Disseminated coccidiodomycosis presentig as acute respiratory distress syndrome in a liver postrasplant recipient

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Abstract
Acute respiratory distress syndrome (ARDS) is a respiratory process of acute onset, showing on X rays as bilateral pulmonary infiltrates and severe respiratory failu-
re. Coccidiodomycosis is a unusual cause of acute respiratory distress syndrome, the incidence of coccidiomycosis in a solid organ transplant recipients ranges from
1.4% a 6.9%, inadequacy of cellular immunity is a well established risk factor for development of coccidiodomycosis, less than 1% of patients develop disseminated
infection and carrying high mortality, the case that we are presenting add to the small list of reports documenting the occasionally acute and aggressive nature of
the disseminated clinical form of coccidiodomycosis.

Key words: Acute respiratory distress syndrome, Coccidiodomycosis, solid organ transplant.

Introduction
Primary pulmonary coccidiomycosis is usually a self limi-
ted illnes, the presenting as acute respiratory failure is dis-
tinctly uncommon, and has been most frequently associated
with underlying immunosuppressive conditions, particulary ste-
roid therapy and massive exposure to C immitis. The highest
risk of coccidiomycosis after solid organ transplant occurs
in the first year postransplant, accounting for as many as
70% of cases in one series, in areas of high endemicity, the
risk of symptomatic posttransplant coccidiomycosis is in-
creased with history of prior infection, positive serology be-
fore transplant, or antirejection therapy, the dissemination is
more common in transplant patients occurring in up to 75%
of cases, mortality is reported to be from 30 % to 63 %.

Case description
A 59 year-old male post transplant liver recipient presented
to the emergency department complaining of abdominal
pain, nausea, diarrhea and fever. The initial physical exam
revealed his blood pressure was 100/62 mm Hg, heart rate
of 125/min, temperature 100 °F, respiratory rate 27/min,
and oxygen saturation 88 % on room air and 92% on 40%
venti-mask, the heart exam revealed tachycardia but regu-
lar rhythm, a normal S1 and S2 and no murmurs, gallops or
rubs. On auscultation of the lung fields, breath sounds were
diminished without the presence of adventitious sounds.
The abdomen was benign without organomegaly, extremi-
ties were normal with absence of clubbing or edema. the
patient appeared in discomfort.
The white blood cell count was 5.5 (reference range 5.0 – 12.0 x 10^3), with 95% of neutrophils, the hemoglobin was 11.3 gr (reference range 13 – 15.7 gr/dl in men), the platelets count was 76 (reference range 150-450 K/ul). The serum creatinine was 0.94 mg/dl (reference range 0.6-1.2mg/dl), serum sodium was 127 mmol/L (reference range 135-145 mmol/L), serum potassium was 4.3 mmol/L (reference range 3.5-4.5 mmol/L). Serum albumine was 2.8 (reference range 3.4 to 5.4 g/dl) Total Bilirubin 1.26 (reference range 1 to 1.2 mg/dl ) ALT 34 AST 29.50 (reference ranges for both 8-40 U/L). Arterial blood gas analysis reported pH 7.46 (7.35-7.45), paCO2 20.9 mmHg (reference range 35-45 mmHg), HCO3 14.4 mmol/L (reference range 22.2-28 mmol/L). Chest CT imaging revealed consolidation areas, multiple lung nodules and ground-glass areas (Figure 1).

Due to the suspicion of invasive fungal infection a bronchoalveolar lavage was requested, after bronchoscopy the patient condition worsened, needing mechaninal ventilation, vasopressor suport, transferred to the ICU due to severe respiratory fai-ure, a chest X ray revealed lungs with bilateral diffuse consolidation areas (figure 2). The Arterial blood gas analysis reported pH: 7.06 PO2: 137 PCO2: 32 HCO3: 8.8 LACT: 8.76, Pa02/FiO2 ratio < 100. Upon admission to the critical care unit, the patient placed under mechanical ventilation pressure control mode and continue antibiotic therapy for adquiried community pneumonia, and amphotericin B was added, however the patient died 24 hours after his admission.

The bronchoalveolar lavage culture was negative for bacteria, but the fungus culture produced suspicious filamentous colonies, the cotton blue stain reveled thin and septate hyphae and arthroconidia. (figure 3). Post mortem macroscopic pieces shows a multiple nodular lesions in the lung and liver (figure 4), microscopic description has typical histologic features, granulomatous inflammation, large thick walled spherules contain variable sized daughter endospores. (figure 5).

**Brief discussion**

Acute respiratory distress syndrome (ARDS) is a respiratory process of acute onset, showing on X rays as bilateral pulmonary infiltrates and severe respiratory failure, disorders associated with ARDS include direct lesions of the pulmonary parenchyma and lesions indirectly affecting the lung occurs most often in the setting of pneumonia, sepsis, aspiration of gastric contents or severe trauma and is present in ~10% of all patients in intensive care units worldwide. Despite some improvements, mortality remains high at 30-40% in most studies. Coccidioidomycosis is a unusual cause of acute respiratory distress syndrome.

Coccidioidomycosis is caused by the dimorphic fungi *Coccidiodes immitis*, is found in nature as a saprophytic filament (mould) that produces propagules (arthroconidia) which spread easily in the air, infection caused by *Coccidioides* species occurs after inhalation of aerosolized arthroconidia, with the organism potentially becoming latent within resident and recruited pulmonary phagocytes and cells of the reticuloendothelial system, is endemic to areas of Southwestern United States, Northern Mexico and parts of Central and South America with particular presence in Argentina and Paraguay, are highly infectious to susceptible humans, presents variability of symptoms, 60-80% mild respiratory symptoms, 15 - 35% develop respiratory symptoms in 1 to 4 weeks, 5% will develop progressive symptoms, 1- 5 % disseminated forms, dissemination to any organ or tissue can occur, establishing secondary mycosis foci, the fungus can remain viable and latent at and cause clinical manifestation.
The present report describes a old man patient post transplant liver recipient, no residing in the traditional areas of endemicity of *C. Immitis*, a immunocompromised host, with multiple risk factors for a disseminated disease such as age, gender, diabetes mellitus as concurrent immunosuppressing illness, use high-dose corticosteroid treatment and other immnosuppressant drugs tacrolimus and mycophenolate, and your previously labor activities to contact with contaminated dust, especially from uncultivated areas in endemic areas, his relatives comment in the past he works as a civil engineer as a construction operations supervisor in the northern region of Mexico, an endemic area of coccidiodomycosis, with the suspicion of exposure of airborne soil particles.

Coccidiodomycosis has been reported in solid organ transplant (SOT) recipients since 1967, the diseases occurs in the first year after transplant and the incidence of these patients in the endemic areas has been reported as 5 %⁴.

Figure 2. lungs with bilateral diffuse consolidation areas.

A recent coccidioidal infection or a positive serologic test result at the time of organ transplantation is associated with a rate of dissemination of 75% and a mortality of 30% to 63% without the use of antifungal prophylaxis⁵. Coccidioidal disease in the immunocompromised host can result from primary infection or from reactivation of old infection. T-cell function deficiencies add the patient at risk for severe or disseminated infection. The receipt of anti-rejection medications or of tumor necrosis factor α inhibitors increases the risk of disseminated coccidioidal disease because of their effect on T-cell function⁶,⁷.

In solid organ transplantation is associated with reactivation of latent infection or primary infection in areas where it is an endemic. In the patient that we are presenting the suspicion is that the reactivation of latent coccidiodomycosis, is the most common probable cause form of the disease, which is the most frequent in transplanted patients, since the acquisition through the organ donor was ruled out.

Donor organs may be a source of transmissible agents, particularly viruses, has been a significant concern throughout the era of solid-organ transplantation, Although it is less common, the transmission of fungi⁸,⁹. In this case the results of postmortem coccidioidal serological tests for the donor were negative, the donor no residing in the traditional areas of endemicity of *C. Immitis*, none other recipients of the donor presented coccidiomycosis manifestations over the time. Primary pulmonary coccidiomycosis is usually a self limited illness, the presenting as acute respiraory failure is distinctly uncommon, and has been most frequently associated with underlying immunosupresive conditions, particulary steroind therapy and massive exposure to *C. immitis*, very rarely primary pneumonia is overwhelming and complicated by respiratory failure and the mortality of acute disseminated coccidiomycosis is high, and the outcome may not be altered by antifungal therapy⁸.

Figure 3. filamentous colonies, the cotton blue stain 40 x, reveled thin septate hyphae and arthroconidia.

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Figure 5. Granulomatous inflammation, large thick walled spherules contain variable sized daughter endospores.

The case that we are presenting add to the small list of reports documenting the occasionally acute and aggressive nature of the disseminated clinical form of coccidiodomycosis.

Ethical disclosure

Conflict of interest. None

Sources of funding for our research. Authors

Protection of human and animal subjects. Consent Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Confidentiality of data. No data that identifies patient are revealed

References:


