Wegener Granulomatosis

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Wegener granulomatosis (WG) is an idiopathic, nonneoplastic, aseptic, necrotizing disease characterized by vasculitis and destructive properties. In general, affected patients exhibit disease in the sinonasal tract, lungs, and kidney, in some cases metachronously. Patients may present with systemic or localized disease; patients with systemic disease are usually quite sick. Disease progression may be seen when localized disease becomes systemic, but many patients will remain with limited disease.

The ELK classification system is used to define the disease: E indicates ear, nose, and throat involvement; L indicates lung involvement; and K indicates kidney involvement. Localized upper aerodigestive tract WG (WG-E) tends to affect men more often than women, although laryngeal disease is seen predominantly in women. The sinonasal tract is affected more often than the nasopharynx, larynx, or oral cavity. Symptoms are usually nonspecific and can include sinusitis, rhinorrhea, obstruction, pain, epistaxis, and headaches, depending on which anatomic site is affected.

One of the critical elements of the diagnostic evaluation is laboratory testing for antineutrophil cytoplasmic antibody (ANCA) and proteinase 3 (PR3). There is usually an elevation of ANCA and PR3, with a specificity between 85 and 98%. There are two types of ANCA-cytoplasmic (c-ANCA) and perinuclear (p-ANCA). WG is much more frequently associated with c-ANCA (figure 1). PR3-ANCA is highly specific for WG. Laboratory results vary according to the extent of disease and disease activity, and they normalize 6 to 8 weeks after remission.

Figure 1. A: A vessel wall is destroyed by an inflammatory infiltrate. A zone of fibrinoid necrosis is seen. B: A couple of multinucleated giant cells are seen; they are usually isolated. C and D: ANCA can be either cytoplasmic (C) or perinuclear (D). WG is most often associated with c-ANCA.
It is important to note that a negative test does not exclude WG, and positive results can be seen in other vasculitides, including microscopic polyangiitis and allergic granulomatous angiitis. Various treatment regimens can result in a complete remission, although relapses do occur. Renal or pulmonary insufficiency and/or complications from therapy can result in morbidity and death.

WG presents clinically as ulcerative and crusted lesions with tissue destruction. The histologic triad of vasculitis, granulomatous inflammation, and biocollagenolytic necrosis is characteristic, but all three findings are uncommon in a single biopsy. The vasculitis involves destruction of small to medium-sized arteries that contain an inflammatory infiltrate within the vessel wall and subendothelial space, leading to destruction of the elastic lamina (figure 1).

A smudgy, dirty, basophilic, ischemic or geographic type of biocollagenolytic necrosis, in which the stromal collagen is destroyed, is quite characteristic (figure 2). Surface ulceration is nonspecific. Granulomatous inflammation is often limited and difficult to find. There are often isolated multinucleated giant cells (figure 1) and occasional epithelioid histiocytes, but well-formed granulomas are not seen. The background inflammation is composed of lymphocytes, histiocytes, neutrophils, eosinophils, and plasma cells.

**Figure 2.** A: Biocollagenolytic necrosis has a dark-blue granular appearance in a geographic arrangement. Note a vessel with sclerosis in the middle of the field. B: The blue granular collagen destruction yields a very characteristic appearance for Wegener granulomatosis.

Histologically, the diagnosis of WG is often one of exclusion. The pathologist must ensure that infections (fungal, mycobacterial, bacterial, viral, and parasitic), cocaine abuse, lymphoma, and Churg-Strauss syndrome, among others, have been ruled out by special studies or clinical evaluation.

**Suggested reading**


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