Pulmonary Coccidioidomycosis After a Renal Transplant in a Nonendemic Region

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Abstract
Coccidioidomycosis is a fungal infection caused by the Coccidioides species, endemic to the southwestern United States. In healthy people, manifestations range mainly from asymptomatic to mild influenzalike signs, whereas in immunosuppressed patients (eg, transplant recipients) this infection is often a severe disseminated disease. We report a case of primary pulmonary coccidioidomycosis in a 61-year-old man with a renal transplant 7 months earlier. The patient had nonspecific symptoms of pulmonary infection, including weakness, anorexia, and weight loss. Both spherules and endospores of Coccidioides immitis were seen histologically after a transbronchial biopsy of a cavitary lesion. The patient was treated with amphotericin B. At the time of this writing (8 months), he remains disease free.

Key words: Coccidioides immitis, Fungal infection, Solid-organ transplant

Introduction
Coccidioidomycosis is a pulmonary mycosis caused by inhalation of fungal spores from the diphasic fungus, and C. immitis. The organism is endemic to the southwestern United States, northern and central Mexico, and regions of Central and South America.1,2 Approximately 100,000 infections occur in the United States each year.3,4 Most infected patients have no symptoms and recover without evidence of persistence disease. Primary pulmonary infection may be acute, persistent, chronic fibrocavitary, chronic progressive, and nodular, with or without, cavities. Risk factors for coccidioidomycosis include older age; living in, or travel to, an endemic area; or an immunosuppressed state.4,5,6 The unsuspected diagnosis of coccidioidomycosis eventually is made based on identifying the filamentous fungus in mycologic culture of the lung tissue, and presence of the typical spherules with endospores upon histopathologic examination.1,5

Certain populations are at higher risk for dissemination, including persons with compromised cellular immunity. This group includes patients with human immunodeficiency virus, patients undergoing immunosuppression for rheumatologic disorders, and patients receiving antirejection therapy after organ transplant.1,6

We report a case of primary pulmonary coccidioidomycosis in a 61-year-old man with a renal transplant 7 months earlier. To the best of our knowledge, this is the first reported case in Turkey.

Case Report
A 61-year-old man with a history of chronic glomerulonephritis and resultant end-stage renal disease had a renal transplant from deceased donor in April 2011. The donor was a 49-year-old man who died of injuries sustained in a motor vehicle accident. The surgery and postoperative course were uneventful. The patient was discharged on posttransplant day 9 with a serum creatinine concentration of 1.6 μmol/L. His immunosuppressive regimen consisted of mycophenolate mofetil, prednisone, and tacrolimus. Seven months after transplant, the patient presented to our institution with weakness, anorexia, and weight loss of 4 weeks’ duration.
The results of a physical examination were normal. All of his laboratory findings were within normal limits. A high-resolution computed tomography of the chest showed an irregular, thick-walled, cavitary lesion in the inferior lobe of the right lung (Figure 1A). A transbronchial biopsy of a cavitary lesion was performed; histopathology showed granulomatous inflammation with epithelioid cells, Langhans giant cells, and lymphocytes (Figure 2A). Necrosis was seen in the center of some granulomas. Conversely, acute suppurative inflammation with neutrophilic infiltrates were detected around the granulomas (Figure 2B). In the serial sections, many thick-walled, round spherules that contained endospores could be seen within the neutrophilic infiltrates and the necrotic zones (Figure 2C). Periodic acid-Schiff stain highlighted the spherule wall and the endospores, which were consistent with *C. immitis*.

Treatment with amphotericin B had been started empirically before the histopathologic diagnosis and was continued for 3 weeks. After 3 weeks, high-resolution computed tomography was performed showing that the cavitary lesion in the right inferior lobe had been almost totally healed (Figure 1B). Currently, his renal functional tests are within the normal limits, with a serum creatinine concentration of 1.6 μmol/L.

**Discussion**

*C. immitis* is a dimorphic fungus endemic to the desert regions of the southwestern United States. Infections are acquired by inhaling airborne arthrospores. The symptoms in most immunocompetent persons range from none to a mild or moderate flulike illness. Infections are acquired by inhaling airborne arthrospores. The symptoms in most immunocompetent persons range from none to a mild or moderate flulike illness.1,2,3 Coccidioidomycosis is often thought only to be of interest to those regions in which it is endemic. However, with increased travel and migration to the endemic regions, many individuals are exposed to *C. immitis*. Inadequacy of cellular immunity is a well-established risk factor for developing coccidiomycosis. Solid-organ transplant recipients require life-long suppression of cell-mediated immunity to prevent organ rejection, thus increasing their risk of coccidioidal infection or other opportunistic infections.3,4 Coccidioidomycosis in organ transplant recipients can result from one of 3 mechanisms: acquisition of primary infection after organ transplant, reactivation of previously acquired infection, or infection derived from the transplanted organ.3-5 Clinical manifestations of coccidioidomycosis are variable and nonspecific, but may include respiratory symptoms, nodules or other abnormalities on chest radiographs, and constitutional symptoms.1,2,5

The early histologic reaction associated with primary pulmonary coccidioidomycosis consists of an acute suppurative pneumonitis with neutrophilic

![Figure 1. High-Resolution Computed Tomography of the Thorax](image)

(A) A cavity in the right inferior lung. (B) Computed tomography showing the lesion in the right inferior lobe almost totally healed after 3 weeks.

![Figure 2. Biopsy Pictures](image)

(A) The lung parenchyma showing multiple scattered granulomas, consisting of epithelioid cells, Langhans giant cells, and lymphocytes (hematoxylin and eosin × 40). (B) Acute suppurative inflammation with neutrophilic infiltrates, necrosis, and many giant cells seen around the granulomas. A round spherule consistent with *Coccidioides immitis* also is seen in the center (hematoxylin and eosin × 100). (C) *Coccidioides immitis*; A thick-walled spherule is filled with small endospores (hematoxylin and eosin × 1000).
infiltates. The neutrophilic foci become surrounded by granulomatous inflammation, and these lesions can progress to necrotizing granulomas. The organisms are typically found within the neutrophilic infiltrates of necrotic zones. An accurate diagnosis is established by identifying coccidoidal spherules. In cases in which diagnostic mature spherules are absent or difficult to find, the endospores or immature spherules of *C. immitis* may be confused with other fungi.

The endospores of *C. immitis* may be distinguished from yeast forms of *Histoplasma capsulatum* or *Cryptococcus* by the presence of buds on the latter two. Immature spherules of *C. immitis* may be difficult to separate from the yeast forms of *Blastomyces dermatitidis*, but the presence of broad-based budding would favor the latter. The other major entities in the differential diagnosis are *Mycobacterium tuberculosis*, Sarcoidosis, or Wegener’s granulomatosis. In tuberculosis, detection of acid-fast bacilli by histochemically stain (Ziehl-Neelsen) is essential for diagnosis. When parenchymal necrosis and vasculitis are seen concomitantly with granulomatous inflammation, Wegener’s granulomatosis must be kept in mind. And in Sarcoidosis, noncaseating granulomas are distributed with relative sparing of the intervening lung.¹

Coccidioidomycosis has been reported in solid-organ transplant recipients since 1967. Retrospective analyses show that the frequency of coccidioidomycosis after transplant is 4% to 8% in regions highly endemic for cocci.⁶⁻⁷ Most of these infections occur during the first posttransplant year, an implication that, for many patients, the infection is one of reactivation rather than acquisition.⁶⁻⁷

Transmission from donor organs has rarely been reported in the English literature, with 3 cases reported from donor lungs, and 4 cases of Coccidioides infection from a donor liver and kidney.⁸⁻¹² All patients underwent transplant in a nonendemic area and had no travel history to an endemic area.

We report a case of Coccidioides infection occurring in solid-organ transplant in which the person had not lived in an endemic area or traveled to an endemic area, which made us think that this infection could be donor derived. We had no information about the donor’s travel history. Donor and pretransplant recipient coccidioidal serologies were not performed, as this is not an expected infection in Turkey and is not a standard procedure in our country. None of the recipients received antifungal prophylaxis.

To the best of our knowledge, this case is the first one that is reported in Turkey. In areas where the organism is not endemic and Coccidioides serology is not routinely performed, diagnosis can be delayed. This report demonstrates the need to include coccidioidomycosis the differential diagnosis of a possible cause of pulmonary infection in the patients of transplant.

**References**