

[ CASE REPORT ]

## Organizing Pneumonia as the First Presentation in a Patient with Takayasu Arteritis: A Report of Rare Complication

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### Abstract:

A 48-year-old woman without any medical history visited an outpatient clinic with a chief complaint of cough persisting for more than 1 year and was diagnosed with organizing pneumonia. Computed tomography showed wall thickening with luminal stenosis of the main branch vessels of the aorta, and a detailed examination including fluorodeoxyglucose-positron emission tomography revealed Takayasu arteritis. There have been some reports of combined organizing pneumonia in similar vasculitis cases, but Takayasu arteritis and organizing pneumonia have not been reported to be associated. This case can be referred to when considering the association of lung lesions with Takayasu arteritis.

**Key words:** Takayasu arteritis, organizing pneumonia, fluorodeoxyglucose-positron emission tomography

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### Introduction

Takayasu arteritis is a vasculitis of unknown origin that causes inflammation of the aorta and its main branch vessels, resulting in vascular stenosis, occlusion, and dilatation. The ischemic lesion peculiar to the dominant organ of vascular stenosis or occlusion, or conversely, an aneurysm due to a dilated lesion is central to its clinical picture. Since clinical presentations differ depending on the dominant region of the blood vessel where the lesion occurs, various clinical symptoms manifest.

Respiratory symptoms appear in approximately 10.8% of patients with Takayasu arteritis (1). Recently, it has been reported that 6.3% to 25.9% of patients have pulmonary artery involvement (2, 3). In Takayasu arteritis, pulmonary artery involvement sometimes causes respiratory symptoms without visible pulmonary artery stenosis, pulmonary artery infarction, or pulmonary hypertension.

We herein report a case of Takayasu arteritis with organizing pneumonia.

### Case Report

A 48-year-old woman had experienced gradually worsening cough for more than 1 year. She visited a physician and underwent computed tomography (CT). An infiltration shadow was found in the left lower lung lobe, and organizing pneumonia was considered. She had no remarkable medical history and was not on any medication. She was a never-smoker. None of her family members had vascular or lung diseases.

On visiting our hospital, her height was 165 cm, and her weight was 54.0 kg. Her percutaneous oxygen saturation was 97% on room. Side-to-side differences in arterial blood pressure were recognized (right: 77/40 mmHg, left: 61/44 mmHg), and both were low. Claudication of the upper limb was not apparent, but the left radial artery was not palpable. Vascular murmurs were heard below the neck and right clavicle, and coarse crackles were heard in the lower left lung field. Mild bilateral leg edema was noted. Chest X-ray showed an infiltration shadow in the left lower lung field. No pulmonary congestion or heart enlargement was seen. An electrocardiogram demonstrated a normal sinus rhythm with no significant ST-T changes. The initial laboratory

**Table. Initial Laboratory Findings.**

|                  |   |   |             |
|------------------|---|---|-------------|
| Blood count      |   | Coagulation                               |             |
| White blood cell | 6,200 / $\mu$ L                         | PT  | 105 %       |
| Neutrophils      | 62.1 %                                  | APTT                                      | 32 sec      |
| Lymphocyte       | 25.6 %                                  | ESR (1h)                                  | 29 mm       |
| Monocyte         | 4.2 %                                   | ESR (2h)                                  | 65 mm       |
| Eosinophil       | 7.1 %                                   | Immuno-serological findings               |             |
| Red blood cell   | 449 $\times$ 10 <sup>4</sup> / $\mu$ L  | IgG                                       | 1,290 mg/dL |
| Hemoglobin       | 12.8 g/dL                               | IgG4                                      | 52.6 mg/dL  |
| Platelet count   | 39.0 $\times$ 10 <sup>4</sup> / $\mu$ L | ANA                                       | negative    |
| Biochemistry     |   | CH50                                      | 55.1 U/mL   |
| Total protein    | 7.4 g/dL                                | RF  | <5 IU/mL    |
| Albumin          | 3.9 g/dL                                | $\beta$ -D glucan                         | 7.4 pg/mL   |
| AST              | 17 IU/L                                 | <i>Aspergillus</i> -galactomannan antigen | <0.1        |
| ALT              | 8 IU/L                                  | <i>Cryptococcal</i> antigen               | negative    |
| LDH              | 150 IU/L                                | C7-HRP                                    | negative    |
| $\gamma$ -GTP    | 15 IU/L                                 | PR3-ANCA                                  | <0.5 U/mL   |
| T-Bil            | 0.4 mg/dL                               | MPO-ANCA                                  | <0.5 U/mL   |
| BUN              | 7 mg/dL                                 | KL-6                                      | 208 U/mL    |
| Creatinine       | 0.52 mg/dL                              | CEA                                       | 1.6 ng/mL   |
| Sodium           | 139 mEq/L                               | ProGRP                                    | 52.8 pg/mL  |
| Potassium        | 4.5 mEq/L                               | CYFRA 21-1                                | 2.6 ng/mL   |
| Chlorine         | 105 mEq/L                               |   |             |
| Uric acid        | 3.9 mg/dL                               |   |             |
| Creatine kinase  | 112 IU/L                                |   |             |
| CRP              | 0.53 mg/dL                              |   |             |
| Glucose          | 111 mg/dL                               |   |             |
| HbA1c            | 5.7 %                                   |   |             |

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase,  $\gamma$ -GTP:  $\gamma$ -guanosine triphosphate, T-Bil: total-bilirubin, BUN: blood urea nitrogen, CRP: C-reactive protein, HbA1c: hemoglobin A1c, PT: prothrombin time, APTT: activation partial thromboplastin time, ESR: erythrocyte sedimentation rate, IgG: immunoglobulin G, ANA: antinuclear antibody, CH50: haemolytic complement, RF: rheumatoid factor, C7-HRP: cytomegalovirus antigenemia, PR3-ANCA: proteinase3-antineutrophil cytoplasmic antibody, MPO-ANCA: myeloperoxidase-antineutrophil cytoplasmic antibody, KL-6: Krebs von den lungen-6, CEA: carcinoembryonic antigen, ProGRP: pro-gastrin-releasing peptide, CYFRA 21-1: cytokeratin-19 fragment

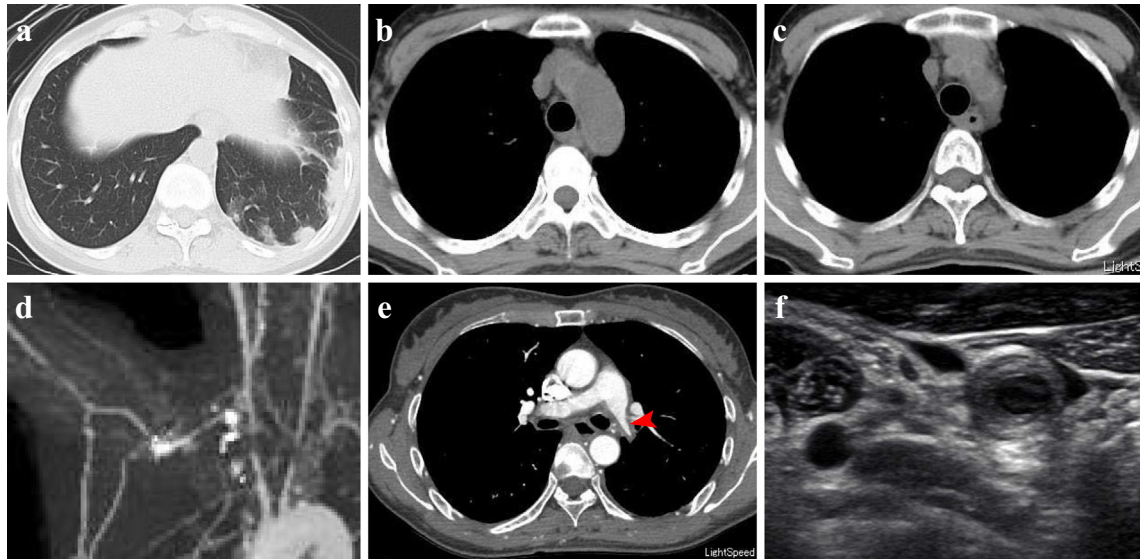
studies showed elevated platelet counts, C-reactive protein (CRP) levels, and erythrocyte sedimentation rate (ESR) (Table). There were no other findings suggesting infection, collagen disease, antineutrophil cytoplasmic antibody-associated vasculitis, or tumor. Transthoracic echocardiography revealed normal left ventricular contraction and no apparent valvular disease. There were no findings suggesting pulmonary hypertension. Chest CT showed a ground-glass shadow with a nodular infiltration shadow on the dorsal side of the left lower lobe (Fig. 1a). In addition, wall thickening of the aortic arch, brachiocephalic artery, left common carotid artery, and subclavian artery was found (Fig. 1b, c). Contrast-enhanced CT [three-dimensional multislice helical CT angiography (3D-CTA)] was performed to evaluate the vascular lesions. All images were acquired using a multi-detector row CT scanner with 64 detectors and a tiltable gantry. 3D-CTA showed stenosis and occlusion consistent with the thickened wall on plain CT (Fig. 1d). In addition, although not apparent on plain CT, wall thickening and stenotic lesions were found in the left lower lobe pulmonary artery (Fig. 1e).

Carotid artery ultrasonography revealed high-echoic and

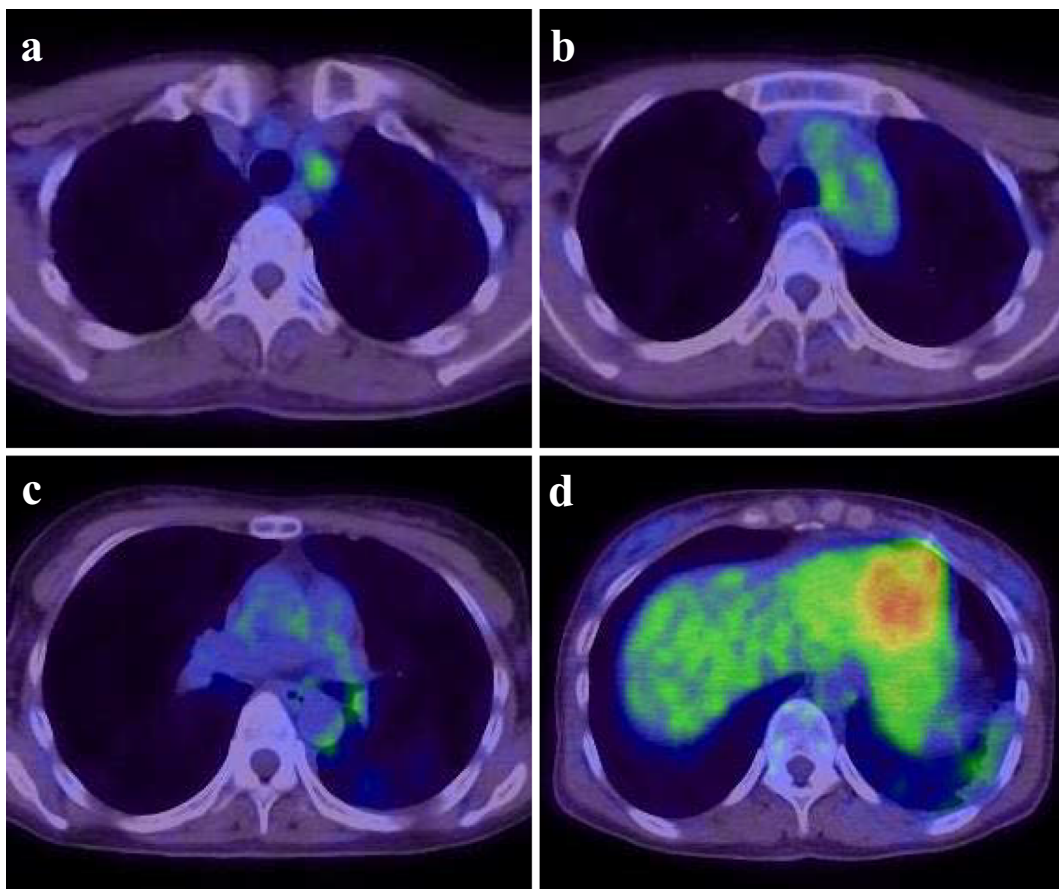
circumferential wall thickening of bilateral internal carotid arteries, described as the “macaroni sign” (4) (Fig. 1f). Fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed a high accumulation in the vascular wall where wall thickening and stenosis were found on contrast-enhanced CT (Fig. 2a, b). Similarly, an enhanced tracer uptake in the left lower lobe pulmonary artery and left lower lobe perimeter were seen (Fig. 2c, d). Based on the Japanese Circulation Society 2017 criteria (5), the definitive diagnosis of Takayasu arteritis was made. Immunosuppressive treatment for Takayasu arteritis requires the exclusion of infectious diseases, so pneumonia images were further examined using a bronchoscope.

Transbronchial lung biopsy specimens showed intra-alveolar spaces containing fibrin deposition and formation of fresh fibroblast foci as signs of organizing pneumonia (Fig. 3).

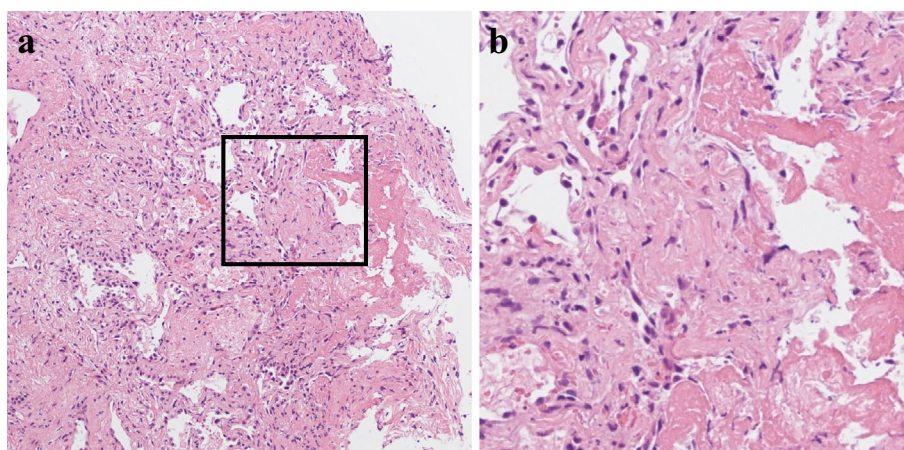
For the treatment, methylprednisolone was started at 30 mg/day. Promptly after the start of the treatment, the CRP concentration and ESR returned to normal, and palpation of the left radial artery improved. The blood pressure in the



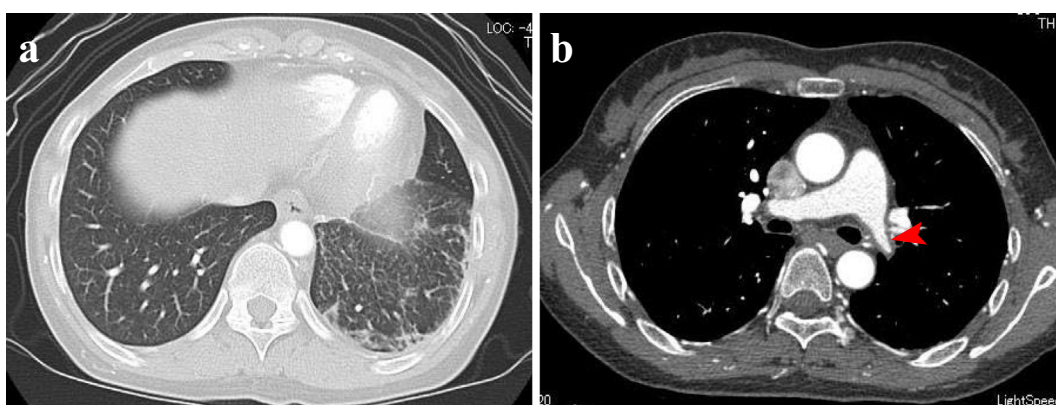
**Figure 1.** Computed tomography (CT) shows a ground-glass shadow with a nodular infiltration shadow on the dorsal side of the left lower lobe (a) and wall thickening of the aortic arch (b), brachiocephalic artery, left common carotid artery, and subclavian artery (c). The anterior view of three-dimensional multislice helical CT angiography shows stenosis and occlusion of the carotid and subclavian arteries (d). Contrast-enhanced CT shows wall thickening and stenotic lesions in the left lower lobe pulmonary artery (arrowhead) (e). Ultrasonography of the right internal carotid artery shows high-echoic and circumferential wall thickening (f).



**Figure 2.** Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). FDG PET/CT shows inflammation of the left common carotid artery (a) and aortic arch (b). The uptake of  $^{18}\text{F}$ -FDG can be seen in the lower lobe pulmonary artery (c) and left lower lobe perimeter (d).



**Figure 3.** Transbronchial lung biopsy specimens show intra-alveolar spaces containing fibrin deposition and the formation of fresh fibroblast foci as signs of organizing pneumonia. a: Low-power view, b: High-power view.



**Figure 4.** Contrast-enhanced computed tomography after one year of methylprednisolone therapy. Pneumonia showed significant improvement (a). However, no marked improvement was seen in the vascular lesions (arrowhead) (b).

arm was 94/52 mmHg on the right and 84/48 mmHg on the left. The dose was gradually reduced to 15 mg while checking for relapse of the inflammatory response. After one year, chest CT was performed again, showing the significant improvement of pneumonia compared to that in the previous examination. However, no marked improvement was seen in vascular lesions (Fig. 4).

## Discussion

We herein report a patient with Takayasu arteritis complicated by organizing pneumonia. Pulmonary lesions associated with Takayasu arteritis are mainly pulmonary artery stenosis or occlusion, and other pulmonary lesions are extremely rare, although acute interstitial pneumonia (6) and pulmonary fibrosis (7) have been reported. Rayner et al. (8) described an 18-year-old woman with Takayasu arteritis diagnosed using angiography who developed pneumonic consolidation that was unresponsive to antibiotics but cleared with prednisone. However, in the present case, whether or not the lung lesion was interstitial pneumonia, particularly

organizing pneumonia, was unclear. In addition, some patients with Takayasu arteritis have been diagnosed with interstitial or other pneumonia, despite their histopathology containing granulation tissues (9). To our knowledge, this is the first case report proving the complication of Takayasu arteritis and organizing pneumonia.

Approximately 25% of cases of polyarteritis nodosa (PAN), which is a similar disease to Takayasu arteritis, have respiratory lesions (10), and organizing pneumonia can occur (11). In microscopic polyangiitis (MPA), the lung is a vulnerable organ, and diffuse alveolar hemorrhaging and pulmonary fibrosis are the most frequent manifestations (12). With MPA, the complication of organizing pneumonia has been reported (13). Takayasu arteritis causes inflammation of the aorta and its main branch vessels, i.e. large arteries, whereas PAN is a disease in which inflammation occurs in the blood vessel wall, mainly of medium-sized arteries. MPA is a disease that causes necrotizing vasculitis primarily in small blood vessels, such as capillaries, venules, and arterioles, and occasionally in medium-sized arteries. The pathogenesis of organizing pneumonia in PAN

and MPA are unclear, but one prevalent theory suggests that neutrophils get activated and injure localized endothelial and alveolar epithelial cells in response to proinflammatory cytokines (14). Organizing is a phenomenon in which granulation tissue surrounds and absorbs pathological substances, such as blood clots and necrotic tissue. The elastic arteries become inflamed in Takayasu arteritis. A characteristic of the pulmonary artery is that the elastic artery extends from the trunk of the pulmonary artery to a fairly peripheral pulmonary artery, unlike the body artery where the elastic artery is limited to the aorta and large branches. Therefore, in Takayasu arteritis, inflammation occurs even in the peripheral pulmonary arteries. Furthermore, unlike the systemic circulation system, the pulmonary artery, which is a low-pressure system, is likely to be occluded by thrombi. These findings suggest that inflammation may spread to the peripheral pulmonary artery wall, resulting in micropulmonary infarction, alveolar hemorrhaging, and fibrin deposited during the healing process, leading to organizing pneumonia. In some cases of Takayasu arteritis, biopsy results of the pneumonia-like lesions indicated hemorrhagic infarction accompanied by fibrinoid necrosis of the small vessels and infiltration of inflammatory cells (3). In the current case, we found inflammatory wall thickening and stenosis in the proximal part of the left lower lobe pulmonary artery but no evidence of vasculitis in the peripheral part. However, repeated micropulmonary infarctions may have occurred due to vasculitis. It seems difficult to separate pneumonia-like symptoms or findings from visible pulmonary artery stenosis in CT or angiography. These findings may only differ with regard to whether the arterial lesion is proximal or distal. In addition, the effects of responses to inflammatory cytokines associated with arterial inflammation may also need to be considered.

Organizing pneumonia is associated with various diseases, and causes such as drugs, collagen diseases, radiation pneumonitis, malignant diseases (such as lymphoma), non-bacterial infections (such as tuberculosis and non-tuberculous mycobacterial disease and mycoplasma), and vasculitis are considered. When encountering a lung infiltrate refractory to antibiotics, the cause should be identified while considering the possibility of organizing pneumonia. Vasculitis is also a cause of organizing pneumonia, so it should be evaluated by myeloperoxidase-antineutrophil cytoplasmic antibody measurement, angiography by contrast CT, and FDG-PET. <sup>18</sup>F-FDG, the typical radiopharmaceutical used for FDG-PET, accumulates at sites of active inflammation. Therefore, FDG-PET is useful for diagnosing the lesions of Takayasu arteritis and their inflammatory activity (15).

In conclusion, we encountered a case of combined Takayasu arteritis and organizing pneumonia. Although elucidating the mechanism underlying organizing pneumonia

was not possible in this case, it was suggestive in considering the lung lesions of Takayasu arteritis, and we have reported it with some opinions.

**The authors state that they have no Conflict of Interest (COI).**

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