# RELAPSING POLYCHONDRITIS

**Nadia K Waheed**

## CASE:

A 19 year-old Asian male presented to the uveitis clinic with a complaint of a red right eye for the past 2 weeks, not relieved by antibiotic eye drops.

The patient had initially presented to the ENT service a few weeks ago with nasal obstruction for a few weeks, which was found to be due to a nasal mass, that on incision and drainage showed neutrophils. This was followed nearly 2 weeks later with hoarseness that was found on laryngoscopy to be associated with tracheal inflammation and edema. He also gave a several month history of episodic ear swelling and tenderness.

On examination, he was found to have scleritis with anterior chamber cells and flare in the right eye. Lab results revealed a negative ANA and ANCA, his ESR was 96, urinalysis showed trace red blood cells, and a cartilage biopsy showed inflammation and destruction of cartilage. A diagnosis of relapsing polychondritis was made and he was started on oral steroids. However, on taper of steroids, his scleritis recurred, and he was advised immunomodulatory therapy. Imuran was started by his rheumatologist.

The patient had imperfect control of symptoms, and progressive shortness of breath on a backpacking trip resulted in a visit to the emergency room where he was found to have severe subglottic stenosis. Despite high dose steroids, and multiple unsuccessful attempts at dilation, a tracheostomy had to be performed.

Inflammation persisted as manifested by ear pain and an elevated ESR; cyclophosphamide was discussed but the patient and his rheumatologist decided to hold back on that due to its side effects. However, when an unsuccessful attempt at revision of tracheostomy made it clear that more immunomodulation was needed, the patient was placed on methotrexate, and the dose adjusted to achieve a quiescence of all inflammatory activity and an ESR within normal limits. The patient then underwent a successful tracheal reconstruction.

Relapsing polychondritis was first described by Wartenhorst in 1923 as ‘polychondropathia,’ in a patient who was described as developing the classic nasal deformity. It is characterized by recurrent, potentially severe episodes of recurrent inflammation of cartilagenous tissue. It has been described most commonly in Caucasians and is equally prevalent in males and females. The average age of onset is in the $4^{th}$ decade, although in the major series on this subject, ages of onset of between 13 and 84 years have been described. A recently published series shows that the delay between when help is first sought for the symptoms and the diagnosis is made may be as long as 2.9 years.

## PATHOLOGY AND PATHOGENESIS

There is evidence to implicate autoimmune mechanisms in the pathogenesis of the disease: circulating immune complexes have been found in these patients, as have antibodies to collagen, the disease responds to immunosuppression and is associated with the HLA DR4 antigen as are many other autoimmune diseases. On histology, there is no pathognomonic pattern, although cartilage tissue may show subtle changes such as a loss of basophilia, necrotic, vacuolated chondrocytes and perichondrial inflammation. **Figure 1.**Vasculitis may also be present.

## CLINICAL CHARACTERISTICS

It is characterized by a sudden, flagrant onset with nearly 91% of patients having external ear pain at presentation. Patients may also present with nasal pain, hoarseness, throat pain, or even with acute obstruction of the upper respiratory tract of unknown cause. Patients may also have polyarthritis or polyarthralgias that may be fleeting and change joints. A few patients may present initially with recurrent scleritis or episcleritis. **Figure 2.**Vestibular or hearing dysfunction due to vasculitic or cartilagenous lesions is a much less common presenting symptom and may be cause confusion with Cogan's syndrome. Various symptoms that can occur later in the disease are presented in **Table 1** and can be seen in **Figure 3**, 4. Larynotracheal inflammation may cause tracheal collapse, long-term cardiovascular deterioration can occur due to destruction of the cartilagenous valve cusps and the roots of the large blood vessels and renal involvement, although uncommon, has important prognostic implications. Diagnosis is made on the basis of clinical criteria summarized in **Table 2**.

Ocular involvement occurs in 14-24% of patients at presentation, and eventually the eye is involved in 51-65% of cases. Although the most common sites of involvement are the conjunctiva, the episclera and the sclera (each involved in nearly 10% of patients), almost any part of the eye can be involved in the disease. Scleritis can be diffuse, nodular or necrotizing; necrotizing scleritis has been shown to be associated with systemic vasculitis, and responds only to aggressive treatment. Iridocyclitis and corneal involvement in the form of peripheral thinning, ulceration or infiltrates is not uncommon. Retinal involvement may also occur occasionally, and neuro-ophthalmologic manifestations are usually a result of vasculitis.

Reviews have shown that most patients with eye disease tend to develop multiple systemic manifestations and that scleritis may be associated with a systemic vasculitis.

**TREATMENT**

Treatment of acute symptoms is through the use of systemic steroids. Immunomodulatory agents, including methotrexate, imuran and cyclosporine have been used, as have dapsone and pencillamine in the less severe cases. Methotrexate is shown to be steroid-sparing and to increase longevity in these patients. However, cyclophosphamide is the gold standard of treatment in severe or refractory cases, and may be the first line agent in certain manifestations of the disease such as necrotizing scleritis that do not respond to azathioprine or methotrexate.

**PROGNOSIS**

The disease is intermittent and fluctuant, but is progressive with some studies showing survival rates of around 75% and 55% at 5 and 10 years of follow-up respectively. However, a more recent study shows a survival of over 90% at an average follow-up of 8 years. Factors that worsen the prognosis are presented in **table 3.** The leading causes of death in patients with relapsing polychondritis are summarized in **table 4**. These patients have an increased risk of developing myelodysplastic malignancies, and when these occur, they are the cause of death rather than the polychondritis itself.

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TABLE 1:

CLINICAL FEATURES IN ESTABLISHED RELAPSING POLYCHONDRITIS

| |
|---|
| Constitutional symptoms |
| Eventual bilateral ear involvement |
| Hearing impairment |
| Joint pain |
| **Laryngotracheal inflammation** |
| Costochondritis |
| Cardiovascular deterioration |
| Arterial and venous thromboses |
| **Renal involvement** |

TABLE 2:

DIAGNOSTIC CRITERIA*

| |
|---|
| Recurrent chondritis, both auricles |
| Non-erosive, inflammatory polyarthritis |
| Nasal chondritis |
| Ocular inflammation |

| |
|---|
| Respiratory tract chondritis |
| Cochlear and/or vestibular dysfunction |

*Diagnosis is made in the presence of:

> 2 clinical signs or

> 1 sign with histologic confirmation

> 2 separate sites of chondritis and response to steroids and immunosuppression

TABLE 3:

FACTORS ASSOCIATED WITH WORSE

**Prognosis**

| |
|---|
| **AT ALL AGES:** |
| Anemia |
| **< 50 YEARS:** |
| Saddle nose deformity |
| Arthritis |
| Tracheolaryngeal strictures |
| Vasculitis |
| Microhematuria |

TABLE 4:

CAUSES OF DEATH IN PATIENTS WITH RELAPSING POLYCHONDRITIS

| |
|---|
| Respiratory complications (airway collapse/ pneumonia) |
| Cardiovascular complications (aneurysm rupture/ vasculitis/ valvular heart disease) |
| Infectious complications |

| Concurrent malignancy |
| --- |

FIGURE LEGENDS

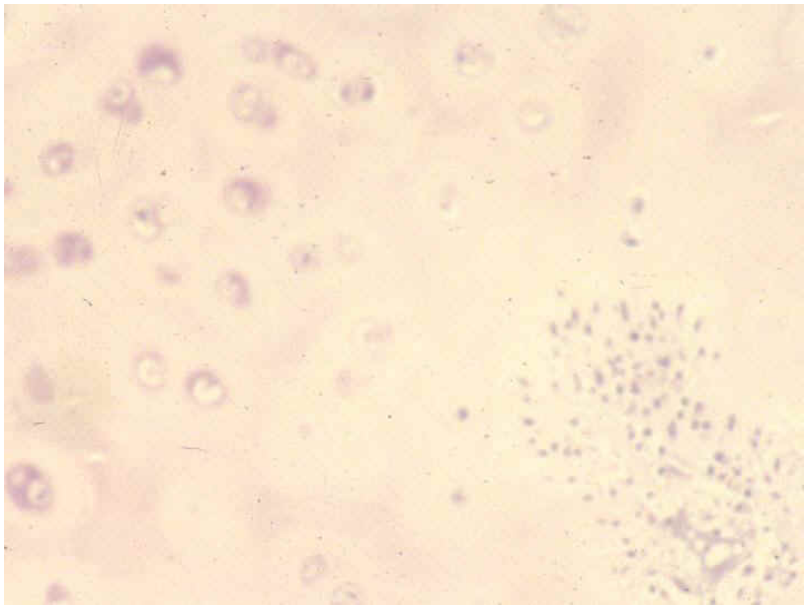

**Figure 1**: Areas of inflammation in cartilage in a patient with relapsing polychondritis

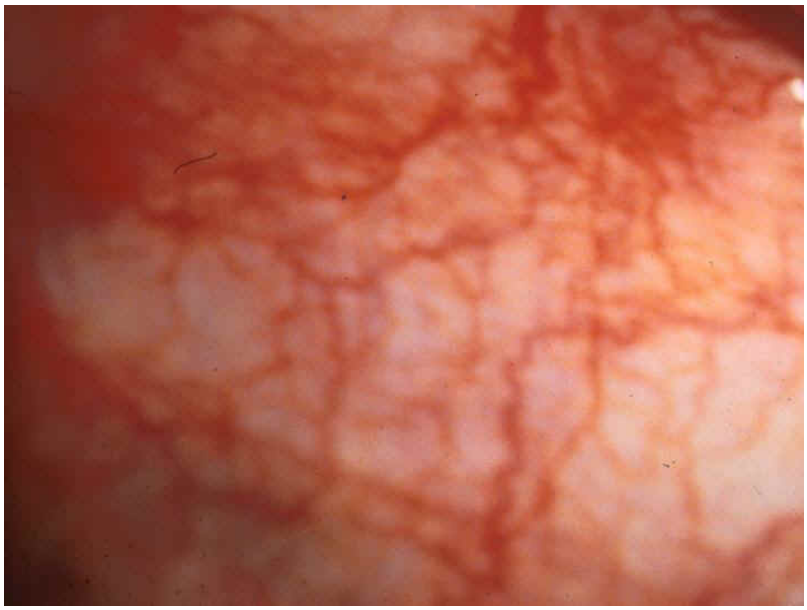

**Figure 2**: Scleritis in a patient with relapsing polychondritis

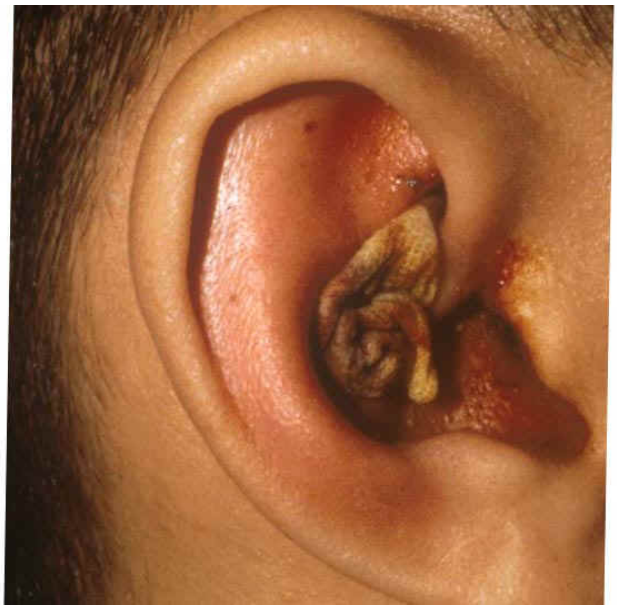

**Figure 3**: Ear cartilage inflammation seen as redness of the ear lobe

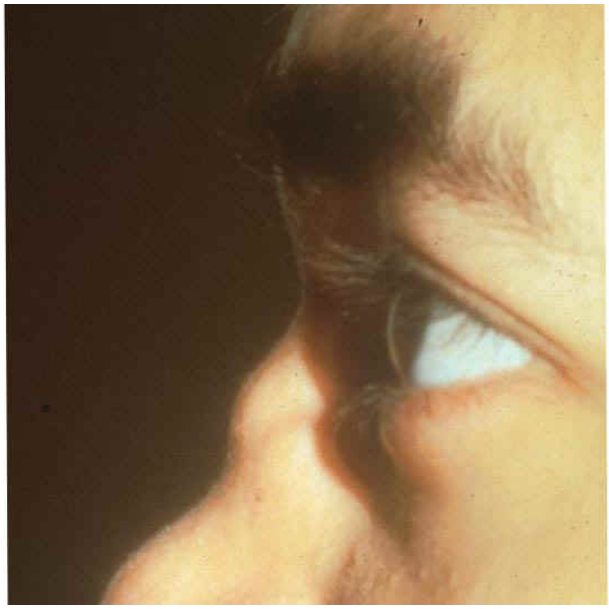

**Figure 4**: Saddle nose deformity

## QUESTIONS

Patients with relapsing polychondritis may have all of the following as part of the disease except:

Recurrent cartilage inflammation

Scleritis

Renal involvement

Colorectal cancer

Vasculitis

The commonest cause of death in patients with relapsing polychondritis is:

Respiratory complications

Cardiovascular complications

Steroid-induced Diabetes

Lung cancer

Fungal infections

Which of the following in a patient with relapsing polychondritis is associated with a high incidence of concurrent systemic vasculitis:

Infections

Diffuse scleritis

Dermatitis

Necrotizing scleritis

Old age

Untreated patients with relapsing polychondritis have a worse prognosis than untreated patients with all of the following diseases except:

Diabetes Mellius

Systemic Lupus Erythematosis

Scleroderma

Wegener’s granulomatosis

Cushing’s syndrome

The pathognomonic feature of relapsing polychondritis on histopathology is:

Cartilage inflammation

Vasculitis

Renal basement membrane staining with anti-C3 antibodies

A lumpy-bumpy pattern on immunofluorescence

None of the above

A 52 year old, 80 kg male patient known to have relapsing polychondritis and controlled on systemic methotrexate now resents with a red eye and a week long history of malaise and fatigue. On examination, he is found to have nodular scleritis. The next most appropriate step in his management would be to:

Reduce methotrexate dose

Start on 30 mg prednisone PO

Consider pulse steroids and alkylating agents

Observe for 2 weeks

Switch to Imuran

The diagnosis of relapsing polychondritis is based on:

Clinical criteria

Blood results

The presence of a saddle nose deformity

Histopathologic features

Response to treatment

All of the following are bad prognostic features for patients with RP except:

a) Hematuria

Age > 25 years

Anemia

Arthritis

Saddle nose deformity

The differential diagnosis of eye and ear involvement in a disease include all of the following except:

RP

Cogan’s

Wegener’s

Syphilis

HLA-B27 associated uveitis

A known case of Relapsing Polchondritis presents to the clinic with scleritis and a 4-day history of shortness of breath. The next most appropriate step in management is:

Send the patient home with reassurance

Evaluate emergently for tracheal collapse

Arrange for an appointment with the ENT service 2 weeks later

Start on 20 mg Prednisone and re-evaluate in 1 week

Inquire about exposure to allergic material

ANSWERS

d

d

d

d

e

c

a

b

e

b