Clinical features of GCA/PMR

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ABSTRACT

Giant cell arteritis (GCA) is a common vasculitis of unknown cause that affects persons in middle age and older. Its incidence rises with increasing age. The inflammatory lesions involve larger arteries that contain an abundance of elastic tissue. Although cranial symptoms such as headache, tender scalp, jaw claudication and visual symptoms are common, the disease presents in many different fashions, often with symptoms not directly related to the arteries. These latter presentations include fever, severe malaise, polymyalgia rheumatica, high erythrocyte sedimentation rate and anemia, thrombocytosis, sore throat, and hepatic dysfunction. GCA appears to have a self-limited course, but is also characterized by relapses and recurrences. Visual loss due to occlusion of the optic arteries is the most important early manifestation and aortic aneurysm is the most important late complication. Patients respond promptly to varying doses of glucocorticoids but drug side effects are common.

Introduction

Giant cell arteritis (GCA) is a chronic vasculitis of large and medium size vessels. It occurs in persons over 50 years of age and mainly in those over age 60 years (1). Although it may be widespread, symptomatic vessel inflammation usually involves the cranial branches of the arteries originating from the aortic arch (2, 3). Its etiology is unknown, but recent studies have suggested a genetic predisposition with an event after the age of 50 years that triggers the disease (1).

Clinical manifestations

Onset and systemic manifestations. The onset tends to be gradual, but can be abrupt. Systemic symptoms are often present and include fever in about half of patients, fatigue, and weight loss. Although the fever is usually low grade, it can reach 39° to 40° in about 15% of cases.

Head pain. A new headache occurs in two-thirds of patients. The pain tends to be located over the temporal areas, but may also occur elsewhere. The headache may be mild or severe, persistent or intermittent.

Jaw claudication. Nearly one-half of patients suffer from jaw claudication. In some cases, a trismis-like symptom occurs rather than fatigue of the chewing muscles. Similar findings that can be seen include tongue or swallowing claudication, and throat pain.

Visual loss. Permanent partial or complete loss of vision in one or both eyes has been observed in 15-20% of patients in most series. Impaired vision is often an early manifestation of the disease. Affected patients typically note an abrupt partial field defect in one eye, which may progress to total blindness. The visual loss is painless. If untreated, the second eye is likely to become affected within one to two weeks. It is rare, however, for patients to become completely blind in both eyes. Transient visual loss or diplopia is less frequent, but may precede permanent visual loss. In patients with visual loss, fundoscopic examination shows changes of ischemic optic neuropathy (4).

Large vessel giant cell arteritis. In approximately 15% of cases, the branches of the aortic arch, particularly the subclavian and axillary arteries, become narrowed to produce claudication (3). Such patients may have few of the usual symptoms of GCA so the diagnosis may be initially overlooked.

Polymyalgia rheumatica (PMR). This syndrome, characterized by proximal aching and morning stiffness, is intimately associated with GCA. The musculoskeletal pain in PMR is caused mainly by proximal joint and periarticular synovitis (5). Patients may have PMR without overt vasculitis or both together at the same time or different times. Much progress has been made in recent years in the investigation of these two processes. Most evidence favors the concept that they are two phases of the same dis-

ease. The etiology and pathogenesis of GCA and PMR are incompletely understood. However, age, genetic factors, ethnic background, and infection may have causative roles (6-11). Patients with PMR alone are treated successfully with lower doses of prednisone than those with PMR plus GCA.

Musculoskeletal symptoms other than PMR. In addition to PMR, some patients may have peripheral synovitis, distal extremity swelling with pitting edema, swelling without pitting edema, tenosynovitis, and carpal tunnel syndrome (12). These symptoms also respond well to glucocorticoids.

Thoracic aortic aneurysms. The development of thoracic aortic aneurysms is a late and potentially serious complication of GCA. It occurs in about 15% of patients as a late event, usually several years after the diagnosis and often after the patient's other symptoms have subsided (13,14). The aneurysm may rupture and cause the patient's death. The development of an aneurysm may or may not be accompanied by other evidence of active vasculitis with an elevated ESR or CRP. Patients with GCA need to be followed periodically for the development of thoracic aortic aneurysm. Annual posterior-anterior and lateral radiographs of the chest are usually adequate for screening unless an aneurysm is present, in which case closer follow-up is needed. Surgical repair may be required in some instances.

Course. The course of GCA is variable, but in the majority of patients tends to gradually go into remission over 1 to 2 years. However, late recurrences occasionally develop.

Physical examination

The patient with GCA often appears chronically ill on physical examination. However, findings related to involvement of characteristic arteries may be present.

Scalp arteries. The frontal or parietal branches of the superficial temporal arteries may be thickened or tender or occasionally erythematous. The occipital arteries, and less often, the post-auricular, or facial arteries may be enlarged or tender. A small, non-tender, hard artery may be related to arteriosclerosis. In uncommon circumstances the temporal artery pulse may be diminished because of arteriosclerotic thrombosis of the external carotid artery.

Bruits. These may be heard on auscultation of the carotid or supraclavicular areas, over the brachial or axillary arteries, or (rarely) over the orbits.

Joints. In patients with PMR, active range of motion of the shoulders, neck, and hips is limited due to pain. In some cases careful passive motion may be full. Generally in PMR joint tenderness is not a prominent finding. In approximately 10-20% of cases a mild to moderate synovitis is present, especially in the knees and wrists. When diffuse swelling is present the entire hand and fingers or foot are swollen and often tender. In some instances, the swelling may follow the path of a tendon sheath such as the posterior tibial tendon.

Laboratory findings

The characteristic laboratory change in most patients with GCA is a very high ESR which may reach 100 mm/hr or more according to the Westergren method. Other acute phase changes may be present, such as increases in C-reactive protein. However, occasional patients have been reported with symptoms and findings typical of PMR or GCA who have a normal ESR.

Anemia. A normochromic anemia is often present. It may become rather marked in chronic untreated cases.

Leukocyte count. The white blood count is usually normal.

Platelet count. Thrombocytosis is usually present and may become very high. We have seen cases with counts of one million.

Immunologic tests. Complement and immunoglobulin levels are generally normal or slightly elevated. Other tests are occasionally abnormal, such as elevated antinuclear antibody titers, but are not diagnostically helpful.

Hepatic enzymes. Increased blood enzyme levels such as AST and alkaline phosphatase, occur in 25% or so of patients. These test revert back to normal with glucocorticoid therapy. Liver biopsy has shown nonspecific changes.

Increased plasma factor VIII/von Willebrand factor levels are found in most patients and are likely related to the vascular inflammation. They revert slowly back toward normal over months after treatment is started. At this time they do not appear to be helpful in the diagnosis or in the management of glucocorticoid therapy.

Elevated interleukin-6 levels in the serum or plasma appear to be closely related to the clinical disease activity. Early studies suggest that this may be the most sensitive test for following the course of disease activity. However, the test is not yet routinely available.

Diagnosis

The diagnosis of GCA should be considered in a patient over the age of 50 years who complains of a new type of headache, abrupt loss of vision, symptoms of PMR, unexplained fever or anemia, and elevated acute phase tests (15). Manifestations of GCA vary considerably from one patient to another and may be transient. As a result, patients in whom the disease is suspected should be questioned carefully about both current and recent symptoms. The arteries of the head, neck, upper torso, and arms should be palpated for tenderness, enlargement, or thrombosis: these arteries should also be auscultated for the presence of bruits. Temporal artery biopsy is suggested in all cases of suspected GCA. The necessity for biopsy in patients with only symptoms of PMR is less clear and depends on the individual case. The chances of a positive biopsy are low when PMR is present but there are no vascular manifestations (16). When an adequate temporal artery biopsy is negative for arteritis, the likelihood of active giant cell arteritis has been only approximately 10%.

GCA can be distinguished from isolated angiitis of the central nervous system, Takayasu's arteritis, and other similar arteritides by the age of the patient and the distribution of the lesions. However, the histopathologic findings and radiographic changes may be indistinguishable from GCA in selected patients.

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