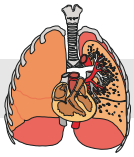

The acquisition of new information, the integration of newer diagnostic methods, and the use of new therapy have occurred with breathtaking rapidity during the past decade in pulmonology, as it has in medicine in general. In order to keep all of us informed, the periodic appearance of review articles written by authorities in the particular field has proven to be effective. The current article by Drs. Hatipoglu and Rubinstein is the first in a series dealing with pulmonary diseases that will appear in *IMAJ*. I believe this covers the specific area of pulmonary vasculitides in a comprehensive manner and sets a high standard for the subsequent articles to meet. A personal gift for me is that this first article is co-authored by a former student of mine, Dr. Rubinstein.

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Pulmonary Vasculitis: A Clinical Overview

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Vasculitides comprise a heterogeneous group of disorders characterized by necrotizing inflammation of blood vessels. Such inflammation may occur as part of a primary disease process or secondary to a variety of disorders. The lungs are frequently involved in both primary and secondary vasculitides. The aim of this review is to provide an overview on lung involvement in primary vasculitides based on articles written in English.

While the clinical presentation may be quite unique for individual entities of primary vasculitis, overlapping features are frequently present. It is for this reason that the classification of primary vasculitides presents a challenge. The American College of Rheumatology published criteria for the classification of vasculitis in 1990 [1]. A committee of experts classified seven categories of primary vasculitis based on over 1,000 cases submitted by rheumatologists from 48 centers in the U.S., Canada and Mexico. The objective was to provide diagnostic categories for individual patients, and not the institution of a nomenclature system. An International Consensus Conference that convened in Chapel Hill, North Carolina, addressed this issue [2]. Based on the size of blood vessels involved, the conference adopted definitions for 10 different clinical entities. In our approach to primary vasculitis involving the lung, we adopt the nomenclature proposed by the Chapel Hill Conference with the addition of two entities: isolated pauci-immune pulmonary capillaritis [3] and Behçet's disease [Table 1].

Pathogenesis

There is general consensus about an immunopathogenic mechanism underlying vasculitis. Immune complexes formed in the bloodstream in the presence of antigen excess localize in the blood vessel wall. Increased vascular permeability enables immune complexes to be trapped along the basement membrane of the blood vessel wall, causing activation of complement and accumulation of complement-derived chemotactic factors. The polymorphonuclear neutrophils attracted to the area of immune complex deposition release lysosomal enzymes that damage the blood vessel wall. Neutrophil infiltration leads to fibrinoid necrosis,

Table 1. Vasculitides with pulmonary involvement

Small vessel
Wegener's granulomatosis
Churg-Strauss syndrome
Microscopic polyangiitis
Isolated pauci-immune pulmonary capillaritis
Behcet's disease
Medium sized vessel
Behcet's disease
Large vessel
Giant cell (temporal) arteritis
Takayasu arteritis
Behcet's disease

culminating in thrombosis and occlusion of the blood vessel. In 1982, a group of Australian investigators reported the finding of an autoantibody that stained the cytoplasm of alcohol-fixed neutrophils in eight patients with nephritis – namely, antineutrophil cytoplasmic antibodies [4]. Interestingly, half of these patients had hemoptysis and/or dyspnea. Three years later, an association was recognized for the first time between ANCA and Wegener's granulomatosis [5].

Two ANCA-staining patterns are seen in ethanol-fixed neutrophils using indirect immunofluorescence: cytoplasmic ANCA and perinuclear ANCA. The target antigen of c-ANCA is a 29 kD serine protease (proteinase 3), an enzyme involved in host defense, residing within azurophil granules of the neutrophils. p-ANCA targets primarily myeloperoxidase, an enzyme with a similar function. Other targets such as elastase, cathepsin G, azurocidin, lactoferrin, lysozyme, enolase, and bactericidal/permeability-increasing protein have been identified as well. Very rarely, myeloperoxidase may be the target for c-ANCA and proteinase 3 the target for p-ANCA. c-ANCA is associated with Wegener's granulomatosis, while p-ANCA is associated with a number of vascular diseases including microscopic polyangiitis, isolated pauci-immune pulmonary capillaritis, and Churg-Strauss syndrome.

Small Blood Vessel Vasculitis

Wegener's Granulomatosis

The ACR defined Wegener's granulomatosis as "a disease of unknown etiology that is characterized by the clinicopathologic complex of necrotizing granulomatous vasculitis of the upper and lower respiratory tract, glomerulonephritis, and variable degrees of small vessel vasculitis." The original description of the disease is ascribed to Friedrich Wegener and Heinz Klinger. Although it is one of the most common pulmonary vasculitides, WG has an estimated prevalence of 3 per 100,000 persons in the United States [6]. No gender predilection has been observed. There is, however, an overwhelming predilection for white Caucasians. The mean age of patients in the largest series was 41 years (range 9–78) [7].

- ***Clinical presentation and diagnosis***

WG characteristically involves the upper and lower respiratory tracts on presentation. Recurrent epistaxis, nasal crusting, chronic rhinosinusitis and serous otitis are common. In most cases, the symptoms are ascribed to infection and/or allergy in the absence of systemic disease, a major pitfall leading to delayed diagnosis. In a stuttering fashion over a period of weeks to years, other organ manifestations ensue. The disease has a characteristic chronic remitting-relapsing course. The kidney is the third most involved organ. Focal segmental necrotizing glomerulonephritis is the most common manifestation. Ocular disease in the form of conjunctivitis, scleritis, uveitis, retinal vasculitis, dacryocystitis, and orbital pseudotumor may be the initial manifestation in 15% of cases, eventually appearing in over half of the patients. Heart, gastrointestinal tract, central nervous system, genital tract, skin, joint, and breasts may be involved.

The ACR developed the following criteria for diagnosing WG: nasal or oral inflammation; abnormal chest X-ray with nodules, infiltrates or cavities; active urinary sediment; and demonstration of granulomatous inflammation in affected organs [8]. A diagnosis of WG is made if at least two of the four criteria are noted, with sensitivity of 88.2% and specificity of 92%

Lung involvement is present in 85% of patients with WG sometime during the course of their illness, making lung involvement the second most common after ear, nose, and throat [7]. Pulmonary infiltrates, nodules, or both are initially present in approximately half of the patients. While these lesions are asymptomatic in the majority, cough, hemoptysis and pleuritic chest pain may be present. The most common site of tracheobronchial involvement is the subglottic region. In the National Institutes of Health series of 189 patients, 43 (23%) had evidence of subglottic stenosis [9] associated with dyspnea (79%), voice changes/hoarseness (61%), and cough (23%). Inflammation in the tracheobronchial tree can also result in intraluminal inflammatory pseudotumors and tracheomalacia. Diffuse alveolar hemorrhage is a potentially fatal complication of WG seen in 40% of patients.

- ***Diagnostic tests***

Bronchoscopy demonstrates abnormalities in more than half the patients [10]. Ulcerating tracheobronchitis, tracheobronchial stenosis, and inflammatory pseudotumors may be seen. Transbronchial biopsy supports the diagnosis. Bronchoscopy could also detect alveolar hemorrhage by demonstrating sequential reddening of the aspirated bronchoalveolar lavage fluid.

Bilateral, multiple, rounded opacities ranging from a few millimeters to 10 cm in diameter are the most common radiographic presentation. These nodules tend to cavitate and form thick walls. Small pleural effusions occur in 20–50% of patients. Computerized tomography scan of the chest shows multiple nodules or masses frequently with cavitation, air bronchogram and wedge-shaped consolidation resting on the pleura [11]. Hilar adenopathy is uncommon.

Serologic testing for ANCA is an important part of diagnosis and possibly follow-up of disease activity. In a meta-analysis by Rao et al. [12], the pooled sensitivity and specificity of c-ANCA in active WG was 91% and 98%, respectively. For inactive disease, however, pooled sensitivity was 63% and specificity 99.5%. In another study [13], the overall sensitivity of c-ANCA in patients evaluated for possible vasculitis was only 28%. These studies suggest that positive c-ANCA serology has diagnostic value in patients with suspected active vasculitis who have an intermediate likelihood of WG, but biopsy confirmation is necessary. The test should not be used to screen for the disease.

- ***Treatment and prognosis***

Before the introduction of combination therapy with glucocorticoids and immunosuppressive drugs, average life expectancy was 5 months. In 1992, Hoffman et al. [7] published an analysis of 158

ANCA = antineutrophil cytoplasmic antibodies
c-ANCA = cytoplasmic ANCA
p-ANCA = perinuclear ANCA
ACR = American College of Rheumatology
WG = Wegener's granulomatosis

patients with WG who had been followed for 6 months to 24 years at the NIH. Treatment with cyclophosphamide and prednisone resulted in a mortality of 13% over a median follow-up of 8 years. The regimen consisted of daily oral therapy with cyclophosphamide (2 mg/kg) and prednisone (1 mg/kg). Prednisone treatment was initiated at 2–15 mg/kg and tapered during 4 weeks, followed by 1–3 months of 60 mg on alternate days. The dose was then tapered off and the patient was maintained on cyclophosphamide alone for at least one year after the achieved clinical remission. Cyclophosphamide was then tapered slowly. Nearly half the patients experienced relapse following complete remission.

Despite improved survival, significant treatment-related complications and toxicity were observed. Forty-six percent of patients experienced serious infection, with pneumonias of diverse etiologies being the most frequent. Infections were less frequent when prednisone was administered on alternate days. Non-infectious complications of therapy included cyclophosphamide cystitis (43%), bladder cancer (2.8%), myelodysplasia (2%), glucocorticoid-related cataracts (21%), fractures (11%), and aseptic necrosis (3%). Close to two-thirds of childbearing-age women were infertile.

In an effort to reduce toxicity, Hoffman and colleagues [14] substituted weekly methotrexate for other cytotoxic agents in 19 patients with WG. In another 10 patients, methotrexate was used when the disease failed to remit in response to prednisone and/or cotrimoxazole. Close to 75% of patients achieved remission.

The use of intravenous pulse cyclophosphamide therapy achieved a 60% reduction in total dose administered, and decreased toxicity. In a prospective multicenter trial, Guillevin et al. [15] randomized treatment for newly diagnosed WG using prednisone plus intravenous pulse cyclophosphamide versus prednisone and oral cyclophosphamide. Both regimens achieved initial remission with fewer side effects noted in the pulse group. However, over a 5 year period, a high relapse rate was seen in the IV pulse group. Haubitz and co-workers [16] noted no difference in patient survival, remission rate, time of remission and relapse rate between 22 patients receiving IV pulse therapy and 25 receiving oral therapy. Over a period of one year a lower rate of leukopenia and severe infections were noted in the pulse group. An important feature of this study was the use of immunosuppressive therapy when ANCA titers were $\geqslant$ 1:64.

Recently, Langford et al. [17] studied 31 patients with WG in whom cyclophosphamide and prednisone were used for remission-induction followed by methotrexate for remission maintenance. Disease relapse occurred in only five patients after a median of 13 months following remission.

Stegeman and associates [18] conducted a prospective, randomized trial of 81 patients who received cotrimoxazole or placebo twice daily for 24 months. Fewer relapses were reported in the cotrimoxazole group. Reduction of relapses involving the upper airways was noted but relapses of renal and pulmonary disease were not affected.

The use of rising c-ANCA titers to predict imminent relapse remains controversial since a rising antibody level is not always followed by a relapse. In one study [20], a rise in c-ANCA titer was observed preceding relapse in only 24% of the patients [19]. In a 2 year study of 100 patients, with ANCA measured at 2 month intervals, 92% of relapses were preceded by a rise in antibody titer as measured by indirect immunofluorescence or an antigen-specific enzyme-linked immunosorbent assay. The ELISA appeared more sensitive than indirect immunofluorescence. The rise in antibodies occurred in 13 of 52 relapse-free patients by immunofluorescence and 11 of 52 patients by ELISA. Moreover, the time between the rise in antibody level and relapse exceeded 6 months in more than 60% of patients. These data suggest that an increase in serial ANCA titers should heighten clinical suspicion of a relapse, but early treatment based on this laboratory finding alone is unwarranted.

Churg-Strauss Syndrome

In 1951, Churg and Strauss described 13 patients with severe asthma, rhinitis and eosinophilia, who were found to have necrotizing vasculitis and extravascular granulomas in resected tissues. Distinguishing it from polyarteritis nodosa by the presence of asthma and allergies, they named this syndrome "allergic granulomatosis and angiitis." More than 30 years after its original description, Lanham et al. [21] published a series of 154 patients with Churg-Strauss syndrome and noted that the classical histopathologic findings were not present in all cases and that clinical criteria better define the syndrome. Their clinical definition included asthma, peripheral eosinophilia in excess of 1.5 x 10^9/L, and systemic vasculitis involving two or more extrapulmonary organs. In 1990, the ACR developed six clinical criteria to describe Churg-Strauss syndrome: asthma, eosinophilia over 10%, history of allergy, mono- or polyneuropathy, migratory/transient pulmonary infiltrates, and paranasal sinus abnormality. Extravascular eosinophils typically were seen on biopsy. When necrotizing vasculitis was noted on histologic examination, the presence of four of six criteria yielded 85% sensitivity and 99.7% specificity. The estimated annual incidence of CSS is 2.4/million.

- ***Clinical presentation and diagnosis***

As described by Lanham et al. [21], patients express three phases of the syndrome that usually span several years. Characteristic presentation is late adult-onset asthma and allergic rhinosinusitis. In the second phase, eosinophilic infiltration of visceral organs occurs. Gastroenteritis and fleeting pulmonary infiltrates are common. The third phase is vasculitis, presenting as mononeuritis multiplex, palpable purpura, cardiomyopathy, pericarditis and focal segmental glomerulonephritis. In 20% of patients, asthma, eosinophilia and vasculitis present simultaneously. Cardiac involvement accounts for half of the deaths in patients with CSS.

Wechsler et al. [22] published a report of eight patients with asthma who developed CSS after being treated with the cysteinyl leukotriene antagonist zafirlukast. Emergence of the syndrome coincided with tapering of prednisone in all patients. Subsequently, the syndrome was associated with montelukast and pranlukast. Similar cases of unmasked CSS were reported during treatment with inhaled corticosteroids or while tapering the dose of prednisone

ELISA = enzyme-linked immunosorbent assay
CSS = Churg-Strauss syndrome

[23]. Since montelukast had a different molecular structure than zafirlukast and unmasking of CSS occurred while on inhaled corticosteroids as well, Wechsler and colleagues [22] postulated that leukotriene antagonists simply unmasked the disease during corticosteroid tapering. This fails to explain cases where CSS occurred in association with leukotriene receptor antagonists but without corticosteroid therapy [24].

- ***Diagnostic tests***

Elevated sedimentation rate, blood eosinophilia, anemia and hypergammaglobulinemia are common laboratory findings. ANCA with perinuclear staining pattern is seen in two-thirds of patients.

In the largest series of CSS, Lanham et al. [21] reported non-segmental air space disease on the chest X-ray of 72% of the patients. Transient and migratory infiltrates were observed in 40%. Pleural effusions (eosinophilic) were present in almost a third of the patients. High resolution CT findings include subpleural consolidation with lobular distribution, centrilobular nodules, increased vessel caliber, and bronchial wall thickening [25]. The presence of thickened bronchial walls on high resolution CT characterizes CSS as compared with other pulmonary infiltrates with eosinophilia [25].

- ***Treatment and prognosis***

Treatment with corticosteroids remarkably improves prognosis in CSS. Fifty percent of untreated patients in the vasculitic phase die within 3 months. Mean survival is more than 9 years in patients treated with steroids.

Unlike WG, in CSS, cyclophosphamide has not been shown to affect mortality. Its use is associated with fewer relapses but this should be weighed against a higher risk of infections. Use of cyclophosphamide should be reserved for severe cases and for patients with multiple relapses.

Since 1980, The French Vasculitis Study Group has undertaken prospective randomized trials to investigate therapies adjunctive to corticosteroids. A mixture of patients with polyarteritis nodosa and CSS were enrolled in these studies. The addition of oral cyclophosphamide to a standard regimen of corticosteroids and plasma exchange had no impact on the 10 year survival rate [26]. Although cyclophosphamide reduced the number of relapses, there were more lethal infections in the cyclophosphamide group. In a study of 62 patients with poor prognostic signs (renal, gastrointestinal, cardiac, central nervous system involvement, age $\geqslant$ 50 years, weight loss >10% of body weight), the addition of plasma exchange to corticosteroids and pulse cyclophosphamide did not affect mortality [27].

Microscopic Polyangiitis

Polyarteritis nodosa is characterized by inflammation and necrosis of medium-sized arterioles with subsequent microaneurysm formation and organ infarction. In 1948, Davson et al. [28] described patients with PAN, characterized by small vessel vasculitis and rapidly progressive glomerulonephritis. These patients did not have hypertension or microaneurysms characteristic of classical PAN. Furthermore, rapidly progressive glomerulonephritis was not a feature of classical PAN. Savage et al. [29] described a group of 34 patients with non-granulomatous small vessel vasculitis affecting the skin and musculoskeletal system, as well as focal segmental necrotizing glomerulonephritis, and coined the term microscopic polyarteritis. In 1994, an international conference defined the syndrome as a distinct entity and renamed it microscopic polyangiitis – MPA, recognizing the involvement of venules and capillaries as well as arterioles.

The mean age of presentation in MPA is 50 years. Necrotizing glomerulonephritis is present in 80–100% of cases. Almost 30% of patients develop alveolar hemorrhage due to pulmonary capillaritis, another feature absent in classical PAN. Alveolar hemorrhage is associated with 25% of MPA-related deaths. Dyspnea, acute decrease in hemoglobin, and alveolar infiltrates in the setting of vasculitis should raise suspicion of alveolar hemorrhage even in the absence of hemoptysis. Recurrent alveolar hemorrhage has been associated with progressive irreversible airflow limitation and hyperinflation [30]. Patients may suffer constitutional symptoms of fever, anorexia and weight loss. Vasculitic involvement with palpable purpura, mononeuritis multiplex, arthralgias, myalgias and gastrointestinal bleeding are commonly observed on presentation. Nearly half the patients with MPA have the p-ANCA staining pattern. Since ANCA is extremely rare in classical PAN, some experts view a positive ANCA as another distinguishing feature of MPA.

The French Vasculitis Study Group published their long-term follow-up of 278 patients with PAN, MPA and CSS [31]. Fifty-eight of these patients had MPA. Patient survival was dependent upon initial disease severity rather than on disease type. A five factors score – comprising serum creatinine level >1.58 mg/dl, proteinuria >1 g/day, presence of severe gastrointestinal tract involvement, cardiomyopathy, and/or central nervous system involvement – correlated best with survival. When patients with a FFS $\geqslant$ 2 were treated with cyclophosphamide and corticosteroids, their survival was significantly better than if they were treated with corticosteroids alone. A survival benefit was not seen when patients with lower FFS were treated with combination therapy. Only patients treated with corticosteroids alone had uncontrolled disease and 15 of them died. Another limitation is that the FFS does not include alveolar hemorrhage as a manifestation of severe disease, a finding that also warrants combination therapy with high dose corticosteroids and cyclophosphamide.

Isolated Pauci-Immune Pulmonary Vasculitis

In 1997, Jennings and colleagues [3] reported on 29 patients with diffuse alveolar hemorrhage and biopsy-proven pulmonary capillaritis. The most common clinicopathologic entity was isolated pulmonary capillaritis (eight patients). These patients did not have serologic or clinical evidence of connective tissue disease. ANCA and anti-basement membrane antibody were negative. The mean age at presentation was 30 years. Although six of eight patients presented with upper respiratory symptoms, none fulfilled further

PAN = polyarteritis nodosa

MPA = microscopic polyangiitis

FFS = five factors score

diagnostic criteria of WG. Two patients had a diagnosis of asthma but without peripheral eosinophilia or other signs of vasculitis suggestive of CSS. None had evidence of kidney involvement, ruling out MPA. Following a median follow-up of 43 months in seven patients (one died of septic complications), no other clinical or serologic systemic vasculitic involvement was observed. Four patients received corticosteroids and/or cyclophosphamide. Two patients experienced recurrent alveolar hemorrhage while the rest remained in remission.

Medium-Sized Blood Vessel Vasculitis

Behçet's Disease

Behçet's disease is a rare systemic inflammatory vasculitis characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis and/or retinitis and skin lesions. Skin pathergy, a curious reaction to skin prick with a hypodermic 20–22 gauge needle and the development of a 2 mm erythematous papule or pustule, is considered a diagnostic criterion.

The disease follows a chronic relapsing course. Although most manifestations are self-limited, ocular involvement can cause blindness and systemic vasculitis may be life-threatening. BD can involve blood vessels of any size, leading to multisystem manifestations. Meningitis, meningoencephalitis, arthritis, gastrointestinal involvement mimicking inflammatory bowel disease, and migratory thrombophlebitis are other features of BD.

Pulmonary involvement in BD is rare. Clinically significant pulmonary disease is usually due to pulmonary artery aneurysms with *in situ* thrombosis. Hemoptysis may be massive and fatal. Radiographically, pulmonary artery aneurysms produce hilar enlargement usually with a lobular appearance. In a review of 2,179 patients with BD, Hamuryudan et al. [32] reported 24 (1.1%) with pulmonary arterial aneurysms. All presented with hemoptysis except for one. Half of the patients died within 10 months after onset of hemoptysis. More recently, serial CT scans were performed to evaluate pulmonary aneurysms due to BD before and after treatment [33]. Forty-six aneurysms in 13 patients were reported. Aneurysms completely disappeared with treatment in nine patients. In the remaining four there was a significant reduction in size. Other radiographic findings include atelectasis, wedge-shaped linear shadows, and reticular or nodular opacities – all presumably associated with foci of pulmonary hemorrhage or infarction [34].

Treatment experience in BD with pulmonary involvement is anecdotal. Severe vasculitis and visceral organ involvement necessitate treatment with immunosuppressive drugs. Combination therapy with cyclophosphamide and methylprednisolone is commonly employed for pulmonary aneurysms; however, FK506, azathioprine and cyclosporin A have been successful. Recently, autologous hematopoietic stem cell transplantation was successfully utilized in two patients with pulmonary involvement who were resistant to therapy with immunosuppressive and anti-inflammatory agents [35]. It is recommended that anticoagulation be used with caution in patients with mural thrombosis and only after administration of immunosuppressive therapy [34].

BD = Behçet's disease

Large Blood Vessel Vasculitis

Giant Cell Arteritis

Giant cell arteritis is a large vessel granulomatous arteritis of the aorta and its major branches with a predilection for extra cranial branches of the carotid artery. GCA is associated with polymyalgia rheumatica and affects individuals over the age of 50. Since the disease usually involves the temporal artery, it is sometimes termed temporal arteritis. The syndrome frequently presents with headache, polymyalgia rheumatica, visual disturbances, and jaw claudication with chewing. Constitutional signs such as fever, weight loss and tenderness upon palpation of the temples and scalp are commonly noted. Although GCA is the most common systemic vasculitis, pulmonary involvement is extremely rare. In an early study, nearly 10% of patients with GCA complained of respiratory symptoms, such as cough, hoarse voice and sore throat, which responded to corticosteroids [36]. In none of these, however, was the chest X-ray abnormal. Pulmonary parenchymal involvement is usually evident, with diffuse interstitial lung disease or multiple nodular lesions [37]. Exudative pleural effusions may occasionally be the presenting manifestation in GCA [38].

Due to the rarity of pulmonary involvement in GCA, it is difficult to make firm recommendations for therapy. Nevertheless, moderate doses of corticosteroids were administered with success for nodular and diffuse interstitial involvement [37] and pleural effusion [38].

Takayasu Arteritis

Takayasu arteritis is a chronic progressive occlusive vasculitis that involves the aorta and its major branches. The ACR developed the following criteria for its diagnosis: onset at age $\geqslant$ 40 years; extremity claudication; decreased brachial artery pulse; >10 mmHg differences in systolic blood pressure between arms; a bruit over the subclavian arteries along with the aorta; and arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities. The presence of three or more of these six criteria has a 90.5% diagnostic sensitivity and 97.8% specificity.

Pulmonary involvement is rare and may present as pleural effusion, diffuse interstitial infiltrates and pulmonary hemorrhage due to rupture of collateral vessels. The common manifestation of TA in the lung is due to involvement of the large and medium-size pulmonary arteries. Lupi et al. [39] reported pulmonary arterial involvement in 11 of 22 patients studied by angiography. In the largest series of patients with TA from North America, there was no clinical evidence of pulmonary arterial involvement in 32 patients with a median follow-up of 5 years [40]. Pulmonary arterial involvement can present as stenosis or total occlusion of the vessel. This represents a diagnostic challenge since angiographic appearance may mimic chronic thromboembolic disease. The response to moderate doses of corticosteroids is dramatic in TA. A 5 year survival rate of 94% has been reported from the Mayo Clinic [40]. In half of the patients who presented with absent pulses, pulses were detected after corticosteroid therapy.

GCA = giant cell arteritis
TA = Takayasu arteritis

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