The Journal of Laryngology and Otology
September 1992, Vol. **106**, pp. 841–844

Relapsing polychondritis—two cases with tracheal stenosis and inner ear involvement

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Abstract
Relapsing polychondritis is a rare disease which often presents firstly to ear, nose and throat (ENT) departments. Its complications, respiratory, cardiovascular, renal and neurological are life-threatening; thus it is important to recognize the disease and its complications early. Treatment for relapsing polychondritis may have serious side-effects which should be taken into account when managing these patients. We report two young patients with relapsing polychondritis and their treatments; both had severe tracheal stenosis responding in one case to pharmacological and in the other to surgical intervention.

Introduction

Relapsing polychondritis (RP) is a systemic disease first described in 1923 by Jaksch-Wartenhorst. It is characterized by recurrent inflammation and degeneration of cartilage, commonly the pinnae, nose, trachea, larynx and joints. It may run an aggressive short course or may be indolent over many years (Cohen and Rapini, 1986). Involvement of major airways is more common in young patients and can be more serious than in adults (Michet *et al.*, 1986). Fluctuating hearing loss, either conductive or sensorineural, tinnitus and vertigo may be overlooked symptoms of audio-vestibular involvement. Numerous treatments have been reported to alleviate symptoms including non-steroidal anti-inflammatory drugs, corticosteroids, dapsone, colchicine, chlorambucil, cyclophosphamide, azathioprine, cyclosporin-A and exchange plasmaphoresis (Barranco *et al.*, 1976; Damiani and Levine, 1979; Askari, 1984; Svenson *et al.*, 1984; 1986) but none are believed to influence disease progression. Comparative trials in this rare condition are lacking.

Case reports

Case 1

A 14-year-old female, was admitted to the dermatology unit with a two-month history of painful swollen erythematous pinnae which had become floppy, the disease sparing the non-cartilagenous tissue. Slight erythema and tenderness of the nose with follicular conjunctivitis of both eyes were also noted. Her ESR was 115 mm/h and haemoglobin 10.5 g/l; all other haematological parameters were normal. A punch biospy of the ear revealed complete replacement of cartilage with fibrous tissue. An abdominal ultrasound revealed moderate hepatosplenomegaly (2 cm greater than normal). Pulmonary function tests showed a decreased peak expiratory flow rate of 340 l/min (predicted 450 l/min) . Initial treatment with 100 mg dapsone was ineffective and 30 mg prednisolone with azathioprine led to a temporary remission. Audiometry carried out on presentation was normal. However, two months later, coinciding with the development of vertigo, tinnitus and nausea with nystagmus, pure tone audiometry revealed a bilateral high frequency hearing loss (Fig. 1). The Unterberger test showed no rotation but she fell to the left. Caloric testing and electronystagmography revealed spontaneous nystagmus to the right without optic fixation and a directional preponderance of 21 per cent. Three months later no response occurred on caloric testing of both ears. At presentation she had a grossly enlarged right tonsil which was removed once her condition stabilized to exclude lymphoma. Histology revealed a simple tonsillolith.

During her treatment with systematic steroids and azathioprine, her renal function deteriorated and she developed haematuria and proteinuria (23 mg/l). Her creatinine clearance was initially normal but dropped to 70 µmol/l. Attempts to reduce her oral prednisolone from 30 mg daily to 12.5 mg resulted in a raised ESR (55 mm/h) and a worsening of her breathlessness and the development of stridor. Laryngeal tomograms showed significant subglottic stenosis over a four-month period. The transverse diameter of the upper trachea was reduced from 13 mm to 8 mm in calibre over a 20 mm segment. In view of this, azathioprine was replaced with cyclosporin (5 mg/kg). However, three months later, her airway was further reduced to 4 mm and a tracheostomy was considered. Flow volume loops carried out at the same time showed an inspired peak flow rate less than 50 per cent of its predicted value and her expiratory peak flow rate was 170 l/min although she only became breathless and developed stridor on moderate to severe exertion. In an attempt to arrest her progressive disease prednisolone was increased from 20 mg to 50 mg and cyclosporin A substituted with cyclophosphamide 50 mg t.i.d. following which there was a marked improvement. Her daily prednisolone dose was gradually reduced to 12.5 mg with a substantial improvement in exercise tolerance and peak flow rate increased to 320 l/min.

Case 2

A 17-year-old female, was seen in December 1985 by the otolaryngology department with secretory otitis media requiring grommet insertion. The diagnosis was confirmed audiometrically and at operation. Over the year, she developed tinnitus which fluctuated along with her conductive hearing loss. Sixteen months after presentation, she developed a cough and wheeze which failed to settle with salbutamol and a reducing course of oral steroids prescribed by her practitioner. Her peak expiratory flow rate was 170 l/min but her FEV_1/FVC wa s normal at 85 per cent (2.55/3.00). Eight weeks later, following a sore throat, she developed a generalized arthopathy and hoarseness which rap-

Accepted for publication: 29 May 1992

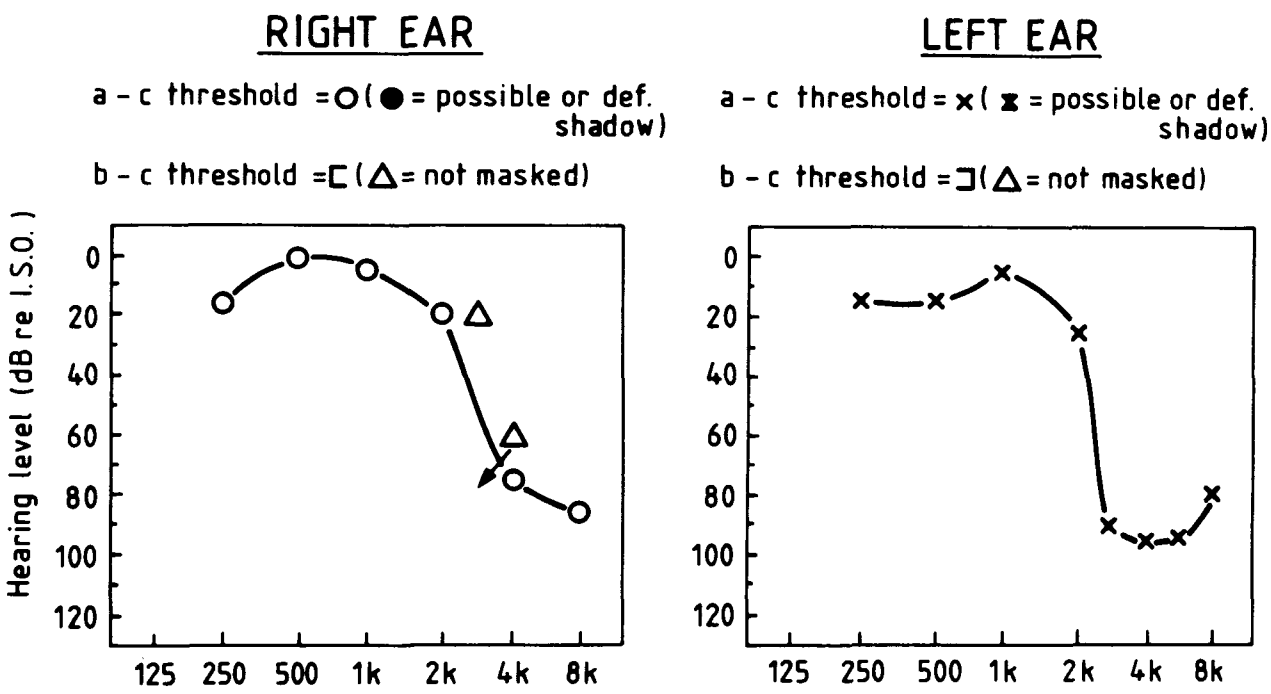

FIG. 1
Audiogram of patient number one, showing a high tone sensorineural loss.

idly progressed to stridor. There was subglottic crusting on indirect laryngoscopy and a soft mid-systolic murmur noted at the apex on auscultation. Her ESR was raised at 89 mm/h and her ASO titre was 1 in 320. Her stridor settled with humidification and oxygen.

Four weeks later, she became acutely ill with a widespread vasculitic eruption, abdominal pain, haematuria and proteinuria. Her blood urea and creatinine were raised and her chest X-ray showed multiple large opacities. A nasal mucosal biopsy revealed marked deposition of IgG in the basement membrane suggestive of Goodpasture's syndrome. She was treated with 60 mg prednisolone daily slowly reducing to 27.5 mg over six weeks with some clinical improvement. However she developed tinnitus, visual blurring, haemoptysis and tender nodules on both pinnae. A biopsy of her pinna showed a cutaneous vasculitis. A lateral soft tissue X-ray of her neck showed a trachea of normal calibre. She had only one episode of acute dysponea over the next two months thus her oral prednisolone was reduced to 15 mg daily. Her ESR fell from 26 to 21 mm/h. She went on to develop a nephrotic syndrome and recurrent haemoptysis. Tracheal tomograms revealed a 5 mm subglottic stenosis (Fig. 2) and her steroid dose was maintained.

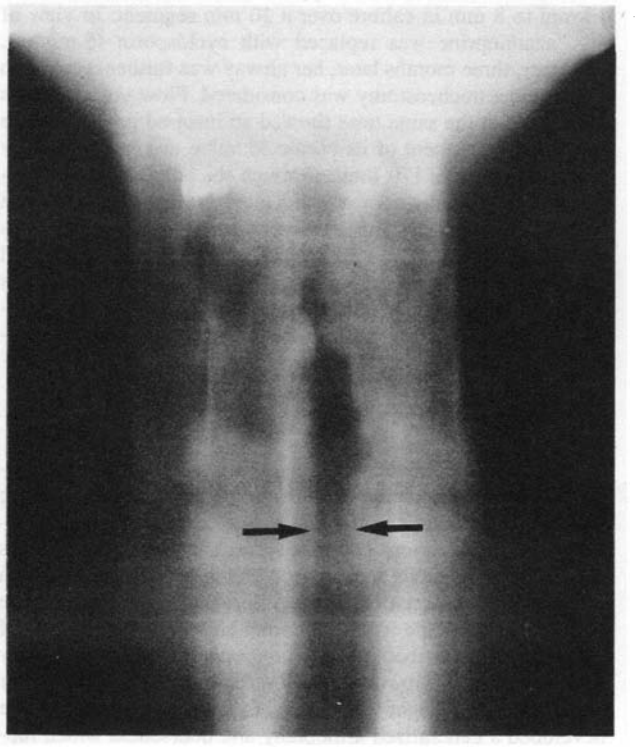

FIG. 2
Tomogram of patient number two, showing the subglottic stenosis as arrowed.

Four months later, two years after presentation, she was urgently admitted with stridor which failed to settle with high dose prednisolone, humidification and oxygen. An elective tracheostomy was performed under local anaesthetic which then allowed direct examination and hydrostatic balloon dilation of her tracheal stenosis under a general anaesthetic. Her tracheal lumen was thus increased from 2 to 6 mm. This was followed by regular monthly dilatations for more than a year. During that period she developed narrowing of the left main bronchus due to trauma from the tracheostomy tube impinging on the carina. Subsequently, she had specifically shortened tracheostomy tubes. Three and a half years after presentation, she remains stable allowing her tracheostomy tube to be replaced with a stoma button. Her renal function has improved with normal urea and creatinine and her spirometry although reduced is still within the normal range.

TABLE I
McADAM'S DIAGNOSTIC CRITERIA FOR RELAPSING POLYCHONDRITIS, THREE OF WHICH ARE SUFFICIENT FOR THE DIAGNOSIS OF RP

1. Recurrent chondritis of both auricles.
2. Non-erosive inflammatory polyarthritis.
3. Chrondritis of the nasal cartilages.
4. Occular inflammation—conjunctivitis, keratitis, scleritis, episcleritis and uveitis.
5. Chondritis of the laryngeal and tracheal cartilages.
6. Cochlear and vestibular damage—sensorineural hearing loss, tinnitus and vertigo.

https://doi.org/10.1017/S002221510012105X Published online by Cambridge University Press

Discussion

McAdam *et al.* in 1976 empirically established a set of diagnostic criteria for relapsing polychondritis (Table I). Three of these would confirm the diagnosis of RP particularly with typical histology. Histology depends on the stage of the disease but in the active phase consists of a loss of basophilic staining of the cartilage matrix, perichondrial inflammation and later cartilage destruction with fibrous tissue replacement.

Increased turnover of collagen leads to a loss of mucopolysaccharides in the urine and raised levels correlate with disease activity (Svenson *et al.*, 1984). An autoimmune pathogensis is supported by the finding of antibodies to type II collagen in two-thirds of patients with RP (Ebringer *et al.*, 1981; Svensen *et al.*, 1986). Type II collagen is the principal type present in cartilagenous structures. The detection of antibodies in the cartilage by direct immunofluorescent microscopy and of circulating immune complexes in the serum of patients with RP would suggest a role for the humoral immune system in RP (Valenzuela *et al.*, 1980; Meyer *et al.*, 1981). A cell-mediated immune response to cartilage has also been demonstrated (McAdam *et al.*, 1976).

The commonest presenting symptom is auricular chondritis (26 per cent), being bilateral in 95 per cent of cases, and occurring in 88 per cent of cases during the course of the disease (McAdam *et al.*, 1976). The next most common presenting signs or symptoms include arthritis, nasal chondritis, occular inflammation, respiratory tract problems and audio-vestibular damage. Thus otorhinolaryngological presentation is common and involvement of major airways with stridor is a potential life-threatening event possibly necessitating tracheostomy. Airway destruction may be localized to the upper or lower airways by use of spirometry and flow-loop volume studies (Mohsenifar *et al.*, 1982).

Middle or inner ear involvement usually develops after the onset of relapsing polychondritis and it is believed that cochlear and vestibular damage is due to involvement of the internal auditory artery (Damiani and Levine, 1979). Middle ear involvement may be due to disease affecting the eustachian tube (Hughes *et al.*, 1972). Inner ear disease has been reported (Rabuzzi, 1970; Cody and Sones, 1971) to be reversible with steroids but this was not the case in our patient.

Mortality rates vary according to the age at presentation. Younger patients, usually with more aggressive disease, have reported mortality rates ranging from 28 per cent (McAdam *et al.*, 1976) to 50 per cent (Cohen and Rapini, 1986) with overall rates of approximately 30 per cent. there is a 20-30 per cent mortality rate in those under 51 years of age with poor prognostic features. These include laryngotracheal strictures, systemic vasculitis, microhaematuria and anaemia. Fifty per cent of deaths are due to airway collapse with resulting respiratory failure or pneumonia. Cardiovascular complications, vasculitis or opportunistic infection due to immunosuppression may also prove fatal. Older patients may have disease that runs a chronic, low grade course over many years, most dying from causes unrelated to their RP (Dolan *et al.*, 1966; Hughes *et al.*, 1972; Cody and Powers, 1983).

The differential diagnosis of RP revolves around each of the diagnostic criteria laid down by McAdam. Thus infective perichondritis may cause collapse of the nasal, laryngeal and tracheal cartilages. Airway narrowing with soft-tissue involvement may be caused by Wegener's granulomatosis and sarcoidosis whilst rheumatoid arthritis, systemic lupus erythematosis, polyarteritis nodosa and other collagen, vasculitic and auto-immune disorders have been linked to RP in about 2–30 per cent of cases.

Treatment

The mainstay of treatment has been corticosteroids but other agents have been used either alone or in conjunction. These include non-steroidal anti-inflammatory agents, dapsone and colchicine which are helpful for mild disease and cyclophosphamide, azathioprine and cyclosporin A for severe cases. Corticosteroids appear to be anti-inflammatory and antichondrolytic (Pearson *et al.*, 1960). However whilst decreasing the frequency and severity of attacks the impression is that they do not stop the progression of the disease in aggressive cases, in which high doses of steroids are often required with the addition of immunosuppressive agents.

Cyclosporin A, an immunosuppressant with specific effects on cytokine production from T lymphocytes, has proved very useful in patients with severe manifestations (Svenson *et al.*, 1986; Rogerson *et al.*, 1987) and in the patient reported by Svenson *et al.* results were dramatic and life-saving. Nonetheless patient 1 deteriorated whilst on cyclosporin and showed a much more favourable response to cyclophosphamide which produces more global immunosuppression suggesting this to be more effective perhaps by suppressing autoantibody production. This has also proven very effective in a patient with RP associated with glomerulonephritis (Ruhlen *et al.*, 1981).

Monitoring progress of the disease may be difficult. Regular measurement of renal and pulmonary function should be carried out by assessing creatinine clearance, GFR and flow-loop volumes along with conventional spirometry. CT may be useful for assessing the degree and sites of airway stenosis if tracheostomy is considered. Measuring the ESR does not appear to correlate with progression of the disease since airway symptoms may occur due to acute inflammatory lesions or fibrosis.

The two patients described both share the ominous problem of tracheal stenosis. Interestingly both had previous surgery requiring intubation and later developed strictures at the level of the cuff of an endotracheal tube. It is possible that slight trauma at the time of intubation could lead to localized disease and should be avoided, whenever possible, in these patients. In both patients tracheal obstruction was improved; in patient 1 by aggressive immunosuppression and in patient 2 by monthly balloon dilatation.

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Key words: Cartilage diseases; Relapsing polychondritis; Tracheal stenosis; Hearing loss; sensorineural.