CASE REPORT

Scrotal mass and unilateral lung masses with pleural effusion mimicking metastatic testicular malignancy: an unusual presentation of sarcoidosis

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SUMMARY

Involvement of the genitourinary tract by sarcoidosis may present with a scrotal mass, mimicking infection or malignancy. Sarcoidosis is a systemic granulomatous disease that affects patients of both sexes worldwide. Sarcoidosis of the genitourinary tract is rare. We describe a case of a 33-year-old African-American man who presents with a scrotal mass, mediastinal mass, unilateral lung masses and pleural effusion mimicking testicular malignancy with pulmonary metastases. The histopathological examination of the right testis and lung biopsy revealed granulomatous inflammation consistent with sarcoidosis. Genitourinary sarcoidosis must be a diagnostic consideration, especially in an African-American patient with a scrotal mass. There is a possible association between sarcoidosis and testicular malignancy; hence, underlying malignancy should always be ruled out. Serum tumour markers, ACE, a biopsy of the accessible tissue and intraoperative frozen section analysis aid in establishing the diagnosis of sarcoidosis and leading to appropriate management.

BACKGROUND

Sarcoidosis is an idiopathic granulomatous disorder with a wide spectrum of organ involvement having worldwide distribution and affecting all racial and ethnic groups. Non-caseating granulomas are the hallmark histological feature.¹ Sarcoidosis involving the genitourinary tract is rare. We report an unusual case of sarcoidosis in a 33-year-old African-American man, who presents with a scrotal mass, asymmetric lung involvement and unilateral pleural effusion mimicking metastatic testicular malignancy.

CASE PRESENTATION

A 33-year-old African-American man with an 8-month history of right upper chest pain, non-productive cough and a significant weight loss presented with a complaint of a right testicular mass discovered by his wife. Physical examination revealed increased fremitus and rhonchi in the right upper lobe of the lung and visible and palpable 2 cm fixed, irregularly shaped, non-tender right epididymal and testicular mass. The small ill-defined non-tender mass measuring less than 1 cm was palpated in the left scrotum. A 1.5 cm right inguinal lymph node was also palpable.

INVESTIGATIONS

A scrotal ultrasound revealed an ill-defined hypoechoic lesion involving the right epididymis and

testis. A CT scan of the chest showed a large right hilar and a mediastinal mass with right bronchial obstruction, scattered right upper lobe nodules involving the pleural surface and a mild to moderate right pleural effusion (figure 1). These findings were interpreted as being consistent with malignancy. The serum tumour markers—lactate dehydrogenase (LDH), β -human chorionic gonadotropin (β -HCG) and α -fetoprotein (AFP) were within the normal limits.

Owing to high suspicion of malignancy, a right radical orchiectomy was performed. Gross examination revealed a firm, enlarged mass with a tan, nodular cut surface involving the epididymis and testis. Intraoperative frozen section analysis of the mass revealed non-caseating granulomatous inflammation. Mycobacterial and fungal cultures were performed on the mass and were negative. Extensive microscopic examination showed non-caseating granulomas involving the epididymis and testis without any evidence of malignancy (figure 2). Subsequently, biopsies of the right upper lobe lung lesions revealed non-caseating granulomatous inflammation. The right bronchial washings revealed multinucleated giant cells and histiocytes consistent with granulomatous inflammation. The tissue special stains for acid-fast organisms and fungi were negative. These findings were consistent with sarcoidosis.

Pertinent laboratory values included reversal of CD4/CD8 ratio with a value of 0.80 (normal >1.0), non-reactive rapid HIV test and HIV ELISA, and increased ACE value of 80 U/l (normal range 9–67 U/l).

TREATMENT

The patient responded to oral prednisone with alleviation of chest pain, significant improvement of the right lung parenchymal disease, dramatic decrease in the mediastinal and hilar masses and a complete resolution of the right pleural effusion.

DISCUSSION

Sarcoidosis is a granulomatous disorder involving a variety of organs. Aetiology is unknown but has been linked to immune dysregulation in individuals with genetic predisposition after exposure to specific environmental or infectious antigenic agents. The antigen-mediated activation of CD4 T-cells leads to clonal proliferation and expression of chemokines and cytokines, causing accumulation of histiocytes and granuloma formation.¹ This

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Figure 1 Chest CT scan showing the right side moderate pleural effusion (A) with mediastinal and the right lung masses (A and B).

widespread sequestration of CD4 T-cells is manifested clinically as inverted CD4/CD8 ratio as seen in our patient. Effusion fluid in a case of pleural sarcoidosis shows increased CD4/CD8 ratio reaffirming the role of CD4 T-cells in the pathogenesis of this disease.²

In the USA, African-Americans have approximately threefold higher annual incidence of sarcoidosis when compared to Caucasian patients.³ Acute presentations with more severe disease are characteristically seen in African-American patients. The associated morbidity and mortality is significantly higher in African-Americans.⁴

The thoracic involvement is the most common manifestation of sarcoidosis and is seen in more than 90% of patients. A high resolution CT scan is highly sensitive in the detection and characterisation of thoracic sarcoidosis. The symmetrical involvement of hilar lymph nodes is the most common manifestation followed by lung parenchymal involvement. In 75–90% of the cases, lung parenchymal involvement is visualised as micronodules with a perilymphatic distribution. Atypical involvement by the lung nodules and masses is seen in 15–25% of the lung sarcoidosis cases. Pleural involvement is seen only in 1–4% of the thoracic sarcoidosis cases. Pleural involvement is manifested as exudative or transudative effusions. The patient had

atypical lung parenchymal and pleural involvement associated with effusion.^{1 5}

Extrathoracic sarcoidosis is seen in 50% of the patients and commonly involved sites in a decreasing order of incidence are skin, eyes, lymph nodes, liver, spleen and nervous system. Genitourinary sarcoidosis is seen in less than 0.2% of all clinically diagnosed cases.^{6 7} Epididymis and testis are the most commonly involved genitourinary organs. Kodama *et al*⁸ reviewed 60 cases of biopsy-proven male reproductive tract sarcoidosis published until 2003. Since then, eight more cases of genitourinary sarcoidosis, including this case, have been reported. Approximately 60% of these patients are African-Americans and most of them are in the age group of 20–40 years. Most of these patients did not have a history of sarcoidosis. Approximately 75% of the patients had epididymal involvement and up to 50% had testicular involvement. Scrotal swelling and pain were the most commonly presenting symptoms; cases of azoospermia owing to testicular sarcoidosis have also been reported. A radical orchiectomy was performed in one-third of the cases.

There is a controversial yet intriguing association between sarcoidosis and malignancy. Multiple observational and epidemiological studies have shown temporal or concomitant association of sarcoidosis and malignancies.^{9 10} This association was more frequent with lymphomas than solid malignancies, leading to the term sarcoidosis lymphoma syndrome.¹¹ The inherent biases associated with the case series and the epidemiological studies have raised a debate regarding the association of sarcoidosis and malignancy. Misclassification of either sarcoidosis or malignancy has been considered to be a significant confounding factor in many studies.^{12 13} Moreover, a phenomenon described as sarcoid reaction is quite frequently associated with malignancies.¹⁴ Sarcoid reaction is a non-caseating granulomatous response most commonly seen in the lymph nodes draining the tumour, but can also be seen in the organ in which the tumour originates and in distant organs. Sarcoid reaction is proposed to be an immunological response to the disintegrated tumour antigens.¹⁵

Figure 2 Microscopic examination demonstrating non-caseating granulomatous inflammation in the right testis (A, magnification $\times 200$; B, magnification $\times 400$), the right epididymis (C, magnification $\times 200$) and the right lung (D, magnification $\times 400$).

The major differential diagnosis in a scrotal mass is testicular malignancy. Sarcoidosis is usually a benign and self-limiting disease and hence it is important to differentiate it from testicular malignancies. Both involve patients of the same age group. There is a possible association between sarcoidosis and malignancy. Studies have shown either concomitant diagnosis of testicular malignancy and sarcoidosis or diagnosis of sarcoidosis in follow-up of testicular malignancy, possibly as a reaction to testicular malignancy or treatment.^{16 17}

The possible association of sarcoidosis and malignancy could pose problems in the management of patients with suspected testicular sarcoidosis. The main goal in patients suspected of having testicular sarcoidosis is to rule out an underlying malignancy.¹⁸ Laboratory tests for serum tumour markers associated with the germ cell testicular malignancies (LDH, AFP, β -HCG) and serum ACE can be helpful in differentiating testicular cancer and sarcoidosis. Serum ACE is increased in 75% of the untreated patients with active sarcoidosis, but not in the testicular cancer patients.¹⁹ Inguinal exploration with the frozen section analysis can be helpful in establishing the diagnosis of sarcoidosis and ruling out malignancy. In patients with localised disease, who wish to preserve fertility, excision of the lesion with maintenance of organ function can be attempted. Orchiectomy should be favoured for any equivocal cases with atypical presentation, indeterminate pathological findings, or diffuse testicular involvement where index of suspicion for malignancy is high.¹⁸

Learning points

- ▶ Genitourinary sarcoidosis is rare, but should be considered in the differential diagnosis of urological conditions, especially in African-American patients.
- ▶ In the cases of suspected testicular sarcoidosis, it is always important to rule out an underlying malignancy.
- ▶ The laboratory assays and intraoperative frozen section analysis aid in establishing the diagnosis of sarcoidosis and ruling out malignancy.

Competing interests None.

Patient consent Obtained.

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