



## Coexisting Rheumatoid Arthritis and Takayasu's Arteritis: a Case Report and Review of the Literature

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The coexistence of rheumatoid arthritis (RA) and Takayasu's arteritis (TA) is a rare combination and described only in case reports in the literature. Although concurrent presence of RA and TA has been described only in a few literatures to date and the number of reports is increasing, the association between RA and TA remains to be clarified.

### Introduction

Takayasu's arteritis (TA) is a rare, idiopathic, chronic inflammatory disease characterized by necrotizing and obliterative segmental panarteritis of unknown aetiology, which attacks the aorta and its major branches (1). Autoimmunity is thought to play an important role, and several cases have been reported an associations between TA and various autoimmune disorders. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by symmetric, multiple arthritis and extra-articular manifestations (EAM), including the skin, eyes, lungs and blood vessels. Rheumatoid vasculitis is an unusual complication of longstanding, severe RA, which involves the small and medium sized arteries in the body (2). The controversy exists about the concurrent presence of both diseases, and it is also unclear whether this disease occurs incidentally or overlaps like other connective tissue diseases. However, the reports of coexistence of RA and TA are increasing in spite of very rare description only in case reports in the literature (4-14). More reports, experience and case control studies will be needed to define the relationship between RA and TA.

We present a case of a female patient with both RA and TA, presenting with polyarthritis. We also reviewed the clinical features of the cases with coexistence of RA and TA.

**Key Words.** Rheumatoid arthritis, Takayasu's arteritis

We here described a case of a young woman with both RA and TA, and reviewed the clinical features of the reported cases with coexistence of RA and TA.

### Case Report

A 40-year-old female patient was visited the private clinic with painful swellings on both knees, elbows, and small joints in hands in March 2000. She was diagnosed as having RA. She had been treated for pulmonary tuberculosis 8 years previously with 4-drug regimen(isoniazid, rifampin, pyrazinamide, ethambutol) and there was no other medical history. In July 2007, the patient was referred to our hospital due to poorly controlled symptoms of RA. She was treated with methotrexate (10 mg/week), leflunomide (10 mg/day) and prednisolone (5 mg/day), which improved her articular symptoms and laboratory findings.

After 6 months later, she presented with exacerbation of RA as well as cough, sputum and hemoptysis. She was found to have both swelling and tenderness in her peripheral joints of both hands and feet. But she didn't experience claudication. On

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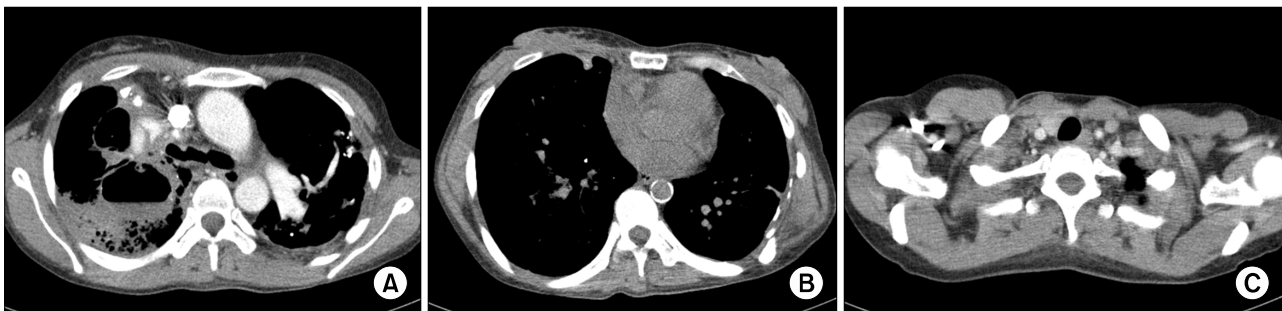
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**Figure 1.** Simple X-ray of right hand in 2007 (A), 2011 (B). Hand X-ray shows narrowing of radio-carpal and carpal bone joint space and irregular bony erosion and sclerosis of carpal bone and distal radius.



**Figure 2.** (A) Computed tomography (CT) with enhancement of chest shows known tuberculosis-destroyed lung with acute pneumonic consolidation. (B) Takayasu's arteritis in late stage of disease. Unenhanced CT scan shows extensive calcification composing abdominal aortic lumen. (C) Enhanced CT scan shows stenosis of left common carotid artery.

physical examinations, her lung sounds were decreased with crackles and there wasn't deformity or rheumatoid nodule on her hands. A blood pressure difference between the left and right arm was not noted. But pulsations of both tibial arteries were reduced. She had a reversed arm-leg systolic blood pressure discrepancy of 50 mmHg (51/50 mmHg vs 102/100 mmHg, leg vs. arm, respectively). There was bruit over abdominal aorta. At admission, laboratory test revealed white blood cell (WBC) of  $16.9 \times 10^3/\text{mL}$  with neutrophilia and hemoglobin 13.4 g/dL, platelet  $299 \times 10^3/\text{mL}$ , erythrocyte sedimentation rate (ESR) 82 mm/hr, C-reactive protein (CRP) 293.05 mg/L. Rheumatoid factor (RF) level was 31.5 IU/mL (normal < 14 IU/mL), and anti-CCP antibody level was 59.08 IU/mL (normal < 5 IU/mL). Her renal function were normal and sputum AFB stains and cultures were negative.

Simple X-ray of right hand showed narrowing of radiocarpal and carpal joint space and irregular bony erosion and sclerosis

of carpal bone and distal radius (Figure 1). Computed tomography (CT) with enhancement of chest showed known tuberculosis-destroyed lung with acute pneumonic consolidation (Figure 2A). And abdominal aorta had incidentally found diffuse calcification with complete obstruction of infrarenal aorta (Figure 2B). To further evaluate aortic abnormality on CT, aortic angiography was performed and showed complete obstruction of infrarenal aorta (Figure 3) with left common carotid artery stenosis (Figure 2C). Considering the age of the patient, bruit over abdominal aorta and abnormal findings of 3D CT scan of aorta and aortic angiography, TA was diagnosed by The American College of Rheumatology. Despite of vascular lesion, she had enough peripheral circulation with good patency around the obstructive lesion, percutaneous transluminal angioplasty or stent insertion on obstructive lesion was not performed. She has been maintained her medication (Figure 4). Under this therapy, she has regular followed



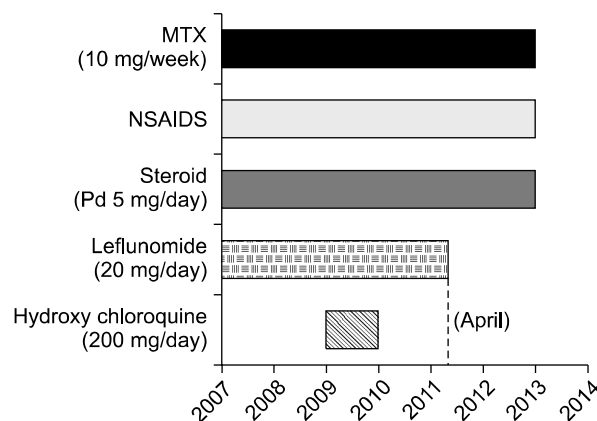
**Figure 3.** Catheter angiography shows infrarenal abdominal aortic stenosis with extensive collateral vessel formation. Although atherosclerosis commonly affects infrarenal abdominal aorta, atherosclerosis usually produces abrupt caliber changes just beyond stenosis sites; the smooth tapered nature of this stenosis favors TA.

up with no recurrence.

### Discussion

Takayasu's arteritis (TA) is a nonspecific large vasculitis, which induces occlusive or dilative lesions in the aorta, its main vessels, and pulmonary or coronary arteries (1). TA most frequently affects young Asian woman, with an age at onset usually between 10 and 40 years and median age at diagnosis of 28 years. The pathogenesis remains to be clarified but has been suggested that the vasculitis may deteriorate via autoimmune mechanism with infiltration of cytotoxic T lymphocyte and release of proinflammatory cytokines (2). This is the reason that TA is a rare pathology associated with other autoimmune disease, such as systemic lupus erythematosus and systemic sclerosis (2). Despite a similar pathogenesis with a prominent role of TNF-, the association between RA and TA is rare (3). The relationship between TA and RA remains unknown.

Despite its predominant articular manifestations, RA is a systemic disease often associated with organ-specific EAM (2). Rheumatoid vasculitis affects from <1% to 5% of RA patients and can occur in any organ, although about 90% of cases have cutaneous lesions (2). Commonly inflammation of the small- and medium-sized arteritis in the extremities may be seen, but aortic root changes and aortitis were reported in RA. RA associated aortitis is almost accompanied by severe extra-articular vasculitic manifestations with positive rheumatoid



**Figure 4.** Drug dosage and duration of treatment are shown.

factor (RF) and subcutaneous nodules (8). Although aortitis is rarely reported in patients with RA, necropsy data suggested that may be seen in up to 15% of cases (8).

In the previous reports of this disease, age at diagnosis of RA or TA, mucocutaneous, articular manifestations and rheumatoid factor were described (Table 1). In addition, results of genotype of human lymphocyte antigen (HLA) and type of involvement of large blood vessels in TA were described (4-14). According to the research on TA in 129 Korean patients, the most common clinical symptom of TA were headache (60%) and the second most common symptom is exertional dyspnea (42%) (15). But in this case, patient present with nonspecific respiratory symptoms and clinical symptoms variety as a cause of late diagnosed Takayasu's arteritis. The concurrent presence of Takayasu arteritis and rheumatoid arthritis (RA) is described in only few cases in the literature to date, these were often in female (18 females and 6 males), and the mean age at the time of RA diagnosis was  $46.5 \pm 14.3$  yr (range 16~74). The mean age at the time of TA diagnosis was  $52.1 \pm 15.7$  yr (range 20~82), and the age at diagnosis of TA in patients with RA have older than patients with isolated TA. Only 3 studies have reported case developed TA before RA (11,13), TA diagnosed after arthritis signs and symptoms in most cases. The average time elapsing between the onset of RA and the development of TA was 5.6 yr. Most of the patients had positive RF and subcutaneous nodules were detected. These studies found that clinical difference regarding arthritis and arthralgias in the course of TA may be attributable to a genetic background, as polymorphic HLA genes and their combinations may have had a role in modulating the clinical findings.

Despite the fact that there is still a debate on the exact nature of the coexistence of RA with TA, we suggest that it can be a very rare rheumatic disease entity or that the development

**Table 1.** Clinical characteristics of our case and previous case reports of coexisting RA and TA

References	Age/Sex	Age at diagnosis (years)		RF	Nodule	Erosion	HLA types	Involvement type	
		RA	TA					Angiography	Necropsy
Sanding et al. (5)	63/F	40	63	+	NR	NR	NR	I	NR
Sanding et al. (5)	65/F	55	65	+	+	NR	NR	I	NR
Falicov et al. (6)	16/F	16	20	NR		+	NR	I	NR
Reimer et al. (7)	49/F	44	49	+	+	NR	NR	NR	III
Rush et al. (8)	37/F	37	26	+	+	+	DR4	III	NR
Sketchler et al. (9)	53/F	50	53	NR	NR	NR	NR	I	NR
Mimura et al. (10)	50/F	48	50	+	NR	NR	NR	NR	III
Gravellese et al. (11)	61/F	50	61	+	+	NR	NR	NR	I
Gravellese et al. (11)	82/F	74	82	NR	NR	NR	NR	NR	I
Gravellese et al. (11)	68/M	47	68	+	+	NR	NR	NR	III
Gravellese et al. (11)	61/F	58	61	+	+	NR	NR	NR	I
Gravellese et al. (11)	52/F	26	52	+	+	NR	NR	NR	I
Gravellese et al. (11)	69/M	68	69	+	+	NR	NR	NR	Aortic root
Gravellese et al. (11)	60/M	48	60	+	+	NR	NR	NR	NR
Gravellese et al. (11)	46/M	37	46	+	+	NR	NR	NR	II
Gravellese et al. (11)	67/M	65	67	+	+	NR	NR	NR	III
Gravellese et al. (11)	64/F	61	64	+	+	NR	NR	NR	III
Towned et al. (12)	44/M	NR	44	+	+	+	NR	Aortic root	NR
Nakabayashi et al. (13)	64/F	60	64	+	NR	+	DR2, 12	III	NR
Jung et al. (14)	30/F	28	24	+	+	+	NR	NR	NR
Korkmaz et al. (15)	36/F	34	36	+	NR	+	DR4, 1	I	NR
Yokoe et al. (16)	50/F	46	39	+	NR	NR	NR	I	NR
Verweij et al. (17)	49/F	48	49	-	NR	NR	NR	I	NR
Our case	45/F	31	39	+	+	+	NR	III	NR

RA: rheumatoid arthritis, TA: Takayasu's arteritis, RF: rheumatoid factor, HLA: human leukocyte antigen, NR: not reported.

of these two diseases in our patient or other previously reported cases might be a complication of the chronic autoimmune inflammatory disease and a nonspecific vascular response to a generalized inflammatory process in association with genetic background predisposing to both RA and TA.

The genetic relationship between RA and TA is not yet clearly established. however, it has been shown that a considerable number of reported cases. Thus, physicians should consider that RA patients with extra-articular manifestations should be monitored carefully for the development of an occlusive arterial involvement such as TA.

Although coexistence of RA and TA were very rarely reported, the inter-relationship between these diseases as an EAM has controversies. The clinical characteristics of coexisting RA and TA were not well known. We found 23 other cases of RA overlapped with TA or aortitis in the English literature (4-14).

### Summary

We report the case of a Asian woman who was diagnosed with TA after being treated for RA for 8 years. As mentioned above, there is still a debate on the coexistence of RA with

TA, it can be a very rare rheumatic disease entity. Physicians should consider that RA patients with extra-articular manifestations should be monitored carefully for the development of an occlusive arterial involvement such as TA.

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