CHAPTER 22

Relapsing Polychondritis

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- Relapsing polychondritis (RP) is a rare disease that occurs worldwide in all age groups and affects men and women equally.
- An associated rheumatologic or hematologic disorder is seen in over 30% of patients with RP. Inflammation of cartilaginous structures with lymphocytic infiltration and association with anticollagen antibodies are consistent with an autoimmune pathogenesis.
- The characteristic clinical findings are acute painful swelling and redness of the external ear, nasal cartilage, and laryngotracheal cartilage. Nonerosive arthritis, ocular inflammation, vestibular symptoms, and involvement of the heart and kidney also occur.
- Diagnosis is made on clinical grounds, though cartilage biopsy may be useful.
- Treatment with nonsteriodal anti-inflammatory drugs (NSAIDs) or corticosteroids may control inflammation, but immunosuppressive and biologic treatments may be required for severe disease.
- Laryngotracheal involvement is a serious complication that may require tracheostomy.

Relapsing polychondritis is a recurring inflammatory disorder of unknown etiology causing inflammatory reactions in the cartilaginous structures of the nose, ears, trachea, and the joints. It is considered an autoimmune disorder. It was first described by Jaksch-Wartenhorst (1), in a patient with systemic illness characterized by external ear swelling, collapse of the nasal bridge, fever, and arthritis. Pearson and colleagues (2) first coined the term *relapsing polychondritis* (RP), and described, in detail, the clinical features of several of their own patients along with those in the literature. Since then, this disorder has been described worldwide and occurs in all age groups, although it peaks in the fifth decade. Over 30% of patients have an associated disorder, usually autoimmune or hematologic. These include systemic vasculitis syndromes, systemic lupus erythematosus (SLE), Sjögren's syndrome, overlap connective tissue disorders, rheumatoid arthritis (RA), spondyloarthropathies, dysmyelopoietic syndromes, Hodgkin's disease, diabetes mellitis, and psoriasis vulgaris (3). It is a rare disease occuring in 3.5 person's per million (Michet, personal communication). The 5-year survival is decreased to approximately 74%. The male : female ratio is equal (4).

The pathology shows destructive changes in the fibrocartilagenous junction by mononuclear cells (Figure 22-1). These cells have been found to be CD4+ lymphocytes (5). Evidence of local complement activation has been observed (6,7). Elevated levels of anticollagen antibodies and cell-mediated immunity to cartilage components have been observed (8,9). Recently, similar changes have been observed in transgenic mice immunized with type II collagen (10). These observations are consistent with the thought that autoimmune mechanisms are involved in this disease.

OTORHINOLARYNGEAL

One of the hallmarks of this disease and the presenting feature in 40% of the patients is acute painful swelling and redness of the external ear (Figure 22-2). This may occur spontaneously or following minor injury, and even though it is unilateral initially, most patients develop it bilaterally. Ultimately 80% of the patients experience this swelling (Table 22-1). The lobule of the external ear is characteristically spared. Recurrent inflammatory episodes lead to destruction of the external ear cartilage, resulting in either a soft flopped ear or a firm fibrotic knobby ear. In rare cases the cartilage of the ear may calcify. The nasal bridge may be similarly involved and can cause nasal bridge collapse. The external auditory canal may be stenosed by the inflammatory swelling and cause conductive deafness. About one third of the patients experience vestibular or auditory abnormalities of varying degrees from vasculitis of the internal auditory artery (11).

RESPIRATORY

Hoarseness, cough, wheezing, and dyspnea are commonly observed. The severity of these depends upon the severity of the inflammation of the tracheal cartilages. Tenderness of the thyroid cartilage and trachea

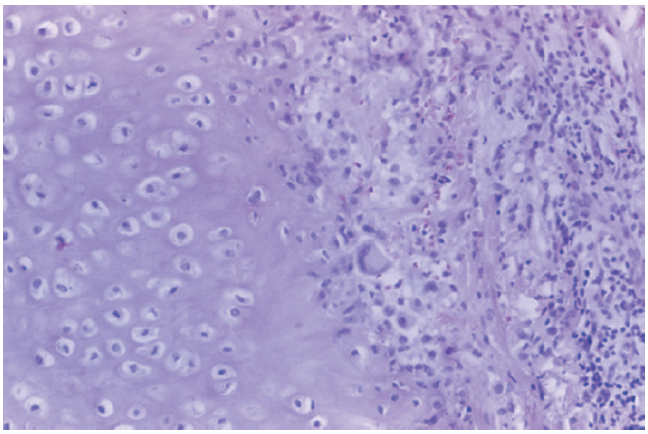

FIGURE 22-1

Histology of the fibrocartilagenous junction of the ear in a patient with relapsing polychondritis. Inflammatory mononuclear cells infiltrate this region with occasional polymorphonuclear leukocytes with damage to the cartilage. Hemotoxylin and eosin stain. Original magnification, ×200. (Courtesy of Dr. Lestor E. Wold.)

TABLE 22-1. Clinical manifestations of relapsing polychondritis.

MANIFESTATION	INITIAL (%)	TOTAL (%)
Auricular chondritis	40	85
Nasal cartilage	20	50
Hearing loss	9	30
Arthritis	35	50
Ocular	20	50
Larynotracheal–bronchial	26	48
Laryngotracheal stricture	15	23
Systemic vasculitis	3	10
Valvular dysfunction	0	6

SOURCE: Adapted from Isaak BL, Liesegang TJ, Michet CJ Jr. Ophthalmology 1986;93:681–689, by permission of *Ophthalmology*.

can be a clue to this involvement. Narrowing of the trachea, either localized or generalized, leads to inability to clear the throat, choking spells, and respiratory infections. These symptoms should be taken seriously because this is a potentially lethal complication. Respiratory symptoms of varying degree may be observed in up to 50% of patients (12).

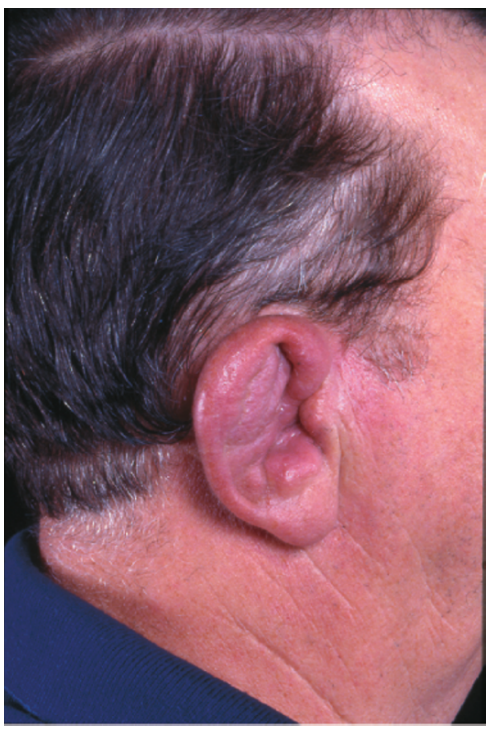

Figure 22-2

Acutely inflamed ear with sparing of the noncartilageneous lobule.

CARDIOVASCULAR

Vasculitis of various varieties can be observed in about 10% of the patients. Small vessel involvement leading to a leukocytoclastic vasculitis, medium size vessel disease of the polyarteritis variety, and large vessel disease of the Takayasu's arteritis variety occur. Signs and symptoms depend upon the type of involvement as well as the associated disease. Inflammation of the root of the aorta can cause aortic valve dysfunction, including aortic incompetence. Myocarditis may manifest as arrhythmias or even heart block (13).

OCULAR

The ocular involvement is very variable with both intra- and extraocular disease. Intraocular changes seen include iridocyclitis and retinal vasculitis. Extraocular disease manifests as periorbital edema, extraocular muscle palsy, conjunctivitis, keratitis, scleritis, and episcleritis. Proptosis is observed rarely (11).

MUSCULOSKELETAL

A seronegative episodic inflammatory oligo- or polyarthritis can be observed in anywhere from 30% to 75% of the patients. This is generally nonerosive and nonde-

forming, affecting both the small and large joints. Articular cartilage damage can cause symmetrical joint space narrowing and costal cartilage damage may lead to a pectus excavatum deformity (14).

OTHER FEATURES

Segmental proliferative glomerulonephritis may be observed in approximately 10% of patients (15). Systemic features, including fever, weight loss, and fatigue, are commonly seen. Several cases of myelodysplastic syndrome have been described (16).

DIAGNOSIS

McAdam and colleagues (17) proposed that the diagnosis of RP require three or more of the following clinical criteria: (1) bilateral auricular chondritis, (2) nonerosive, seronegative inflammatory polyarthritis, (3) nasal chondritis, (4) ocular inflammation (conjunctivitis, keratitis, scleritis/episcleritis, uveitis), (5) respiratory tract chondritis (laryngeal and/or tracheal cartilages), and (6) cochlear and/or vestibular dysfunction (neurosensory hearing loss, tinnitus, and/or vertigo), and a compatible biopsy. The need for a biopsy has not been necessary in retrospective studies (4) and is not necessary in clinical practice if the patient has chondritis of both ears, or chondritis at multiple sites. If, however, the history is recent and the clinical picture unclear or confusing, a biopsy (see Figure 22-1) may be essential to make a diagnosis.

As with other inflammatory diseases there can be anemia of chronic disease, elevated sedimentation rate, and hypergammaglobulinemia. If macrocytosis is observed, the possibility of associated myelodysplasia should be investigated. An abnormal urinalysis generally reflects renal involvement and the possibility of glomerulonephritis should be investigated.

Respiratory involvement is always a serious complication and may go undiagnosed until complications develop. Thus, all patients should undergo pulmonary function tests, as well as inspiratory and expiratory flow volume curves (12). Radiologic assessment by tomography or computed tomography (CT) scan (3,18–20) has been helpful in delineating the inflammatory changes of the trachea and the bronchial tree and the presence of stricture/s (localized or diffuse) and calcification can be accurately assessed.

Echocardiogram may help assess involvement of the cardiac valves and CT/magnetic resonance angiography (MRA) may be necessary to look for large vessel disease. Other investigations depend upon the associated disease.

When faced with a patient with early RP, one is obligated to consider other diagnosis. Chondritis due to streptococcal infection, local fungal infections, syphilis, or leprosy need to be kept in mind. Local trauma may cause inflammatory changes that mimic chondritis. Nasal cartilage damage leading to collapse of the bridge can occur from trauma, infections, granulomatous diseases like Wegener's granulomatosis, as well as from neoplastic diseases. Vasculitis of large and small blood vessels from other connective tissue diseases should be considered.

MANAGEMENT

The management of patients with RP depends upon the manifestations of the disease. If the patients have mild disease with fever, ear cartilage and/ or nasal cartilage inflammation with arthalgias, then nonsteriodal anti-inflammatory drugs (NSAIDs) may be adequate. If, however, the symptoms are severe or resistant to NSAID therapy, then low-to-moderate doses of corticosteroids may be necessary. Presence of respiratory symptoms, renal disease, or vasculitis require high-dose corticosteroids. As the disease is better controlled the steroid dose can be reduced. Immunosuppressives may be necessary as steroid-sparing agents. Other drugs, for example, dapsone and cyclosporine, have been reported to be helpful in small numbers of patients and so have immunosupressive drugs, including azathioprine, methotrexate, chlorambucil, and cyclophosphamide. Recently, anti-CD4 antibodies and anti–tumor necrosis factor (TNF) agents have been used with mixed success. Because of the rarity of this illness, no controlled studies have been done. Involvement of the trachea is a serious complication and necessitates aggressive management, including tracheostomy, use of stents if there is tracheal collapse, high-dose corticosteroids, and immunosuppressives (21). Infection from respiratory compromise and immunosuppressed state, as well as systemic vasculitis have been increasingly common causes of death. Aortic valve disease can be successfully treated by surgery (22).

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