

Chapter 162: Manifestations of Systemic Disease in the External Ear

Thomas J. McDonald

The various diseases that affect the external ear may present identical symptoms and signs; such similar features may create problems in making a diagnosis. On the other hand, when presented with a patient with external ear involvement from a systemic disease, making a diagnosis may be easier by noting whether lesions, if present in other regions of the head and neck or in distant sites are also caused by the same process.

Therefore the approach to take with a patient whose external ear manifests a systemic disease is a complete history and physical examination, thorough head and neck examination, general medical evaluation, key laboratory tests, and often even a biopsy. The later is done not only for routine histopathologic review but also for special tests.

This chapter describes six disorders that are not uncommon and can manifest in the external ear: Wegener's granulomatosis, relapsing polychondritis, lupus erythematosus (LE), gout, ochronosis, and chondrodermatitis helioides.

Wegener's Granulomatosis

This is a systemic vasculitis with preferential involvement of the respiratory tract, named after Friedrich Wegener (1939) who first described the syndrome as a distinct disease entity. In the past, Wegener's granulomatosis was uniformly fatal, but the recent advent of successful immunosuppressive therapy as well as a new diagnostic test (anticytoplasmic autoantibodies (ACPA) test) has led to renewed clinical and scientific interest in this disease as well as a much-improved prognosis (Gaughan et al, 1990; Kallenberg, 1990). The cause of Wegener's granulomatosis is unknown. The disease can be represented by a continuum, beginning with limited organ involvement (usually the upper airway) before progressing to its classic generalized form, disseminated vasculitis with ear, nose, throat, lung, and kidney involvement (DeRemee et al, 1976; McDonald et al, 1974, 1982). Limited forms also occur. A more complete review of Wegener's granulomatosis is presented elsewhere in this book.

Otologic involvement

Twenty-five percent of Mayo Clinic patients with Wegener's granulomatosis involving the upper airway had documented otologic involvement (McCaffrey et al, 1980). In 1989, Kempf (1989) reported that in 16 of 19 patients with biopsy-proven Wegener's granulomatosis the disease's early manifestations were limited to the head and neck region, and that 13 of the 19 cases had ear involvement. The type of involvement he described was very similar to the involvement in the Mayo Clinic series, which took four forms. The first is conductive deafness due to serous otitis media, which is often unilateral and can be the earliest sign of the disease. The second form is suppurative otitis media with thickening of the tympanic membrane or perforation of the tympanic membranes, with or without granulation tissue in the middle ear and mastoids. The third form of involvement is sensorineural hearing loss, often profound and bilateral and, surprisingly, reversible by the early administration of steroid drugs, with or without cytotoxic agents. A fourth form of Wegener's granulomatosis is involvement of the pinna similar to that seen in relapsing

polychondritis, that is, a red, tender, brawny, diffuse swelling of the pinna occurring intermittently during active phases of the disease (Plate 20, A). In a 1990 review of the otorhinolaryngologic manifestations of Wegener's granulomatosis, Murty (1990) noted that the incidence of otologic involvement varied from 19% to 61% and tabulated the otologic manifestations of this disorder under (1) external ear: earlobe atrophy, otitis externa, tympanic membrane granulomata; (2) middle ear: serous otitis media, suppurative otitis media; (3) inner ear: sensorineural deafness and vertigo; and (4) facial nerve palsy.

Diagnosis

The diagnosis is based on a complete history, detection of the classic symptoms and signs - localized or systemic - and specific tests that include chest roentgenograms, erythrocyte sedimentation rate, complete blood cell count, rheumatoid factor, serum creatinine concentration, and urinalysis. The last two tests are reliable indicators of renal involvement.

Obtaining an adequate biopsy specimen is the next step in the diagnosis. In pinna involvement, there should be no reason for pinna biopsy because there is usually enough nasal and paranasal sinus and nasopharyngeal ulceration to allow a biopsy to be performed at these sites.

Anticytoplasmic autoantibodies test (Specks et al, 1989)

The basis of this test, which was recently introduced into clinical practice, is the demonstration of the activity of serum IgG antibodies against cytoplasmic components of neutrophils. For ACPA detection, the indirect immunofluorescence protocol used by Drs. Lüdemann, Gross, and coworkers is followed. An elaboration of this technique and its results is presented elsewhere in this book.

Differentiation from polymorphic reticulosis

For many years, we have published our opinion on these two diseases and have treated them as separate entities, both clinically and histopathologically. We now understand that polymorphic reticulosis is actually a T-cell lymphoma. In the Mayo Clinic series (Pisani and DeRemee, 1990), of 28 patients with the disease, no patients had ear problems.

Relapsing Polychondritis

Relapsing polychondritis is characterized by intermittent episodes of inflammation of the articular and nonarticular cartilage, leading to chondrolysis, dystrophy, and atrophy of the involved cartilage (McCaffrey et al, 1978). The inflammation typically involves the cartilages of the ear, nose, trachea, larynx, ribs, joints, and eustachian tubes. Inflammation of the sclera and audiovisual impairment, anemia, and fever also are associated with the disease.

In the first reports by Jaksch-Wartenhorst in 1923, the disease was called *polychondropathia*. The term *relapsing polychondritis* was coined by Pearson, Kline, and Newcomer in 1960. At the present time, more than 100 cases have been reported, primarily in the American and European literature.

Relapsing polychondritis affects more females than males and most patients are between the ages of 35 and 45 years, with the average age at onset being in the fourth decade. There is no racial predilection.

Otologic involvement

Classically, there is a beefy red involvement of the pinnae with sparing of the ear canals (Plate 20, A). The ear lobes also remain conspicuously normal. The affected areas are swollen and tender. The disease may involve both pinnae simultaneously or there may be alternating involvement.

Relapsing polychondritis is a clinical diagnosis and biopsy is usually not necessary. Two or more sites may be involved at a time. Typically, the disease involves one ear or both ears with nasal involvement and perhaps tenderness over the trachea and hoarseness. In addition, there may be inflammation of the eyes, arthropathies, audiovestibular disturbances (due to involvement of the eustachian tube or otic capsule or both), malaise, fever, anemia, and loss of weight.

Although laboratory findings are nonspecific, they can include an increased erythrocyte sedimentation rate and anemia. A test for rheumatoid factor may be positive.

Histopathologically, biopsy of affected cartilage, when it has to be done, shows condrolysis, chondritis, and perichondritis, with alteration of the cartilaginous matrix. In the active phase, the cartilaginous matrix shows decreased or complete loss of normal basophils and evidence of infiltration by inflammatory cells. Later, in the quiescent phase of the disease, the destroyed cartilage is replaced by granulation tissue and eventually by fibrous tissue (Plate 20, B).

Relapsing polychondritis as immune disease

Autoimmune mechanisms appear to be responsible for this disease (Foidart et al, 1978). Cell-mediated immunity to cartilage has been demonstrated in vitro; the degree of response was related to disease activity. IgG anti-type II collagen antibodies have been documented in these patients in titers corresponding to disease activity. Steroid therapy lowers the antibody titers.

Treatment

Corticosteroids are effective in the treatment of this disease, but more recently 100 mg of dapsone (Avlosulfon) once or twice a day (after 50 mg a day initially) has been successful. Indomethacin and salicylates also have been used with much success, and salicylates in large doses can be more effective than corticosteroids. Rarely, the disease will be characterized by a rapid, fulminant course leading to death from upper airway obstruction. More typically, the course of the disease involves intermittent, painful swelling of cartilaginous structures that can be controlled with either salicylates or corticosteroids. Usually, the external ears become scarred, thickened, and deformed, and there is often a resulting saddle nose deformity or subglottic stenosis when the nose or trachea is involved.

Principles of dapsone treatment

Dapsone can be toxic to erythrocytes and produce anemia (Lang, 1979). This is especially true in patients of Mediterranean descent, who may lack the glucose-6-phosphate dehydrogenase enzyme (G6PD). Therefore, before initiating treatment with dapsone, a G6PD screen should be performed; chemistry group, urinalysis, and measurement of baseline hemoglobin and liver enzymes should be done. Initially, a dose of 50 mg/day for 3 to 4 days should be prescribed and then hemoglobin concentration should be measured. If the hemoglobin value is normal, the dose can be increased to 100 mg/day; the studies mentioned above should be performed every 2 to 3 weeks to monitor the safety of dapsone therapy.

Lupus Erythematosus

This disorder is classified as a collagen disease (see box) because of the widespread fibrinoid degeneration of the collagen fibers in the mesenchymal tissues (Arnold et al, 1990). Basic to all of the connective tissue diseases is a complex array of autoimmune responses.

Box: Lupus erythematosus (LE): a classification

Chronic cutaneous LE

Discoid lupus erythematosus (DLE) localized to the head and neck region

Generalized DLE (lesions above and below the neck)

Hypertrophic discoid LE

Lupus erythematosus profundus (panniculitis)

Subacute cutaneous LE

Papulosquamous type

Annular type

Acute cutaneous LE

Systemic LE (SLE) with localized (malar erythema) generalized lesions

Bullous variant of LE.

Clinical presentation

LE is manifested in many forms and may involve any organ of the body. A current classification includes: (1) chronic cutaneous LE, which includes discoid lupus erythematosus (DLE) localized to the head and neck region, generalized DLE (lesions below and above the neck), hypertrophic DLE, and LE profundus (panniculitis); (2) subacute cutaneous LE, papulosquamous and annular types; and (3) acute cutaneous LE, which includes systemic LE (SLE) with localized (malar erythema) or generalized lesions and the rare bullous variant of LE (bullous eruption of LE or erythema multiforme-like bullous LE).

Cutaneous involvement occurs in 70% to 80% of patients with LE, with skin lesions second only to joint symptoms in the list of manifestations of SLE. DLE is the most common cutaneous manifestation of LE. In more than 90% of patients with DLE, the disease is confined to the skin. Generalized DLE is more frequently associated with SLE than is the localized form of cutaneous disease. Patients with DLE who do have systemic manifestations usually have a more benign course; severe systemic involvement (renal disease) is unusual. Approximately 15% of patients with SLE have lesions of DLE at presentation, and in approximately 25%, DLE will develop during the course of the disease.

DLE typically involves the bridge of the nose, malar areas, ears, and scalp. Contributing factors include exposure to ultraviolet light, cold, thermal burn, and direct physical trauma. The characteristic lesion is a well-circumscribed papule or plaque with follicular plugging (Plate 20, C). Lesions of DLE enlarge slowly and develop areas of scarring and hypopigmentation. Patients with DLE limited to the head and neck area usually lack serologic abnormalities. A subset of patients with DLE has circulating antinuclear antibodies, antibodies to extractable nuclear antigen, or minor hematologic abnormalities.

Subacute cutaneous LE manifests as widespread, non-scarring, intensely photosensitive, coalescing inflammatory papules and plaques. This form of cutaneous LE is more frequently associated with systemic symptoms or serologic abnormalities than is DLE. However, the association is usually with more benign systemic disease (eg, musculoskeletal) rather than renal or central nervous system disease. Subacute cutaneous LE represents approximately 10% to 15% of LE. At least 50% of such patients have diffuse alopecia. Ulcers of the mouth or rhinopharynx affect 15% to 40% of patients with LE and are more commonly seen in association with subacute cutaneous LE than DLE. Lupus profundus, involving subcutaneous tissues, has been noted in approximately 2% of patients with SLE and occurs more commonly alone or with DLE. Calcification may develop in patients with lupus profundus. Patients who have DLE or subacute cutaneous LE without systemic disease or with mild systemic manifestations have an excellent prognosis. The overall survival rate for patients with SLE is greater than 80% to 90% over a 10- to 15-year period, with mortality most commonly attributed to renal disease and less frequently to various other problems, including infection.

Histopathologically, the characteristic changes in cutaneous LE consist of vacuolar/hydropic degeneration at the basement membrane zone, interface lymphocytic inflammation, follicular plugging, hyperkeratosis, and atrophy. Direct immunofluorescence examination of lesional skin shows deposition of immunoglobulins and complement at the basement membrane zone; this is called a *lupus band*. The finding of a lupus band in non-sun-exposed, uninvolved skin is highly specific for SLE, whereas a positive lupus band in

lesional skin may be seen in any type of LE.

Treatment

Treatment of cutaneous LE depends on the extent and severity of disease. All patients should be advised to use sunscreen daily and minimize sun exposure. Patients with localized cutaneous lesions may benefit from topically applied corticosteroids. Antimalarial therapy, such as chloroquine, hydroxychloroquine, quiacrine, or a combination of these medications, may be useful in patients with various forms of cutaneous LE. Dapsone has been beneficial in patients with acute cutaneous LE, particularly patients with bullous LE. Spontaneous improvement may occur, with or without scarring; however, cutaneous LE is characterized by chronicity and recurrence.

Gout

Gout and ochronosis are disorders caused by errors of metabolism, and both involve the external ear (Grahame and Scott, 1970).

Gout is a form of severe recurrent nonarthritic arthritis associated with hyperuricaemia and results from deposition of urates in nonarticular tissue. These deposits in subcutaneous tissues are called *tophi*. They vary from the size of a pinhead to that of a pea and are most commonly found on the rim of the external ear (Plate 20, D).

The disease is a familial one relating to defects of specific enzymes. One of the enzymes, hypoxanthine guanine phosphoribosyltransferase, involves purine metabolism; deficiency of this enzyme is associated with the most severe excess production of uric acid yet found.

The deposits on the helix can be confused with rheumatic nodules. Typically, they are painful subcutaneous nodules that are salmon pink in color. When pressed, they exude a chalky white material containing sodium biurate.

Hyperuricaemia (serum urate level greater than 7 mg/dL) is found in almost all gouty patients, although an occasional patient may have a serum uric acid value in the high normal range, particularly during the acute attack. Additionally, leukocytosis and an increased erythrocyte sedimentation rate are common.

Histopathologic examination shows characteristic long needle-shaped crystals of monosodium urate. Because these deposits are dissolved by routine processing, fixation in absolute ethanol or freezing is necessary for their demonstration.

Treatment

Treatment for the extreme arthritic pain of gout is directed toward complete rest and analgesic agents. Colchicine, 0.5 mg, can be given hourly and is the drug of choice. If decreased renal excretion is the problem, uricosuric agents such as probenecid (Benemid) are useful. If the overproduction of uric acid is the basis, a xanthine oxidase inhibitor such as allopurinol is helpful. There is no treatment necessary for the small tophi on the helical areas.

Ochronosis

Ochronosis is the other disorder caused by an error of metabolism that has external ear manifestation (Lawrence et al, 1988). It is really a form of alkaptonuria. Alkaptonuria, an inherited autosomal recessive trait, is caused by the lack of renal and hepatic homogentisic acid oxidase, the enzyme necessary for the metabolism of homogentisic acid to acido-acetic and fumaric acids. It is characterized by the excretion of homogentisic acid in urine (producing a dark-staining urine) and the deposition of a grossly brown-black pigment in the connective tissue, which is ochre in color microscopically - hence the term *ochronosis*.

Patients present with ochronosis in the third decade of life. Cartilage is a favored site. The early sign is the pigmentation of the sclera (Osler's sign) and the cartilage of the ears. Additionally, blue or mottled-brown macules can appear (Plate 20, E). The bluish macules have a predilection for the fingers, the external ears, the nose, and the buccal mucosa. The cerumen is often black. This brown pigmentation can be deposited in the larynx, tonsils, and esophagus.

Ochronotic arthropathy involves the spinal joints. At first it resembles osteoarthritis and then it is followed by arthropathy involving the knees, shoulders, and hips.

Treatment

There is no effective treatment; however, recent studies indicated that the inhibition of lysyl hydroxylase activity by homogentisic acid can be counteracted by ascorbic acid and that treatment with ascorbic acid may be helpful. Other treatments include a low-protein but adequate diet in order to decrease the accumulation of homogentisic acid.

Chondrodermatitis Helicis

This is a disease caused by degeneration of collagen and it is important to the head and neck surgeon because these lesions are quite commonly on the superior rim of the helix and can be clinically misdiagnosed as either squamous or basal cell carcinoma of the helix (Arnold et al, 1990). They are small, nodular, tender, chronic inflammatory lesions occurring on the helix, anthelix, concha, and tragus (Plate 20, F). There are usually multiple lesions, and as many as 10 nodules may arrange themselves along the upper edge of the auricle. They are ovaloid, slightly reddish, extremely tender, and 2 to 4-mm in diameter. They are densely attached to the underlying cartilage. There is no tendency for malignant change.

Often, there is a history of trauma or acute exposure to cold. Histologically, degenerative changes of the collagen are the chief features. Acanthosis and hyperkeratosis may also occur. Treatment is removal of the lesion for correct histopathologic diagnosis. When the clinical diagnosis is confirmed, mostly intralesional triamcinolone diacetate or triamcinolone acetonide injections (20-40 mg/mL) are useful.