Systemic Sarcoidosis with Significant Granulomatous Swelling of the Pharyngeal Tonsil

Yukiko Onishi*, Yasufumi Imai**, Hitoshi Tojima***, Kotaro Nakajima**** and Atsushi Takahashi*****

A pharyngeal tonsil biopsy specimen from a 27-year-old male revealed epithelioid cell granulomas with noncaseating necrosis. Systemic enlargement of the lymph nodes was present. Plain chest radiographic and computed tomography (CT) images showed ground-glass attenuation in the lungs and bilateral hilar lymphadenopathy. Biopsy of inguinal region nodes confirmed the diagnosis of systemic sarcoidosis. Detailed examination of the nasopharynx should be performed in any case presenting with systemic sarcoidosis because the specimen is readily removable and the pathologic findings of the local lesion may support the diagnosis.


Key words: epipharyngeal sarcoidosis, sarcoid granuloma, rhinolaryngologic biopsy

Introduction

Sarcoidosis is a systemic noncaseating granulomatous disease of unknown etiology predominantly involving lymph nodes, lungs, eyes and skin, with the lesions indistinguishable from those of other granulomatous conditions (1, 2). Head and neck involvement in sarcoidosis including the upper respiratory tract occurs as an isolated phenomenon or coexists with systemic disease (3), and, on rare occasions, diffuse tracheal stenosis results from sarcoidosis (4). In systemic sarcoidosis, the upper respiratory tract may be involved more frequently than generally believed, as rhinolaryngologic examinations are rarely done in these cases (3). We report a case of systemic sarcoidosis in which the pharyngeal tonsil exhibited significant swelling and a granular surface.

Case Report

A 27-year-old Japanese male was first seen in Hitachi General Hospital on October 31, 1995 with complaints of low-grade fever, malaise, and inguinal lymph node swelling with tenderness. The patient had been well until about one year before admission, when he began to complain of loss of appetite and malaise, and there had been an 8 kg weight loss in the previous half year. In September 1995, low-grade fever, headache, enlargement of the bilateral inguinal lymph nodes with tenderness, and numbness of the bilateral toes became apparent. There were no nasopharyngeal symptoms. Physical examination findings included a body temperature of 36.8°C, a full and strong pulse of 80/min with a regular rate, and blood pressure of 116/64 mmHg. Neither pathologic breath sounds nor a heart murmur was heard. There were no abdominal abnormalities. No skin eruption was detected. The lymph nodes of the cervical, axillary, and inguinal regions were palpable. Several lymph nodes in the bilateral inguinal regions were swollen to thumb tip size, and the patient complained of tenderness on palpation of these nodes. No wound of the lower extremities was found. Other than the dysesthesia of the bilateral toes, there were no neurologic abnormalities.

Urinalysis was normal. Peripheral blood data were as follows: white blood cell count (WBC) 5,400/mm³ (band form neutrophils 12%, segmented neutrophils 59%, eosinophils 2%, basophils 1%, monocytes 8%, lymphocytes 18%), red blood cell count (RBC) 540x10⁶/mm³, platelet count 23.2x10⁶/mm³, hemoglobin 16.0 g/dl. Total protein was elevated to 8.4 g/dl with an increased γ-globulin fraction (albumin 57.8%, α₁-globulin 2.9%, α₂-globulin 9.7%, β-globulin 8.9%, γ-globulin 20.7%). Immunoglobulin tests showed no abnormalities: immunoglobulin (Ig)G 1,970 mg/dl, IgA 283 mg/dl, IgM 156 mg/dl, IgG 1,970 mg/dl, IgA 283 mg/dl, IgM 156 mg/dl, C3 98 mg/dl and C4 43 mg/dl. Lactate dehydrogenase (LDH) was high, 899 IU/l. Angiotensin-converting enzyme was slightly elevated to 24.2 IU/l (normal range 8.3 IU/l to 21.4 IU/l). The serum calcium, phosphorus, sodium, chloride, potassium, C-reactive protein (CRP), erythrocyte sedimentation rate

From **the Department of Internal Medicine, ***the Department of Otorhinolaryngology, ****the Department of Radiology and *****the Department of Pathology, Hitachi General Hospital, Hitachi, *present address: the Third Department of Internal Medicine, University of Tokyo, Tokyo
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Reprint requests should be addressed to Dr. Yukiko Onishi, the Third Department of Internal Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655

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(ESR), serum lysozyme, and 1,25-(OH)2 vitamin D values were all within normal range. Serologic tests for rheumatoid factor and antinuclear antibodies were normal. Antibodies to human immunodeficiency virus (HIV) and human T cell leukemia virus were not present in sera. Syphilis test results were negative. The Mantoux reaction was negative and Mycobacterium tuberculosis cultures of sputum and nasal exudates were negative. Blood, urine, nasal exudate and sputum cultures revealed no significant bacteria. Respiratory function tests and Holter electrocardiogram showed no abnormalities. Chest radiography showed swelling of the bilateral hilar lymph nodes and ground glass attenuations of the right upper lobe, and the left upper and lower lobes of the lungs (Fig. 1).

A computed tomographic (CT) scan of the chest revealed multiple and systemic, occasionally conglomerated swelling of the lymph nodes of the superior mediastinal, anterior mediastinal, bilateral hilar, right axillary, and periaortic regions, up to walnut size. Diffuse interlobular septal attenuation was seen in the bilateral lung fields representing coalescent minute granulomas. Irregular-shaped ground-glass opacifications without cavitation were disclosed in both lungs, consistent with the chest radiograph. Thickening of bronchovascular bundles with accumulation of densities was seen in the right upper lobe (Fig. 2).

CT findings of the abdomen included swelling of lymph nodes in the hepatoduodenal, parapancreatic, and iliac regions. There was moderate splenomegaly. Furthermore, CT scans of the neck and throat revealed swelling of multiple lymph nodes and thickening in the posterior nasopharyngeal wall, and CT scan of the nasopharynx was carried out disclosing diffuse swelling of the posterior wall of the epipharynx (Fig. 3). A gallium scintigram showed swelling of the bilateral hilar and inguinal lymph nodes, but no significant changes in the lung fields.

Rhinolaryngologic examinations confirmed the diffuse thickening of the epipharynx which had been noted on the CT scan. The surface of the swollen tegmentum (Tonsilla pharyngea) was granular in appearance, being indistinguishable from a malignant lymphoma or a squamous cell carcinoma. On the other hand, the nasal mucosa including the Rosenmüller fossa, the opening of the auditory tube, and bilateral palatine tonsils showed no granulomatous change. Chronic maxillary sinusitis

Figure 1. Chest X-ray showing ill-defined ground-glass densities in the right upper lobe (arched arrow) and left upper and lower lobes (arrows) of the lungs. Bilateral hilar lymphadenopathy is seen.

Figure 2. Thickening of bronchovascular bundles and accumulation of granular densities (arrow) can be seen in the lungs.

Figure 3. CT scan of the nasopharynx showing diffuse swelling of the posterior wall of the epipharynx (arrow). Chronic maxillary sinusitis is seen on the right side.
was recognized on the right side. There were no granulomatous findings in other areas of the ear-nose-throat system.

On ophthalmologic examination, granulomatous uveitis was seen in both eyes, although the patient did not complain of visual disturbance. Cerebrospinal fluid examination was normal. Sural nerve conduction velocity was slightly decreased indicating peripheral neuropathy of the lower extremities. These clinical findings were considered to be attributable to sarcoidosis, although the hallmark granuloma had not yet been disclosed at this point.

Pathologic examination of small specimens obtained from the epipharyngeal tonsil revealed accumulation of epithelioid cell granulomas. These granulomas were composed of a small, sharply delimited collection of epithelioid cells including Langhans giant cells surrounded by an ill-defined zone of lymphocytes, plasma cells and histiocytes (Fig. 4). Further histological study of the lymph nodes biopsied from the bilateral inguinal regions demonstrated an accumulation of multiple epithelioid cell granulomas without caseating necrosis. Cell surface marker analysis by flow cytometry and southern blot analysis of DNA using lymph node cells revealed no clonal proliferation of lymphocytes.

Thus, based on the clinical and pathologic observations, the diagnosis of systemic sarcoidosis was made. The pulmonary attenuation was estimated to represent accumulation of sarcoid granulomas of interstitial tissue. Dysesthesia of the toes disappeared after resection of the swollen inguinal lymph nodes. Administration of antibiotics improved the chronic maxillary sinusitis and also ameliorated the low-grade fever and headache. The patient’s appetite was restored, and his weight is currently stable. Although he suffers occasional low-grade fever and malaise, his general condition has been good to date. Prednisolone has not been administered as there are no symptoms of pulmonary or cardiologic disorders, and no evidence of neurosarcoïdosis. The epipharyngeal sarcoïd granuloma remains stable showing neither progression nor regression. The ground-glass attenuation of the lung and the bilateral hilar lymphadenopathy has shown no change to date.

Discussion

Sarcoidosis is a multisystem granulomatous disorder of unknown cause. Presenting features of sarcoidosis are protein, ranging from asymptomatic but abnormal findings on chest radiography in many patients to progressive multiorgan failure in an unfortunate minority (5). On chest radiography, pulmonary involvement with enlargement of the hilar lymph nodes and swelling of the peripheral lymph nodes are demonstrated as early signs. However, virtually any organ or tissue may be involved in cases with disseminated granulomas. Symptoms caused by pulmonary, cardiac, neural, gastrointestinal, hepatic, renal, cutaneous, ophthalmic, and endocrine involvement manifest in the later stage of the disease (1, 2). It is noteworthy that many cases appear to be asymptomatic and are diagnosed only when enlarged hilar nodes are seen on chest radiography or, more often, when respiratory symptoms or nonspecific features such as fever, fatigue and weight loss, as in the present case, develop (4).

Sarcoidosis of the ear-nose-throat system is relatively rare, accounting for 2–18% of generalized sarcoidosis cases (4–6), and can affect the ear and temporal bones, sinonasal region, salivary glands, pharynx, tonsils and larynx (3–14). Among cases of ear-nose-throat sarcoidosis, nasal mucosal lesions are frequently recognized (69%), while laryngeal and pharyngeal involvement is less frequent (15%) (4). Nasal cavity involvement is present in all cases with laryngeal and pharyngeal involvement (4). The present case did not have cutaneous involvement, in contrast to the high prevalence of skin invasion in reported cases (92%) with ear-nose-throat sarcoidosis (4).

Only a small number of cases with nasopharyngeal involvement of sarcoidosis have been reported to date. However, the actual number of such cases may be underestimated, because rhinolaryngologic examinations are not generally performed in patients with systemic sarcoidosis (3). However, patients with sarcoidosis often initially seek treatment from an otorhinolaryngologist, because the earliest signs and symptoms of sarcoidosis may be identical to those of other forms of chronic sinonasal inflammation (10). In the present case, CT scans delineated the epipharyngeal granulomatous change very clearly, but malignant lymphoma or squamous cell carcinoma could not be ruled out without a histopathologic examination. Interestingly, the granulomatous lesion was limited to the tegmental tonsillar tissue of the epipharynx, while no sarcoidosis was noted in the nasal mucosa, palatine tonsils, or in other rhinolaryngologic tissues, in the present case.

Although the cause of sarcoidosis remains obscure, its development is attributed to an excessive, antigen-driven cellular immune response occurring within target organs which promotes nonspecific systemic inflammation (15). Since the pharyngeal tonsil is exposed to antigens in inspired air, immune activation may have occurred at this site, subsequently leading to systemic sarcoidosis. In this respect, it merits empha-
size that a careful and detailed rhinolaryngologic examination including biopsy of the nasopharynx should be performed routinely in any patient suspected to have systemic sarcoidosis, because the lesion can be biopsied, and even excised without difficulty via a rhinologic approach.

References