Pearls & Oy-sters: Cogan syndrome

A potentially grave disorder of audiovestibulopathy with many faces

Sun-Uk Lee, MD, Ji-Soo Kim, MD, PhD, Joon Young Hyon, MD, PhD, You-Jung Ha, MD, PhD, Hyo-Jung Kim, PhD, Jae-Jin Song, MD, PhD, Jeong-Yoon Choi, MD, PhD, and Xu Yang, MD

Neurology® 2019;93:39-41. doi:10.1212/WNL.0000000000007733

Correspondence
Dr. J.-S. Kim
jisookim@snu.ac.kr

MORE ONLINE

Video

Pearls

- Cogan syndrome refers to a chronic inflammatory disorder that typically presents with ocular inflammation and audiovestibular dysfunction.
- Cogan syndrome may mimic Ménière disease (MD) by presenting recurrent audiovestibulopathy.

Oy-sters

- Cogan syndrome can present the features of benign paroxysmal positional vertigo (BPPV) initially, followed by sequential bilateral labyrinthitis, and finally ocular inflammation.
- Cogan syndrome should be suspected even in unilateral audiovestibulopathy of unknown cause, especially in the presence of systemic symptoms, elevated serologic markers for inflammation, or bilateral labyrinthine enhancements on MRI.

A 60-year-old previously healthy man had recurrent positional vertigo for 2 months refractory to canalith repositioning maneuvers (CRMs) for BPPV. Two weeks before referral to our hospital, he developed hearing loss and fluctuating tinnitus in the right ear, and the positional vertigo changed into recurrent spontaneous vertigo lasting about 2 hours. The patient also reported intermittent febrile sensation and myalgia for 2 months.

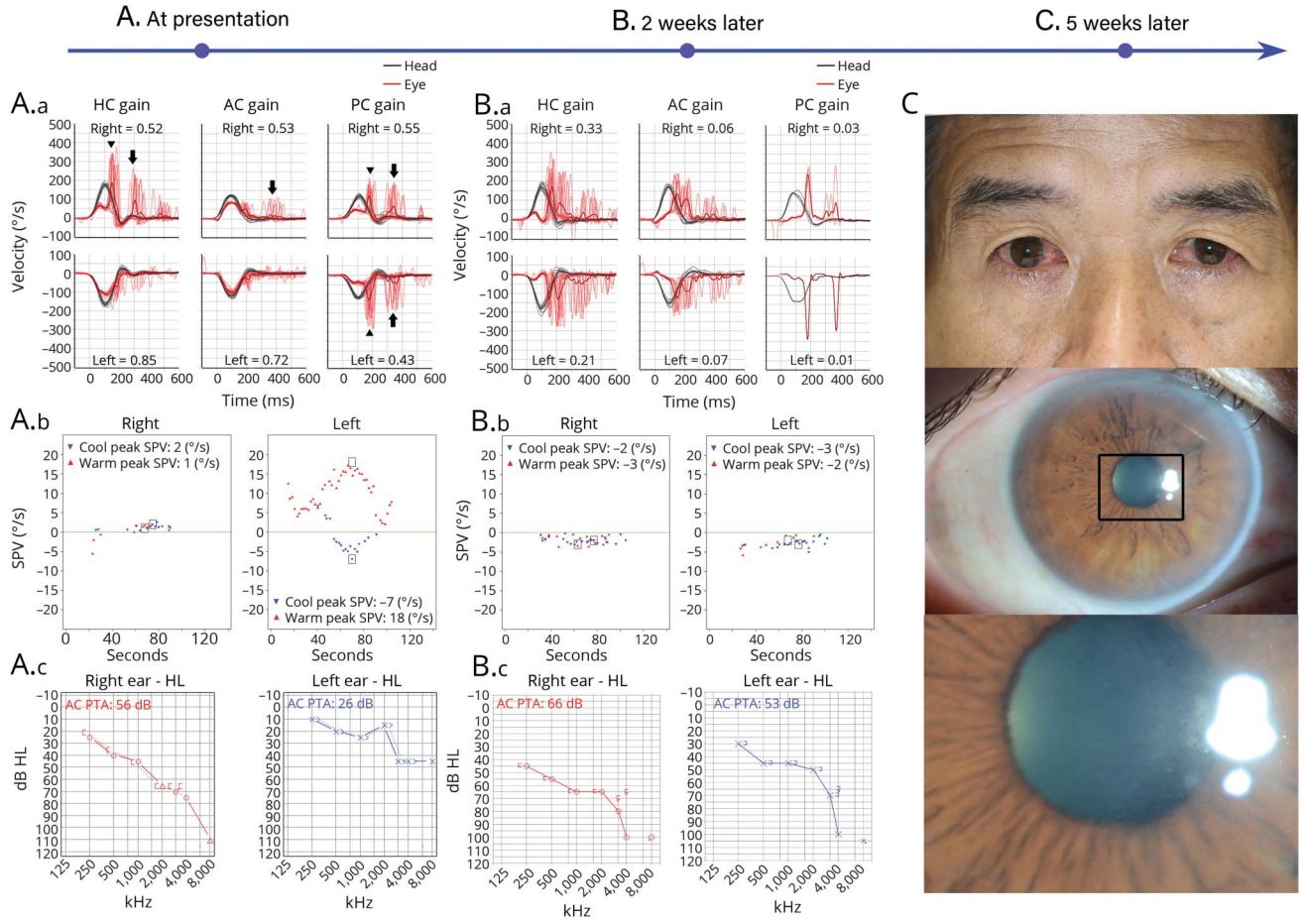
At admission, the body temperature was 38.4°C. The patient showed spontaneous nystagmus beating leftward, downward, and counterclockwise (the upper poles of the eyes beating to the left shoulder). Bedside head impulse tests (HITs) were positive for right horizontal semicircular canal. The patient also showed persistent apogeotropic nystagmus after head turning to either side while supine, more intense while turning the head to the right. In addition, left Dix-Hallpike maneuver evoked nystagmus beating upward and counterclockwise (video 1). The positional nystagmus did not respond to repeated CRMs.

Video HITs were positive for all right semicircular canals and left posterior canal (figure, A.a). Bithermal caloric tests showed right canal paresis (figure, A.b). The patient showed absent cervical vestibular-evoked myogenic potentials (VEMPs) and decreased ocular VEMPs with an interaural difference at 42.9% (normal range < 21.5%) during right ear stimulation. He also showed right sensorineural hearing loss (figure, A.c), leukocytosis of 12,700/μL (neutrophil 76%), hemoglobin of 12.4 g/dL (hematocrit at 36.9%), and platelet counts at 413 k/μL. The erythrocyte sedimentation rate (ESR, 120 mm/h) and C-reactive protein (CRP, 23.4 mg/dL) were elevated. Internal auditory canal MRIs revealed abnormal enhancements in both labyrinths, and magnetic resonance angiography revealed a stenosis of left middle cerebral artery at the M1 portion. The patient's fever and vertigo resolved 1 week later without specific treatments even though the positional nystagmus persisted. He was discharged with a diagnosis of right labyrinthitis and concomitant BPPV involving the contralateral ear.

From the Department of Neurology (S.-U.L.), Korea University Anam Hospital; Department of Neurology (S.-U.L., J.-S.K., J.-Y.C.), Dizziness Center, Clinical Neuroscience Center, and Department of Neurology (J.-S.K., J.-Y.C.), Department of Ophthalmology (J.Y.H.), and Department of Otolaryngology–Head and Neck Surgery (J.-J.S.), Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine (Y.-J.H.), and Research Administration Team (H.-J.K.), Seoul National University Bundang Hospital, Seongnam, South Korea; and Department of Neurology (X.Y.), Aerospace Center Hospital, Peking University Aerospace School of Clinical Medicine, Peking, China.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure Presentation of the findings



(A) At presentation, 2 months after symptom onset, the patient showed positive video head impulse tests (HITs) with decreased gain and corrective covert (arrowheads) and overt (arrows) saccades for all right semicircular canals and left posterior canal (A.a), right canal paresis of 92% (A.b), and right sensorineural hearing with a pure tone average at 56 dB (A.c). (B) Two weeks later, the gains of video HITs were markedly decreased for all 6 canals (B.a) with bilateral canal paralysis (B.b) and bilateral sensorineural hearing loss (B.c). (C) Five weeks later, the patient shows a conjunctival and episcleral injection and diffuse stromal edema with keratic precipitates (black box) in both eyes suggesting interstitial keratitis. AC = anterior semicircular canal; HC = horizontal semicircular canal; HL = hearing level; PC = posterior semicircular canal; SPV = slow-phase velocity.

Two weeks later, the patient redeveloped vertigo, imbalance, bilateral fluctuating tinnitus, and sudden hearing loss in the left ear. Examination showed spontaneous nystagmus beating rightward and upward, which changed its direction into left-beating during leftward gaze. The gains of video HITs were markedly decreased for all 6 canals (figure, B.a). Bithermal caloric tests showed bilateral canal paralysis (figure, B.b). Audiometry documented symmetric sensorineural hearing loss on both sides (figure, B.c). With an impression of inflammatory disorder involving both labyrinths, he was placed on 20 mg of IV dexamethasone for 5 consecutive days, and his vertigo and hearing loss improved.

The patient was discharged with oral methylprednisolone 60 mg per day for 2 weeks, and 3 days after discontinuation of the medication, he reported deterioration of his balance and hearing again. Examination this time showed a marked conjunctival and episcleral injection and diffuse stromal edema in both eyes suggesting interstitial keratitis (figure, C). Echocardiogram and abdomen and chest CT results were normal without any evidence of vasculitis involving other organs. With a diagnosis of Cogan syndrome, he was placed on aspirin 100 mg, azathioprine 100 mg, and methylprednisolone 30 mg per day. One month later, his dizziness and eye injection improved markedly, while the hearing impairments and abnormal HITs persisted in both ears.

This study followed the tenets of the Declaration of Helsinki and was performed according to the guidelines of the Institutional Review Board of Seoul National University Bundang Hospital (B-1807-480-701).

Discussion

The patient sequentially developed positional vertigo and nystagmus mimicking BPPV, recurrent spontaneous vertigo, tinnitus, and hearing loss mimicking MD, and sequential bilateral audiovestibulopathy along with fever and myalgia. The later development of ocular inflammation delayed the diagnosis of Cogan syndrome.

Cogan syndrome is caused by autoantibodies against the peptide expressed in the sensory epithelia of the inner ear.[1] The serum antibodies against the inner ear tissue can also have an affinity to the epithelial structure of the cornea.[2] Besides the inner ear and eye, 30%–50% of patients may show vasculitis affecting any size of vessels.[3,4] Systemic symptoms, such as headache, arthralgia, fever, and myalgia, are common, along with leukocytosis, thrombocytosis, or elevated CRP and ESR.[4] Unilateral audiovestibular involvement is found in 65% of patients initially.[5] Early diagnosis and prompt treatments are important since nearly half (~44%) of the patients become deaf in both ears within 3 months.[4] Cogan syndrome is known to occur almost equally in men and women without a sex predilection.[6] The average age at symptom onset is around the third to fourth decade, with a range from 4 to 70 years in previous reports.[6,7]

Our patient showed positional nystagmus that mimicked posterior and apogeotropic horizontal canal type of BPPVs from the ear contralateral to audiovestibulopathy. Of interest, the positional nystagmus was refractory to repeated CRMs, which is inconsistent with BPPV due to canalithiasis. Indeed, persistent geotropic or apogeotropic nystagmus may be observed in labyrinthitis[8,9] and has been ascribed to heavy or light cupula due to changes in the specific gravity of the endolymph from inflammation. Otherwise, given the paroxysmal nature of the positional nystagmus during Dix-Hallpike maneuver, it may be ascribed to secondary BPPV due to labyrinthine inflammation. This implicates that positional nystagmus mimicking BPPVs can precede full-blown audiovestibulopathy in Cogan syndrome.

Cogan syndrome may mimic MD by presenting recurrent spontaneous vertigo.[4,7] However, the associated fever and myalgia, elevated inflammation markers, and progression from unilateral to bilateral audiovestibulopathy within a few months are all atypical for MD.[10] Moreover, abnormal HITs on both sides and gaze-evoked nystagmus also stand against the diagnosis of MD.[11] Additional lists for differential diagnosis of Cogan syndrome include neurosyphilis and other systematic autoimmune disorders such as Susac syndrome, Wegener granulomatosis, systemic lupus erythematous, Behçet disease, and Vogt-Koyanagi-Harada syndrome. Therefore, a scrutinized physical examination, history taking, and thorough laboratory workups are essential for differentiation of these disorders.

Given the wide spectrum of audiovestibular findings and later development of ocular inflammation in our patient, Cogan syndrome should be suspected even in unilateral audiovestibulopathy of unknown cause, especially in the presence of systemic symptoms, elevated serologic markers for inflammation, and bilateral labyrinthine enhancements on MRIs.

Author contributions

S.-U. Lee analyzed and interpreted the data and wrote the manuscript. J.Y. Hyon, Y.-J. Ha, H.-J. Kim, J.-J. Song, J.-Y. Choi, and X. Yang analyzed and interpreted the data and revised the manuscript. J.-S. Kim designed and conceptualized the study, interpreted the data, and revised the manuscript.

Study funding

This study was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (no. NRF-2016R1D1A1B04935568).

Disclosure

S.-U. Lee reports no disclosures relevant to the manuscript. J.-S. Kim serves as an associate editor of *Frontiers in Neurotology* and on the editorial boards of *Journal of Clinical Neurology*, *Frontiers in Neuro-ophthalmology*, *Journal of Neuro-ophthalmology*, *Journal of Vestibular Research*, *Journal of Neurology*, and *Medicine*. J.Y. Hyon, Y.-J. Ha, H.-J. Kim, J.-J. Song, J.-Y. Choi, and X. Yang report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

References

1. Lunardi C, Bason C, Leandri M, et al. Autoantibodies to inner ear and endothelial antigens in Cogan's syndrome. Lancet 2002;360:915–921.
2. Arnold W, Pfaltz R, Altermatt H-J. Evidence of serum antibodies against inner ear tissues in the blood of patients with certain sensorineural hearing disorders. Acta Otolaryngol 1985;99:437–444.
3. Kessel A, Vadasz Z, Toubi E. Cogan syndrome: pathogenesis, clinical variants and treatment approaches. Autoimmun Rev 2014;13:351–354.
4. Vollertsen RS, McDonald TJ, Younge BR, Banks PM, Stanson AW, Ilstrup DM. Cogan's syndrome: 18 cases and a review of the literature. Mayo Clin Proc 1986;61:344–361.
5. McDonald TJ, Vollertsen RS, Younge BR. Cogan's syndrome: audiovestibular involvement and prognosis in 18 patients. Laryngoscope 1985;95:650–654.
6. McCallum RM, Clair EWS. Cogan's syndrome. In: Hoffman GS, Weyand CM, Langford CA, Goronzy JJ, eds. Inflammatory Diseases of Blood Vessels. 2nd ed. Hoboken: Wiley-Blackwell; 2012:299–311.
7. Gluth MB, Baratz KH, Matteson EL, Driscoll CL. Cogan syndrome: a retrospective review of 60 patients throughout a half century. Mayo Clin Proc 2006;81:483–488.
8. Ahmed S, Heidenreich KD, McHugh JB, Altschuler RA, Carender WJ, Telian SA. Refractory positional vertigo with apogeotropic horizontal nystagmus after labyrinthitis: surgical treatment and identification of dysmorphic ampullae. Otol Neurotol 2015;36:1417–1420.
9. Kim CH, Choi JM, Jung HV, Park HJ, Shin JE. Sudden sensorineural hearing loss with simultaneous positional vertigo showing persistent geotropic direction-changing positional nystagmus. Otol Neurotol 2014;35:1626–1632.
10. House JW, Doherty JK, Fisher LM, Derebery MJ, Berliner KI. Meniere's disease: prevalence of contralateral ear involvement. Otol Neurotol 2006;27:355–361.
11. Lee SU, Kim HJ, Koo JW, Kim JS. Comparison of caloric and head-impulse tests during the attacks of Meniere's disease. Laryngoscope 2016;127:702–708.