

## Case report

# Pulmonary artery involvement in Wegener's granulomatosis

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### ABSTRACT

*Classification and nomenclature schemes are guidelines and are not intended to recognize and distinguish the entire spectrum of any single disease. It may in fact be misleading to suggest that a classic presentation of a given disease plus atypical features should be considered an "overlap" of two separate, often rare, conditions.*

*We report a case of typical Wegener's granulomatosis (WG), with the coexistence of pulmonary artery stenosis, a lesion more commonly observed in TA. This is not the first or only example of large vessel vasculitis occurring in patients with WG. This observation cautions clinicians to avoid rigid application of classification and nomenclature systems and raises questions about determinants of vasculitis subsets and organ targeting.*

### Introduction

Vascular injury in Wegener's granulomatosis (WG) classically occurs in small and medium-sized vessels (1). Although, the upper and lower respiratory tract and kidneys (glomerulonephritis) are most commonly involved in WG, virtually any organ can be affected including joints, skin, peripheral nerves, skeletal muscle, heart, brain, eye, genitourinary, and gynecologic organs (1). Takayasu's arteritis (TA), another form of vasculitis, is quite distinct from WG. It affects large elastic and muscular arteries such as the aorta and its primary branches and the coronary and pulmonary arteries (2). Apart from ischemia or infarction, TA rarely produces tissue parenchymal lesions.

Classification and nomenclature schemes are man-made formulae to aid physicians in the exercises of diagnosis, prognosis and planning treatment. However, such schemes are only guidelines and are not intended to recognize and distinguish the entire spectrum of any single disease (3,4). This is in part

reflected by reports of patients with overlapping features such as rheumatoid arthritis and lupus (SLE) or in the case of vasculitides: WG and polyarteritis nodosa (PAN) (5), sarcoidosis and TA (6), WG and TA (7-10), and SLE and TA (8). It may in fact be misleading to suggest that a classic presentation of a given disease plus atypical features should be considered an "overlap" of two separate, often rare, conditions.

We report the case of a 37-year-old female with typical features of WG, who 5 years later developed pulmonary artery stenosis, a lesion more commonly observed in TA.

### Case report

In 1997, a 37-year-old woman developed muscle and joint discomfort, bilateral otitis media, nasal and sinus pain and discharge, pulmonary infiltrates and nodules. She had positive serologic studies for ANCA (C-pattern by immunofluorescence and anti-proteinase 3 antibodies detected by ELISA). Her physicians initially provided treatment with antibiotics, which were not effective. Corticosteroids and placement of myringotomy tubes provided transient improvement. Corticosteroid dose reduction was followed by worsening symptoms. Severe leg pain precluded walking. Hemoptysis led to imaging studies and recognition of pulmonary nodules. Open lung biopsy revealed granulomatous inflammation and vasculitis. The diagnosis of WG was made and she was treated with methotrexate (15 mg/week) and prednisone (60 mg/day). Marked improvement followed and methotrexate was maintained at a dose of 22.5 mg per week. Her illness remained stable until 1999, when attempts were made to reduce prednisone below 20 mg QD she developed rhinitis, sinusitis, hemoptysis, shortness of breath, and recurrent pulmonary nodules.

In 2000, a relapse included pulmonary

infiltrates, otitis media, and newly diagnosed subglottic stenosis, which required focal corticosteroid intra-lesional injection and dilatation. The procedure led to increased tracheal patency, stabilization of the airway and improved function (11). Corticosteroids were increased to 40 mg QD, methotrexate was increased to 25 mg per week, and the patient was enrolled in a Phase III trial to evaluate the utility of adjuvant treatment with etanercept versus placebo. Corticosteroid-free remission was not subsequently achieved. In September 2001, a cardiac exam revealed a marked increase in intensity of a previously noted systolic murmur. A trans-thoracic echocardiogram and a pulmonary artery angiogram demonstrated narrowing of the distal main and right pulmonary arteries (Figure 1). Intravascular ultrasound revealed smooth-walled thickening of the primary branches of the pulmonary arteries, which was felt to be compatible with an inflammatory process. By February 2002, recurrent otitis media, rhinitis, sinusitis, malaise and dyspnea on exertion led to increasing prednisone to 60mg QD and changing methotrexate to cyclophosphamide (125 mg QD). Dramatic improvement followed. At 3 months follow-up, energy level was much improved, she was walking 20 minutes per day, and sinus and nasal symptoms had resolved. Follow-up angiography did not reveal progression of pulmonary artery stenoses.

**Fig. 1.** Pulmonary angiogram: pulmonary artery stenosis.



### Discussion

This patient's illness includes classical features of WG. Her illness meets both the ACR criteria (12) and the Chapel Hill (13) nomenclature guidelines for WG. However, she also developed large vessel disease in the form of pulmonary artery stenosis, not heretofore reported as part of WG. Angiography is only a surrogate marker and does not represent as rigorous proof of vasculitis as histopathology. One could argue for the observed lesion may have been congenital and non-inflammatory. However, the lesion was discovered in concert with worsening of WG and a dramatic change in a murmur that, by

echocardiography, was attributed to the pulmonary artery lesion. Angiographic and MR characteristics were most compatible with an inflammatory lesion. One might also argue that our patient's illness is an "overlap syndrome" of both WG and TA. However, she did not have involvement of the aortic arch, subclavian, innominate or carotid vessels, which are the most frequent sites of disease in TA. Others (Table I) have previously recognized large vessel disease in WG. This experience supports the notion that WG, a disease usually of small and medium-sized vessels, may rarely involve large muscular and elastic vessels.

**Table I.** Studies reporting large vessel disease in Wegener's granulomatosis.

Author	Age	Gender	TA features	WG features
Jolly <i>et al.</i> (3)	29	Female	Aortic insufficiency, left subclavian stenosis, arm claudication, and pericarditis	Scleritis (perforation from scleritis, enucleation), nasal crusting and epistaxis, maxillary and ethmoid sinus involvement, +nasal and sinus biopsy, ANCA+, C- pattern
Yamasaki <i>et al.</i> (4)	27	Female	MRI-thickening of aortic arch, complete occlusion of left subclavian and common carotid, arm claudication	Conjunctivitis, epistaxis (+nasal biopsy), maxillary sinus involvement, destruction of nasal septum, ANCA+, C-pattern
Dabague <i>et al.</i> (5)	29	Female	Aortogram-proximal obstruction and irregularities in the vessels emerging from the aortic arch, asymmetric pulses	Nodular pulmonary infiltrates, nasal and renal biopsy +, ANCA+, P-pattern
Rojo-Leyva <i>et al.</i> (8)	67	Female	Aortogram-ascending aortic aneurysm. Histopathology-giant cell aortitis	Pulmonary infiltrates. Open lung biopsy compatible with WG, ANCA+, C-pattern

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