*The Journal of Laryngology and Otology*
October 1992, Vol. **106**, pp. 911–914

# Relapsing polychondritis—A study of four cases

B. S. Irani, M.S., D. P. Martin-Hirsch, D. Clark, F.R.C.S., D. W. Hand, F.R.C.S., C. E. Vize, F.R.C.S., J. Black, F.R.C.S. (Bradford)

**Abstract**
Four case reports of relapsing polychondritis, (RP), are presented, together with a literature review and management suggestions. There are approximately 211 reported cases in world literature making RP an uncommon condition associated with high morbidity and mortality rates. The key to the management of RP is based on accurate and early diagnosis though the ideal medical regimen has yet to be elucidated.

## Introduction

Relapsing polychondritis is a rare disease of unknown aetiology, first described by Jaksch-Wartenhorst in 1923 and is characterized by an inflammatory reaction occurring in the cartilages of several different organs, the commonest being the auricular cartilage. Other sites affected are the nose, the upper respiratory tract, including the larynx and the trachea, cochlea and vestibule, and costal cartilages. Ocular inflammation and arthropathy are also seen. It was McAdam *et al.* (1976) who initially defined the diagnostic criteria of RP:

1. Recurrent chondritis of both auricles.
2. Non-erosive inflammatory arthritis.
3. Chrondritis of nasal cartilages.
4. Ocular inflammation including conjunctivitis, keratitis, scleritis/episcleritis and/or uveitis.
5. Chondritis of the upper respiratory tract involving the laryngeal and/or tracheal cartilages.
6. Cochlear and/or vestibular damage manifested by senorineural hearing loss, tinnitus and/or vertigo.

A definite diagnosis of RP was made when three or more of the above signs were present; histological confirmation was unnecessary. McAdam's diagnostic criteria were later modified by Damiani and Levine (1979).

1. At least three or more diagnostic criteria (McAdam's) histological confirmation not necessary. OR
2. One or more of McAdam's signs with a positive histological confirmation. OR
3. Chondritis in two or more separate anatomical locations with response to steroids and/or dapsone.

In this study, the diagnosis was made on the basis of the modified criteria by Damiani and Levine though instead of dapsone, other immunosuppressants such as azathioprine and cyclophosphamide were used.

## Case reports

*Case 1*

A 57-year-old man presented with a painful swelling of his right pinna which had progressively worsened over one week. He had concomitant pain over his nasal cartilage and malaise. There was a past history of Menière's disease, rheumatic fever involving both his ankles and knees, Q fever and conjunctivitis.

On examination, his right pinna was erythematous, swollen and exquisitely tender. The swelling extended on to his right postauricular region but there was no associated mastoid tenderness. The rest of his right ear and the left were normal.

His nasal examination revealed an erythematous tender swelling of his left lower lateral cartilage with crusting. The rest of the ENT and general examination was normal.

The only significant haematological finding was a raised ESR which was 113 mm/h. His audiogram showed a moderate high tone sensorineural loss in the left ear. Despite antibiotics and anti-inflammatory analgesics, there was no improvement in his symptoms. Instead, two days later, he developed left conjunctivitis. His vision was unaffected and eye movements were normal. Considering his clinical signs and failure to respond to antibiotics, a provisional diagnosis of RP was made and the patient was started on oral prednisolone 40 mg/d following which he improved dramatically.

A wedge biopsy from the right pinna showed chronic inflammatory changes.

Oral prednisolone was continued in a dose of 40 mg/d for one week and then gradually tapered over two weeks to 20 mg/d. By then, the nasal lesion and conjunctivitis had completely resolved. The right pinna was gradually returning to normal.

After being maintained on oral prednisolone 20 mg/d for one month, the patient developed pain in his right pinna again and his ESR, which had reduced from 113 mm to 40 mm/h increased to 46 mm/h. Hence the dose of prednisolone was increased to 30 mg/d and then tapered to 25 mg/d over two months. The patient has been symptom-free since, with a recent ESR of 32 mm/h.

*Case 2*

An 80-year-old lady presented with right auricular chondritis and chondritis of the nasal lower lateral cartilage which failed to respond to routine antibiotics and anti-inflammatory analgesics. She later developed chondritis of her left auricular cartilage and bilateral scleritis and iritis which progressed to glaucoma in one eye. She also had severe sensorineural deafness and poor balance from the bilateral loss of labyrinthine function.

The only significant findings were a raised ESR which was 117 mm/h and a biopsy from her left pinna which was suggestive of vasculitis. The rest of the haematological investigations were normal. A diagnosis of relapsing polychondritis was thus made and she was treated with oral prednisolone 40 mg/d for

Accepted for publication: 29 May 1992.

one week, tapered to 10 mg/d by which time her symptoms and signs had completely resolved except for her hearing and balance which showed no change. Her ESR had reduced to 7 mm/h. She later developed secretory otitis media in her right ear for which myringotomy was done and a grommet inserted. Since then her condition has been stable.

*Case 3*

A 58-year-old housewife was admitted as an emergency with dyspnoea and hoarseness of acute onset. She also had a few vasculitic skin lesions, macular in type, on the lateral aspect of her left leg. Direct laryngoscopy and fibreoptic bronchoscopy showed slight thickening of the posterior third of the left vocal fold. The rest of the larynx was normal.

The trachea and both main bronchi were of normal calibre and did not show any paradox on inspiration or expiration. However, the tracheal cartilaginous rings were less distinct, their normal corrugation effect was absent and the tracheal submucosal venous plexus was markedly prominent. Biopsy from the posterior third of the left vocal fold and from the leg lesion showed chronic inflammatory changes with evidence of vasculitis, suggestive of RP. Her ESR was 70 mm/h. An X-ray of the chest showed no significant abnormality.

She was started on oral prednisolone 15 mg/d to which she responded well and the laryngeal lesions resolved completely. The ESR returned to normal and prednisolone was tapered to a maintenance dose of 5 mg/d and azathioprine was added in a dose of 50 mg twice a day as repeat bronchoscopy showed persistence of previous tracheal findings. With this combination an excellent control of the expression of the RP was achieved.

*Case 4*

A 53-year-old man presented with malaise and saddle nose deformity which was preceded by tender swelling of his nasal cartilages. He also suffered from arthritis involving his knees for three years. A few days later he developed intermittent stridor.

His ESR was 108 mm/h but the other haematological investigations were normal. The chest X-ray showed pleural thickening in the inferior segment of the lingula.

Bronchoscopy showed purulent bronchitis with tracheal softening, posterior bulging of membraneous part of distal trachea up to carina and narrowing of the left main bronchus. At the same time a biopsy was taken from the trachea and a Montgomery 'T' tube was inserted. The biopsy was reported as chronic inflammation with vasculitis suggestive of RP.

The Montgomery 'T' tube had to be removed after a few days, as it was causing airway obstruction and internal wire springs were inserted within the lower trachea for internal splinting.

Once the diagnosis of RP was made, the patient was commenced on a regimen of methylprednisolone 1 gm IV for three days with cyclophosphamide 15 mg/kg IV for one day. This cycle was repeated fortnightly for three such cycles. Oral prednisolone 60 mg/d was given in between the above fortnightly pulses and was omitted when the patient was receiving methylprednisolone. The dose of prednisolone was gradually tapered over a few weeks to 5 mg/d. On starting the medical treatment, the ESR dropped to 45 mm/h and the patient's condition appeared stable. An augmentation rhinoplasty was performed using iliac crest graft at the patient's request.

However, a few months later, his WBC count dropped and the immuno-suppressive treatment had to be omitted following which, the patient developed uveitis and scleritis with repeated episodes of respiratory distress. A posterior membrane fixation of the trachea, and the main bronchi was performed using Prolene mesh and histoacrylate tissue. This had temporary beneficial effect and the patient had to be kept on a ventilator.

His cardiovascular system became unstable with episodes of hypertension and hypotension, with poor gaseous exchange and the patient died from respiratory failure.

## Discussion

In the four cases presented here, it is seen that RP can present with varying clinical pictures and thus pose a diagnostic enigma. Auricular chondritis is the commonest presenting feature observed in 90 per cent of the cases. It is typically bilateral but may be unilateral, and of sudden onset. There is an erythematous swelling of the pinnae which are tender to palpate.

The other otological features seen are:

1. Secretory otitis media due to involvement of the Eustachian tube cartilage. (Hughes and Berry, 1972).
2. Sensorineural or mixed deafness which may be bilateral or unilateral, sudden or progressive over weeks.

This may be associated with vestibular symptoms. It is thought that the end-organ hearing loss may be due to RP involving the internal auditory artery—(Cody and Sones, 1971). The hearing loss may be brought on either by an abrupt cessation of steroid therapy or by a drastic reduction in the dose. Cody and Sones (1971) and Rabuzzi (1970) reported cases with reversal of sensorineural hearing loss with steroid treatment. This was not the case in this series.

The other clinical feature of RP commonly observed are:

*Arthropathy*: The joints commonly involved are the costochondrial joints, spinal joints and other peripheral joints.

*Nasal chondritis*: There is tender erythematous dorsal swelling of the nose.

*Chrondritis of the respiratory system*: There is a laryngotracheo-bronchial chondritis, chondromalacia and narrowing of the tracheobronchial tree. Subglottic stenosis due to RP has been reported. RP may involve the cardiovascular system resulting in aortic incompetence, mitral regurgitation, pericarditis, cardiac ischaemia, aneurysm of large arteries, vasculitis of CNS, phlebitis and Raynaud's phenomenon.

Skin involvement causes cutaneous vasculitis, erythema nodosum-like lesions or non-specific eruptions. Ocular involvement may be present as well, the commonest manifestation being episcleritis. Other ocular manifestations are scleritis, conjunctivitis, iritis, keratitis. Extra-ocular muscle palsies, optic neuritis, exophthalmos, and kerato-conjunctivitis may be seen occasionally.

A review of world literature shows on average age incidence of 44 years and an equal incidence between the sexes. Neither a specific racial predilection nor a familial predisposition has been recorded except in one series in which a pregnant woman with RP delivered a child affected at birth. (Damiani and Levine, 1979).

In this study, the ages of the patients ranged from 53–80 years and most of the clinical features of RP have been observed in different combinations.

Two patients presented with auricular chondritis; one had unilateral involvement, and the other bilateral, neither developed collapse of the cartilage. Two patients had involvement of the respiratory cartilages, more marked in the 53-year-old man who developed respiratory obstruction and respiratory failure from collapse of the tracheal and bronchial cartilages.

One patient developed nasal collapse. Nasal collapse can be seen in RP, congenital syphilis, Wegener's granulomatosis, but other clinical features and serological tests should aid the diagnosis. It is worth noting that positive serology for syphilis has been observed in cases of RP though all patients in this study had negative serology for syphilis.

Arthropathy involving the knee joints, was observed in two patients. In one, it was diagnosed as rheumatic fever but this may well have been a manifestation of RP.

Ocular manifestations observed in this study were conjunctivitis in one patient and bilateral scleritis and iritis which progressed to glaucoma and uveitis in another.

The common laboratory findings reported are normocytic normochromic anaemia, mild leucocytosis and a raised ESR which follows the progress of the disease as was demonstrated in all four cases. The significance of the changes in the blood levels of immunoglobulins is questionable.

No abnormalities in the immunoglobulin levels were detected in the present series.

Radiology is not of much help in the diagnosis of RP. The histological changes in RP are similar in all the affected cartilaginous structures. There is basophilic staining of cartilage matrix, perichondrial inflammation, cartilage destruction with replacement of fibrous tissue. There is lacunar breakdown and infiltration of neutrophils. As infiltration continues, there is condensation into irregular whorls of collagen with plasma cell and lymphocytic infiltration. Chondrocytes de-differentiate forming fibroblasts and collagen fibrils. Occasionally small sites of cartilage regenerate. There is loss of matrix acid mucopolysaccharides. Electron microscopic studies have shown many chondrocytes containing increased lysosomes and lipids. Direct immunofluorescence of auricular cartilage shows deposits of immunoglobulins IgA, IgG, and C3 component of the complement system at the chondro-fibrous junction (Valenzuela, 1980).

In this series, an auricular biopsy from case 1 revealed chronic inflammatory changes, auricular biopsy from case 2, laryngeal biopsy from case 3 and tracheal biopsy from case 4 revealed evidence of vasculitis and a picture suggestive of RP. It is important to include cartilage in the biopsy.

The pathogenesis and aetiology of RP are not clearly defined. It has been considered an auto-immune disorder mainly because of undoubted efficiency of cortico-steroids in reducing inflammatory response. Herman and Dennis (1973) have demonstrated that delayed hypersensitivity may play a role in RP.

They have suggested that cellular immune mechanisms may, in some way, aid antigenic cartilaginous components facilitating the continuous process of cartilaginous inflammation. They were, however, unable to identify a circulating antibody to the cartilaginous matrix. Fiodart and Shigeto (1978) demonstrated circulating antibodies to type 2 collagen during the acute phase of RP by indirect immuno-fluorescence. Hydralazine-induced RP has been recorded as an adverse reaction to this drug, developing almost exclusively in patients who are slow acetylators.

In case one, an anti-type 2 collagen, auto-immunity could have developed because of his preceding fever but thus far, no specific association has been observed. In the other cases, the aetiological factor could not be determined.

Medical treatment of RP consists primarily of corticosteroids, immuno-suppressive drugs and dapsone. Salicylates, phenylbutazone and indomethacin have been tried with little effect. Prednisolone is the drug of choice. It reduces the inflammatory response by stabilizing the lysozymes that come from the leucocytes with some recovery of hearing in patients with early sensorineural involvement although, relapses tend to occur when this drug is discontinued or dosage markedly reduced. It may not be possible to withdraw completely some patients from the medication without exacerbation of RP.

Oral prednisolone 5 mg four times a day up to 200 mg four times a day for acute exacerbation has been used.

The duration of treatment varies from three weeks to six years. ACTH gel 80 units can be given for acute episodes. Dapsone (DDs) has been thought to inhibit lysosomal enzyme release and thereby prevent chondrocyte damage. Stendahl (1978) believes that the drug interferes primarily with myeloperoxidase $H_2O_2$ halide mediated cytotoxic system in the polymorpho-nuclear leukocyte and this achieves anti-microbial and anti-inflammatory effects.

The dose range for DDs is 25 mg–200 mg qds for one week to two years, the average being 75 mg qds for four months. The drug may be required to be discontinued because of its side-effects of nausea, and haemolytic anaemia. Combination treatment with steroids and DDs does not appear to have any special advantage as far as recurrence of RP is concerned. Immunosuppressive drugs have been used in RP with some success and frequently in conjunction with steroids. Hughes and Berry (1972) have tried azathioprine and steroids with good response. Other immuno-suppressive drugs that may be used are methotrexate, cyclophosphamide, six mercaptopurine, and nitrogen mustard. Immuno-suppressive drugs appear to have only moderate value in controlling RP and are generally used only as adjuvants to steroids and/or dapsone.

One of the suggested regimens of RP is methylprednisolone IV one gram for three days with cyclophosphamide IV 15 mg/kg for one day—to be repeated at two weekly intervals with maintenance steroids (prednisolone in tapering doses) in between the fortnightly pulses—maintenance dose of steroids to be omitted when receiving methylprednisolone. This regimen was used in case 4 considering the severity of the involvement of his respiratory system but had to be discontinued as there was a marked reduction in the patient's white blood cell count.

In two patients, only prednisolone was used and in one a combination of prednisolone and azathioprine was used with good control of the disease process.

Temporary or permanent tracheostomy may be needed for respiratory distress secondary to tracheal/laryngeal/bronchial chondritis despite the risk that polychondritis may progress.

Incision, drainage and debridement of necrotic tissue from the involved site may be needed.

In cases with involvement of the cardiovascular system, valve replacement or resection of aneurysms may be indicated. Cosmetic surgery for collapsed nasal cartilage and laryngeal reconstruction is of debatable value, though some surgeons have achieved satisfactory results with cosmetic surgery for nasal cartilage collapse. Damiani and Levine (1979) think that considering the relapsing nature of the disease, cosmetic surgery is not indicated unless the disease has been quiescent for a number of years. If there is a recurrence and further collapse following surgery, the question could be raised as to whether the recurrent deformity was secondary to the recurrence or was initiated by the surgery. In case 4, augmentation rhinoplasty was attempted as the patient's condition seemed to have stabilized with medical treatment and the patient requested it. The rhinoplasty was a success though the patient succumbed to the disease a few months later.

As for laryngeal reconstruction, though excision of the diseased tissue with stenting has been successful in establishing satisfactory airway and averting a permanent tracheostomy, the general consensus is that laryngeal reconstruction should await resolution of the disease.

In case 4, Montgomery 'T' tube insertion and internal wire springs were used to prevent tracheal collapse but they failed to relieve the obstruction and so did posterior membrane fixation of the trachea and the main bronchi. The patient succumbed to the disease.

## Acknowledgements

We would like to thank Dr Paterson, consultant dermatologist, Carlisle.

Thanks are also due to Sarah Rafferty and Eileen Barraclough for their secretarial help in the reference preparation of this article.

## References

Cody, D. T. R., Sones, D. A. (1971) Relapsing polychondritis: Audio vestibular manifestations. *Laryngoscope*, **81:** 1208.

Damiani, J. M., Levine, H. L. (1979) Relapsing polychondritis. *Laryngoscope*, **89:** 929–946.

Fiodart, J. M., Shigeto, A. (1978) Antibodies to type 2 collagen in relapsing polychondritis. *New England Journal of Medicine*, **299:** 1203–1207.

Herman, J. H., Dennis, M. V. (1973) Immunopathologic studies in relapsing polychondritis. *Journal of Clinical Investigation*, **52:** 549–558.

Hughes, R. A., Berry, C. L. (1972) Relapsing polychondritis. *Quarterly Journal of Medicine*, **41:** 363–380.

Jaksch-Wartenhorst, R. (1923) Polychondropathia. *Archives of Internal Medicine (Vienna)*, **6:** 93–97.

McAdam, L. P., O'Hanlon, M. A., Bluestone, R., Pearson, C. M. (1976) Relapsing polychondritis: Prospective study of 23 patients and a review of literature. *Medicine, Baltimore*, **55:** 193–215.
Rabuzzi, D. D. (1970) Relapsing polychondritis. *Archives of Otolaryngology*, **91:** 188–194.
Stendahl, O., Molin, L., Dahlgren, C. (1978) The inhibition of polymorphonuclear leukocyte cytotoxicity by dapsone. A possible mechanism in the treatment of dermatitis herpitiformis. *Journal of Clinical Investigation*, **62:** 214–220.
Valenzuela, R. (1980) Relapsing polychondritis. Immunomicroscopic findings in cartilage ear biopsy specimens. *Human Pathology*, **11:** 19–26.

Address for correspondence:
Dr B. S. Irani,
E.N.T. Department,
Ninewells Hospital and Medical School,
Ninewells,
Dundee DD1 9SY.

**Key words: Polychondritis, relapsing.**