Sarcoidosis with Bilateral Epididymal and Testicular Lesions

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Abstract

We report a case of genital sarcoidosis that presented characteristic features on MRI. A 25-year-old man sarcoidosis patient with ocular and lung lesions presented a painful mass in the left scrotum together with systemic symptoms of fever, appetite loss, headache, and stomachache during the tapering of steroids. The patient was hypercalcemic, and this was thought to be the cause of his systemic symptoms. MRI showed multiple nodules of bilateral testes and enlargement of bilateral epididymis; the patient was diagnosed with testicular and epididymal lesions of sarcoidosis. An increased steroid dosage improved his hypercalcemia and genital lesions.

Key words: MRI, hypercalcemia, epididymitis

Introduction

Sarcoidosis is a systemic disease characterized by the presence of non-caseous epithelioid cell granulomas in all affected tissues. The prevalence of sarcoidosis varies from fewer than 1 to 64 cases per 100,000 people, depending on the country, area, and race evaluated (1). A variety of clinical manifestations may hinder the epidemiological evaluation. Hyperimmune response at the lesion sites is thought to be the principal pathophysiology, but the causative agents are still unknown. All of the organs but the adrenal gland have been reported to be involved, and the most frequently affected organ is the lung. According to the description by Katz (2), the disease clears spontaneously within 1 to 2 years in 60% to 80% of patients with stage I sarcoidosis. Radiographic resolution can even be expected in a substantial number of patients with stage II or stage III sarcoidosis, though some develop irreversible pulmonary fibrosis. In a series of 337 pulmonary sarcoidosis cases examined by Nagai et al (3), overall clearance rates of shadows on chest radiograph were 34% within 1 year from detection, 64% within 3 years, 72% within 5 years, and 76% within 10 years. On this basis, we can assess symptoms persisting into the fifth year as pulmonary sarcoidosis in the chronic stage. At the time of detection in Nagai’s series, the following features were more characteristic in the patients whose shadows ultimately persisted than in those whose shadows cleared up: a higher mean age, stage II or higher, the presence of symptoms, the presence of extrathoracic lesions, and a previous history of treatment with corticosteroids. The organs involved and the course of the disease differ greatly between countries, areas, races, and individuals (4). Though hypercalcemia has been considered rare in Japanese sarcoidosis patients, Hamada et al found that nearly 40% of patients had increased levels of ionized calcium (5). In the female reproductive system, asymptomatic granulomatous lesions can occur in any organ, though the uterus is most commonly affected (6). The male reproductive tract is rarely affected, and testicular lesions are rare. We report a case of systemic sarcoidosis with bilateral epididymal and testicular lesions, and review previous reports on genital sarcoidosis.

Case Report

In April 2001, a 25-year-old Japanese man visited a clinic for a cold and was found to have bilateral hilar lymphadenopathy and multiple nodules in both lung fields on a chest X-ray. He was clinically diagnosed with sarcoidosis the following month at another hospital, based on findings of bilateral enlargement of parotid glands, left supraclavicular lymph node swelling, and uveitis. In June he began showing ophthalmic symptoms and was placed on oral betamethasone at an initial dose of 4 mg/day. When his ophthalmic symptoms improved the betamethasone was tapered. However, in August 2001, when the betamethasone dose stood at 0.5 mg every other day, he began to suffer several new symptoms. On September 18, he was admitted to our hospital due to loss of appetite, fever, headache, stomachache and a left scrotal
Table 1. Laboratory Tests on Admission

<table>
<thead>
<tr>
<th>Test Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td></td>
</tr>
<tr>
<td>White blood cell</td>
<td>5.6x10^7/\mu l</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>4.8x10^7/\mu l</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>14.8 g/dl</td>
</tr>
<tr>
<td>Platelet</td>
<td>240x10^7/\mu l</td>
</tr>
<tr>
<td>Tumor markers</td>
<td></td>
</tr>
<tr>
<td>HCG</td>
<td>&lt;0.5 mIU/ml</td>
</tr>
<tr>
<td>AFP</td>
<td>&lt;3.0 ng/ml</td>
</tr>
<tr>
<td>CA19-9</td>
<td>48 U/ml</td>
</tr>
<tr>
<td>CEA</td>
<td>&lt;1.0 ng/ml</td>
</tr>
<tr>
<td>Serology</td>
<td></td>
</tr>
<tr>
<td>CRP (0.3)</td>
<td>0.4 mg/dl</td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>12.7 mg/dl</td>
</tr>
<tr>
<td>β2-MG (8.5–9.9)</td>
<td></td>
</tr>
<tr>
<td>ACE (8.3–21.4)</td>
<td>39.4 IU/\mu l</td>
</tr>
<tr>
<td>1,25-(OH)_2-Vitamin D (20–60)</td>
<td>104 pg/ml</td>
</tr>
<tr>
<td>Ionized calcium (1.1–1.34)</td>
<td>1.67 mM</td>
</tr>
<tr>
<td>KL-6 (≤500)</td>
<td>673 U/ml</td>
</tr>
<tr>
<td>Arterial blood gas (room air)</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.502</td>
</tr>
<tr>
<td>PaCO_2</td>
<td>33.0 mmHg</td>
</tr>
<tr>
<td>PaO_2</td>
<td>104.0 mmHg</td>
</tr>
<tr>
<td>HCO_3^-</td>
<td>25.6 mmol/l</td>
</tr>
<tr>
<td>Bronchoalveolar lavage (right B'b)</td>
<td></td>
</tr>
<tr>
<td>Recovery</td>
<td>95/150 ml</td>
</tr>
<tr>
<td>Total cell count</td>
<td>2.93x10^7/\mu l</td>
</tr>
<tr>
<td>Macrophage</td>
<td>64.2%</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>34.9%</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>0.9%</td>
</tr>
<tr>
<td>CD4/CD8 ratio</td>
<td>4.5</td>
</tr>
</tbody>
</table>


Figure 1. Chest X-ray (A, the first presentation; B, on admission; C, after the increase of steroid dosage). The mediastinal and hilar lymph node swelling and nodular shadows in the right upper and left middle lung fields were exacerbated on admission, and later improved after the steroid dosage was increased.
mass with pain. Physical examination revealed a body temperature of 37.0°C, blood pressure of 108/72 mmHg, and pulse of 104/min with a regular rhythm. Heart and lung auscultation and neurological examination were normal. Liver was palpable beneath the right costal margin. Bilateral parotid glands were slightly enlarged. Right cervical and supraclavicular lymph nodes were enlarged to 1 cm and 1.5 cm, respectively. A movable tender nodule of 1 cm in diameter was palpable in the left scrotum. The patient had no history of smoking or previous illnesses. The laboratory tests (Table 1) showed mild elevation of CRP (0.4 mg/dl). Serum angiotensin converting enzyme (39.4 IU/l), KL-6 (673 U/ml), and soluble IL-2 receptor (3,220 U/ml) were moderately elevated, and 1,25-(OH)2-vitamin D (104 pg/ml) and ionized calcium (1.67 mM) were markedly elevated. PPD skin test (0.05 µg i.d.) was negative. Serum human chorionic gonadotropin and α-fetoprotein were within normal range, and urinary N-acetyl-β-D-glucosaminidase and β; microglobulin were mildly elevated. Arterial blood gas revealed mild hypocapnia (PaCO2 33.0 mmHg). Pulmonary function tests were within the normal range. Bronchoalveolar lavage fluid showed an increased total cell recovery (2.93×10⁷/ml), with a decrease in the macrophage ratio (64%), an increase in the lymphocyte ratio (34%), and an increase in the neutrophil ratio (0.9%). The CD4/CD8 ratio in BALF was elevated to 4.5. Electrocardiogram and Holter electrocardiogram revealed no abnormality. Chest X-ray on admission (Fig. 1B) showed mediastinal and hilar lymph node swelling and nodular shadows in the right upper and left middle lung fields. In comparison with the findings of his first presentation at the previous hospital (Fig. 1A), his lymph nodes were further enlarged and his nodular shadows were more extensive. Chest computed tomography (Fig. 2) showed nodular shadows along the bronchovascular bundles on the right upper lobe. Transbronchial lung biopsy (Fig. 3 A, B) revealed non-caseous epithelioid cell granuloma and multinuclear giant cells. A postauricular lymph node biopsy performed simultaneously also revealed epithelioid cell granuloma. Ga scintigram (Fig. 4) showed uptake in bilateral parotid glands, the hilum and mediastinum, bilateral supraclavicular lymph nodes, and around the left scrotum. MRI of testis on admission (Fig. 5A) showed enlargement of bilateral epididymis, and multiple testicular lesions de-

![Figure 2. Chest CT. Nodular shadows in the right upper lobe are seen along the bronchovascular bundles.](image)

![Figure 3. (A, B) Transbronchial lung biopsy at right B2 (HE stain, ×100). Non-caseous epithelioid cell granulomas and polynuclear giant cells (arrows) were found.](image)
Testicular Sarcoidosis

- Anterior 2
- Posterior 2

Figure 4. Ga scintigram. Uptake was seen on bilateral parotid glands, the hilum and mediastinum, bilateral supraclavicular lymph nodes, and around the left scrotum.

We encountered a patient with systemic sarcoidosis who initially presented with pulmonary, ocular, parotid, and lymph node lesions. The patient was given oral steroids due to exacerbated uveitis. As the steroid was being tapered, the patient became hypercalcemic, his pulmonary and lymph node lesions relapsed, and new bilateral testicular and epididymal lesions appeared. An increase in the steroid dosage improved these lesions, and the steroid is now being tapered again.

Genital lesions are rare in sarcoidosis cases. Clinically they are diagnosed in approximately 0.5% of cases (7, 8), and at autopsy they appear in fewer than 5% of cases (7, 9). Most of the lesions involve the epididymis, and far fewer appear in the testes. According to one report (10), testicular lesions are diagnosed clinically in fewer than 0.2% of all sarcoidosis cases. In a review of the literature, we found reports of only 1 case in Japan (11) and 14 cases in other countries. According to a review of 12 cases by Toyoshima et al (11), 10 cases were blacks and 9 had unilateral lesions. The unilateral lesions were mostly painless, and multiple lesions in organs such as the epididymis, lung, articular and skin were often seen. Differential diagnoses of the testicular mass include testicular tumor, metastatic tumor, tuberculosis, syphilis, lymphogranuloma inguinale, fungal infections, and Wegener’s granulomatosis. As with the primary tumors of the testes, most of the metastatic tumors are unilateral.

It is important to differentiate genital lesions of tuberculosis due to the similarity to sarcoidosis. In almost all cases of testicular tuberculosis, epididymal lesions coexist (12) and the sarcoidosis may co-present with tuberculosis (13). Definitive diagnosis is based on transinguinal testicular biopsy or castration. When benign disease is suspected, preservation of the testis by testicular biopsy is recommended. Leydig cell dysfunction due to testicular lesions and ductal obstruction due to epididymal lesions can result in infertility (14, 15), but the frequency with which this occurs is unknown.

Many cases respond to corticosteroid therapy, but there is no consensus on the indication or effect of therapy to preserve reproductive function. Like other cases, the present patient presented multiple organ involvement. However, none of the previous cases of testicular sarcoidosis presented with hypercalcemia. Based on our experience, hypercalcemia in sarcoidosis rarely causes symptoms as severe as those we encountered in the present case.

There are no reports on the MRI findings of testicular lesions of sarcoidosis. However, when testicular nodules are seen bilaterally, or in combination with an epididymal lesion, or in patients with systemic sarcoidosis, benign diseases such as sarcoidosis or tuberculosis are suspected (16). Thus, we diagnosed the condition as testicular and epididymal lesions of the genital lesion. The steroid is now being tapered, albeit very slowly to avoid a relapse.

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of sarcoidosis. Among the reported cases of testicular lesions, including bilateral lesions, the size of the nodules ranges from several millimeters to 3 cm. It seems that MRI is very useful for the diagnosis of testicular sarcoidosis, a condition that generally should not be diagnosed by computed tomography. More cases should be investigated to establish the utility of MRI definitively.

As epididymal lesions of sarcoidosis are also known to be a potential cause of epididymitis with pain (17), combined epididymitis was suspected. The present patient had already sired a child before the onset of the disease, hence the effect of the lesions on fertility remains unclear. The lesions responded well to steroid therapy, but we are carefully observing him as we taper the steroid, or the patient may experience another relapse of the type encountered the last time the steroid was being tapered. In previous reports on testicular sarcoidosis, at least two other cases developed testicular lesions after steroids had been withdrawn (for a period ranging from several weeks to one year).

In conclusion, our experience with this case of sarcoidosis with bilateral testicular and epididymal lesions suggests that MRI is very useful for the diagnosis of genital sarcoidosis.

References

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Testicular Sarcoidosis