

# Concomitant pulmonary sarcoidosis and HIV infection

## A case report

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### Abstract

**Rationale:** Sarcoidosis is an immune-mediated systemic disease, and the increase in CD4+ T lymphocyte cells is considered as a key factor for the development of sarcoidosis. The acquired immune deficiency syndrome (AIDS) is well known as the impaired immune system and characterized by relative lack of CD4+ T lymphocytes. Thus, the coexistence of sarcoidosis and HIV infection has rarely been reported.

**Patient concerns:** A 65-year-old female patient was admitted to our respiratory ward complained of fatigue, chest distress, and a persistent dry cough for 2 months.

**Diagnoses:** The chest computed tomography scan showed diffuse reticulonodular infiltrates and mediastinal and hilar lymphadenopathy. Fiberoptic bronchoscopy along with transbronchial biopsy and transbronchial needle aspiration was performed. The pathological findings revealed noncaseating granulomas, and the patient was found to be HIV-seropositive through enzyme-linked immunosorbent assay and confirmed as HIV by the centers for disease control and prevention.

**Interventions:** The patient was administered oral methylprednisolone 20 mg/day for pulmonary sarcoidosis and then referred to the hospital for infectious diseases receiving subsequent treatment for HIV.

**Outcomes:** clinical symptoms relieved 3 months later after treatment.

**Lessons:** The coexistence of sarcoidosis and HIV infection is rare because of paradoxical roles of CD4-positive T cells in the pathogenesis of AIDS and sarcoidosis.

**Abbreviations:** AIDS = acquired immune deficiency syndrome, CT = computed tomography, HAART = highly active antiretroviral therapy, HIV = human immunodeficiency virus, IRIS = immune reconstitution inflammatory syndrome.

**Keywords:** AIDS, HIV infection, pulmonary sarcoidosis

## 1. Introduction

The acquired immune deficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV) infection leading to high mortality without effective treatment, which has drawn increasing concerns globally.<sup>[1,2]</sup> It is characterized by

progressive loss of CD4-positive T cell and immunological abnormalities, which usually leads to increased risks of opportunistic infection. Sarcoidosis is an immune disorder disease featured with granulomas formation with exact cause. Pulmonary is one of the most commonly involved organs in sarcoidosis. Factors for the development of sarcoidosis include genetic predisposition triggered by bacteria, viruses, dust, or chemicals, which lead to over reaction of immune system, and then formation of granulomas consisted of immune cells, especially CD4-positive T cell. Owing to paradoxical roles of CD4-positive T cells in the pathogenesis of AIDS and sarcoidosis, concomitant AIDS and sarcoidosis are rare.<sup>[3]</sup> Here, we report a female patient with pulmonary sarcoidosis and HIV infection in China.

## 2. Case presentation

A 65-year-old female patient was admitted to our respiratory ward complained of fatigue, chest distress, and a persistent dry cough for 2 months. Physical examinations including skin, eyes, and nervous system were normal. The chest computed tomography (CT) scan showed diffuse reticulonodular infiltrates and mediastinal and hilar lymphadenopathy (Fig. 1). Laboratory tests including the complete blood count, leukocyte differential count, serum electrolytes including calcium, myocardial enzyme, tumor biomarkers, liver function, and renal function were

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**Informed Consent:** Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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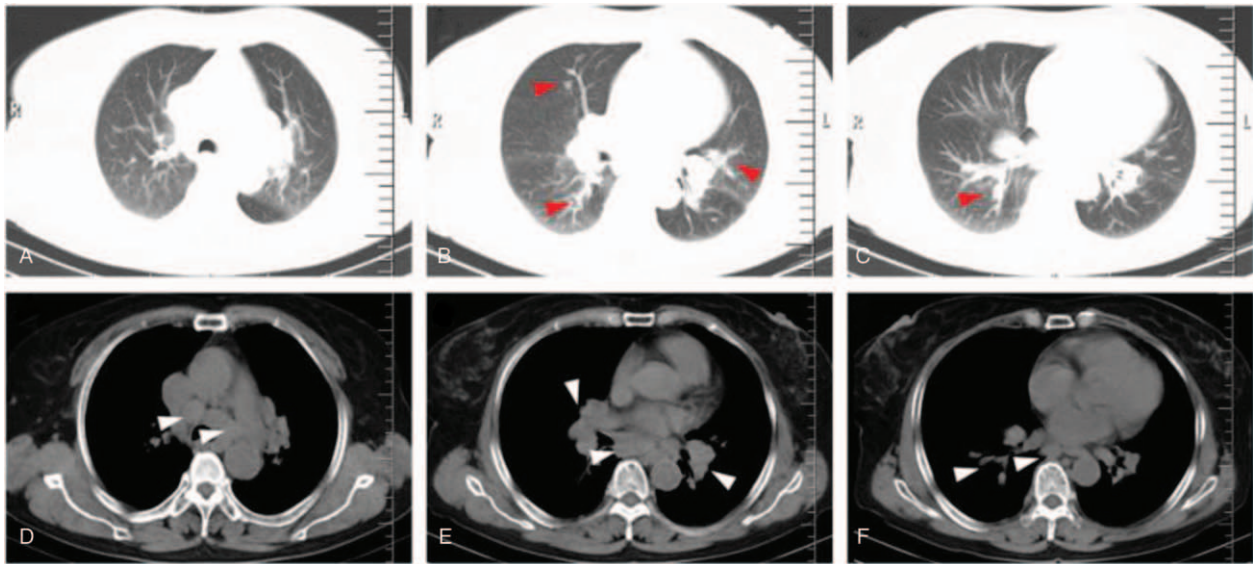
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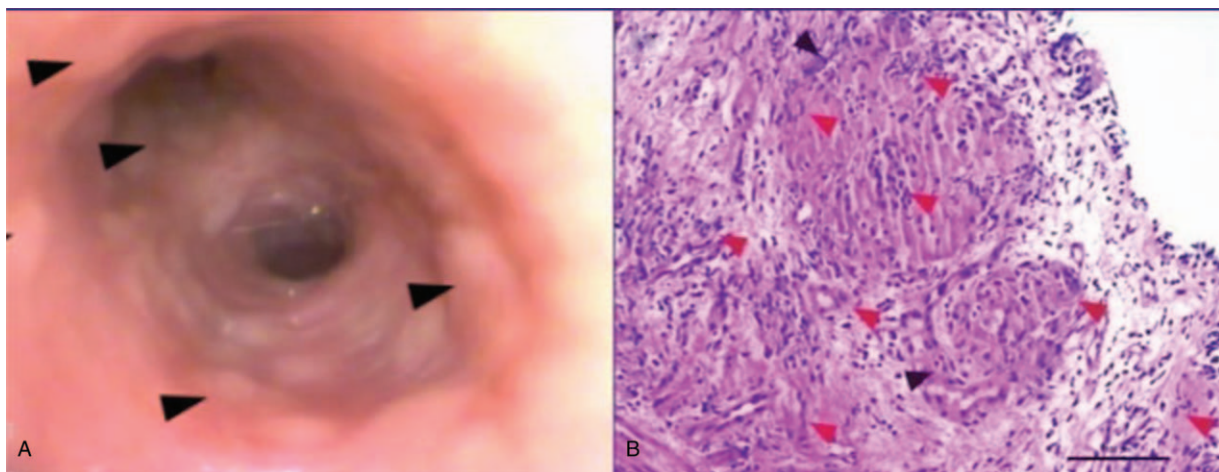
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**Figure 1.** The images of computed tomography scan showed diffuse reticulonodular infiltrates, mediastinal and hilar lymphadenopathy (A–F).

revealed normal. Both the number of blood CD4-positive T cells and CD4/CD8 ratio were in normal range. Electrocardiogram was normal. Pulmonary function tests showed moderately reduced diffusion capacity of the lung carbon monoxide and forced vital capacity. Fiberoptic bronchoscopy along with transbronchial biopsy and transbronchial needle aspiration was performed. Multiple nodules in bronchial mucosa were seen and the pathological findings showed noncaseating granulomas (Fig. 2). The diagnosis of sarcoidosis was considered. Further tests were done for differential diagnosis. Acid-fast bacilli in sputum, tuberculin skin test, and T-Spot test were performed to exclude tuberculosis. And all these results were negative. Subsequent cultures performed on blood and sputum were negative for bacteria, mycobacteria, fungi. Serological investigations of respiratory viruses were also negative. The serum angiotensin-converting enzyme revealed an increased level, 116 UI/mL (normal value, <50 UI/mL). Abdominal CT was normal.

During the hospitalization, the patient was found to be HIV-seropositive through enzyme-linked immunosorbent assay and confirmed as HIV by the centers for disease control and prevention. Therefore, this patient was finally diagnosed as having pulmonary sarcoidosis and AIDS. A regimen of 20 mg oral methylprednisolone once daily was administered and the patient was asked to follow-up every 2 weeks at the outpatient department. Then the patient was referred to the hospital for infectious diseases receiving subsequent treatment for HIV infection. Three months later, we did a telephone follow-up. The patient's clinical manifestations including fatigue, chest distress, and a persistent dry cough were relieved obviously about 2 weeks after the administration of methylprednisolone and the regimen was gradually tapered to a maintenance dose of 8 mg orally once daily. Highly active antiretroviral therapy (HAART) was started for the treatment of HIV infection. Both the condition of pulmonary sarcoidosis and HIV infection were stable so far.



**Figure 2.** Multiple nodules were seen in bronchial mucosa (A). Histological findings of transbronchial needle aspiration revealed noncaseating granulomas (B). (Hematoxylin-eosin stain, original magnification  $\times 400$  magnified).

The symptoms of pulmonary sarcoidosis did not aggravate during HAART.

### 3. Discussion

HIV infection can alter immune response and lead to immune disorder disease with granuloma formation.<sup>[4,5]</sup> However, because of the paradoxical roles of CD4-positive T cells in the pathogenesis of AIDS and sarcoidosis, coexistence of these 2 diseases is rare. Sarcoidosis and HIV infection are both characterized by a reduction in circulating CD4-positive T lymphocytes. In patients with HIV infection, the number of blood CD4 T cell is progressively destroyed leading to increased risks of infections.<sup>[6]</sup> The reduction of circulating CD4 T cells in patients with sarcoidosis is because of their accumulation in granuloma formation, and high activity of CD4 T cells is the key factor of the development of granuloma.<sup>[7,8]</sup> Thus, coexistence of sarcoidosis and HIV infection was infrequently reported. However, with the coming of HAART era, the occurrence of immune reconstitution inflammatory syndrome (IRIS) is more commonly observed after HAART in patients with AIDS.<sup>[9]</sup> Sarcoidosis was sometimes diagnosed in HIV patients after receiving HAART.<sup>[10]</sup> It is considered that the increased numbers of CD4-positive T cells with high activity in IRIS may play a role in the development of sarcoidosis.<sup>[11–13]</sup> There were 55 cases reported with coexistence of AIDS and sarcoidosis, 14 of those before the HAART era.<sup>[14]</sup> Miranda et al reviewed these cases and found that 13 patients who presented with sarcoidosis preceded HIV infection revealed the CD4+ T cell counts above 200 cells/ $\mu$ L. And interestingly, in the remaining 1 patient who was diagnosed with HIV infection before sarcoidosis, the CD4+ T cell count was  $>600$  cells/ $\mu$ L.<sup>[15]</sup> In our case, the patient was diagnosed with sarcoidosis and HIV infection nearly at the same time, and presented with normal range of CD4-positive T cells. Like the cases reported before, there were no significant differences between the clinical presentation, radiological characteristics, and pathology of sarcoidosis in patients with HIV infection and that of noninfected patients.<sup>[16,17]</sup> The patient's clinical manifestations were relieved obviously about 2 weeks after the administration of methylprednisolone and did not aggravate after the initiation of HAART. The condition of both pulmonary sarcoidosis and HIV infection was stable so far and was still in follow-up.

Up to now, it is considered that coexistence of these 2 diseases without HAART might be “an occurrence of 2 independent conditions in the same patient rather than a causal relationship between the 2 diseases.”<sup>[15]</sup> However, this conclusion was based on current case reports. The underlying mechanisms of the development of sarcoidosis in AIDS need further investigation. One thing we should be concerned about is that sarcoidosis symptoms could be worse after HAART as the CD4+ cell count raises, which requires close attention from physicians during treatment.<sup>[17]</sup>

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### Author contributions

**Supervision:** Cheng Yusheng

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### References

- [1] Salehi B, Kumar NVA, Şener B, et al. Medicinal plants used in the treatment of human immunodeficiency virus. *Int J Mol Sci* 2018;19: pii: E1459.
- [2] Deeks SG, Overbaugh J, Phillips A, et al. HIV infection. *Nat Rev Dis Primers* 2015;1: 15035.
- [3] Wurm K, Ewert G, Löhr G. Sarcoidosis complicated by HTLV III-infection: steroid therapy in combination with thymostimulin. *Sarcoidosis* 1987;4:68–70.
- [4] Fauci AS. Multifactorial nature of human immunodeficiency virus disease: implications for therapy. *Science* 1993;262:1011–8.
- [5] Maggi E, Mazzetti M, Ravina A, et al. Ability of HIV to promote a TH1 to TH0 shift and to replicate preferentially in TH2 and TH0 cells. *Science* 1994;265:244–8.
- [6] Gowda KS, Mayers I, Shafran SD. Concomitant sarcoidosis and HIV infection. *CMAJ* 1990;142:136–7.
- [7] Lowery WS, Whitlock WL, Dietrich RA, et al. Sarcoidosis complicated by HIV infection: three case reports and a review of the literature. *Am Rev Respir Dis* 1990;142:887–9.
- [8] Amin DN, Sperber K, Brown LK, et al. Positive Kveim test in patients with coexisting sarcoidosis and human immunodeficiency virus infection. *Chest* 1992;101:1454–6.
- [9] Shelburne SA3rd, Hamill RJ, Rodriguez-Barradas MC, et al. Immune reconstitution inflammatory syndrome: emergence of a unique syndrome during highly active antiretroviral therapy. *Medicine (Baltimore)* 2002;81:213–27.
- [10] Foulon G, Wislez M, Naccache JM, et al. Sarcoidosis in HIV-infected patients in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2004;38:418–25.
- [11] Naccache JM, Antoine M, Wislez M, et al. Sarcoid-like pulmonary disorder in human immunodeficiency virus-infected patients receiving antiretroviral therapy. *Am J Respir Crit Care Med* 1999;159:2009–13.
- [12] Almeida FAJr, Sager JS, Eiger G. Coexistent sarcoidosis and HIV infection: an immunological paradox. *J Infect* 2006;52:195–201.
- [13] Gomez V, Smith PR, Burack J, et al. Sarcoidosis after antiretroviral therapy in a patient with acquired immunodeficiency syndrome. *Clin Infect Dis* 2000;31:1278–80.
- [14] Miranda EJ, Leite OH, Duarte MI. Immune reconstitution inflammatory syndrome associated with pulmonary sarcoidosis in an HIV-infected patient: an immunohistochemical study. *Braz J Infect Dis* 2011;15: 601–6.
- [15] Trevenzoli M, Cattelan AM, Marino F, et al. Sarcoidosis and HIV infection: a case report and a review of the literature. *Postgrad Med J* 2003;79:535–8.
- [16] Viroit E, Duclos A, Adelaide L, et al. Autoimmune diseases and HIV infection: a cross-sectional study. *Medicine (Baltimore)* 2017;96:e5769.
- [17] Ibrahim IA, Estaitieh OM, Alrabee HA, et al. Sarcoidosis and HIV infection in a native Saudi man. *BMJ Case Rep* 2018;doi:10.1136/bcr-2018-224386.