Relapsing polychondritis: A rare cause of sudden severe sensorineural hearing loss

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ABSTRACT

Relapsing polychondritis (RP) is a very rare disease, and the symptoms can be vague. This case report serves as a reminder to take RP into consideration in patients with sudden hearing loss, with concurrent features of recurrent cartilaginous inflammation. A young lady presented with recurrent eye inflammation for two years and sought treatments from various general practitioners and ophthalmologists. Each attack was successfully controlled with a short course of oral or topical steroids. She later developed sudden onset aural perichondritis and severe bilateral sensorineural hearing loss and a diagnosis of RP was made after clinical and laboratory assessments. Delay in the diagnosis and treatment has led to permanent hearing loss in this patient.

Keywords: Relapsing polychondritis, deafness, conjunctivitis, cartilage diseases

INTRODUCTION

Relapsing polychondritis (RP) is a rare, episodic, and progressive inflammatory disease of the cartilaginous structures. It is an autoimmune disease and like other autoimmune disorders can present in a highly ambiguous fashion. Hence, diagnosis can be delayed and result in potentially permanent complications. We report a case of RP presenting with a rare inner ear manifestation, sensorineural hearing loss, and provide a literature review of this disease.

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CASE REPORT

A 32-year-old Malay lady presented with recurrent red eyes of two and a half years duration that was associated with mild pruritus and watery discharge. She experienced this almost alternate months and had frequently sought treatment from her general practitioners. Each time, she was prescribed topical steroids and the condition usually resolved within three days of treatment. Occasionally, the attacks were severe and warranted oral steroid treatment for two weeks prescribed by the ophthalmologists. She was diagnosed as having recurrent conjunctivitis. Unfortunately, no further assessment was done at the time.

She presented again with conjunctivi-

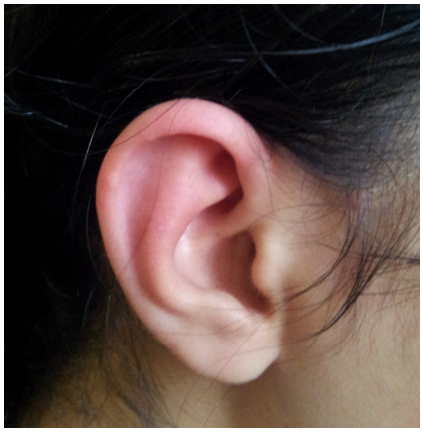

Fig. 1. Inflammation of the auricle with sparing of the non-cartilaginous ear lobe.

tis and severe pain in both her pinna. She was again prescribed oral steroid and analgesia by her general practitioner. However, she developed sudden onset hearing loss in both ears the following day after waking up. She initially ignored the symptom, thinking that it may be a side-effect of the prescribed medications. She only presented to our Otolaryngology Clinic three days later. Upon reviewing her history, she denied having any recent hearing problem, fever, ear discharge, trauma to the head or ear, vertigo, or taking any medications except for the steroid and analgesia prescribed to her. There were no symptoms and signs of arthralgia, arthritis or any skin or genital rashes, pigmentation or ulceration and any family history of autoimmune disease or cancer. She again provided a history of painful red ears in association with conjunctivitis which settled with steroid treatment.

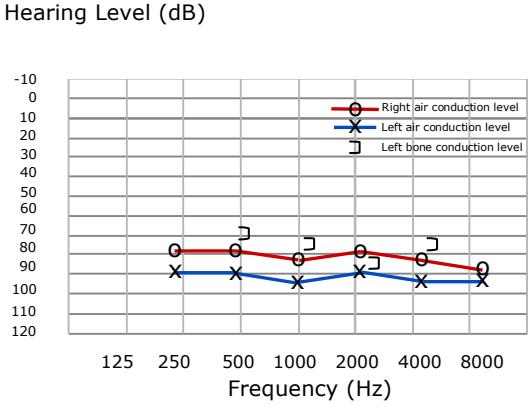

Fig. 2: Pure tone audiometry at presentation.

On examination, she was afebrile but both her pinna were erythematous, and tender (Figure 1). Otoscopic examination revealed an inflamed cartilaginous ear canal, with normal tympanic membrane bilaterally. Pure tone audiometry (PTA) showed bilateral severe mixed hearing loss, slightly worse on the left ear (Figure 2). Conjunctivitis was noted on ophthalmological examination.

Blood investigations revealed leukocytosis, thrombocytosis, and raised erythrocyte sedimentation rate (ESR) at 107mm (Normal <10). Rheumatoid factor (RF) and antinuclear antibody (ANA) were positive, and C3 was at 22.6 mg/dl, while other connective tissue disease screening tests were negative. Thyroid, renal and lipid profiles were normal. Syphilis serology (VDRL/TPHA) and tuberculin tests were also negative. Her urine analysis was negative for red blood cells and cellular cast. Chest radiography, echocardiography and magnetic resonance imaging (MRI) of the brain were all normal.

A tissue biopsy obtained from the aural cartilage revealed mixed inflammatory infiltrate of lymphocytes, neutrophils, and plasma cells in the perichondrium and mild disruption of the cartilage. She was referred to the rheumatologist. A diagnosis of RP was made based on the clinical history, examination and investigations.

She was admitted and was started on

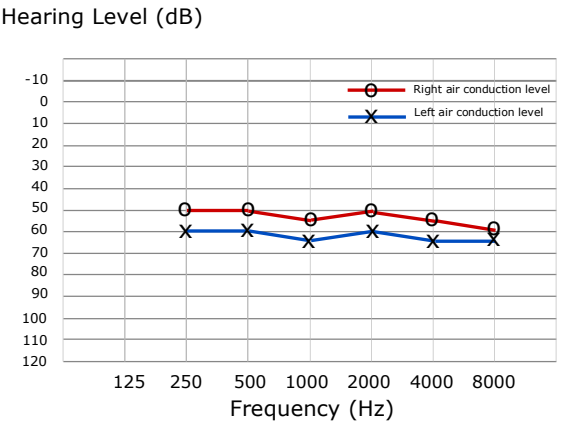

Fig. 3: Pure tone audiometry showing persistent hearing loss despite resolution of her RP.

intravenous steroids (methylprednisolone 250mg daily for three days) followed by oral prednisolone (50mg daily). In addition, oral betahistine (24mg twice daily) and oral ciprofloxacin (500mg twice daily) were also started. After three days of treatment, oral methotrexate (10mg per week) along with calcium and vitamin D supplements were initiated. There was good response within three days of therapy with improvement of the aural perichondritis and conjunctivitis. However, the hearing status remained unchanged. She was discharged on the sixth day to continue the oral steroids (prednisone 40mg daily) therapy on a tapering schedule and weekly methotrexate (10mg).

On the follow-up visit four weeks later, there was total resolution of aural perichondritis and conjunctivitis, without history of recurrent inflammation. Repeat PTA showed only slight improvement of hearing. She was continued on weekly methotrexate for the next five months. A year later, the patient reported no recurrence of her disease off treatment. However, her sensorineural hearing loss persisted at 50-60 dB bilaterally (Figure 3).

DISCUSSION

RP is an autoimmune disease affecting the cartilaginous tissues, predominantly affecting the ears, nose, joints and airways. RP can manifest independently or in association with other autoimmune diseases such as systemic lupus erythematous (SLE), rheumatoid arthritis (RA) and Sjögren syndrome. [1, 2] The mean age at diagnosis is between 44 and 51 years, with a female to male ratio of 3:1.[3]

There is evidence for an autoimmune basis of this disease. A study has shown cellular and humoural responses directing against collagen type II and other cartilage-specific collagen (types IX and XI) during acute RP episodes, with the levels correlating with the severity of an episode. [4] Levels of antibodies to matrilin 1, an extracellular matrix protein that is predominantly expressed in the tracheal cartilage, were significantly higher in patients with RP, which reflects a tissue-specific response to airway cartilage in this disease. [5] Other evidence for an autoimmune aetiology includes pathological findings of infiltrating T-cells and other immune mediators directed against collagen type II, [6] the presence of antigen-antibody complexes in the affected cartilage, [7] and observation in many reported cases showing response to immunosuppressive therapies. Despite the clear immune-mediated mechanism, the trigger for inflammation affecting the cartilaginous tissue in this rare disease is still unknown.

Diagnosis of RP is made based on several criteria; inflammation that involves at least two of the typical sites - auricular, nasal, laryngotracheal or one of the typical sites and two other - ocular inflammation, audio

vestibular damage (hearing loss/vertigo), or sero-negative inflammatory arthritis. [8] Aural perichondritis is the most common manifestation of RP, followed by joint inflammation, nasal chondritis, eye manifestations (scleritis, conjunctivitis, uveitis, optic neuritis) and laryngotracheal cartilage involvement. [2, 3, 8] Less commonly, the associated immune reaction causes inflammation in non-cartilaginous tissues like kidney, cardiovascular system, gastrointestinal tract, middle and inner ear, skin, and central nervous system. [2]

Due to the general manifestations of the disease, patients with RP often present to multidisciplinary physicians; usually to primary care doctors, otolaryngologists, rheumatologists, orthopaedic surgeons and ophthalmologists. With the ambiguity of the symptoms, the diagnosis is often delayed. In a group of 36 patients with RP, the mean delay from the onset of symptoms to a correct diagnosis being made was reported to be around 2.9 years. [3] In addition, patients had already seen on average five or more physicians before being diagnosed. [3] This delay can potentially lead to permanent complications.

This case highlights the inconsistency of the presentation of RP, which may have complicated and delayed the diagnosis. Our patient initially presented with an eye symptom for a few years, before the onset of aural perichondritis, later followed by sudden hearing loss. Although ocular involvement occurs in 50-60%, it is rare to have eye symptoms as a sole presentation of RP. [3, 8] The most common eye manifestation is non-necrotising recurrent scleritis. Other forms of ocular manifestation are rare. [3, 8] When a patient presents with isolated eye symptoms as in our case, there is very little clue to specifically suspect the diagnosis of RP.

Previous studies have reported that 28-40% present with hearing loss during the course of their disease. [3, 8, 9] The incidence of sensorineural hearing loss is higher than conductive hearing loss. [10] In our patient, the duration from disease onset to the cochlear manifestation was around three years. This is the same as the mean duration reported by Tretham *et al*. [3] The hearing loss can be unilateral or bilateral and progression can be slow or rapid. [3, 10] Most of the cases reported presented with mild to moderate hearing loss, and the incidence of progression to profound loss as in our case is rare. [10]

There is no cartilage present in the inner ear, thus, the mechanism of hearing loss in RP is still unknown. Earlier theories suggested the possibility of concomitant viral labyrinthitis causing the hearing loss based on some observation on the temporal bone of RP patients with degeneration of organ of Corti and sensory cells. [11] Another postulated mechanism is hearing loss due to obliterative circulatory disorder caused by vasculitis in the cochlear branch of the internal auditory artery. [9, 12] Autoantibodies against the labyrinth which may induce inflammation in the inner ear causing problems to hearing loss have been detected in the serum of patients with RP with audiovestibular dysfunction.[4] Abnormal enhancement of the membranous labyrinth has been described in a case of RP, which further strengthens the inner ear inflammation theory. [13]

Due to the rarity of the disease, the current treatment of RP is only based on clini-

clinical observations. To date no randomised controlled trials have been performed. The mainstay of treatment is systemic corticosteroids, which are used in acute flares and for long-term suppression of inflammation. Initial treatment can be oral or intravenous depending on the disease severity and organ involvement. In a severe manifestation e.g. involving the airway, intravenous pulsed methylprednisolone of 250mg to 1gm/day should be started for three days, followed by the oral prednisolone. [2] Milder cases are often treated with a starting dose of oral prednisone ranging from 0.5 to 1.0mg/kg per day. In patients who require higher and prolonged maintenance doses of prednisolone, a disease modifying and steroid-sparing agent like methotrexate (up to 25mg weekly) is often administered. Some patients may eventually be maintained with methotrexate alone without steroid treatment.

Currently, there is no clear guideline on how long the maintenance treatment should be, but it is usually recommended for years. [14] A recent review article on other treatments of RP mentioned some other drugs that have been used and reportedly successful, which include colchicine (0.6mg twice daily), dapsone (25–200mg/day), azathioprine (2mg/kg/day), cyclophosphamide (1–2mg/kg up to 150mg/day in life threatening RP) and cyclosporin A. [2] More recently, Lekta *et al*. reviewed the outcome of 61 patients treated with different biologic therapies for RP; TNFα blockers (n = 43), rituximab (n = 11), anakinra (n = 5), tocilizumab (n = 2), and abatacept (n = 1).[1] They found that biologics were effective in 44% patients, and partially effective in 8%. The authors conclude that biologic therapy for RP should only be used in very severe refractory forms of RP. Biologic therapy may have a future role, but more trials are needed to test this.

In our case, the aural perichondritis and conjunctivitis had totally resolved following therapy, but not the hearing loss. While in some less severe cases hearing loss fully recovered with treatment, [3, 12] some authors have also reported similar long-term or permanent complication of hearing in their patients despite rigorous medical treatment.[3,15] In our case, the severity of the hearing loss at diagnosis, together with the substantial delay in the diagnosis and initiation of steroid treatment may have led to the permanent complication of hearing loss. It is hard to say whether a more aggressive therapeutic approach (e.g. azathioprine, cyclophosphamide, or biologics) may have been more efficacious in recovering the hearing.

Recent evidence has shown that cochlear implantation is successful in cases of RP with progressive bilateral profound sensorineural hearing loss resistance to multiple drugs treatment. [15] With proper selection of candidates, cochlear implants can be used to treat patients with immune-mediated inner ear disease, such as RP cases.

In conclusion, our case highlighted that the possibility of an autoimmune disease causing sudden sensorineural hearing loss cannot be overlooked, and one must try very hard to rule out such a condition. Although RP is a very rare disease, it should be suspected as a cause of hearing loss in patients with cartilaginous inflammation. Delay in diagnosis and management can lead to permanent hearing loss.

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