

Otosyphilis: a cause of hearing loss in adults with HIV

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Clinical records

Patient 1

A 59-year-old man infected with HIV presented to hospital with sudden onset of tinnitus, vertigo and hearing loss in his right ear. An audiogram showed moderate bilateral sensorineural hearing loss, which was worse on the right. A magnetic resonance imaging scan of his brain showed no abnormalities. He was diagnosed with Meniere's disease and managed symptomatically. Symptoms worsened over the following months, and he was reviewed in the neurology and ear, nose and throat (ENT) clinics of another tertiary hospital. Both clinics agreed with the diagnosis of Meniere's disease. Serological tests for syphilis were performed 12 months after symptom onset. The rapid plasma reagin (RPR) and *Treponema pallidum* particle agglutination (TPPA) test results were reactive, with the RPR test showing a titre of 1:128. Cerebrospinal fluid (CSF) examination showed a mild lymphocytic pleocytosis and a reactive TPPA test result but a negative RPR test result (Box 1). A diagnosis of otosyphilis was made and the patient was treated with intravenous benzylpenicillin 2.4 million units 4 hourly and oral probenecid 2 g daily for 2 weeks, followed by three doses of weekly benzathine penicillin 2.4 million units intramuscularly. His symptoms stabilised but did not improve.

Patient 2

A 30-year-old man infected with HIV presented to an HIV clinic having had tinnitus, hearing loss and imbalance for 3 months. He was referred to ENT clinics in two tertiary hospitals, both of which diagnosed Meniere's disease. Audiological tests showed mild right sensorineural hearing loss. Serum RPR and TPPA test results were reactive, with an RPR titre of 1:516. CSF examination showed a mildly elevated protein level, but no other abnormalities (Box 1). A diagnosis of otosyphilis was made, and the patient was treated for 2 weeks with benzylpenicillin 2.4 million units 4 hourly. His symptoms resolved completely, and an audiogram performed 6 months after treatment showed that his hearing had returned to normal. ♦

The recent increase in early syphilis infections in Australia has been accompanied by the re-emergence of disease manifestations unfamiliar to modern clinicians. Otosyphilis is a rare cause of sensorineural hearing loss and dizziness, and is important for clinicians to consider because the hearing loss is potentially reversible with early diagnosis and treatment. We report two cases of otosyphilis occurring in patients infected with HIV. In both cases, the diagnosis of otosyphilis was initially missed, despite review by several specialist medical units.

Cochleovestibular dysfunction is a well described complication of congenital and acquired syphilis. In acquired syphilis, it can occur at any stage of infection. In the pre-penicillin era, hearing loss was reported in 17% of patients with early latent infection and in 80% with symptomatic neurosyphilis.¹

Cochleovestibular symptoms of neurosyphilis can occur via two main mechanisms. First, the eighth cranial nerve may be affected, for example in acute syphilitic meningitis. In these situations, hearing loss is usually accompanied by other neurological deficits, and findings on cerebrospinal fluid (CSF) examination will usually be abnormal. Second, and more commonly, hearing loss and vestibular symptoms present without features of

coexisting neurosyphilis. These symptoms may occur at any stage of syphilis and are thought to result from direct damage to the vestibulocochlear apparatus. During dissemination, spirochaetes invade the inner ear perilymph, leading to inflammation of the labyrinthine structures and otic capsule. CSF parameters are usually found to be normal but, histologically, fibrosis and ischaemic necrosis of labyrinthine structures are seen² and endolymphatic hydrops is common. These pathological findings are identical to those of Meniere's disease, explaining the similar clinical features.

Symptoms may be sudden or insidious in onset, and include bilateral (but often asymmetrical) sensorineural hearing loss, tinnitus and vestibular symptoms ranging from dizziness to severe vertigo. These symptoms closely resemble those of Meniere's disease. Audiological testing shows sensorineural hearing loss, classically affecting low or high frequencies while sparing middle frequencies, and speech discrimination is poor.

Without treatment, otosyphilis will progress to profound deafness over months to years. Symptoms can fluctuate markedly over time, but the overall course is one of deterioration.³

There is no established case definition for otosyphilis, but the diagnosis should be made on the basis of a typical clinical presentation and positive serological test results for syphilis. This approach is purposely "over inclusive", as otosyphilis is a potentially reversible cause of hearing loss.

The optimal treatment for otosyphilis is not established. The published literature is limited, consisting of case reports and small case series, but indicates that intravenous therapy is required. Intramuscular penicillin penetrates the perilymph poorly, and there are numerous reports of treatment failure when patients with otosyphilis are treated with penicillin regimens for latent syphilis. In one report, spirochaetes were recovered directly from a patient's perilymph after treatment.⁴

Intravenous penicillin G at a dose of 18–24 million units per day, administered as 3–4 million units every 4 hours for 14 days, is the regimen recommended by the United States Centers for Disease Control and Prevention for treatment of otosyphilis. Probenecid is sometimes added, as are subsequent courses of intramuscular or intravenous penicillin.⁵ There is no high-level evidence to support any of these approaches.

Steroids are commonly coadministered, although there are few supporting clinical data. The rationale is that inflammation of the endolymphatic duct appears crucial to the pathogenesis of otosyphilis. A typical steroid treatment regimen is prednisolone at a dose of 0.5–1.0 mg/kg tapered over 1–2 months.

Regardless of the penicillin regimen used or whether steroids are employed, treatment outcomes are uniformly poor. Studies consistently show that auditory symptoms abate for only 30% of patients, while 7%–15% have improved results in audiological or speech discrimination tests. Tinnitus and dizziness have better outcomes, with 70%–80% of patients reporting improvement. Factors associated with better outcomes include duration of symptoms less than 5 years, age less than 60 years and fluctuating hearing loss.⁶

Both of these patients had HIV infection. Rates of syphilis are known to be substantially higher in the HIV-positive population.⁷ Otosyphilis has previously been described in patients infected with

1 Cerebrospinal fluid and serological test results for two patients with HIV and otosyphilis

	Patient 1	Patient 2
Cerebrospinal fluid		
Appearance	Clear, colourless	Clear, colourless
White cell count ($\times 10^6/L$)	1 polymorph 8 lymphocytes	0 polymorphs 1 lymphocyte
Red cell count ($\times 10^6/L$)	0	0
Protein (g/L) (reference range, 0.15–0.45 g/L)	0.52	0.7
Glucose (mmol/L) (reference range, 2.5–5 mmol/L)	2.7	2.7
Microbiological culture and sensitivity	Nil	Nil
<i>Treponema pallidum</i> DNA polymerase chain reaction test	Not detected	Not detected
Serum		
Rapid plasma reagin (titre)	Reactive (1:128)	Reactive (1:516)
<i>T. pallidum</i> particle agglutination	Reactive	Reactive

HIV, but relevant published literature is sparse. Patients co-infected with HIV and syphilis appear no different to HIV-negative patients in their clinical features, severity of disease or likelihood of developing this manifestation of syphilis.

In both of the cases we report, the diagnosis of otosyphilis was missed despite review by several specialist medical units. In the past few years, rates of early syphilis have risen markedly in Australia, predominantly among homosexual men.⁸ Relevant practitioners should be aware of this diagnosis in patients presenting with the symptoms described here, especially those at risk of syphilis, such as sexually active homosexual men, including those with HIV infection. Current guidelines recommend syphilis screening in sexually active homosexual men at least annually (up to every 3 months in those at higher risk) and at regular intervals in individuals infected with HIV.⁹

Competing interests

None identified.

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Lessons from practice

- Consider the possibility of otosyphilis in any patient (especially those with HIV infection or at risk of syphilis and/or HIV infection) presenting with auditory symptoms, particularly sensorineural hearing loss with tinnitus and vestibular dysfunction.
- Positive serological test results for syphilis will establish the diagnosis.
- All sexually active men who have sex with men should be screened for syphilis at regular intervals.
- Otosyphilis must be treated with intravenous penicillin regardless of findings of cerebrospinal fluid testing. ♦

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