The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

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Relapsing polychondritis

Manfred Herold

1 Introduction

Relapsing polychondritis (RPC) is a rare, chronic, inflammatory, autoimmune disease of unknown origin characterized by recurrent inflammation with the possible destruction of cartilage and neighboring connective tissue. It was first described in 1923 by Jaksch-Wartenhorst [reviewed in 1 & 2]. The name *relapsing polychondritis* (RPC) was suggested by Pearson and coworkers in 1962 (reviewed in [1 & 2]) because of its episodic nature as an active, cartilage-destroying disease. Autoimmune reactions to antigens present in cartilages such as type II collagen [3] and matrilin seem to be triggers for clinical symptoms. Polychondritis may attack cartilages in different parts of the body [1]. A painful inflammation of the ear (Fig. 1) is the most commonly seen symptom (Table 1).

RPC is a rare disease. In Rochester, USA, the estimated prevalence of RPC is about 3.5 cases per million The ratio of female to male cases seems to be equal and the disease has been reported in all races and ages between 13 and 84 years [1]. The mean age of patients at diagnosis is in the late forties.

2 Diagnostic criteria

Diagnosis is still based on criteria defined by McAdam et al. (reviewed in [2]) in 1976 (Table 2). Nowadays the diagnosis of RPC can be made on the basis of chondritis in two of three sites (auricular, nasal, laryngotracheal) or on the basis of chondritis in one of these sites (auricular, nasal, laryngotracheal) plus two additional features such as ocular inflammation, audio vestibular damage or inflammatory arthritis [3] or on the basis of one or more clinical signs with histological confirmation of chondritis.

RPC-specific laboratory tests are unknown. Only non-specific laboratory signs of inflammation including elevated erythrocyte sedimentation rate (ESR), increased C-reactive protein (CRP), moderate leukocytosis and thrombocytosis are seen. Antinuclear antibodies (ANA) may be present but no specific ANA-subtypes are known.

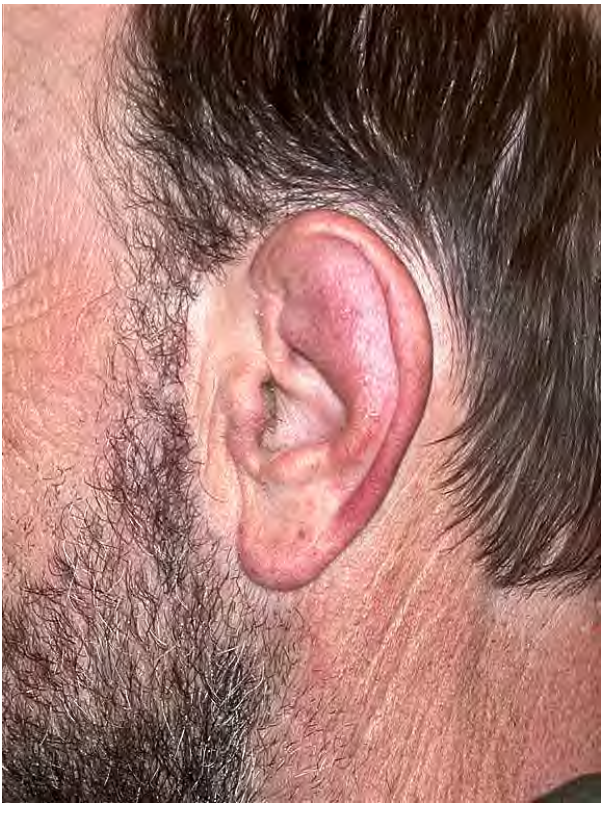

Figure 1. Man of 50 years of age who has suffered from relapsing polychondritis in both ears for several years (picture M. Herold 2008).

3 Requirements for the family practitioner

The most frequent clinical manifestation is an inflammation of the cartilage of the ear either unilaterally or bilaterally presenting as acute pain with swelling and redness (Fig. 1). Painful joints are the second most common feature in RPC. Parasternal joints including sternoclaviclar, manubriosternal or costosternal may be involved as well as peripheral joints presenting as nonerosive, asymmetrical oligo- or polyarthritis.

RPC, as primarily a disease of the cartilage, also affects the respiratory system where most parts, from the external nares, nasal septum, epiglottis and larynx, to the trachea and bronchioli, contain cartilage. Airway involvement is potentially serious and responsible for the significant morbidity and mortality seen in patients with RPC [4]. Nasal chondritis causes stuffiness, crusting, rhinorrhea,

Table 1. Estimated incidence of signs and symptoms in relapsing polychondritis*.

	Presentation (%)	Cumulative (%)
ESR increase	74	82
Anaemia	50	53
Auricular chondritis	40	85
Arthritis	37	57
Laryngotracheal symptoms	25	49
Nasal chondritis	25	57
Ocular symptoms	20	52
Saddle nose	18	29
Airway stricture	15	23
Dermatologic	10	28
Hearing loss	9	32
Systemic vasculitis	3	12
Vestibular dysfunction	0	17
Cardiac valve	0	6
Aneurysm	0	5

* modified from Staats et al. 2002 with estimated percentages abstracted from Michet et al. 1986.

Table 2. Diagnostic criteria for relapsing polychondritis according to McAdam et al. 1976 (reviewed in [5]).

Three or more clinical signs must be present:

1. Recurrent chondritis in both auricles
2. Non-erosive inflammatory polyarthritis
3. Nasal chondritis
4. Ocular inflammation
5. Respiratory tract chondritis
6. Audio vestibular dysfunction and damage

epistaxis and cartilage destruction with saddle nose deformity. Involvement of the larynx results in hoarseness, aphonia, wheezing and inspiratory stridor. Chondritis of the tracheobronchial tree causes effects varying from subtle, asymptomatic inflammation to life-limiting complications. Bronchial inflammation may cause stenosis, wall thickening, obstruction and hyperdynamic airway collapse. Symptoms include cough, dyspnoea and wheezing. In the early stages of the disease,

pulmonary function tests may indicate lower airway involvement of RPC even in asymptomatic patients. In cases of airway manifestations of RCP, it is important to diagnose early and to start treatment before irreversible damage occurs within the tracheobronchial system.

Beside the typical cartilage-including organs, other proteoglycan-rich structures such as eyes, inner ear, blood vessels and heart can also be involved. More than 50 % of patients (Table 1) develop ocular inflammation mainly as scleritis and episcleritis, but also in the form of keratoconjunctivitis Sicca, uveitis, ulcerative keratitis and optic neuritis.

4 Management

In regards to treatment of RPC, there are no evidence-based recommendations as randomised, controlled trials have not been published. Treatment is based on empirical clinical observations and usually starts with anti-inflammatory drugs targeting symptoms. In patients with mild symptoms of nasal or auricular chondritis or peripheral arthritis, nonsteroidal anti-inflammatory drugs (NSAIDs) may be sufficient. If NSAIDs are not effective, or a more rigorous anti-inflammatory treatment is indicated, glucocorticoids are the treatment of choice usually starting with 0.5 to 1 mg prednisone equivalents per kg bodyweight with the dose reducing to the minimal required amount. In life-threatening situations, with acute airway obstructions, pulse therapy with 1000 mg methylprednisolone intravenously for 3 days may be used.

Long term glucocorticoid therapy is associated with undesirable side effects but discontinuation of glucocorticoids often results in disease relapse. As in other chronic, inflammatory rheumatic diseases such as rheumatoid arthritis, several immunomodulatory and anti-inflammatory drugs have been used to reduce reliance on glucocorticoids. Disease modifying antirheumatic drugs (DMARDs) including methotrexate, leflunomide, azathioprine, cyclophoshamide, cyclosporine have been tried as has intravenous immungloulin. A treatment of choice has not yet been defined. Within the last few years, in some patients with a catastrophic course or symptoms refractory to all therapeutic regimes, biologicals, as used in refractory, chronic, inflammatory rheumatic diseases, have been tried. Successful treatment of refractory RPC was described with drugs targeting proinflammatory cytokines [5] such as anakinra (blocking IL-1 signalling), tocilizumab (blocking IL-6 signalling) and TNF-inhibitors (blocking TNF-alpha) including infliximab, etanercept and adalimumab. With rituximab (anti-CD20 resulting in B-cell depletion), only a partial response was seen. Abatacept, a T-cell co-stimulation inhibitor, was successfully administered to patients with RPC and is currently being tested in RCP in a phase 1 trial.

RPC is a rare, systemic, inflammatory, autoimmune disease with variable features and which targets cartilage. The clinical symptoms show a wide rage from

mild attacks, easily handled with NSAIDs on demand, up to acute-onset and life-limiting airway-destructing inflammation. Early diagnosis is important to limit irreversible cartilage destruction and fatal complications. Glucocorticoids are the most important medical treatment. Biologicals may be the treatment of choice to minimise glucocorticoids or in cases of refractory disease.

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