

**INTRODUCTION**

The systemic vasculitides (SV) are a heterogeneous group of rare affections, characterized by a primary process of inflammation and damage of the vessel wall, resulting in blood flow impairment and, ultimately, in ischemia of the distal tissues. Pulmonary vasculitis usually is a component of a systemic small vessel vasculitis. Pulmonary vasculitides can be classified into three major groups: a) those in which lung is the major organ involved, b) those in which lung may be involved as part of a systemic vasculitis, c) diseases in which pulmonary vasculitis may be part of the spectrum of pathology<sup>1</sup>. Three major forms of small vessel vasculitis that often affect the lungs are Wegener's granulomatosis (WG), microscopic polyangiitis (MPA) and Churg-Strauss syndrome (CSS). These forms of vasculitis are strongly associated with antineutrophil cytoplasmic auto antibodies (ANCA) directed against enzymes contained in the primary granules of neutrophils and peroxidase-positive lysosomes of monocytes). Large vessel vasculitides, such as giant cell arteritis and Takayasu's arteritis, occasionally affect the lungs. Medium-sized vessel vasculitis, such as polyarteritis nodosa and Kawasaki disease rarely affect the lungs. The immunologic mechanisms that cause vasculitis include cell-mediated inflammation, immune complex-mediated inflammation and inflammation induced by ANCA. ANCA associated vasculitis is more common cause for pulmonary vasculitis.

**LARGE VESSEL VASCULITIDES**

The large vessel vasculitides include giant cell arteritis (GCA) and Takayasu arteritis (TA).

**Giant Cell Arteritis**

GCA is a granulomatous vasculitis of the aorta and its major branches, with a predilection for the extracranial branches of the carotid artery. GCA mainly affects people older than 50 years and is often associated with polymyalgia rheumatica (PMR). GCA can affect the main pulmonary arteries, as well as large and medium sized pulmonary elastic arteries. The vasculitic process is characterized by medial and adventitial chronic inflammation with giant cells with elastic laminae destruction and focal fibrinoid necrosis in the media. Involvement of the respiratory system has been reported with a frequency ranging from 9-31 percent<sup>2</sup>. The most common respiratory symptom is cough often associated with fever. It responds with corticosteroid therapy. Less common respiratory symptoms are sore throat, hoarseness and chest pain. Pleural effusion is a rare manifestation. Interstitial lung disease (ILD) has been reported in GCA patients.

**Takayasu's Arteritis**

Takayasu's arteritis is an uncommon arteritis that affects the aorta and its proximal branches and, less commonly, the pulmonary arteries. Approximately 90% of cases occur in women and the majority of cases occur in South-east Asia<sup>3</sup>. Pulmonary disease in TA usually presents as cough, dyspnea, and/or hemoptysis. The reported incidence of the pulmonary artery involvement by angiography ranges widely, from 14-100 percent, with an average of 56% in nine series totaling more than 250 cases<sup>4</sup>. The histopathological findings of the pulmonary artery are very similar to those of the aorta and its branches. The adventitia, media, and intima are

infiltrated by mononuclear and giant cells, forming necrotizing or non-necrotizing granulomas. Diffuse or nodular fibrosis may predominate and result in stenosis or obliteration of the vascular lumen.

### **MEDIUM-SIZED VESSEL VASCULITIDES**

Medium-sized vessel vasculitides refer to “classical” polyarteritis nodosa (PAN) and Kawasaki disease (KD).

#### **Polyarteritis Nodosa**

The respiratory system involvement in PAN is very rare.

#### **Kawasaki Disease**

KD is a vasculitis usually occurring in children, involving large, medium sized and small arteries, and associated with mucocutaneous lymph node syndrome. Coronary arteries are often involved. The prevalence of the respiratory system involvement in KD likely depends on the ethnic origin of patients. In a series of 129 Japanese patients, abnormal chest X-ray findings were found in 14.7% mostly appeared within 10 days of the disease onset<sup>5</sup>. In a multicenter, retrospective study of 250 Italian patients with KD, pulmonary involvement has not been described<sup>6</sup>.

### **SMALL VESSEL VASCULITIDES**

Small vessel vasculitides include WG, CSS, MPA, Henoch-Schönlein purpura (HSP), essential cryoglobulinemic vasculitis (CV).

#### **Wegener’s Granulomatosis**

WG is a systemic granulomatous inflammatory process with variable clinical expression. It classically involves the upper and lower respiratory tracts and kidneys. In some patients it can be manifested primarily or exclusively in the respiratory tract, a form known as limited WG. The characteristic pathological findings of WG include necrotizing granulomata of the respiratory tract, necrotizing vasculitis affecting medium to small pulmonary arteries and veins, and a focal glomerulonephritis. Clinical manifestations related to lower respiratory tract disease include cough, dyspnea, pleuritic pain and hemoptysis. Tracheobronchial involvement is a significant cause of morbidity<sup>7</sup>. Diffuse alveolar hemorrhage (DAH) due to alveolar capillaritis is increasingly recognized as a prominent pulmonary manifestation of WG, reported in 5-45 percent of cases<sup>8</sup>. Patients with DAH present with cough, dyspnea,

hemoptysis and anemia. Chest radiograph showing new unexplained bilateral alveolar infiltrates in the face of falling hemoglobin levels must alert physicians about the presence of symptom-free DAH, since the mortality is very high.

On pulmonary function tests (PFTs) airflow obstruction is the most frequent functional abnormality in WG, often associated with a reduced diffusing capacity for carbon monoxide (DLCO) and reduction of lung volumes. The most common radiological manifestation of pulmonary WG consists of multiple nodules which may range from 0.3-10 cm in diameter and are usually bilateral. The nodules may be smooth or spiculated; ~50% eventually demonstrate cavitation which may have thick walls and shaggy, irregular inner borders. CT is superior to chest radiographs in demonstrating the presence and number of nodules and presence of cavitation. Another common radiological finding is the presence of areas of air space consolidation or ground-glass opacities. The main pathological lung findings include parenchymal necrosis, vasculitis, and granulomatous inflammation, characterized by an infiltrate composed of a mixture of neutrophils, lymphocytes, plasma cells, histiocytes, and eosinophils. Immunohistology and electron microscopy rarely demonstrate immune deposits (“pauciimmune” capillaritis).

#### **Churg-Strauss Syndrome**

Churg-Strauss syndrome is a rare condition seen almost exclusively in patients with asthma and characterized by the presence of systemic vasculitis, extravascular granulomatous inflammation and eosinophilia. Asthma usually precedes vasculitis for an average of 3 to 8 years. Pulmonary transient and patchy alveolar infiltrates, without a lobar or segmental distribution, represent the most frequent radiological findings.

#### **Microscopic Polyangiitis**

Microscopic polyangiitis is a systemic disease characterized by necrotizing vasculitis with few or no immune deposits that involves predominantly small vessels. The most common clinical manifestations are glomerulonephritis, dyspnea, cough, hemoptysis, myalgia and arthralgia. The radiological manifestations consist of patchy or confluent bilateral areas of consolidation due to diffuse pulmonary hemorrhage. The airspace consolidation tends to involve mainly the lower lung zones.

## Treatment

To manage pulmonary vasculitis effectively, the clinician must establish the diagnosis without delay, recognize variability in clinical course, closely monitor disease activity and anticipate disease and treatment related morbidity. Therapeutic decision making should be based on a critical assessment of disease activity. Meticulous attention should be paid to complications of therapy. Sometimes, certain complications (infections, drug reactions, etc.) may be confused with active disease. The significant toxicity of currently available therapeutic agents led to the development of new drugs and innovative approaches for the treatment of systemic vasculitides.

Glucocorticoids are most commonly used in combination with cytotoxic agents in WG. Prednisolone is given at 1 mg/kg per day or higher until all manifestations such as resolution of pulmonary infiltrates have abated. Another approach is to initiate the therapy by intravenous pulse methyl prednisolone (1 gm × 3 days). Oral cyclophosphamide is combined at doses of 2 mg/kg per day. Biologic agents such as rituximab are given for resistant cases<sup>9</sup>.

## REFERENCES

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