

# A Frequent Co-Occurrence of Two Rare Diseases: The Relationship Between Takayasu Arteritis and Ulcerative Colitis

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## ABSTRACT

Takayasu arteritis (TAK) is a rare, medium- to large-vessel vasculitis characterized by inflammation and obliteration of arteries, most commonly the aorta and its proximal branches. Pulmonary artery involvement in TAK may also occur; this is characterized by nonspecific symptoms including dyspnea, chest pain or cough. TAK occurs predominantly in females with an average age of onset between 10-40 years. Additionally, TAK has been found to co-occur with ulcerative colitis (UC). This co-occurrence is thought to be related to the HLA-B\*52:01 allele or other associated autoimmune cross-reactivity. In this case series, we explore the relationship between TAK and UC through two case reports involving this co-occurrence.

**Keywords:** *Inflammatory Bowel Syndrome, Pulmonary Artery Inflammation, Pulmonary Hypertension*

## Introduction

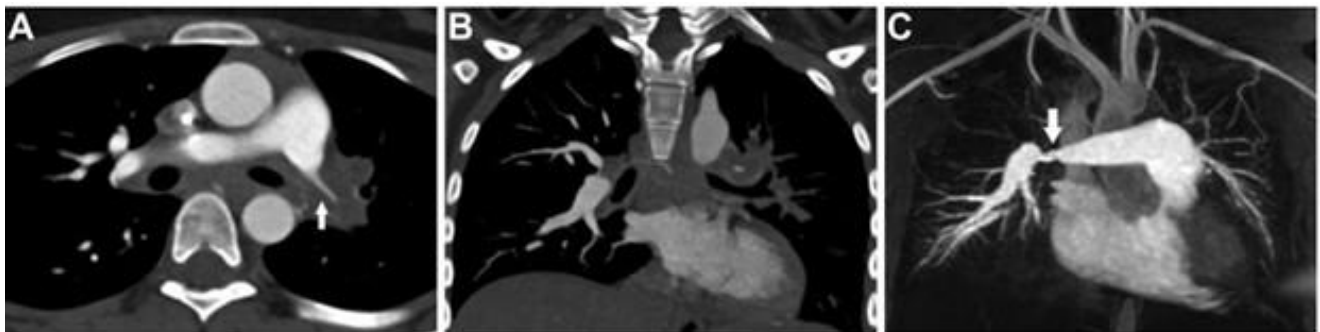
Takayasu arteritis (TAK) is a vasculitis most commonly affecting the aorta, carotid and subclavian arteries (Yang *et al.*, 2019). Pulmonary artery (PA) involvement in TAK ranges from 0-50%, and presents with dyspnea, cough, and chest pain (Yang *et al.*, 2019; Toledano *et al.*, 2011). TAK is thought to be associated with human leukocyte antigen HLA-B52 allele, similar to ulcerative colitis (Ortiz-Fernandez *et al.*, 2021). Previous studies have found a 6-7% co-occurrence rate of UC in patients with TAK (Terao *et al.*, 2015; Watanabe *et al.*, 2014). This case series describes two young females with ulcerative colitis and newly diagnosed Takayasu arteritis with pulmonary artery involvement.

## Case 1

A 24-year-old female with ulcerative colitis on vedolizumab presented to transition care for previously diagnosed fibrosing mediastinitis. Two years prior to current presentation, the patient developed progressive cough and dyspnea. Computed tomography (CT) scans were notable for left hilar lymphadenopathy with progressive occlusion of the left upper lobe pulmonary artery and veins. Bronchoscopy with bronchoalveolar lavage (BAL) and lymph node sampling were negative for infection and malignancy. She was therefore presumed to have fibrosing mediastinitis and started corticosteroids and three doses of rituximab without symptomatic improvement.

Eight months after her last rituximab infusion, she continued to note dyspnea on exertion and dry cough without hemoptysis, fevers or chills. Her vitals, exam and laboratory evaluation were unremarkable, including a normal ESR, CRP and autoimmune workup. Ventilation/perfusion nuclear medicine lung scan revealed mildly decreased ventilation throughout the left lung with associated markedly decreased perfusion throughout the left lung and the right upper lobe. Echocardiogram was notable for mild pulmonary hypertension.

She therefore underwent right heart catheterization notable for a hypoplastic left pulmonary artery without discrete focal stenosis. Serial repeat chest imaging visualized further narrowing of the right middle lobe pulmonary artery along with diminished opacification of the apical posterior segment of the left upper lobe pulmonary artery (Fig. 1).



**Figure 1:** 24-year-old female with ulcerative colitis and Takayasu arteritis. Contrast-enhanced axial (A) and coronal reformatted (B) CT images show severe narrowing of the left pulmonary artery (*arrow*) with surrounding soft tissue thickening. (C) Coronal maximum intensity projection shows severe narrowing of the distal right main pulmonary artery (*arrow*).

Due to the lack of clinical response to prior rituximab infusions along with the absence of typical mediastinal or hilar calcification, a diagnosis other than fibrosing mediastinitis was explored. Thoracic Radiology consulted other experts and felt imaging was more consistent with an underlying vasculitis.

The patient was ultimately diagnosed with Takayasu arteritis (TAK) and started on prednisone, methotrexate, and transitioned to Infliximab. Roughly one year later the patient's imaging remains stable without further pulmonary artery stenoses.

## Case 2

A 27-year-old female with iron deficiency anemia, history of a pulmonary embolism (PE), and ulcerative colitis status-post colectomy not on disease-modifying therapy presented to pulmonary clinic for worsening dyspnea on exertion and persistent pleuritic chest pain. Her PE was three years prior and thought to be precipitated by oral contraceptives. She completed six months of rivaroxaban therapy, however since treatment noted waxing and waning right-sided chest discomfort and progressive dyspnea on minimal exertion. She denied any fevers, chills, or weight loss.

Exam revealed a blood pressure of 168/105 mmHg in the left arm (unable to obtain in the right upper extremity) and normal oxygen saturation. Cardiopulmonary exam was within normal limits, she had 2+ left radial pulse, unable to palpate right radial pulse, and no peripheral edema or clubbing.

Laboratory evaluation included a WBC count 10,500/mL; hemoglobin 10.4 g/dL with MCV 74; and platelets, 593 K/mL. Complete metabolic panel was within normal limits. Her autoimmune workup was negative, CRP normal and ESR of 30 mm/hr (10-20). Chest CT angiogram showed a narrowing of the right main pulmonary artery with reduced flow. MRA of the right upper extremity revealed an 11 cm segment of right axillary artery narrowing with associated perivascular enhancement (Fig. 2).



**Figure 2:** 27-year-old female with ulcerative colitis and Takayasu arteritis. Coronal thin-slab maximum intensity projection (A) and contrast-enhanced axial CT image (B) show narrowing of the right interlobar pulmonary artery (arrow). (C) Coronal thick-slab maximum intensity projection shows attenuated right upper lobe peripheral pulmonary arteritis.

Given symptoms and imaging findings, rheumatology confirmed the diagnosis of TAK. Patient was started on prednisone and adalimumab therapy with improvement in symptoms. Repeat imaging was arranged, however the patient was lost to follow up.

## Discussion

Takayasu arteritis (TAK) is a medium- to large-vessel vasculitis characterized by inflammation that may present as fever, fatigue, myalgias and weight loss (Sharma *et al.*, 1996). As arterial inflammation progresses to fibrosis this can lead to limb claudication, hypertension, unequal peripheral pulses or light-headedness (Sharma *et al.*, 1996). Pulmonary artery (PA) involvement is variable and symptoms are nonspecific and include dyspnea, cough, hemoptysis and chest pain that may delay diagnosis (Yang *et al.*, 2019, Toledano *et al.*, 2011). TAK typically affects Asian women between ages 10-40 (Keser *et al.*, 2014). The pathogenesis of TAK is believed to be autoimmune and genetically associated with the HLA-B52 subtype (Ortiz-Fernandez *et al.*, 2021). On physical examination, patients may have unequal peripheral pulses and bruits on auscultation. Laboratory evaluation may include an elevated ESR, CRP, leukocytosis or thrombocytosis (Sharma *et al.*, 1996). On imaging, CTA and MRA findings of active disease include vessel wall thickening with enhancement (Barra *et al.*, 2018).

In each case, patients had a pre-existing diagnosis of ulcerative colitis (UC). As previously discussed, UC and TAK share the HLA-B\*52:01 subtype as a genetic determinant, and studies have found a 6-7% co-occurrence rate of UC in patients with TAK (Terao *et al.*, 2015; Watanabe *et al.*, 2014). It is postulated HLA-B\*52:01 contributes to the co-occurrence of these two diseases in a dominant manner, given lack of enhancement with homozygosity (Terao *et al.*, 2015). Additionally, whether this association is directly related to this shared allele is yet to be determined as non-HLA markers have also been associated with increased rates of disease co-occurrence (Terao *et al.*, 2015). The pathophysiology related to this relationship is not understood but may be secondary to autoimmune cross-reactivity, as various studies have displayed antibodies against both aortic tissue and colonic mucosa amongst these patients (Terao *et al.*, 2015; Reny *et al.*, 2003). TA can also be seen in patients with Crohn's disease (Reny *et al.*, 2003). Unfortunately, the patients in this case series were unable to undergo genetic or immunologic testing to evaluate for this underlying association.

Patients with IBD are typically diagnosed with TAK around 8-10 years earlier than average if these diseases co-occur (Terao *et al.*, 2015; Sy *et al.*, 2016). In addition, most studies describe the development of TAK after the diagnosis of IBD, and the patient population with disease coexistence is predominantly female (Takahashi *et al.*, 2011; Terao *et al.*, 2015; Sy *et al.*, 2016). The patients in this case series are reflective of s. Additionally, TAK is initially treated with high-dose corticosteroids in the inflammatory phase of disease, with long-term therapies including conventional immunosuppressive medications such as methotrexate, azathioprine or anti-TNF agents for refractory disease (Keser *et al.*, 2014).

Thus, the association between ulcerative colitis and Takayasu arteritis is important to keep in mind when evaluating patients with pre-existing IBD and nonspecific complaints of fatigue/malaise or respiratory symptoms. In regard to PA involvement, a delay in diagnosis of TAK may lead to the development of pulmonary hypertension, which portends worse clinical outcomes (Toledano *et al.*, 2011). Therefore, as research continues to investigate the pathophysiology underlying this association, it is important to raise clinical awareness regarding the connection between TAK and UC to decrease time to diagnosis and initiation of appropriate disease-modifying therapies.

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