American Journal of Ophthalmology Case Reports 19 (2020) 100793

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Vogt-Koyanagi-Harada disease presenting secondary to a post-infectious *Mycoplasma pneumoniae* autoimmune response

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ARTICLE INFO

Keywords:
Mycoplasma pneumoniae
Panuveitis
Uveitis
Vogt-koyanagi-harada disease

ABSTRACT

Purpose: To report a rare case of Vogt-Koyanagi-Harada disease likely secondary to post-infectious *Mycoplasma pneumoniae* autoimmune response in a 14-year-old Hispanic female.

Observations: On presentation, visual acuity was 20/400 in the right eye and 20/20 in the left eye. The patient also had bilateral hyperemia, subretinal fluid, and vitreous cell graded at 1+. Fluorescein angiography and indocyanine green chorioangiography showed bilateral peripapillary hypofluorescence consistent with blocking and hyperflourescence consistent with staining. Laboratory testing showed elevated *M. pneumoniae* IgM and rising IgG antibodies. Topical steroids and oral steroids helped mitigate the systemic disease process and fully restore visual acuity through the 7-week mark.

Conclusions and Importance: The patient had elevated *M. pneumoniae* IgM and rising IgG antibodies resulting in ocular inflammation likely secondary to an autoimmune response. In this case of post-infectious *M. pneumoniae*, topical corticosteroids were beneficial in mitigating ocular manifestations initially, although oral steroids were needed and tapered over 6 weeks.

1. Introduction

Autoimmune conditions are on the rise, and infections or exposure to bacteria or other infectious microorganisms may be major triggers of autoimmunity.[1] *Mycoplasma pneumoniae* infection has often been associated with various autoimmune disorders and antibody production including ankylosing spondylitis[2] and rheumatoid arthritis.[3] In an active infection, the most common neurologic presentations are encephalitis and transverse myelitis.[4] In non-active infectious status however, immune dysregulation can cause cerebellar dysfunction, peripheral nerve involvement, and cranial nerve palsies.[4]

We present a case of Vogt-Koyanagi-Harada (VKH) disease likely secondary to post-infectious *M. pneumoniae* autoimmune response. VKH, or uveomenigoencephalitic syndrome, is a systemic autoimmune disease targeting melanocyte-rich tissues.[5] The etiology of the disease is a matter of debate, however a viral infectious trigger is the most widely accepted.[5–7] The disease has specific diagnostic criteria which the patient had no history of penetrating ocular trauma or surgery, had bilateral ocular involvement with diffuse choroiditis presenting as serous retinal detachments and iridocyclitis, and meningismus.[8]

2. Case report

A 14-year-old Hispanic female presented to the Emergency Department at Brooke Army Medical Center with a two-week history of decreased vision, redness, and central scotoma in her right eye. Two weeks prior to the start of visual symptoms, the patient had fever, myalgias, headache, nuchal rigidity, nausea, and vomiting, which resolved two days after starting a regimen of oseltamivir phosphate for presumed viral influenza. Other past medical and family history were noncontributory. The Ophthalmology Service was consulted to evaluate for possible papilledema.

On examination, her visual acuity was 20/400 in the right eye, and 20/20 in the left eye. The right eye had a 2+ relative afferent pupillary

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https://doi.org/10.1016/j.ajoc.2020.100793
Received 20 June 2019; Received in revised form 13 June 2020; Accepted 16 June 2020
Available online 22 June 2020
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defect. Intraocular pressure, ocular motility, and confrontational fields were found to be normal bilaterally. She correctly identified 4/12 and 12/12 Hardy Rand and Rittler (HRR) color plates for the right and left eyes, respectively. The anterior segment examination showed bilateral trace anterior chamber cell as well as conjunctival injection in the right eye. The right eye showed a 0.3 cup-to-disc ratio with hyperemia and subretinal edema (Fig. 1a, b). The exam in the right eye was also remarkable for vitreous cell graded at 1+ and subretinal fluid, which was also seen on optical coherence tomography (OCT) of the macula (Fig. 1c). The left eye had a 0.3 cup-to-disc ratio with hyperemia and macular striae, and vitreous cell graded at 1+ as well. B-scan showed choroidal thickening bilaterally but right greater than left without a T-sign. Fluorescein angiography and indocyanine green chorioangiography showed bilateral peripapillary hypofluorescence consistent with blocking and hyperflourescence consistent with staining (Fig. 1d). Pediatric Infectious Diseases, Pediatric Neurology, and Rheumatology were consulted. Initial treatment included topical 1% prednisolone acetate ophthalmic suspension every 2 h but was subsequently replaced with 0.05% difluprednate ophthalmic emulsion every 2 h upon admission.

Magnetic resonance imaging (MRI) of the brain/orbits was negative for any optic nerve thickening, intracranial masses, or orbital masses. Serologic testing obtained in coordination with Pediatric ID revealed a normal complete blood count and erythrocyte sedimentation rate, and was negative for *Borrelia burgdorferi*, *Bartonella henselae*, *Treponema pallidum*, *Mycobacterium tuberculosis*, West Nile virus, *Human alphaherpesvirus 1* and *2* (HSV-1/HSV-2), *Human betaherpesvirus 5* (HCMV), *Cryptococcus neoformans*, *Neisseria meningitidis*, *Neisseria gonorrhoeae, Streptococcus*, Epstein-Barr virus (EBV, formally *Human gammaherpesvirus 4*), *Listeria monocytogenes*, Human Immunodeficiency Virus 1 and 2, and HLA-B27/A29/DR15. However, *Mycoplasma* IgM and IgG levels were elevated at 1286 and 777, respectively. C-reactive protein was also elevated and attributed to the ongoing inflammatory process. A subsequent lumbar puncture revealed normal opening pressure, absence of oligoclonal bands, no neutrophils, normal glucose, but elevated protein at 92 mg/dL. Polymerase chain reaction (PCR) of the cerebral spinal fluid was negative for *Mycoplasma pneumoniae*. PCR DNA sampling was not, however, obtained from intraocular fluid samples.

Pediatric Infectious Disease concluded that the *Mycoplasma* infection was not active, but rather the current level of systemic and ocular inflammation was likely a post-infectious autoimmune response, and therefore recommended against antibiotics. Pediatric Neurology felt that the subacute onset and temporal relationship to her febrile illness made an infectious, para-infectious, or autoimmune etiology most

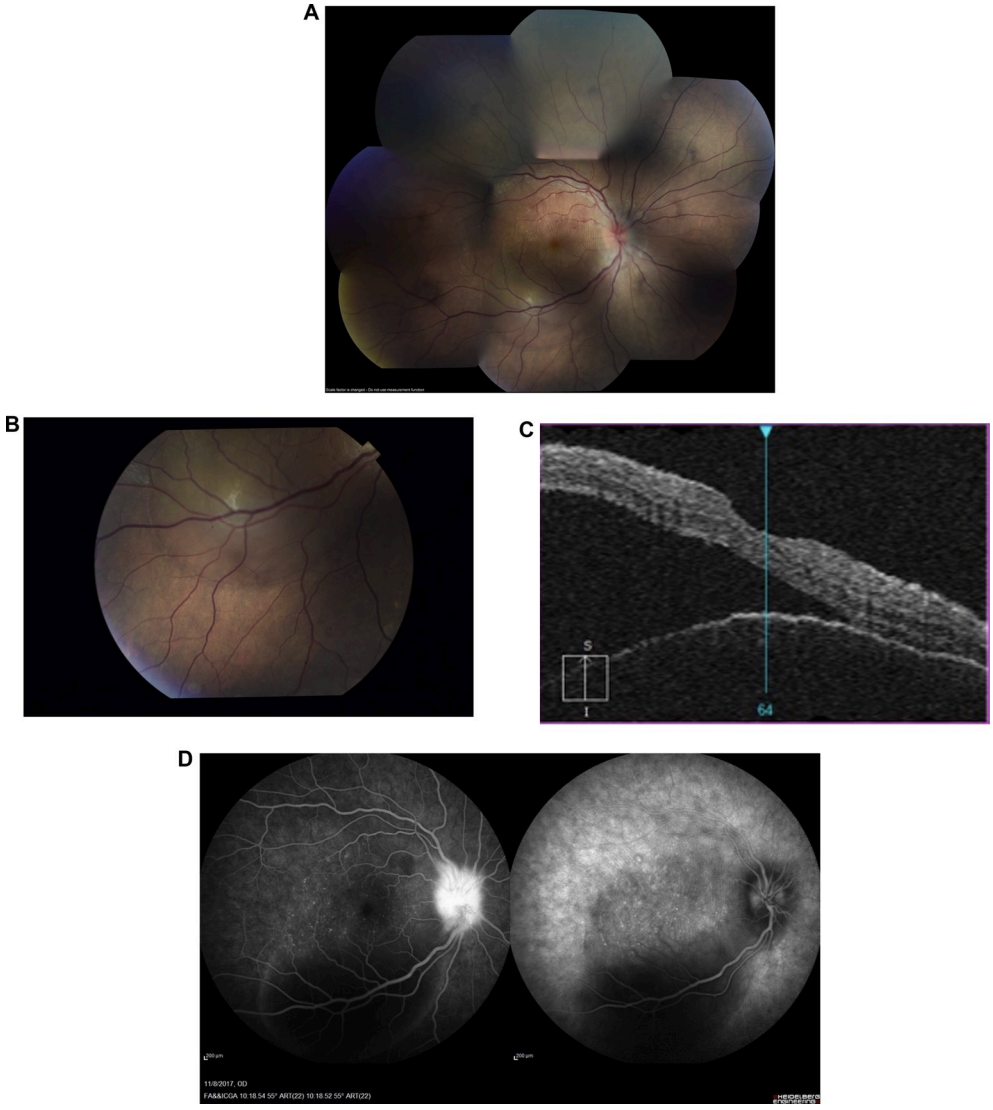

Fig. 1. a,b. Fundus photography of the right eye showing macular striae, hyperemia, and subretinal fluid under the inferior arcade. Fig. 1 c. OCT Macula demonstrating subretinal fluid. Fig 1 d. IFA (left) and ICG (right) of the right eye. Note optic nerve staining and leakage, and inferior arcade blockage.

likely. In addition, the service also felt that the findings could be consistent with Vogt-Koyanagi-Harada disease.

Visual acuity improved to 20/50 OD at day six solely on topic steroids. The patient's visual acuity improved further to 20/40 by day 10; and after discussion with Pediatric Infectious Disease who ruled out an active infection, the patient was started on 40mg of oral prednisone and was tapered over the next 6 weeks. Her visual acuity continued to improve to 20/30 at day 16, and finally 20/20 bilaterally at the 7-week mark. Interestingly, at the 3-week mark, the IgG level was at 1247, which was suggestive of a rising immune response. Two months after presentation, the patient empirically received a ten-day course of 100 mg doxycycline twice daily by Dermatology for a rash that was later thought to be an allergic reaction to an unrelated medication. However, this course of doxycycline would also be considered the treatment dose for *Mycoplasma pneumoniae*. Fortunately, the patient has continued to remain without recurrence for 6 months.

3. Discussion

M. pneumoniae has been demonstrated to cause infectious uveitis requiring treatment with antibiotics to induce resolution of symptoms.[9,10] However, in this case report, the patient, without evidence of active *M. pneumoniae* infection, presented with elevated antibody titers and signs of VKH disease. VKH disease was high on the differential list given a Hispanic female with bilateral serous detachments and choroidal thickening, anterior chamber inflammation, headache, nuchal rigidity, and nausea and vomiting. Her presentation met most of the criteria for VKH: bilateral choroiditis, neuropathologic findings – in this case, meningismus – without any history of ocular trauma or evidence of other disease processes.[8] VKH commonly presents in the following stages: prodromal (resembling a viral illness), acute uveitic (most commonly an initial posterior uveitis that develops later into panuveitis), convalescent (occurring weeks after uveitic stage with systemic signs like Sugiura's sign and choroidal depigmentation resulting in a "sunset-glow" fundus), and recurrent stages (commonly occurs with vision threatening complications like glaucoma, cataract and subretinal neovascularization).[5]

The mainstay of diagnosis of *M. pneumoniae* is through serological diagnosis, but there can be poor correlation between PCR and serology, with frequent negative CSF PCR results as in this patient's case.[11] Although the serology was positive, Pediatric Infectious Disease felt that in the absence of ongoing respiratory symptoms that there was not an active infection, but rather an autoimmune response to a previous resolved *M. pneumoniae* infection. *M. pneumoniae* has been associated with autoimmunity through cross-reaction of bacterial cell components and the human cell.[11] Furthermore, cross-reactivity with Epstein-Barr virus (EBV) is common.[4] EBV infection has been associated with the development of VKH disease.[6] Our patient's vague symptoms of intermittent headache, upper respiratory symptoms and nausea and vomiting could have been associated with an EBV infection leading to *M. pneumoniae* serologic elevation. However, EBV virus testing was negative – though it is important to note that heterophile antibody testing carries a 25% false-negative rate early in the disease course.[12]

The management of this case is also of interest. Initially, the patient was treated solely with topical prednisolone and then difluprednate resulting in a significant improvement in vision (from 20/400 to 20/40), the presence of anterior chamber cell, choroidal thickening and subretinal fluid on OCT. All of these changes occurred prior to initiation of oral steroids which were started after Pediatric Infectious Disease deemed a non-active infection status, and were critical to reducing any recurrences.[13] Although anterior uveitis in patients with VKH can be treated with topical corticosteroids[14]; in general, VKH is treated with high dose corticosteroids at 1–1.5mg/kg/day over a six-month taper.[5,13,15] Therefore, although our patient has not had any known recurrences, on hindsight a longer taper may have been more appropriate for the patient.

In conclusion, we present an interesting case of a young Hispanic female with 2 weeks of headache and URI symptoms that presented with elevated *M. pneumoniae* antibodies with VKH disease. Her disease signs and symptoms resolved initially with topical corticosteroids, but she was further treated with oral systemic steroids.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

Financial support

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: CIW, KEE, GAJ, MLW.

Acknowledgments

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army, the Department of Defense, the Uniformed Services University of the Health Sciences or any other agency of the U.S. Government.

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