

Posterior scleritis and acute posterior multifocal placoid pigment epitheliopathy: A case of painful chorioretinitis and review of the current literature

Thérèse M. Sassalos^a, Albert T. Vitale^b, Christopher D. Conrady^{a,*}

^a Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, University of Michigan, Ann Arbor, MI, USA

^b Department of Ophthalmology and Visual Sciences, John A. Moran Eye Center, University of Utah, Salt Lake City, UT, USA

ARTICLE INFO

Keywords:

Choroiditis
Posterior scleritis
T-sign
APMPPE
Uveitis

ABSTRACT

Purpose: To describe a patient who developed concurrent acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and posterior scleritis.

Observations: We describe a middle-aged woman that developed eye pain and photopsia. She was found to have a “T-sign” on ultrasound of the right eye and multiple, nearly confluent, ill-defined subretinal whitish lesions in both eyes. After an extensive laboratory evaluation and neuroimaging, her photopsia, pain with eye movements, and subretinal lesions began to regress on high dose systemic corticosteroids.

Conclusions and Importance: This is the first reported case of bilateral APMPPE and concurrent posterior scleritis. Our case highlights the importance of performing a full review of systems, specifically eliciting neurological changes, and dilated eye examination in all new uveitis cases.

Introduction

Posterior scleritis is defined by painful inflammation of the posterior sclera exacerbated by eye movements and represents only 1 in 10 of all cases of scleritis.¹ While rare, this entity can be associated with underlying systemic diseases (19.4–37.7% of cases).¹ Misdiagnosis, at least initially, is not uncommon with vague symptoms and subtle clinical findings. As such, ultrasonography has become a mainstay in evaluation.^{1,2} Other anatomic regions of the eye can be affected by posterior scleritis such as an anterior chamber reaction, optic nerve edema, choroidal nodules, and neurosensory retinal detachments.

Unlike posterior scleritis, acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is not frequently associated with underlying systemic conditions. However, like posterior scleritis, it is rare with an estimated incidence of 0.15 cases per 100,000 persons.³ Patients can develop photopsia, metamorphopsia, and varying levels of vision loss that may be preceded by a viral prodrome. This typically self-limited, bilateral, inflammatory chorioretinopathy is defined by multiple subretinal, yellowish-white, 1/8th – 1/4th optic disc diameter placoid lesions of the posterior pole that block early and stain late on fluorescein angiography.⁴ There can be some involvement of the anterior segment (cells and flare) and vitritis at the time of presentation. Similarly,

serpiginous choroiditis is a rare, bilateral inflammatory chorioretinopathy, but unlike APMPPE, is typically a single, yellowish, larger lesion that extends centrifugally from the peripapillary region in a “snake-like” manner. Ampiginous choroidopathy is on the spectrum of APMPPE and serpiginous chorioretinitis in which the APMPPE-like placoid lesions tend to fuse creating larger subretinal lesions and has a predictable fundus autofluorescence pattern in which subtle hyperautofluorescence in areas of activity are seen early in the disease course that then become hypoautofluorescent as activity subsides.^{5–7} Ampiginous lesions can then become recurrent compared to the chronic activity of serpiginous chorioretinitis.⁵

As with any acute uveitis flare, multiple anatomical structures within the eye can be affected simultaneously. For example, it is not uncommon to have macular edema with an anterior uveitis or vascular leakage in pars planitis. However, to our knowledge, concurrent APMPPE and posterior scleritis have not been reported to occur contemporaneously. In the following manuscript, we describe the first case and our management of ampiginous choroiditis with concurrent posterior scleritis.

Case report

A 62-year-old-woman with past medical history significant for a

* Corresponding author.

E-mail address: cconrady1984@gmail.com (C.D. Conrady).

prior infection with histoplasmosis requiring a partial lung resection thirty years prior to presentation was referred to our uveitis clinic due to worsening pain with eye movements of several weeks' duration and photopsia of unclear etiology. At the time of evaluation, her BCVA was 20/30 in her right eye (OD) and 20/20 in her left eye (OS) and her intraocular pressures measured 12 mmHg in both eyes (OU). Her ocular motility examination was unremarkable except that she noted pain in all gazes. Her anterior segment exam was remarkable for tenderness to palpation of OD greater than OS and the lack of cell and flare. Dilated fundus examination revealed no cell or haze within the vitreous, but there were large, irregular patches of whitish, ill-defined, subretinal lesions most prominent around the optic nerve and within the macula (Fig. 1). These were in contrast to the other well-circumscribed, partially pigmented, atrophic choroidal lesions within this same area (Fig. 1). Multimodal imaging further defined the irregular subretinal lesions discovered on clinical examination. On autofluorescence, these lesions were hyper- and hypoautofluorescent, while on fluorescein angiography these lesions appeared to block early and stain late with late leakage around the borders of the lesions (Fig. 1). B-scan ultrasonography identified a "T-sign" OD with fundus thickening and infiltration of Tenon's space, but no definitive "T-sign" OS (Fig. 1).

A review of systems, past medical history, and focused laboratory evaluation were unremarkable for granulomatosis with polyangiitis, tuberculosis, sarcoidosis, syphilis, rheumatoid arthritis, and basic metabolic or hematologic derangements, known underlying systemic conditions associated with posterior scleritis, or chorioiditis except for positive HLA-B27 haplotyping (Table 1). These symptoms and clinical findings (multiple, large creamy subretinal lesions of various ages) we felt were consistent with a posterior scleritis and concurrent APMPE/ampiginous chorioiditis spectrum disease OU.

Due to concern for progression of the lesions into the fovea, irreversible vision loss, and worsening eye pain, the patient was started on oral prednisone (1mg/kg/day). Three days after starting steroids, the patient developed what she described as the "worst headache of her

life," while her pain with eye movements and tenderness to palpation of both globes had completely resolved. Given the well-established association of APMPE with cerebral vasculitis and/or concurrent central nervous system (CNS) disease,^{8,9} the patient was admitted to the hospital for expedited neuro-imaging, a lumbar puncture, more extensive laboratory evaluation, and consultation with neurology.

Despite an exhaustive search, the only abnormal findings on systemic workup were multiple non-enhancing, hyperintense lesions on FLAIR sequences of the patient's brain MRI of unclear significance (Table 1/ Fig. 1). In addition, the patient began to endorse bilateral hearing loss and tinnitus shortly after being discharged from the hospital. She was found to have mild high frequency hearing loss in the right ear and moderate high-frequency hearing loss in the left by audiogram (data not shown).

As the chorioretinal lesions began to regress (Fig. 2), the patient was started on 20mg per week of oral methotrexate to reduce risk of foveal involvement with ocular recurrence and ongoing concern for CNS involvement (headaches and hearing loss). Her high dose systemic steroids were tapered during this time.

Three months after initiating treatment, the patient's BCVA remains stable (20/20 OD, 20/25 OS), her ocular lesions have nearly resolved with only mild, residual pigmentary changes (Fig. 2). Repeat neuro-imaging has remained essentially unchanged from prior examination.

Discussion

To our knowledge, this is the first reported case of a bilateral, concurrent posterior scleritis and ampiginous/APMPE spectrum chorioretinopathy. There has been only one other case of posterior scleritis and APMPE reported but this was a monocular process.¹⁰ We felt that our patient's presentation had many features of APMPE, but the pigmented lesions suggested various ages of lesions that would be more typical of ampiginous chorioretinopathy. There are previous reports that have described patients developing scleritis two years after an episode of

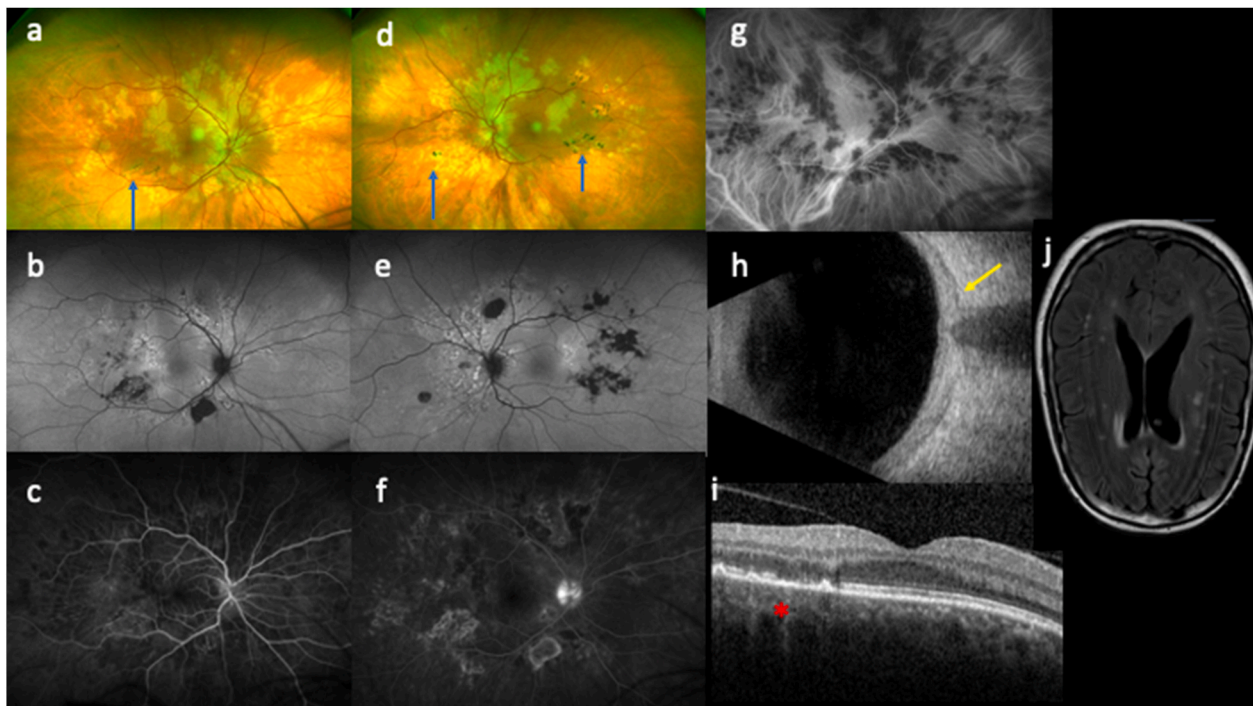


Fig. 1. Imaging findings at time of evaluation. (a) The right eye had multiple, large whitish subretinal lesions as well as pigmented lesions (blue arrow) with mottled hyper- and hypoautofluorescence of the areas (b) that blocked early on fluorescein angiogram (c) and stained late (f). These same areas were hypofluorescent on ICG imaging (g). Similar findings could be found in the left eye (d-e). There was a "T-sign" on B-scan (h, yellow arrow), choroidal thickening on OCT (i, red asterisk), and multiple, scattered hyperintensities on FLAIR MRI sequences within the brain (j). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Laboratory and imaging evaluation.

Serum	
HLA-B27	Pos
HLA-B51	Neg
Quantiferon Gold	Neg
ACE/Lysozyme	WNL
Rheumatoid factor	WNL
ANA	WNL
FTA/RPR	Neg
Bartonella Serology	Neg
ANCA	Neg
Brucella	Neg
Borellia	Neg
anti-dsDNA	Neg
Toxoplasmosis Serology	Neg
HIV	Neg
ESR	WNL
CRP	WNL
TSH	WNL
T4	WNL
CSF	
Protein	WNL
Glucose	WNL
Cell Count	WNL
Culture	Unremarkable
HSV PCR	Neg
VZV PCR	Neg
Cryptococcal antigen	Neg
Oligoclonal Bands	Neg
VDRL	Neg
Cytology	Unremarkable
Flow cytometry	Unremarkable
Imaging	
CT Chest	Remote infection, no signs of sarcoidosis
MRI Brain	Hyperintense lesions of the brain

ACE, angiotensin-converting enzyme; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmic antibodies; CRP, C-reactive protein; CSF, cerebrospinal fluid; dsDNA, double stranded DNA; ESR, erythrocyte sedimentation rate; FTA, fluorescent treponemal antibody; HIV, Human immunodeficiency virus; HLA, Human leukocyte antigen; HSV, Herpes simplex virus; Neg, negative; PCR, polymerase chain reaction; Pos, positive; RPR, rapid plasmin reagin; T4, thyroxine 4; TSH, thyroid stimulating hormone; VDRL, venereal disease research laboratory; VZV, Varicella zoster virus; WNL, within normal limits.

APMPPE had resolved or posterior necrotizing scleritis with concomitant overlying sectoral chorioretinitis.^{11,12} Additionally, there have been more atypical cases of nodular scleritis in which the patient is found to have significant intraocular inflammation.¹³ However, these reports are exceptionally rare. We hypothesize that prolonged profound intraocular or scleral inflammation can extend beyond the initial affected site to include surrounding tissues of the eye and may even lead to fluid accumulation in potential spaces (i.e. T-sign). This is supported, in part, by patients with Behcet's posterior uveitis or those with posterior scleritis with increased choroidal thicknesses that are corticosteroid-responsive.¹⁴⁻¹⁶ These findings suggest that there are underlying inflammatory changes of the choroid in conditions of either the retina or sclera despite no obvious clinical examination findings to suggest it. This was also seen in our patient as she had fundus thickening on ultrasound and significant choroidal thickening on OCT. We hypothesize that our patient's ocular inflammatory disorder started in the sclera and extended internally to the choroid and pigment epithelium or started in the choroid/retinal pigment epithelium and extended externally to include the sclera, since one of these mechanisms seems more plausible than developing two rare, independent ocular conditions simultaneously.

CNS involvement with APMPPE is well-documented and can include headaches, vasculitis, sagittal sinus thromboses, strokes, and even death.^{8,9,17,18} As such, clinicians should have a low threshold to perform neuroimaging with any neurological symptoms as, unlike APMPPE, CNS pathology warrants aggressive inflammatory control with systemic

steroids and immune modulatory therapy to reduce the risk of significant morbidity and mortality.¹⁹ Due to the patient's development of severe headaches and hearing loss, we and our neuroimmunology colleagues felt that these were manifestations of CNS disease and warranted treatment as such with systemic corticosteroids and immune modulatory therapy as others have advocated.^{1,9,20}

The management of APMPPE/ampiginous choroiditis remains controversial within the uveitis community as many cases of APMPPE spontaneously resolve with minimal-to-no sequelae. However, we, and others, have argued that if we were to personally develop the disease, we would prefer the most aggressive management to prevent subfoveal involvement and potentially disabling poor visual outcomes as well as possibly hasten resolution of intraocular and scleral inflammation.²¹ This is in contrast to ampiginous that recurs, that others have advocated for initiating immunosuppressive therapy.⁵ To reduce the risk of ocular recurrence (commonly reported in ampiginous choroiditis) and treat the previously mentioned CNS findings, our patient was started on immunomodulatory therapy as advocated by others.⁵ It remains to be seen if our patient will develop ocular or CNS recurrence of disease.

Conclusion

Posterior scleritis and APMPPE/ampiginous choroiditis can concurrently occur. A low threshold for further ocular or CNS imaging should be considered in any case of APMPPE.

Patient consent

The patient has given both verbal and written consent to publish this report.

Disclosures

All authors have no conflicts of interest to disclose and attest that they meet the current ICMJE criteria for authorship.

Author declaration

[Instructions: Please check all applicable boxes and provide additional information as requested.]

Funding

No funding was received for this work.

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

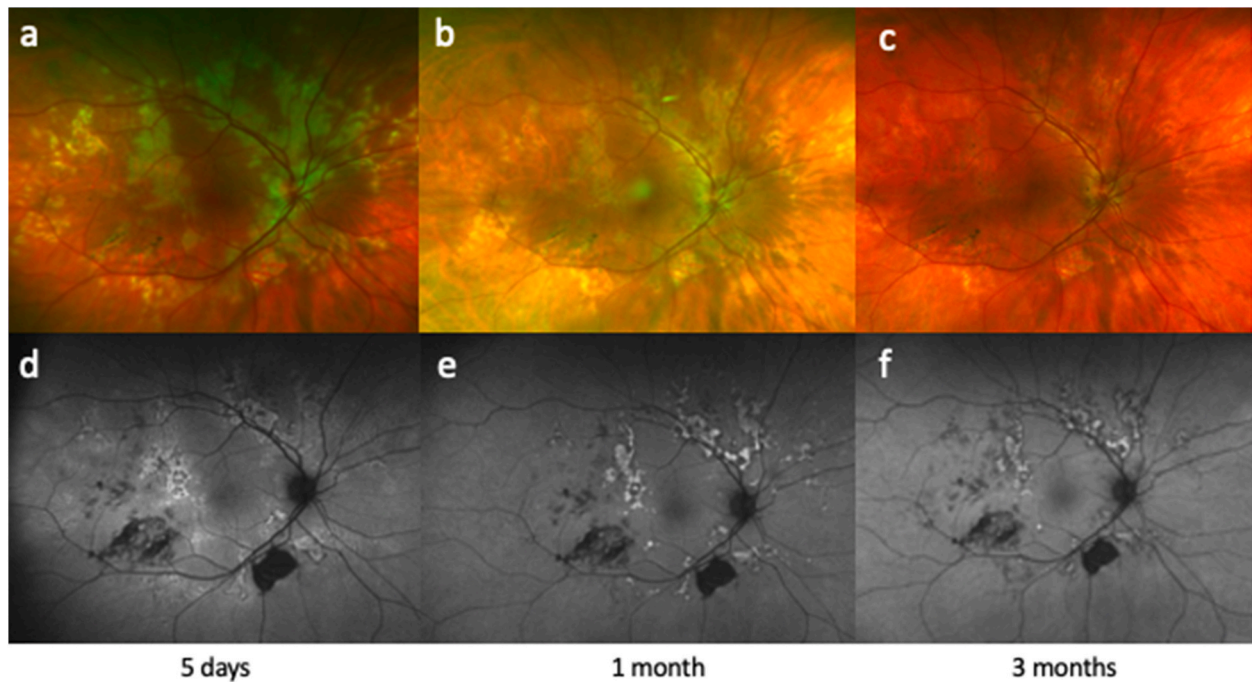


Fig. 2. Clinical course of retinal findings. (a-c) The subretinal lesions were followed over time and notable regression can be seen when comparing the lesion sizes 5 days, 1 month, and finally 3 months later within the right eye. This is more striking in the autofluorescent images in which the hyperautofluorescent lesions shrink in size over the same time period (d-f).

Authorship

We confirm that the manuscript has been read and approved by all named authors.

We confirm that the order of authors listed in the manuscript has been approved by all named authors.

Contact with the editorial office

The Corresponding Author declared on the title page of the manuscript is:

Christopher Conrady, MD, PhD.

This author submitted this manuscript using his/her account in EVISE.

We understand that this Corresponding Author is the sole contact for the Editorial process (including EVISE and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

We confirm that the email address shown below is accessible by the Corresponding Author, is the address to which Corresponding Author's EVISE account is linked, and has been configured to accept email from the editorial office of American Journal of Ophthalmology Case Reports: cconrady@med.umich.edu.

Someone other than the Corresponding Author declared above submitted this manuscript from his/her account in EVISE:

N/A.

We understand that this author is the sole contact for the Editorial process (including EVISE and direct communications with the office). He/she is responsible for communicating with the other authors, including the Corresponding Author, about progress, submissions of revisions and final approval of proofs.

Declaration of competing interest

Potential conflict of interest exists:

We wish to draw the attention of the Editor to the following facts, which may be considered as potential conflicts of interest, and to significant financial contributions to this work:

The nature of potential conflict of interest is described below:

No conflict of interest exists.

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Acknowledgements

All authors have no grant or funding sources to disclose.

References

- Sielert LA, Harris AR, Pyun JM, Campbell BJ, Swan RT. Posterior scleritis. *Expet Rev Ophthalmol.* 2016;11(6):475–484. <https://doi.org/10.1080/17469899.2016.1251313>.
- Cheung CMG, Chee S-P. Posterior scleritis in children: clinical features and treatment. *Ophthalmology.* 2012;119(1):59–65. <https://doi.org/10.1016/j.ophtha.2011.09.030>.
- Abu-Yaghi NE, Hartono SP, Hodge DO, Pulido JS, Bakri SJ. White dot syndromes: a 20-year study of incidence, clinical features and outcomes. *Ocul Immunol Inflamm.* 2011;19(6):426–430. <https://doi.org/10.3109/09273948.2011.624287>.
- Gass JDM. Acute posterior multifocal placoid pigment epitheliopathy. *Arch Ophthalmol.* 1968;80(2):177–185. <https://doi.org/10.1001/archophth.1968.00980050179005>.
- Jyotirmay B, Jafferji SS, Sudharshan S, Kalpana B. Clinical profile, treatment, and visual outcome of ampinginous choroiditis. *Ocul Immunol Inflamm.* 2010;18(1):46–51. <https://doi.org/10.3109/09273940903402637>.
- Gupta A, Bansal R, Gupta V, Sharma A. Fundus autofluorescence IN SERPIGINOUSLIKE choroiditis. *Retina.* 2012;32(4). https://journals.lww.com/retinajournal/Fulltext/2012/04000/FUNDUS_AUTOFLUORESCENCE_IN_SERPIGINOUSLIKE.25.aspx.
- Patel M, Vavvas D. Fundus autofluorescence in ampinginous choroiditis. *Ophthalmic Surg Lasers Imaging Retina.* 2013;44:393–397. <https://doi.org/10.3928/23258160-20130715-10>.
- Algahtani H, Alkhotani A, Shirah B. Neurological manifestations of acute posterior multifocal placoid pigment epitheliopathy. *J Clin Neurol Seoul Korea.* 2016;12(4): 460–467. <https://doi.org/10.3988/jcn.2016.12.4.460>.
- O'Halloran HS, Berger JR, Lee WB, et al. Acute multifocal placoid pigment epitheliopathy and central nervous system involvement: nine new cases and a

- review of the literature. *Ophthalmology*. 2001;108(5):861–868. [https://doi.org/10.1016/S0161-6420\(01\)00565-6](https://doi.org/10.1016/S0161-6420(01)00565-6).
10. Laghmari M, Boutimzine N, Karim A, et al. Sclérite postérieure simulant une épithéliopathie en plaques. *J Fr Ophtalmol*. 2004;27(2):174–178. [https://doi.org/10.1016/S0181-5512\(04\)96115-3](https://doi.org/10.1016/S0181-5512(04)96115-3).
 11. Matsuo T, Horikoshi T, Nagai C. Acute posterior multifocal placoid pigment epitheliopathy and scleritis in a patient with pANCA-positive systemic vasculitis. *Am J Ophthalmol*. 2002;133(4):566–568. [https://doi.org/10.1016/S0002-9394\(01\)01369-1](https://doi.org/10.1016/S0002-9394(01)01369-1).
 12. Stacy RC, Uchiyama E, Jakobiec FA, Sobrin L. Posterior necrotizing scleritis presenting as sectoral chorioretinitis. *Ocul Immunol Inflamm*. 2015;23(5):412–415. <https://doi.org/10.3109/09273948.2014.896467>.
 13. Murthy SI, Sati A, Sangwan V. Infectious scleritis mimicking severe ocular inflammation: atypical initial presentation. *BMJ Case Rep*. 2013;2013, bcr2013008686. <https://doi.org/10.1136/bcr-2013-008686>.
 14. Kim M, Kim H, Kwon HJ, Kim SS, Koh HJ, Lee SC. Choroidal thickness in Behcet's uveitis: an enhanced depth imaging-optical coherence tomography and its association with angiographic changes. *Invest Ophthalmol Vis Sci*. 2013;54(9):6033–6039. <https://doi.org/10.1167/iovs.13-12231>.
 15. Uchihori H, Nakai K, Ikuno Y, et al. Choroidal observations in posterior scleritis using high-penetration optical coherence tomography. *Int Ophthalmol*. 2014;34(4):937–943. <https://doi.org/10.1007/s10792-013-9894-4>.
 16. Yanagida C, Usui Y, Sakai J-I, Goto H. An unusual case of Behcet disease with posterior scleritis: a case report. *Medicine (Baltim)*. 2019;98(35). <https://doi.org/10.1097/MD.00000000000016886>. e16886-e16886.
 17. Hammer ME, Grizzard WS, Travies D. Death associated with acute, multifocal, placoid pigment epitheliopathy. *Arch Ophthalmol*. 1989;107(2):170–171. <https://doi.org/10.1001/archoph.1989.01070010176014>.
 18. Bewermeyer H, Nelles G, Huber M, Althaus C, Neuen-Jacob E, Assheuer J. Pontine infarction in acute posterior multifocal placoid pigment epitheliopathy. *J Neurol*. 1993;241(1):22–26. <https://doi.org/10.1007/BF00870667>.
 19. Tsuboyama M, Chandler JV, Scharf E, et al. Neurologic complications of acute posterior multifocal placoid pigment epitheliopathy: a case series of 4 patients. *The Neurohospitalist*. 2018;8(3):146–151. <https://doi.org/10.1177/1941874417749379>.
 20. Clearkin L, Hung S. Acute posterior multifocal placoid pigment epitheliopathy associated with transient hearing loss. *Trans Ophthalmol Soc U K*. 1983;103:562–564.
 21. *Diagnosis and Treatment of Uveitis*. second ed. Jaypee Brothers Medical Publishers; 2013.