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Presumed Ocular Histoplasmosis Syndrome with Choroidal Neovascularization: Case Report

M. A. Krichene[1*], S. Hassina[1], N. Tebbay[1], I. Hasnaoui[1], Y. Akannour[1], L. Serghini[1], E. Abdellah[1]

[1]University Mohammed V Rabat, Morocco

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***Corresponding author:** M. A. Krichene
University Mohammed V Rabat, Morocco

Abstract **Case Report**

Presumed Ocular Histoplasmosis Syndrome (PHOS) is a clinical condition characterized by chronic inflammation of the choroid and retina, often accompanied by the growth of abnormal blood vessels in the macula known as choroidal neovascularization (CNV). While PHOS is typically seen in regions where Histoplasma capsulatum is endemic, there have been reported cases in non-endemic areas. This case report presents the details of a 32-year-old Moroccan patient with PHOS and macular CNV, highlighting the diagnostic, therapeutic, and practical considerations involved in their treatment. The patient, who had no significant medical history, came to us with a six-month history of central vision loss, intermittent metamorphopsia, and central scotomas in the left eye. Despite having no exposure to environmental risk factors or travel to areas where histoplasmosis is prevalent, our clinical examination revealed choroidal and retinal lesions consistent with histospots and active CNV. Further tests such as fluorescein angiography and optical coherence tomography (OCT) confirmed the presence of CNV, revealing a subretinal fibrovascular membrane and serohemorrhagic detachment. Based on these findings, we diagnosed the patient with PHOS and CNV. We proceeded with treatment using intravitreal ranibizumab, a monoclonal antibody that targets vascular endothelial growth factor (VEGF). Monthly injections resulted in the stabilization of the patient's condition, both clinically and anatomically. The CNV regressed, the serohemorrhagic detachment resolved, and there was a significant improvement in the patient's visual acuity. The discussion in this report highlights the fact that while PHOS is typically associated with Histoplasma capsulatum infection, the occurrence of cases in non-endemic areas raises questions about its etiology and diagnosis. In this particular instance, the patient's exposure to the fungus or potential infection by other fungal species complicates the process of making a definitive diagnosis, as serological tests and fungal cultures are often inconclusive. The development of CNV in PHOS is believed to be a result of chronic inflammation, which leads to alterations in the blood-retinal barrier, tissue hypoxia, and the release of angiogenic factors. Anti VEGF agents, such as ranibizumab, have proven to be an effective alternative to laser photocoagulation for treating CNV in PHOS, with a "pro re nata" approach commonly employed. In conclusion, this case highlights the challenges faced in diagnosing and treating PHOS, even in non-endemic areas. It underscores the efficacy of anti-VEGF medications, particularly ranibizumab. However, further research is needed to enhance our understanding of PHOS epidemiology, pathogenesis, and the optimal therapeutic strategies. Regular observation and personalized approaches are crucial for the early detection and management of this rare yet potentially debilitating condition.

Keywords: Presumed Ocular Histoplasmosis Syndrome (PHOS), Choroid, Retina, fungus or potential infection.

INTRODUCTION

The presumptive histoplasmosis ocular syndrome (PHOS) is a clinical entity distinguished by chronic choroidal and retinal inflammation, which is frequently associated with macular choroidal neovascularization (CNV). Despite the fact that this pathology is frequently observed in the endemism zones of Histoplasma capsulatum, the dimorphe responsible for systemic histoplasmosis, cases of PHOS have been reported in non-endemism zones. We present here the case of a Moroccan patient with PHOS with macular CNV. We also talk about diagnostic, therapeutic, and practical issues that come up when dealing with this condition.

CASE REPORT

A 32-year-old man with no significant medical history presented with central vision loss in his left eye for 6 months. He also reported intermittent metamorphopsia and central scotomas. He had no family

history of eye disease, nor exposure to environmental risk factors such as birds, bats or caves. He had not traveled to histoplasmosis-endemic areas, including the Mississippi and Ohio valleys in the United States. He had no signs or symptoms of systemic histoplasmosis, such as fever, night sweats, cough, dyspnea, hepatosplenomegaly or adenopathy.

On physical examination, his corrected visual acuity was 10/10ths in the right eye and a finger count of 3 metres in the left. Intraocular pressure was normal in both eyes. A slit-lamp examination showed no intraocular inflammation. Fundus examination of the left eye revealed multiple choroidal and retinal lesions, round or oval in shape, pale yellow in color, less than a quarter of papillary diameter, located nasal to the papilla and inferior parafoveolar, corresponding to histospots. There was also active choroidal neovascularization, in the form of a subretinal fibrovascular membrane, associated with serohemorrhagic detachment of the pigment epithelium and neurosensory retina, encompassing the fovea (Fig 1, 2, 4). The right eye showed no abnormalities, with the exception of discrete peripapillary atrophy (Fig 3).

Fluorescein angiography and optical coherence tomography (OCT) confirmed the presence of choroidal neovascularization. Fluorescein angiography showed a deep vascular meshwork corresponding to subretinal neovessels in the early stages and intense diffusion of subretinal neovessels with a window effect at histospots in the late stages (figs. 5, 6, and 7). OCT revealed macular thickening with intraretinal cystic spaces, serous detachment of the pigment epithelium and neurosensory retina, and a subretinal fibrovascular membrane (Figure 8, 9).

The diagnosis of presumed ocular histoplasmosis syndrome (PHOS) with choroidal neovascularization was made, and the patient was treated with intravitreal injections of ranibizumab, a humanized monoclonal antibody directed against vascular endothelial growth factor (VEGF). He received an initial injection of 0.5 mg, followed by monthly injections until clinical and anatomical stabilization. After six injections, there was regression of choroidal neovascularization, resorption of macular serohemorrhagic detachment, and a significant improvement in visual acuity to 6/10ths in the left eye. The patient was kept under regular surveillance, with additional injections in the event of a recurrence of neovascular activity.

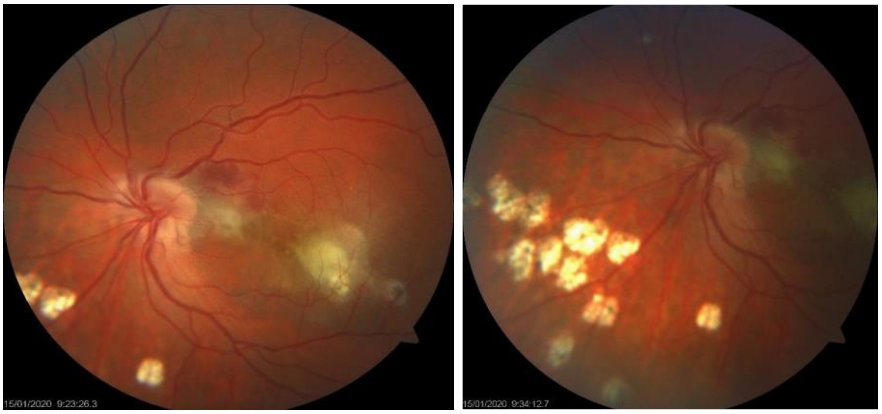

Fig 1, 2: Fundoscopy of the left eye demonstrating a large yellow white lesion with irregular margins involving the macula, numerous small peri papillare retinal scars were also found

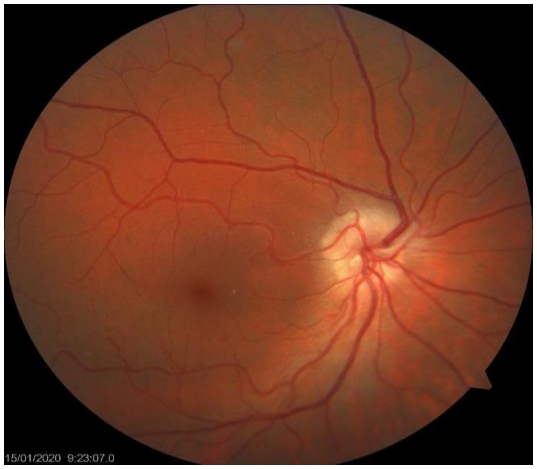

Fig 3: Fundoscopy of the right eye with no abnormalitie

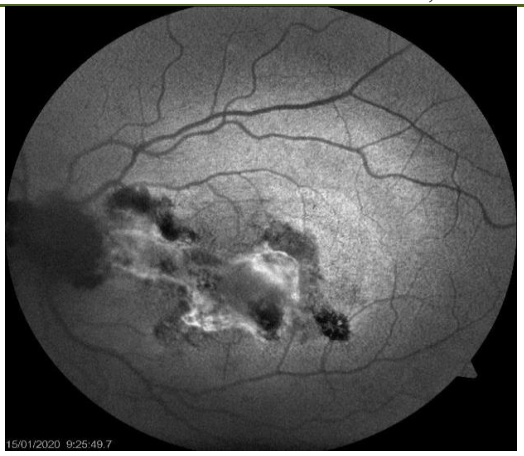

Fig 4: Fundus autofluorescence of the left eye showing the hyper auto fluorescent lesion with subretinal hemorrhage

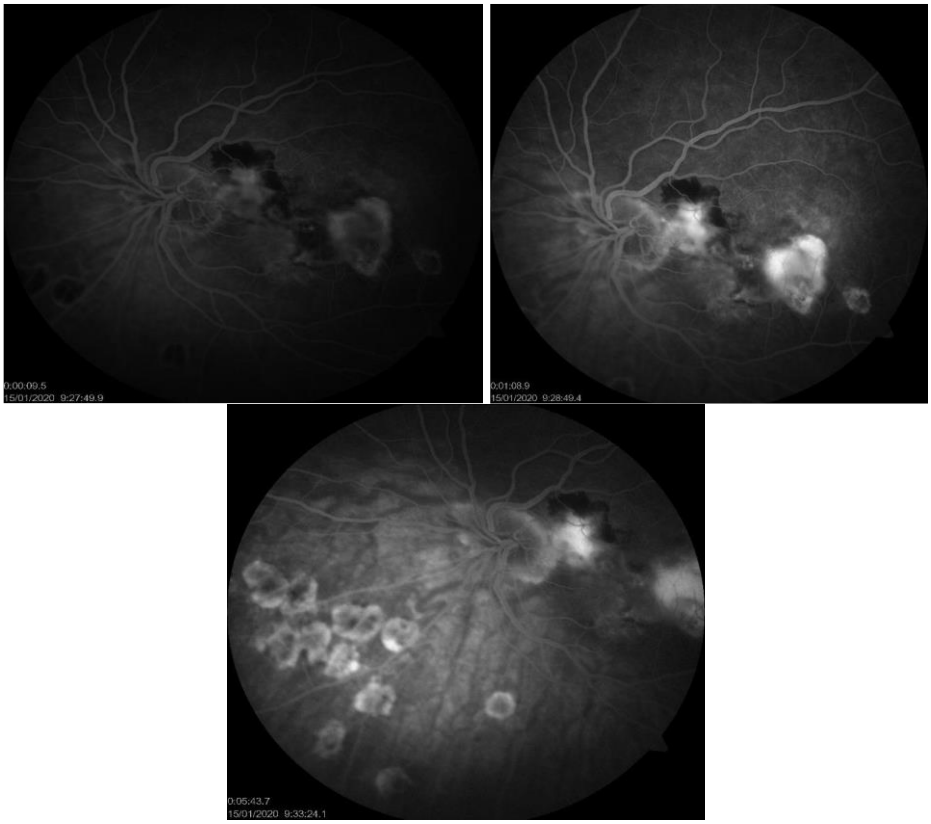

Figure 5, 6, 7: Fluorescein angiography of the left eye; early (figure 5) and late phase (figure 6) showing the staining of the lesion; with window defect of the peripheral scars (figure 7)

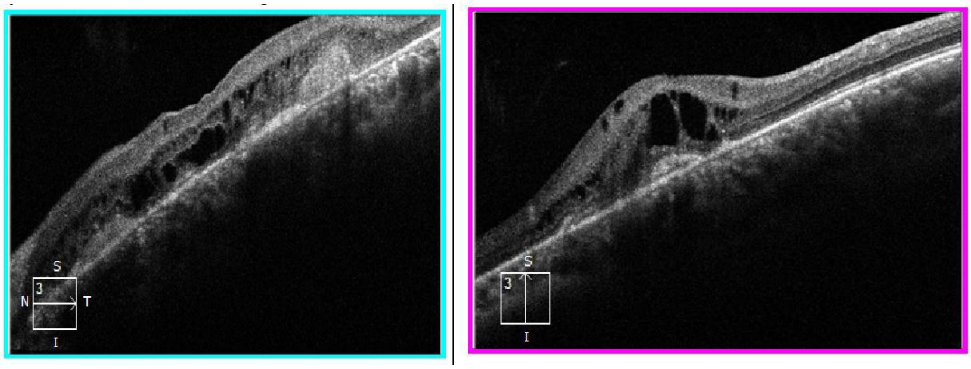

Figure 8, 9: Spectral domain OCT of the macula of the left eye demonstrating the retinal thickening with depiction of the intraretinal cystic edema

DISCUSSION

Presumed ocular histoplasmosis syndrome (PHOS) is a chronic inflammatory disease of the choroid and retina, characterized by the presence of chorioretinal atrophic scarring (histospots), peripapillary scarring, and macular choroidal neovascularization (CNV) [1]. PHOS is considered an ocular manifestation of systemic infection with Histoplasma capsulatum, a dimorphic fungus found mainly in endemic regions of North, Central, and South America [2]. However, PHOS can also occur in non-endemic areas, such as Europe and Africa, where histoplasmosis seroprevalence is low or non-existent [3]. In these cases, the term presumed ocular histoplasmosis is used, as the etiological link between the fungus and the disease is not clearly established.

We report the case of a native Moroccan patient, with no particular history, who presented with decreased visual acuity in the right eye due to macular CNV associated with histospots. The diagnosis of PHOS was made on the basis of clinical, angiographic and tomographic data. The patient was treated with intravitreal injection of ranibizumab, an anti-VEGF monoclonal antibody, with improvement of vision and regression of CNV.

Our observation raises several questions about the pathogenesis, diagnosis and treatment of PHOS. Firstly, H. capsulatum infection in our patient could be due to previous exposure in an endemic area, or to infection by another fungal species. It is possible that the patient was exposed to the fungus during a trip to an endemic area, or that he was infected by an unidentified local environmental source. It is also possible that the patient has been infected by another fungal species, such as Blastomyces dermatitidis or Coccidioides immitis, which can cause eye lesions similar to those of PHOS [4]. It is difficult to confirm the etiological diagnosis of PHOS, as serological tests and fungal cultures are often negative, and choroidal biopsies are rarely performed due to the risk of complications [5]. As a result, diagnosis is based primarily on clinical criteria and imaging studies.

CNV in PHOS results from a chronic inflammatory reaction to fungal antigen, leading to alteration of the blood-retinal barrier, tissue hypoxia, and the release of angiogenic factors. CNV is the main complication of PHOS and the main cause of visual loss in affected patients. CVN develops from chorioretinal scars, which are the result of a chronic inflammatory reaction to fungal antigens. The exact mechanism of CVN is not elucidated but probably involves alteration of the blood-retinal barrier, tissue hypoxia, the release of angiogenic factors such as VEGF, and the activation of inflammatory cells such as macrophages and lymphocytes [6]. CVN can be classified into two types according to its angiographic appearance: type 1, which corresponds to occult CVN, located beneath the retinal pigment (RPE), and type 2, which corresponds to classic CVN, located above the RPE [7]. In our case, the patient presented with a type 2 CVN, manifested by a deep vascular laceration in the early phase and intense diffusion in the late phase of angiography.

Anti-VEGFs represent an effective alternative to laser photocoagulation in the treatment of CNV in PHOS, but the optimal therapeutic regimen remains to be defined. Treatment of PHOS CNV aims to preserve vision and prevent complications such as hemorrhage, retinal detachment, or fibrosis. The conventional treatment for CNV in PHOS is laser photocoagulation, which involves destroying abnormal vessels by thermal burning. However, this treatment has its drawbacks, such as the risk of recurrence, extrafoveolar growth, and loss of central vision [8]. Since the advent of anti-VEGF agents, the treatment of CNV in PHOS has evolved towards a more conservative approach, which involves injecting pharmacological agents into the vitreous to block the action of VEGF, the main factor involved in pathological angiogenesis. Several studies have demonstrated the efficacy and safety of anti-VEGF agents, such as ranibizumab, bevacizumab, or aflibercept, in the treatment of CNV in PHOS, with an improvement in visual acuity, a reduction in macular thickness, and a decrease in angiographic activity [9]. The optimal treatment regimen has yet to be defined but is generally based on a "pro re nata" (PRN) approach, which involves injecting anti-VEGFs as required, depending on clinical and imaging trends. In our case, the patient received three injections of ranibizumab one month apart, with a good anatomical and functional response.

In conclusion, we report A case of PHOS in Morocco, a rare and potentially disabling disease whose diagnosis and treatment remain a challenge. Our observation illustrates the interest of anti-VEGFs in the management of CVN in PHOS, which represent an effective alternative to laser photocoagulation. Further studies are needed to better understand the epidemiology, pathogenesis and prognosis of PHOS, and to optimize the treatment of associated CNV.

CONCLUSION

Even in non-endemic areas, PHOS remains a diagnostic and therapeutic challenge. Our case study sheds light on the efficacy of anti-VEGF medicines, particularly ranibizumab, in the treatment of PHOS-related CNV. However, additional research is required to better understand pathogenesis, epidemiology, and the appropriate therapeutic scheme. This case emphasizes the significance of regular observation and a personalized approach to improving early detection and treatment of this rare but potentially fatal illness.

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