopy/biopsy of the larynx, trachea and bronchial tube were also performed. Histopathological evaluation with haematoxylin-eosin of larynx tissue revealed granulomatous tissue reaction and inflammatory infiltrate with macrophages, lym-

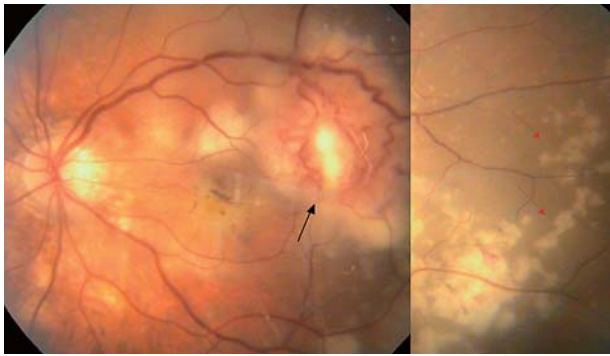


Fig. 1. Image of the fundus of the left eye showing a perimacular choroidal granuloma (black arrow), multiple whitish peripapilar lesion and exudative retinal detachment of all peripheral retina (red arrows) seen through a vitreous cellular haze.



Fig. 3. Ocular echography identified the presence of choroidal nodule measuring 11.2 × 3.0 mm with adjacent serous retinal detachment.

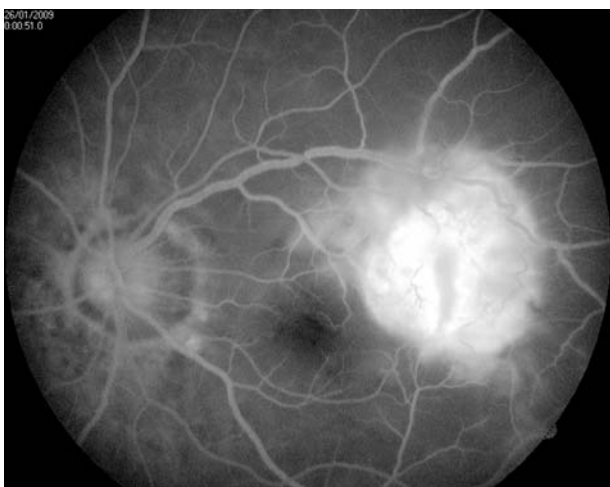


Fig. 2. Angiofluoresceinography showed hyperfluorescence in the lesion area with late leakage.

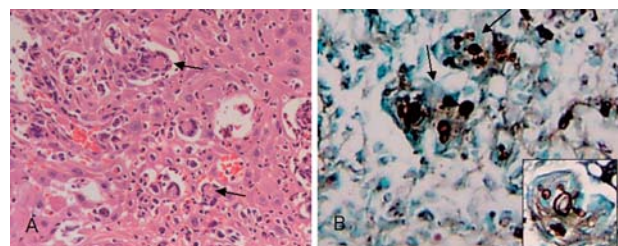


Fig. 4. Larynx lesion of paracoccidioidomycosis: (A) histopathological evaluation with haematoxylin-eosin, presenting granulomatous tissue reaction and inflammatory infiltrate with macrophages, lymphocytes and abundant fungal forms in the cytoplasm of multi-nucleated giant cells (arrows). (B) Grocott staining revealing abundant multiple budding yeasts, typical of *Paracoccidioides brasiliensis* (in black) in the cytoplasm of giant cells and macrophages. In detail, it is possible to observe the “pilot-wheel” cell, characteristic of these fungi.

phocytes and abundant fungal forms in the cytoplasm of multinucleated giant cells (Fig. 4A). Grocott staining detected abundant multiple budding yeasts, typical of *Paracoccidioides brasiliensis* in the cytoplasm of giant cells and macrophages (Fig. 4B). It was also possible to observe the “pilot-wheel” cell, characteristic of this fungus [1, 9]. Other infections such as fungus, mycobacterium, tuberculosis and BAAR were overruled as a result of the tissue analysis.

During the clinical investigation, the patient reported worsening of visual acuity in his left eye (hand movement). Ophthalmological examination also showed worsening of the vitreous and retinal condition.

After consultation with infectologists, the patient was treated with oral sulphadiazine (1.5 g/day). After three months of irregular treatment, the choroidal lesions decreased in size forming atrophic scars and fibrotic spots. However, visual acuity did not show any improvement (Fig. 5). After six months of follow up, no reactivation of disease was noted, and the subretinal fluid slowly vanished.

This case report was approved by the local institutional review board under protocol number 359/11 (Santa Casa de

São Paulo). Informed consent for this article was obtained from the patient.

DISCUSSION

PCM, also known as South American blastomycosis, is a fungus infection acquired by inhalation during handling of contaminated dust, making the lungs the primary location. Most contaminated patients have been engaged in agricultural activities during the first two decades of life and exposed persistently to endogenous latent foci, since plants and soil can be a natural source of *Paracoccidioides brasiliensis* [2, 4, 10–12]. Several cases of systemic paracoccidioidomycosis have also been reported outside endemic areas among travelers, aid workers and immigrants [3, 13–15].

PCM presents as acute, sub-acute (juvenile type) or chronic (adult type) types. The chronic form is responsible for more than 90% of cases, affecting predominantly male Caucasian rural workers aged between 30 and 50 years [1, 2, 16].

The incidence of ocular involvement in PCM is very low, and most cases are limited to the eyelid and conjunctiva [6, 8, 11]. Belfort Jr et al. described 50 cases of systemic PCM with ocular involvement, among which 38% were eyelid lesions, 12% conjunctival lesions and 4% corneal involvement [6]. Cases of retinal and choroidal involvement of PCM are even rarer and have been described by only a few authors (Table 1) [5, 7, 17–20].

Conti-Diaz first described choroidal involvement in systemic PCM in 1964 [19]. Brick et al. described probable initial retinal lesion but did not make laboratory, therapeutic or retinal observation. The follow-up of this patient was lost after the first ocular examination [5]. Dantas et al. reported systemic PCM associated with retinal and choroidal lesions very similar to tuberculosis [21]. Arruda et al. described the pathological characteristics of the retina and choroid [7]. Finamor et al. reported retinal and choroidal involvement in acquired immunodeficiency syndrome [20]. Bonomo et al. presented the first description of the angiographic charac-



Fig. 5. Image of the fundus of the left eye showing atrophic scars and fibrotic spots.

Table 1 Paracoccidiomycosis cases with choroid involvement.

Author (year)	involvement	Drug administered	prognosis
Conti-diaz et al. (1964)	choroid	Amphotericin B	No improvement
Brick M et al. (1969)	Retina, choroid	Prednisone + Amphotericin B	No improvement
Bonomo et al. (1982)	choroid	Amphotericin B + hydrocortisone	No improvement
Arruda et al. (1986)	choroid	Amphotericin B + hydrocortisone	enucleation
Finamor et al. (2002)	choroid, optic nerve	Sulphamethoxazole-trimedoprim	enucleated
Bovo et al. (2005)	Retina, choroid	Sulphamethoxazole-trimedoprim	20/200 to 20/20

teristics of a choroidal granuloma caused by this fungus, both the angiofluoresceinographic and fundoscopic aspects being similar to those of the present case [17]. Bovo et al. presented the most recent description of retinal and choroidal involvement in systemic PCM [18].

The above authors described different therapeutic strategies (Table). The lesion caused by *Paracoccidioides brasiliensis* in the retina and choroid is described as an exudative granulomatous reaction with edema and neovascularization. The treatment of systemic PCM can reach up to 24 months in duration depending on severity. Favorable therapeutical results have been observed using oral sulphamidics (sulphadiazine, sulphamethoxazole-trimedoprim) and azoles (itraconazole, ketoconazole, saperconazole) or endovenous amphotericin B [1, 2, 16].

When choroidal involvement is detected, oral sulphamidics and amphotericin B associated with systemic steroids are recommended by other authors [5, 7, 17–20].

Systemic PCM diagnosis is confirmed by direct mycological testing, culture, and histopathological exam [1, 2, 16].

The gold standard for diagnosis of systemic PCM is the presence of fungal elements suggestive of *Paracoccidioides* in fresh sputum and other specimens, such as biopsy fragments suspected to be affected. In that case, they are stained with Gomori-Grocott or periodic acid Schiff (PAS). Multiple budding with “pilot-wheel” aspect is pathognomonic of *Paracoccidioides brasiliensis* [1, 2, 9, 16]. However, to assure the diagnosis of choroidal granuloma caused by PBM, only pathological or mycological examination of the eye can provide confirmation. When microscopic examination of the eye lesion is not feasible, the diagnosis can be reached only by excluding other possible causes of choroidal granuloma and positive therapeutic test results. Arruda et al. described for the first time a case where the parasite was identified in the choroid and retina in anatomopathologic examination after enucleation [7]. In this case report, the treatment was based on the identification of the fungus in other organs, even though the patient initially presented with ocular symptoms.

The mechanism of eye involvement remains unclear, but it is believed that the fungus spreads most commonly through the blood or lymphatic system. Attention should also be paid to the exclusion of other diseases that present granulomatous ocular setting similar to that of PCM, such as tuberculosis, syphilis and sarcoidosis. The fungus can also be among the agents causing opportunistic eye diseases in immunocompromised individuals such as AIDS patients or heavy drinkers.

PCM should not be forgotten when retinal characteristics similar to those described in this article are found in im-

munocompromised individuals, because some cases may be misdiagnosed because of the rare clinical characteristics in the eye.

ACKNOWLEDGMENT

Drs, Igami and Hida contributed equally to this study and should be considered joint first authors.

CONFLICT OF INTEREST

No authors have any financial/conflicting interests to disclose.

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