Cochlear hydrops after Cialis induced hearing loss

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Abstract

Objectives: Discuss a unique case of sudden sensorineural hearing loss after Cialis use, a phosphodiesterase 5 (PDE5) inhibitor, and the implication of ipsilateral cochlear endolymphatic hydrops (EH) seen on imaging.

Methods: case report and review of literature

Results: We report a case of a 64-year-old male with unilateral low frequency sudden sensorineural hearing loss (SSNHL) after ingestion of Cialis. The SSNHL occurred six hours after ingestion and was associated with aural fullness and tinnitus. There were no symptoms of vertigo. Imaging was obtained using delayed intravenous contrast-enhanced 3D FLAIR MRI which revealed ipsilateral dilation of the cochlear duct without any hydronic change in the vestibular system. He received oral prednisone immediately after the onset of hearing loss without any improvement. To the best of our knowledge, this is the first case of cochlear EH visualized on imaging after PDE5 inhibitor induced SSNHL.

Conclusion: Cialis and other PDE5 inhibitors have a known association with SSNHL. Despite several proposed mechanisms, however, there is inconclusive evidence of a causal relationship. Our presented case suggests that cochlear EH may be one of the possible mechanism of PDE5 induced SSNHL.

Introduction

Phosphodiesterase-5 (PDE5) inhibitors are commonly used in the treatment of erectile dysfunction. The mechanism of action of these drugs involves the nitrous oxide-cyclic guanosine monophosphate (NO/cGMP) pathway and is well described.[1] Sudden sensorineural hearing loss (SSNHL) is a known risk associated with the use of PDE5 inhibitors since the first case reported in 2007.[2] Though the mechanism for SSNHL associated with PDE5 inhibitor use remains unknown, it has been recently reported that inhibition of PDE5 in mice results in EH.[3] With advances in imaging techniques, MRI now allows us to study EH and others pathologic changes seen in inner ear conditions such as Meniere's disease and SSNHL.[4] To our knowledge, this is the first case of cochlear EH identified in a patient presenting with PDE5 inhibitor associated SSNHL.

Case Report

A 53-year-old male presented to a local Otolaryngologist with right sided, low pitch "white noise" tinnitus, aural fullness and unilateral hearing loss 24-48 hours after Cialis ingestion. He had been taking Cialis for ED and reported taking a slightly larger than normal dose. He was given a 4-day course of oral prednisone and started on nasal steroids without relief. He then presented to our neurotology clinic several months later with continued symptoms and an audiogram which showed moderate low-frequency SNHL rising to mild SNHL on the right with a SRT of 35dB. The left side showed mild high frequency SNHL and SRT of 20dB. Tympanogram was normal bilaterally. The patient was otherwise healthy with no prior history of hearing loss. He had no symptoms of vertigo and otologic exam was normal. Imaging was obtained showing dilation of the right cochlear duct without any hydronic change in the vestibular system (Fig 1). The Patient was started on Diamox 250mg daily and at the time of follow up reported hearing improvement and resolution of symptoms. Repeat audiogram showed an increase in threshold of 15dB in the low frequencies on the right with improved SRT. His Speech discrimination score was excellent.

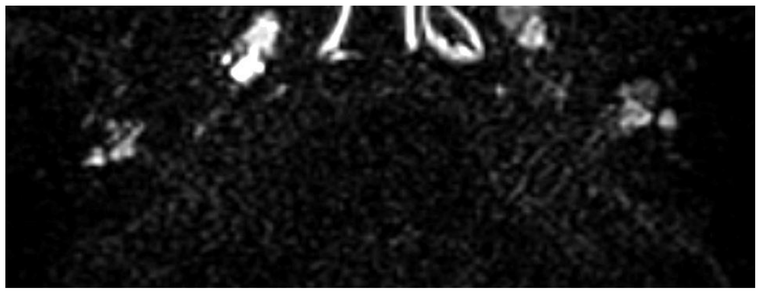

Figure 1. Heavily T2 weighted delayed post contrast FLAIR MRI. Axial image taken at the level of the cochlea.

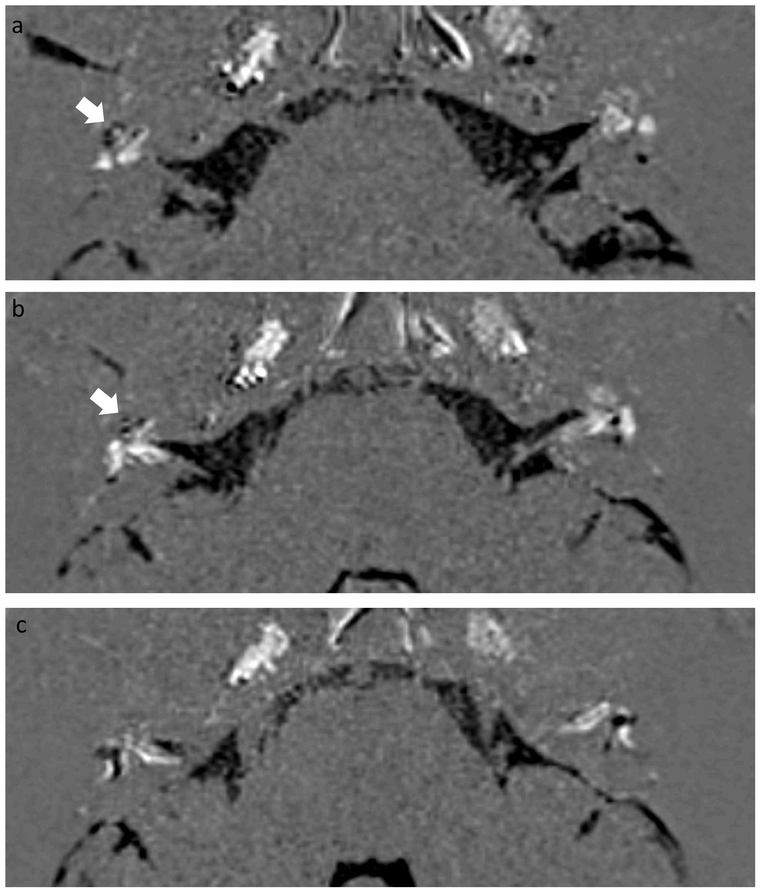

Figure 2. Subtracted images of T2 weighted delayed post contrast FLAIR MRI. Axial images taken at the levels of the cochlea (a), saccule (b) and utricle (c). Cochlear hydrops is identified by an arrow on images *a* and *b*. Image *b* shows absence of saccule hydrops. Image *c* shows absence of utricle hydrops.

Conclusions

To our knowledge, this is the first reported case of EH identified on delayed contrast MRI after PDE5 inhibitor associated SSNHL. Though a paucity of studies exists and experimental data has not shown causal relationship, we feel that our case illustrates EH as a possible mechanism of PDE5 associated SSNHL. Recognition of EH on MRI allowed for treatment initiation with diuretic therapy which ultimately improved hearing outcomes in our patient.

Discussion

Although SSNHL is an uncommon and debated side effect of PDE5 inhibitors (post-marketing reports of 0.01%), most reported cases occur within 24 hours of ingestion suggesting a temporal relationship.[5] However, understanding the underlying mechanism of PDE5 inhibitor associated SSNHL has been challenging given the inherit difficulty of studying the inner ear, as well as inconclusive animal studies.[6] Ultimately, causal relationship remains to be shown.

Recently, Degerman et al., (2016) showed that mice given continuous administration of selective phosphodiesterase inhibitors (including PDE5) all developed EH seen on 9.4 Tesla MRI. The authors postulated that EH may develop due to the downstream MAP kinase effects of increased cGMP levels from PDE5 inhibition, thus leading to altered fluid balance.[3] Several authors have suggested a direct role of the NO/cGMP pathway for hearing loss after PDE5 inhibitor ingestion.[5,7] This pathway has been shown to mediate ototoxicity and regulate normal cochlear hair cell function. By blocking cGMP degradation, PDE5 inhibitors may cause excess cGMP resulting in endothelial dysfunction and oxidative stress.[7] Khan et al. further outlined the downstream effects of specific MAP kinases (JNKs and p38) which may be responsible for cellular damage.[5]

Oxidative stress and reactive oxygen species have been proposed as a risk factor for microvascular damage and thought to be involved in the pathophysiology of both SSNHL and Meniere's disease.[8] Oxidative stress is also implicated in the pathogenicity of EH.[9] Gadolinium-based MRI has enabled us to visualization EH in living patients and has additionally sparked interest in blood labyrinth barrier (BLB) permeability as a promising area of study in inner ear disorders. Greater contrast enhancement is seen in the perilymph of the affected ear in Meniere's disease, as well as in SSNHL suggesting permeability of the BLB.[4]

We have previously shown that the level of hearing loss may be directly related to the degree EH, and that EH is a reversible condition with use of diuretics.[10] Our patient had both low frequency hearing loss as well as improvement in hearing after Diamox use, which clinically supports our findings of EH on MRI. Thus, we feel that the temporal relation to Cialis ingestion is suggestive of causation. We further assert the virtues of delayed intravenous contrast-enhanced 3D FLAIR MRI in detecting EH in suspected patients; as in our case presented, which prompted treatment with Diamox and resulted in reversal of hearing loss.

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