A CASE REPORT

A Case of Concurrent Sarcoidosis, Aortitis Syndrome and Crohn’s Disease

Koichi Izumikawa¹, Noriko Motoi², Hisashi Takaya¹, Atsushi Miyamoto¹, Yoshinobu Eishi³, Kunihiko Yoshimura¹ and Kazuma Kishi¹

Abstract

A 24-year-old man was referred to our hospital due to bilateral hilar lymphadenopathy on chest radiography. He had been under medication for aortitis syndrome and Crohn’s disease for 12 years. Surgical biopsy from the anterior segment of the left upper lobe and mediastinal lymph nodes was performed under video-assisted thoracoscopic. Histopathological examination revealed epithelioid cell granulomas without caseous necrosis, compatible with sarcoidosis. Full sequence analysis of the CARD15 gene, which is reportedly related to the formation of granulomatous lesions in Crohn’s disease and sarcoidosis revealed no mutation of CARD15 gene. This is the first report of concurrent sarcoidosis, Crohn’s disease and aortitis syndrome in an individual.

Key words: sarcoidosis, aortitis syndrome, Crohn’s disease

(Intern Med 50: 2915-2917, 2011)

DOI: 10.2169/internalmedicine.50.5298)

Introduction

Sarcoidosis and Crohn’s disease are both inflammatory disorders characterized by granuloma formation of unknown origin (1, 2). In sarcoidosis, granulomatous lesions develop systemically, whereas in Crohn’s disease granulomas are formed mainly in the gastrointestinal system not in the lung (1, 2). Aortitis syndrome also known as Takayasu arteritis is a chronic vasculitis with undetermined etiology. It primarily affects the aorta and its primary branches; it has been estimated that 150 new cases occur each year in Japan (3). We describe herein the first case of concurrent sarcoidosis, Crohn’s disease and aortitis syndrome.

Case Report

A 24-year-old asymptomatic man was referred to Toranomon Hospital in July 2004 due to bilateral hilar lymphadenopathy on chest radiography (Fig. 1) during regular follow-up for aortitis syndrome and Crohn’s disease, which developed in 1992 and 2003, respectively. He had complained of persistent fever and joint aches in 1991. After several intensive examinations for etiology, arteriography was performed in 1992. Abnormalities such as wall irregularity of the thoracic aorta, narrowing of the abdominal aorta and proximal subclavian artery with some areas of dilatation, and stenosis of the left renal artery were found. These findings were compatible with aortitis syndrome. In 2003, diarrhea, oral ulcer and subcutaneous nodules of the right shoulder had emerged. Colonoscopy revealed longitudinal and aphthous ulcers with skipped lesions in the ileum and colon (Fig. 2). The biopsy of the colon demonstrated epithelioid cell granulomas and these findings were consistent with Crohn’s disease. Oral prednisolone (5-7.5 mg/day every other day) had been administered since 1992 and mesalazine was added after the diagnosis of Crohn’s disease. The condition of both aortitis syndrome and Crohn’s disease was stable with these treatments.

On admission, the vital signs of the patient were as follows: body temperature, 36.8°C; heart rate, 74 beats/minute with a regular rhythm; SpO₂, 98% (on room air); and blood pressure, 138/98 mmHg. Physical examination on admission revealed obesity (height, 158.7 cm; weight, 75.0 kg) and

¹Department of Respiratory Medicine, Respiratory Center, Toranomon Hospital, Japan, ²Department of Pathology, Toranomon Hospital, Japan and ³Department of Human Pathology, Tokyo Medical and Dental University, Japan

Received for publication February 9, 2011; Accepted for publication July 26, 2011

Correspondence to Dr. Koichi Izumikawa, koizumik@nagasaki-u.ac.jp
Cushingoid appearance caused by long-term steroid treatment. No abnormal respiratory sounds were heard in either the right or left lung field. No signs of systemic lymphadenopathy, hepatosplenomegaly, or pre-tibial edema were seen. Laboratory findings on admission were: white blood cell count, 5,100/μL; C-reactive proteins, 0.2 mg/dL; erythrocyte sedimentation rate, 5 mm/hr; serum angiotensin-converting enzyme, 26.8 U/L (normal range: 7.0-25.0 U/L) and serum lysozyme, 8.7 mg/L (5.0-10.2 mg/L). Chest computed tomography also showed swelling of bilateral hilar and mediastinal lymph nodes, ground-glass opacities and small nodular lesions (diameter, 1-2 cm) in both upper lobes (Fig. 3a, b). Although electrocardiography showed normal sinus rhythm, 24-hr continuous electrocardiography indicated atrioventricular block of Mobitz type I (Wenckebach’s block). Gallium-67 scintigraphy revealed typical Panda sign, in which an accumulation of radioisotope was noted in the parotid glands, peripheries of both eyes, supraclavicular regions, and right upper mediastinum. Pulmonary function testing showed no abnormalities. Tuberculin skin test was negative. Bronchoalveolar lavage and transbronchial lung biopsy were performed under bronchoscopy, but no findings typical of sarcoidosis were observed. Lung tissues from the anterior segment of the left upper lobe and mediastinal lymph nodes were resected under video-assisted thoracoscopic surgery. Histopathological examination revealed epithelioid cell granulomas without caseous necrosis, compatible with sarcoidosis, in both lung specimens and lymph nodes (Fig. 4a, b). Since no new clinical symptoms were found, the same dose of oral prednisolone (5 mg/day, every other day) was continuously administered. However, due to deterioration of Crohn’s disease at the end of 2004, prednisolone was increased to 30 mg/day temporarily and gradually tapered along with improvement of Crohn’s disease. Bilateral hilar and mediastinal lymph nodes, ground-glass opacities and small nodular lesions in both upper lobes were gradually improved and disappeared by three years after diagnosis (2007). Oral prednisolone (2 mg/day) has been continuously administered since 2008 and no deterioration of aortitis syndrome, Crohn’s disease and sarcoidosis have occurred to date.

**Discussion**

Overlapping disorders of sarcoidosis and Crohn’s disease, Crohn’s disease and aortitis syndrome, and sarcoidosis and aortitis syndrome have been previously reported in 33, 18 and 5 cases, respectively (4-6). However, to our knowledge, no concurrent case of all three diseases has previously been

---

**Figure 1.** Chest radiography on admission. Bilateral hilar lymphadenopathy with ground-glass opacities in both lung fields was seen.

**Figure 2.** Colonoscopy demonstrated longitudinal ulcers from the sigmoid colon through the terminal ileum.

**Figure 3.** Chest computed tomography on admission. a) Ground-glass opacities and small nodular lesions in the anterior segment of the left upper lobe. b) Bulging of hilar and mediastinal lymph nodes.
Figure 4. Pathological findings of resected specimens by video-assisted thoracoscopic surgery. a) Lung tissues. b) Lymph node. Note formation of epithelioid cell granulomas and giant cells without necrosis, compatible with sarcoidosis. Hematoxylin and Eosin staining, magnification ×400.

reported. Although both sarcoidosis and Crohn’s disease are characterized by the formation of epithelioid cell granulomas, sarcoidosis is not generally associated with gastrointestinal complications, nor is Crohn’s disease associated with lung diseases including bilateral hilar and mediastinal lymphadenopathy (1, 2).

CARD15 (or NOD2), a member of the growing family of nucleotide-binding oligomerization domain (NOD) proteins regulating cellular apoptosis, has recently been found to cause granuloma formation (7). The CARD15 product comprises 2 amino-terminal caspase recruitment domains (CARDs), one NOD and carboxyl-terminal leucine-rich repeats (LRRs) (8). Frameshift mutations in LRRs and mutations in the NOD of CARD15 are reportedly linked with Crohn’s disease and Blau syndrome, respectively (9, 10). Mutations to LRRs in Crohn’s disease would cause impairment in bacterial component-dependent NFκB activation, whereas mutations of the NOD in Blau syndrome promote bacterial component-independent activation of NFκB, causing granuloma formation (7).

We performed full sequence analysis of all 11 exons of the CARD15 gene (EMBL accession number AJ303140) using DNA extracted from a blood sample from the patient. No previously reported missense or frameshift mutations were observed.

Weiler et al (6) reported that sarcoidosis generally preceeds aortitis syndrome and the time lag between the diagnosis of sarcoidosis and that of aortitis syndrome is several years (eight or more) in most of the patients in concurrent cases of sarcoidosis and aortitis syndrome. Although aortitis syndrome preceded sarcoidosis, there was a 14-year time-lag between the diagnoses in the current case which matched a previous report.

In conclusion, this is the first case of concurrent sarcoidosis, Crohn’s disease and aortitis syndrome. However, no mutation of the CARD15 gene, which is involved in granuloma formation, was found.

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

References