

Faheem Sheriff, MD
Nandakumar S.
Narayanan, MD, PhD
Anita J. Huttner, MD
Joachim M. Baehring,
MD

*Neurol Neuroimmunol
Neuroinflamm*
2014;1:e49; doi: 10.1212/
NXL.0000000000000049

VOGT-KOYANAGI-HARADA SYNDROME: A NOVEL CASE AND BRIEF REVIEW OF FOCAL NEUROLOGIC PRESENTATIONS

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Vogt-Koyanagi-Harada syndrome (VKH) is a multi-systemic granulomatous autoimmune disease affecting organs with high melanocyte concentrations including the eye, CNS, inner ear, and skin. Neurologic manifestations of VKH typically include aseptic meningitis and headache. Focal neurologic signs such as cranial nerve palsies, hemiparesis, and optic neuritis are relatively uncommon.

A 58-year-old Caucasian woman with a previous history of recurrent episodes of aseptic meningitis presented with a 2-week history of ataxia, hearing loss, numbness over the right cheek, and difficulty closing her right eye. A neurologic examination revealed decreased sensation in right cranial nerve V2 distribution, right peripheral facial palsy, and right hypoglossal nerve dysfunction. She had profound hearing impairment bilaterally. She also had dysdiadochokinesia and dysmetria on the right. An ophthalmologic examination revealed that her left eye had no light perception, and there were signs of phthisis bulbi, a dense cataract, and posterior synechiae. The right eye had 20/40 vision and was status post cataract extraction. There was no evidence of poliosis, vitiligo, or alopecia, and she denied prior ocular trauma.

She had an erythrocyte sedimentation rate of 41 mm/hour, normal angiotensin-converting enzyme, and a slightly elevated rheumatoid factor at 22 IU/mL. CSF analysis revealed 37 nucleated cells/mm³ (91% lymphocytes), glucose 92 mg/dL, and protein 257 mg/dL. CSF flow cytometry failed to reveal monoclonal lymphoproliferation. Infectious serologies were negative. Coronal and axial gadolinium-enhanced T1-weighted sequences showed diffuse pachymeningeal enhancement and thickening (figure, A and B). There was a heterogeneously enhancing soft tissue mass in the right cerebellopontine angle (CPA) arising from the dura on a broad base extending into the right internal auditory canal (figure, A and B). Biopsy of the frontal dura revealed a diffuse, thickened brown appearance (figure, C). Histopathologic analysis revealed an inflammatory infiltrate composed of numerous CD3-positive T lymphocytes and a few

CD20-positive B lymphocytes. In addition, numerous CD68-positive macrophages were found to contain melanin, which was confirmed by Fontana-Masson staining (figure, D–F). Stains for fungi and acid-fast bacilli were negative and no granulomas were seen.

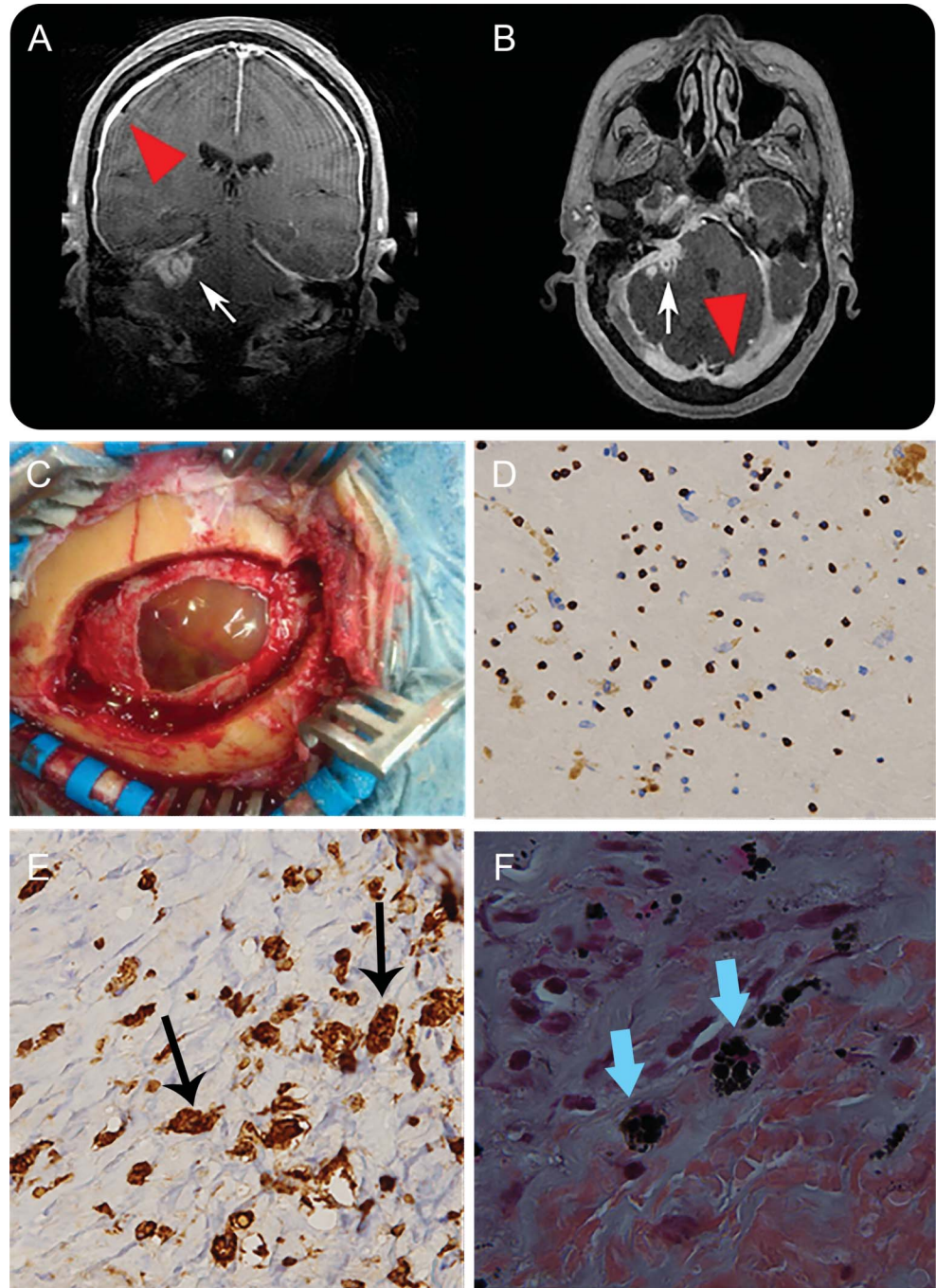
During her hospitalization, she was started on IV dexamethasone 4 mg every 4 hours with a rapid taper. There was marked improvement in her ataxia and cranial neuropathies. Repeat T1 sequences with contrast showed almost complete resolution of the right CPA mass. Ten days after stopping the corticosteroids, she developed a bifrontal headache and tinnitus necessitating readmission and corticosteroid therapy. She was discharged on a gradual corticosteroid taper. Six-month follow-up revealed complete resolution of all neurologic deficits except bilateral hearing loss.

VKH typically presents with granulomatous panuveitis, the characteristic “sunset glow” fundus (due to loss of choroidal melanocytes), vitiligo, poliosis, and sensorineural hearing loss. This patient met criteria for a diagnosis of “incomplete VKH” given absence of integumentary findings.¹ Melanin-laden macrophages on CSF cytology are highly suggestive.² Occasionally in the chronic phase there may be an absence of granulomatous changes on biopsy, as seen in this case.

The antigenic targets for VKH are the tyrosinase family proteins and gp100, against which specific T cells are directed.³ This explains the predilection for melanocyte-rich organs. These CD4⁺ T cells may be triggered by an infectious agent; this process is facilitated by presence of certain HLA types, including HLA-DRB1*0405 and HLA DR 4/DR53, which may unmask cryptic self-epitopes on the surface of melanocyte-specific proteins and activate T cells that would otherwise be silent.³ Focal parenchymal lesions with associated neurologic deficits have been reported in relatively few VKH cases.^{4–6} One case presented with Wallenberg syndrome⁴ and another with brainstem encephalitis and multiple cranial nerve palsies.⁵ It is interesting that our patient had the highest disease burden in the CPA, given the higher concentration of melanocytes over the ventrolateral medulla in humans.⁷ In a recently published case, a predilection for pontomesencephalic and cerebellar areas was also noted.⁶

Given the paucity of reported VKH cases involving the posterior fossa, no inferences can be made at

Figure MRI and leptomeningeal biopsy findings in Vogt-Koyanagi-Harada syndrome involving the cerebellopontine angle



(A) Coronal and (B) axial gadolinium-enhanced T1-weighted sequences before initiation of corticosteroid therapy showing diffuse nodular pachymeningeal thickening and enhancement (red arrowheads). Also seen is a heterogeneously enhancing soft tissue mass in the right cerebellopontine angle (white arrows) extending into the internal auditory canal. Of note, there is mild truncation (or Gibbs) artifact in (A). (C-F) Pathology of leptomeningeal biopsy. (C) Gross view of surgical field, revealing diffuse brown discoloration of dura mater. (D) CD3-positive (40 \times) T lymphocytes are present. (E) Numerous CD68-positive (40 \times) macrophages (black arrows) containing melanin granules. (F) Fontana-Masson stain (100 \times oil immersion) demonstrates melanin granules within macrophages (light blue arrows).

this point in time. The differential concentration of the tyrosinase family proteins in leptomeningeal melanocytes in various brain regions has not yet been studied and may hold the key to understanding why certain sites are more affected than others

and may provide useful insight into other neurologic diseases affecting tyrosinase family proteins and melanocytes.

Given the potential for improved neurologic outcomes with timely immunosuppressive therapy, this

disorder should be considered in the differential diagnosis of patients presenting with ocular disease and recurrent aseptic meningitis with or without focal neurologic deficits.

From the Department of Neurology (F.S.), Oregon Health & Science University, Portland; Department of Neurology (N.S.N.), University of Iowa, Iowa City; and Department of Pathology (A.J.H.) and Departments of Neurology, Neurosurgery, and Medicine (J.M.B.), Yale School of Medicine, New Haven, CT.

Author contributions: Fabeem Sheriff, Nandakumar Narayanan, and Joachim Baehring were involved in clinical data collection, discussion, and authoring the manuscript. Anita Huttner was involved in arriving at a histopathologic diagnosis and providing useful clinical insight into the case.

Acknowledgment: The authors sincerely thank Dennis Bourdette, MD, FANA, FAAN (Chair and Roy and Eulalia Swank Family Research Professor, Dept of Neurology, Oregon Health & Science University) and Daniel Gibbs, MD, PhD (Dept of Neurology, Oregon Health & Science University) for providing invaluable insight into the case.

Study funding: No targeted funding reported.

Disclosure: F.G. Sheriff reports no disclosures. N.S. Narayanan has received research support from Brain and Behavior Research Foundation and Carver Medical Trust. A.J. Huttner and J.M. Baehring report no disclosures. Go to Neurology.org/nn for full disclosures. The Article Processing Charge was paid by Oregon Health and Science University. This is an open access article distributed under the terms of the Creative Commons Attribution-Noncommercial No Derivative

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Received June 2, 2014. Accepted in final form October 17, 2014.

Correspondence to Dr. Sheriff: sheriff@ohsu.edu

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