Curr Rheumatol Rep (2010) 12:420–428
DOI 10.1007/s11926-010-0136-8

Pulmonary Vasculitis: Clinical Presentation, Differential Diagnosis, and Management

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Published online: 30 September 2010

Abstract This review focuses on vasculitides with prominent pulmonary manifestations and discusses key contributions from the recent literature. Pulmonary vasculitis should be considered when clinical findings include alveolar hemorrhage, nodular and cavitary lung disease, airway stenosis, pulmonary artery aneurysms, or pulmonary artery stenosis. The differential diagnostic considerations for common clinical presentations of vasculitis in the lung are important, and several recent additions are discussed. Treatment for established pulmonary vasculitis is effective and has decreased the morbidity and mortality associated with these diseases while introducing an increased risk of infectious complications. Advances in immunosuppressive therapy have improved treatment of refractory disease and are likely to change initial treatment strategies in the future.

Keywords Lung · Vasculitis · Alveolar hemorrhage · Pulmonary artery aneurysm · Tracheal stenosis

Introduction

Vasculitis may affect small vessels in the lung and cause alveolar hemorrhage or granulomatous infiltration of the parenchyma, and inflammation of large vessels can cause aneurysmal dilatation, thrombosis, or obstruction. These findings in combination with distinctive patterns of extrapulmonary organ involvement narrow the diagnostic considerations. Pathologic evaluation and serologic testing can assist in establishing the diagnosis in many patients. In this review, we focus on diseases that cause systemic vascular inflammation in which the lungs are commonly affected, including antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), Goodpasture's syndrome (GS), Behcet's syndrome (BS), and Takayasu's arteritis (TA) (Table 1). As pulmonary vasculitis is relatively uncommon, even when the clinical features are suggestive of vasculitis, a growing number of alternative diagnoses should be considered. Treatment of vasculitides that affect the lung is evolving rapidly as newer targeted immunosuppressive therapies are tested in large cohorts and in randomized clinical trials around the world (Table 2). Advances from these areas in the recent literature are reviewed below.

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Clinical Presentation

ANCA-Associated Vasculitis

The discovery of ANCAs has revealed a large subset of patients with pulmonary vasculitis. AAV includes necrotizing granulomatous vasculitis (NGV), microscopic polyangiitis (MPA), and Churg-Strauss syndrome (CSS). AAV affects small vessels and lacks antibody deposits yielding a pauci-immune pattern on histology. ANCA screening by indirect immunoflorescence on alcohol-fixed neutrophils yields two suggestive staining patterns: cytoplasmic ANCA (cANCA) and perinuclear ANCA (pANCA). When ANCA is detected by indirect immunofluorescence, confirmatory testing with an

Table 1 Clinical findings in pulmonary vasculitis

Finding	Pulmonary	Nonpulmonary	Laboratory findings	Lung pathology
Small vessel vasculitis				
ANCA associated				
Microscopic polyangiitis	Alveolar hemorrhage, pulmonary fibrosis, pleural effusion, VTE	Glomerulonephritis	50%–75% ANCA positive; most have pANCA+ MPO-ANCA	Capillaritis, arteriolitis, venulitis
Necrotizing granulomatous vasculitis	Lung nodules, cavitary masses, alveolar hemorrhage, airway stenosis, pleural effusion, VTE	Glomerulonephritis, otitis media, nasal deformity, skin involvement, central nervous system involvement	90% ANCA positive with active systemic; 50%–75% ANCA positive with pulmonary involvement limited; most have cANCA+PR3-ANCA	Capillaritis, arteriolitis, venulitis, necrosis, granulomas
Churg-Strauss syndrome	Pulmonary infiltrates, asthma, alveolar hemorrhage, eosinophilic pleural effusion, VTE	Eosinophilia, glomerulonephritis, central nervous system involvement, skin involvement, gastrointestinal involvement	30%–50% ANCA positive; pANCA+MPO-ANCA	Eosinophilic infiltrate, granulomatous inflammation, capillaritis, arteriolitis, venulitis
Non–ANCA associated				
Goodpasture's syndrome	Alveolar hemorrhage	Glomerulonephritis	Antiglomerular basement membrane antibody (~ 90%)	Capillaritis, linear antibody deposition on basement membrane
Large vessel vasculitis				
Behcet's syndrome	PAA, thrombosis	Aphthous ulcers, genital ulcers, uveitis, retinal occlusion, skin lesions, positive pathergy test	None diagnostic	Mononuclear infiltrate, thrombus, recanalization, small vessel proliferation, breakdown of lamina elastica
Takayasu's arteritis	Pulmonary artery stenosis	Aortitis, great vessel occlusion	None diagnostic	Stenosis/recanalization of pulmonary elastic arteries, cellular infiltration of muscular arteries

ANCA antineutrophil cytoplasmic antibodies, *cANCA* cytoplasmic ANCA, *MPO* myeloperoxidase, *PAA* pulmonary artery aneurysm, *pANCA* perinuclear ANCA, *PR3* proteinase-3, *VTE* venous thromboembolism

enzyme-linked immunosorbent assay (ELISA) for specific target antigen reactivity to myeloperoxidase (MPO-ANCA) and proteinase-3 (PR3-ANCA) is performed. The ELISA assays are positive in most patients with active vasculitis, and antigen targets continue to be refined to maximize sensitivity [1]. The cANCA pattern is strongly associated with PR3-ANCA, although exceptions are reported. The pANCA pattern has more limited diagnostic specificity and is observed with MPO-ANCA and other cationic proteins. When immunofluorescence and ELISA testing are considered together, the presence of cANCA with PR3-ANCA and of pANCA with MPO-ANCA positivity are highly specific for the diagnosis of small vessel vasculitis. Autoantibodies to human lysosomal membrane protein-2 (LAMP-2) can be found in more than 90% of patients with AAV and pauci-immune glomerulonephritis, and these antibodies are pathogenic in animals immunized with a homologous bacterial protein, FimH [2••]. This discovery suggests a mechanism for renal disease in AAV (molecular mimicry) and may provide a new diagnostic test. A role for LAMP-2 autoantibodies in the evaluation of pulmonary vasculitis has not been determined.

MPA is a nongranulomatous vasculitis of small vessels. MPA patients typically have pANCA and MPO-ANCA positivity; however, MPA may also occur with a positive cANCA and PR3-ANCA. Changes in serum MPO-ANCA levels seem to correlate with MPA disease activity and can predict relapse in most patients [3]. Murine models and human observations support a pathogenic role for MPO-ANCA via activation of neutrophils to damage endothelial cells; however, a recent report of transplacental transfer of MPO-ANCA from a mother with MPA to her newborn found no clinical manifestations of vasculitis over a 4-month period, suggesting that additional factors are required [4]. Renal involvement in MPA is nearly universal, and the histologic finding is rapidly progressive glomerulonephritis. Alveolar hemorrhage is seen in up to one third of patients with MPA. This vasculitis does not exhibit a strong gender predilection, and the average age at onset is greater than 50 years. A recent report of AAV among patients older than 65 years of age found that they were more likely to have MPA, had more prevalent and more severe pulmonary involvement, and were at higher risk of pulmonary infection,

Table 2 Treatment of pulmonary vasculitis

Disease	Initial therapy	Maintenance therapy
Small vessel vasculitis		
ANCA associated		
Microscopic polyangiitis, necrotizing granulomatous vasculitis	Nonsevere with normal renal function: methotrexate (oral or parenteral) and glucocorticoids Severe: cyclophosphamide (oral or intravenous pulse) and glucocorticoids	Azathioprine or methotrexate and glucocorticoid taper
	Severe with advanced renal dysfunction (> 5.6 mg/dL): add plasmapheresis	
	Refractory: rituximab[a] and mycophenolate mofetil[a]	
	No randomized studies of plasmapheresis reported for alveolar hemorrhage in AAV	
Churg-Strauss syndrome	Pulse cyclophosphamide and corticosteroids if≥1 poor prognosis factor	Corticosteroids
Non–ANCA associated		
Goodpasture's syndrome	Plasmapheresis, cyclophosphamide, and glucocorticoids	Recurrence uncommon
Large vessel vasculitis		
Behcet's syndrome	Cyclophosphamide and glucocorticoids	Glucocorticoids
Takayasu's arteritis	Cyclophosphamide, azathioprine, or methotrexate and glucocorticoids	Glucocorticoids

[a] Emerging role in induction therapy; controlled trials under way

AAV ANCA-associated vasculitis, *ANCA* antineutrophil cytoplasmic antibodies

pulmonary fibrosis, and death [5•]. Recent studies suggest that pulmonary fibrosis may be a common manifestation in patients with MPA. Radiographic evidence of fibrosis was present in one third of patients at the time of diagnosis when routine high-resolution CT of the chest was performed [6••]. The diagnosis of pulmonary fibrosis can precede or follow that of MPA and is an important cause of death in these patients [7••].

NGV typically presents as a triad of upper airway, pulmonary, and renal involvement, and the upper airway findings help distinguish this vasculitis from MPA. Lower respiratory manifestations include pulmonary nodules and cavities, alveolar hemorrhage, and airway stenosis. Multiple nodules and masses occur in about half of patients with NGV at presentation and cavitate as they become larger [8]. Ground glass opacities and lung consolidation are seen in 30% of patients at presentation on high-resolution CT and may result from hemorrhage. Airway disease can be focal or multifocal, and subglottic stenosis is a common finding in patients with active NGV (~ 20%). Quantitative ELISA testing for antibody to PR3 can detect an increase in titer that predicts relapse [9]. Early reports suggested that chronic nasal carriage of *Staphylococcus aureus* increases the risk of relapse, and in a recent study of 33 consecutive patients with new or relapsing NGV, two thirds had bacterial growth in lower respiratory samples, and 40% of recovered organisms were *S. aureus* [10].

Diagnosis of CSS requires the presence of asthma, which may precede the diagnosis of CSS by years or be diagnosed concomitantly. Pulmonary infiltrates and eosinophilia are common, and parenchymal involvement appears as ground glass opacity or consolidation on chest CT scans. The radiographic findings correspond to eosinophilic infiltration early in disease and necrotizing granulomas and vasculitis later in the course. CSS is considered an AAV despite the fact that patients have positive ANCA studies in only one third of cases (most are MPO-ANCA positive) [11]. Among ANCA-positive patients, renal and neurologic involvement is more common, whereas more cardiac involvement and fever have been observed in ANCA-negative patients. Histologic evidence of vasculitis and eosinophilic tissue infiltration is observed in both subsets. Many reports have found an association between CSS and initiation of leukotriene receptor antagonist therapy, and omalizumab therapy was also implicated recently [12]. CSS seems to be exceedingly rare in childhood, with only 33 cases reported from 1951 to 2007, but pulmonary and cardiac involvement and mortality seem to be higher among children than adults [13].

Among all patients with AAV, recent reports suggest important additional risks. Up to 12% of patients with AAV will develop venous thromboembolism, and more than 50% of these cases occur during active disease [14•]. Cardiovascular events also seem to be increased in patients with AAV compared with patients with chronic kidney disease and controlled for coronary artery disease risk factors.

Goodpasture's Syndrome

Antiglomerular basement membrane antibody (ABMA) disease is a disorder in which circulating antibodies bind to epitopes in the basement membrane of the kidney and lung and cause vascular inflammation. Less than one third of patients with these ABMAs present with glomerulonephritis alone, and most present with the combination of diffuse alveolar hemorrhage (DAH) and glomerulonephritis, referred to as *Goodpasture's syndrome*. ABMA disease is rarely confined to the lungs. At least 90% of patients with GS reported in the literature have detectable circulating ABMAs, and the distribution of the disease is bimodal, affecting young adults (predominantly males) and older adults. GS has been strongly associated with major histocompatibility complex *HLA-DRB1*1501* in populations around the world. In animal models of GS, targets within type IV collagen in the basement membranes of capillaries in lungs and kidneys are hidden from immune attack and may be exposed by injury. A contribution of lung injury to the pathogenesis of GS in humans is suggested by the association between pulmonary hemorrhage and cigarette smoking, exposure to hydrocarbons, and respiratory infection.

About one third of patients with ABMA also have positive ANCA studies, and more than 90% of these are MPO-ANCA. Patients with dual positive studies are older than patients with ABMA alone and are at increased risk of relapse due to the ANCA component of their disease [15•].

Behcet's Syndrome

BS is a vasculitis that affects predominantly large vessels (less commonly small vessels) and is diagnosed clinically when a patient presents with a history of recurrent oral ulcers and any two of the following: recurrent genital ulceration, eye lesions (eg, uveitis or retinal vasculitis), skin lesions (eg, erythema nodosum or pseudofolliculitis), or a positive pathergy test. The vascular involvement can lead to venous occlusion, arterial occlusion, and arterial aneurysm. Intrathoracic manifestations are seen in fewer than 10% of cases, the most common of which are pulmonary artery aneurysms (PAAs) and thrombosis.

PAAs are the major cause of death in BS, and when present are multiple and bilateral in more than 90% of cases. BS affects men and women. However, men are at higher risk of developing PAAs. The most common presenting symptom of PAAs is hemoptysis. Pulmonary artery enlargement due to aneurysmal dilatation is the most frequent abnormality seen on routine chest radiograph and is confirmed by CT or MRI angiography. Deep venous thrombosis or extrapulmonary superficial thrombosis accompanies PAA in most patients with BS. Pulmonary artery thrombi are commonly seen on CT and appear to result from in situ thrombus formation at the site of the inflamed aneurysm [16•]. Pulmonary infarcts occur as a consequence of local thrombosis or distant embolism and can manifest as wedge-shaped infiltrates and hemoptysis.

Takayasu's Arteritis

In TA, the pulmonary arteries are frequently affected in patients with large vessel involvement. Brachiocephalic disease is particularly likely to be accompanied by pulmonary arterial stenosis or occlusion. However, isolated symptomatic pulmonary vessel involvement is reported [17].

Differential Diagnosis

Distinctive presentations of pulmonary vasculitis include alveolar hemorrhage, nodular or cavitary lung disease, airway stenosis, and PAAs. Recent reports have added to the differential diagnostic considerations in these clinical situations.

Diffuse Alveolar Hemorrhage

Ground glass opacities or consolidation are the characteristic radiologic finding of DAH, and the diagnosis is often suggested by the presence of hemoptysis and/or anemia. A recent retrospective report of 97 consecutive patients with DAH found that only one third were caused by vasculitis [18], and another report of 37 patients admitted with DAH to the intensive care unit found vasculitis in 20% [19••]. Common alternative diagnoses established in these two series included congestive heart failure (due to systolic dysfunction, diastolic dysfunction, or valvular heart disease), infection, drug toxicity, coagulation disorders, and complications of stem cell transplantation.

Infections may contribute to lung injury directly or indirectly and be complicated by alveolar hemorrhage, particularly in the setting of coagulopathy. Specific infections strongly associated with alveolar hemorrhage include novel swine-origin influenza A (H1N1) virus and leptospirosis. Early in the 2009 influenza pandemic, hemoptysis with respiratory failure and alveolar hemorrhage confirmed by bronchoscopy were reported in patients with severe H1N1 infection. Detailed pathological studies of patients who died from this illness showed necrosis of the alveolar walls, alveolar hemorrhage, neutrophilic infiltrate, and diffuse alveolar damage (Fig. 1) [20•]. Leptospirosis is a zoonotic disease transmitted from water or soil contaminated by rodents infected with *Leptospira* spp, particularly after summer floods in endemic areas. It affects more than 500,000 people worldwide annually and is a major cause of febrile pulmonary hemorrhage, with a mortality rate greater

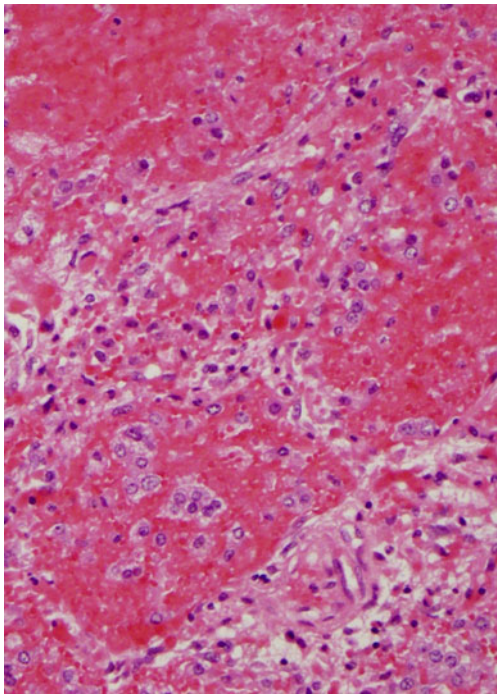

Fig 1 Alveolar hemorrhage in novel swine-origin influenza A (H1N1) influenza infection. Pulmonary histopathology shows a patient with fatal H1N1 and diffuse, bilateral, recent pulmonary hemorrhage characterized by intra-alveolar red cells admixed with occasional intra-alveolar and perialveolar neutrophils and lymphocytes. (*Courtesy of* Dr. Robin McGoey, Louisiana State University Health Sciences Center, New Orleans, LA.)

than 50%. Immunoglobulin and complement deposits have been identified along the alveolar septa in humans with leptospirosis, raising the possibility of an immune mechanism for pulmonary hemorrhage [21]. Nonrandomized studies of patients with leptospirosis and pulmonary hemorrhage treated with cyclophosphamide or cyclophosphamide and plasmapheresis suggest improved outcomes with immunosuppression.

Drug toxicity can lead to alveolar hemorrhage, and recent reports emphasize the importance of antithyroid medications, immunosuppressive drugs, platelet inhibitors, illicit drug use, and silicone injection. Propylthiouracil causes ANCA and MPO-ANCA positivity in up to one third of patients and correlates with treatment duration. While clinical vasculitis with major complications is uncommon in this group, a review of 31 cases of ANCA-positive vasculitis associated with use of antithyroid medication reported that 12 developed DAH [22•]. Most patients had glomerulonephritis or hematuria, and onset ranged from 2 months to 10 years after the initiation of antithyroid treatment. Cessation of the drug and the addition of steroid therapy for severe disease resulted in improvement in all cases. MPO-ANCA titers gradually decrease but can remain positive for more than 5 years, and relapses are uncommon. Mammalian target of rapamycin inhibitors (sirolimus, everolimus) are used widely in solid organ transplantation, and recent reports have added pulmonary hemorrhage to the more common interstitial pneumonitis associated with these drugs [23]. Platelet glycoprotein IIb/IIIa receptor inhibitors (eptifibatide, abciximab) have been reported to cause alveolar hemorrhage, with an incidence of between 1 in 100 and 1 in 700 patients exposed, with onset 30 minutes to 4 hours after administration [24]. This complication has a high mortality rate in most case series. Crack cocaine use continues to be reported as a cause of mild to life-threatening alveolar hemorrhage in populations susceptible to drug addiction [25]. Subcutaneous injection of silicone, a chemically stable, nonimmunogenic liquid polymer, has been associated with pulmonary embolism, lung injury, and death. More than half of reported cases develop clinical findings of alveolar hemorrhage with peripheral ground glass opacity on chest CT [26].

Nodular Lung Disease

Nodular lung disease in patients with NGV is typically multiple, bilateral, and cavitary. These findings can be mimicked by a wide variety of nodular and cavitary lung diseases, including necrotizing pneumonia, mycobacterial and fungal disease, nocardia, and cavitary malignancy [27].

Airway Stenosis

Even relatively short-term mechanical ventilation can lead to tracheal stenosis. In a series of 11 patients with symptomatic stenosis after orotracheal intubation, duration of mechanical ventilation ranged from 2 to 10 days [28]. Endobronchial tuberculosis can present as granulomatous inflamed airway with irregular thickening or an endobronchial mass in 10% to 40% of active tuberculosis cases. With cavitary lung disease, it can mimic NGV. Postinflammatory bronchial stenosis may present several years after antimycobacterial therapy, and among patients requiring intervention, the left mainstem bronchus was the primary site of disease [29].

In relapsing polychondritis, inflammation of cartilaginous structures with destruction of the pinna, saddle nose deformity, and deafness are common findings, and the combination of nasal deformity and tracheal disease can suggest NGV. Airways were involved in one fifth of patients evaluated at a tertiary referral center and included subglottic stenosis and focal stenosis of the mainstem bronchi [30]. Characteristic CT findings are airway wall thickening, malacia, stenosis, and calcification. Adenoid cystic carcinoma is a very slow growing infiltrative tumor that causes irregular narrowing of the airway with nodular thickening of the bronchial wall, and can mimic a benign inflammatory process [31].

Sarcoidosis is a common granulomatous disease that typically affects the lung parenchyma, and airway involvement with granulomatous inflammation with obstruction or stenosis is less common but well-described [32•]. Isolated idiopathic tracheal stenosis is a rare condition recently reported in 63 women and characterized by gradual onset of dyspnea (> 2 years) and excessive keloidal fibrosis with preservation of normal cartilage [33].

Pulmonary Artery Aneurysms

Aneurysms and pseudoaneurysms may accompany infection within or adjacent to the pulmonary artery, and recent series have included tuberculosis (Rasmussen aneurysm), lung abscess, invasive fungal disease, and mycetoma among the causes [34]. PAAs are commonly bilateral and proximal in the presence of chronic pulmonary hypertension, and may be very large with sudden death occurring as a result of dissection or rupture. Peripheral PAAs are uncommon but are reported in these patients. Penetrating trauma and iatrogenic injury during pulmonary artery catheterization can cause PAAs, and cases of aneurysm and pseudoaneurysm due to lung carcinoma have been reported.

Treatment

ANCA-Associated Vasculitis

In early series of therapy for NGV, the benefit of cyclophosphamide plus steroid induction was apparent, with 75% of treated patients achieving complete remission in this highly lethal disease. During the past decade, large randomized controlled trials of therapy have refined the approach to AAV [35••]. Most patients enrolled in these trials have demonstrated evidence of pulmonary involvement. These studies have demonstrated that methotrexate can replace cyclophosphamide as the induction agent for early vasculitis, and that for severe but non–life-threatening vasculitis, a pulse cyclophosphamide regimen is as effective as a daily oral regimen for induction of remission [36•]. For maintenance therapy, azathioprine can be substituted for cyclophosphamide, and methotrexate is comparable to azathioprine [37]. Relapse rates are unacceptably high if maintenance therapy is discontinued after 1 year. The role of plasmapheresis remains uncertain in patients with active pulmonary vasculitis. In patients with kidney failure due to AAV, plasma exchange is more effective than high-dose methylprednisolone for preserving organ function [38]. Plasmapheresis has been used for alveolar hemorrhage due to AAV; however, this approach has not been subjected to a controlled study [39••]. For hypoxemic respiratory failure due to DAH, extracorporeal membrane oxygenation support also has been used, with a good outcome.

The reported experience with targeted immune cell depletion for AAV is promising in children and adults with severe refractory AAV. In a retrospective study of 65 consecutive patients with relapsing or refractory AAV treated with rituximab to deplete B cells, complete remission was achieved in 75% [40]. However, more than half of these patients relapsed (median time to relapse, 1 year), and in half of the relapsed patients, peripheral B-cell populations had not yet recovered. B-cell infiltration in affected tissues can occur after administration of rituximab even while circulating B-cell counts are low. Several randomized controlled trials are currently evaluating the role of rituximab compared with cyclophosphamide in the treatment of AAV. Other cell depletion strategies targeting T cells or both T and B cells have been used with success for refractory AAV; however, remissions are not durable, and infectious complications are frequent. A recent retrospective report of 71 patients treated with anti-CD52 found that although remission was induced in most patients, two thirds relapsed (median time to relapse, 9 months), and one half of the treated patients died, most commonly of infection [41].

Mycophenolate mofetil has been evaluated in the treatment of AAV during the past decade, with experience in patients with NGV or MPA and mild to moderate renal involvement, and compares favorably with standard therapy for induction and maintenance of remission in this setting. Tumor necrosis factor (TNF)-α and its receptor are upregulated at the site of vasculitis and provide attractive targets for available biological reagents. However, etanercept, a soluble p75 receptor, is ineffective in maintenance of remission in NGV, and a chimeric monoclonal antibody to TNF-α (adalimumab) modestly decreased steroid requirement when administered with cyclophosphamide in treatment of acute, severe AAV [42].

Symptomatic subglottic stenosis in NGV can present early or late in this disease and may not respond to systemic immunosuppressive therapy. In these cases, recent reports have found that intralesional treatment with long-acting steroids coupled with mechanical dilation can be effective [43].

Several recent series of patients with AAV demonstrated that complications after administration of potent immunosuppressive therapy are major causes of mortality. In a study of 524 patients with a new diagnosis of AAV, the mortality rate during the first year was 11%; 59% of these deaths were attributed to complications of therapy, including infection and 14% to vasculitis [44••]. Adding to the spectrum of infections reported in patients with vasculitis, a recent report described invasive pulmonary aspergillosis in 7 of 157 consecutive patients treated for AAV [45]. The

outcomes for vasculitis with primary pulmonary manifestations may differ somewhat from those for AAV in general. In 12 patients with AAV and DAH, 3 died rapidly of respiratory failure, 3 died later of infectious complications, and 1 died of heart failure [39••]. In a series of patients with MPA, death was most frequently a result of alveolar hemorrhage [46].

The French Vasculitis Study Group has used a five-factor score to investigate prognosis and treatment of CSS. For patients without one of the five poor prognosis factors (elevated creatinine, proteinuria, gastrointestinal tract involvement, heart involvement, or central nervous system involvement), corticosteroids are highly effective in inducing remission (93%). Relapses occurred in one third of patients, most of which were responsive to pulse cyclophosphamide or daily azathioprine [47]. Corticosteroids were continued in most patients, and the 5-year survival rate was 97%. Among patients with at least one poor prognosis factor, treatment with corticosteroids and pulse cyclophosphamide yielded complete remission in 86%, and relapses occurred in 60% to 80%, with a benefit in preventing mild relapses noted using a 12- versus 6-pulse regimen [48]. Successful treatment of refractory CSS has been reported with rituximab. Mepolizumab, an antibody to interleukin-5, may have a role in treating CSS and is currently in clinical trials. Immune modulators interferon-α and intravenous immunoglobulin have been used in a limited number of patients, with apparent success. Coronary arteritis and myocarditis are major causes of death and morbidity in patients with CSS.

Goodpasture's Syndrome

Therapy for GS has been directed at inhibiting production and enhancing clearance of these antibodies, and the mainstay of therapy in published reports has been plasmapheresis, frequently in combination with steroids and cyclophosphamide. Recent therapeutic modifications include use of higher efficiency plasmapheresis to remove immunoglobulins with less albumin and crystalloid replacement. Recurrence of anti–glomerular basement membrane antibody with linear deposits after kidney transplantation can be decreased via suppression of circulating antibody, and therapy for refractory disease has included mycophenolate mofetil. Recurrence of clinical disease is uncommon in patients treated for GS.

Behcet's Syndrome

PAAs and in situ thrombosis of pulmonary vessels are well-described large vessel manifestations in BS, and medical therapy is effective in the vast majority of cases [49••]. Glucocorticoid and cyclophosphamide treatment results in resolution or regression of aneurysmal dilatations, typically with formation and evolution of mural thrombus during treatment. Surgical management is occasionally feasible; however, postoperative hemorrhage from suture line has been reported, and recurrent anastomotic aneurysms are common.

Takayasu's Arteritis

A recent report of 248 patients with TA in Turkey found that aortic disease remission was induced in more than 90% using a combination of corticosteroid and immunosuppressive therapy (most received methotrexate or azathioprine), and remission was durable in 70% with prolonged therapy [50•]. In symptomatic patients unresponsive to medical therapy, balloon angioplasty with stent placement has been performed, with good outcomes.

Conclusions

Recent reports have added to the expected clinical presentations that occur when systemic disease causes vascular inflammation of the lung. In addition, characteristic features of pulmonary vasculitis are frequently mimicked by non-vasculitic conditions, and the differential diagnosis needed to evaluate these patients continues to expand. Immunosuppressive treatment options for systemic vasculitis affecting the lung are frequently effective and have improved outcomes but have altered the natural history of these conditions to include more infectious complications. Emerging immunosuppressive approaches are promising and are likely to add to the primary management options in the near future.

Disclosure No potential conflicts of interest relevant to this article were reported.

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- • Of importance
- •• Of major importance

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