J MEDICINE 2011; 12 : 163-165

Case Reports

Disseminated Histoplasmosis in a Renal Transplant Recipient – A Fatal combination

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Abstract:

Histoplasmosis is an infectious disease caused by the dimorphic fungus Histoplasma capsulatum**.** *The disseminated form is usually found in immunocompromised patients. A 53 year-old man, renal transplant recipient, was admitted with fever, dyspnea, productive cough, adynamia and weight loss. He was septic, but hemodynamically stable. The tracheal aspirate found intracellular fungi and the peripheral blood exam was compatible with histoplasmosis. The patient presented a progressive worsening of respiratory pattern and needed mechanical ventilation, vasoactive drugs and hemodialysis. A large spectrum antimicrobial therapy was started, including amphotericin B, but the patient died.*

Keyword: *Disseminated histoplasmosis. Kidney transplantation. Immunosuppression*

Introduction:

Histoplasmosis is an infectious disease caused by the dimorphic fungus *Histoplasma capsulatum*, which is endemic in Latin America and is characterized by a broad spectrum of clinical manifestations, from asymptomatic cases to disseminated form, affecting different organs and systems. The disseminated form is usually found in immuno-suppressed patients.[1]

The incidence in Brazil is not known. Disseminated histoplasmosis (DH) has been the second most notified infection in AIDS patients in the city of Fortaleza.[2] DH is more frequent in AIDS patients, being rarely found in transplanted patients.[3]

We report the case of a kidney transplant recipient with DH with fatal outcome.

Case Report:

A 53 year-old man, from Paracuru (State of Ceará, Brazil), was admitted with complaints of high degree fever (38-39ºC), productive cough, adynamia, anorexia and weight loss for 15 days. He developed progressive dyspnea 7 days before admission.

He reported history of systemic arterial hypertension, kidney transplant in 2005 and smoking. He was taking tacrolimus 5mg/day, mycophenolate mofetil 500mg/day, prednisone 5mg/

Fig.-1: *Chest x-ray showing a bilateral diffuse interstitial infiltrate, mainly in the left lung.*

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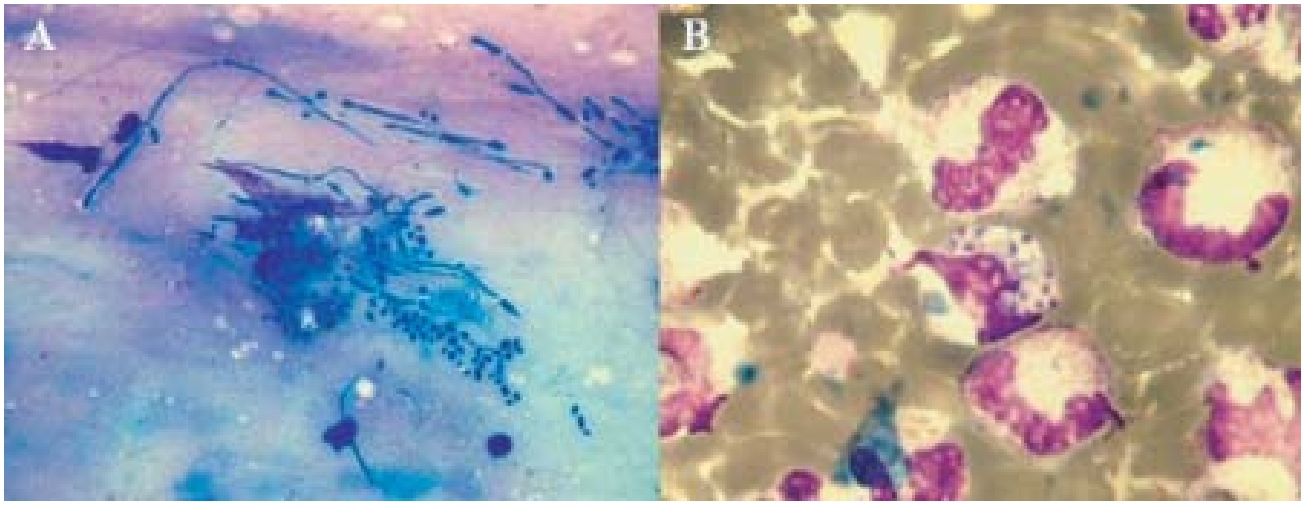

Fig.-2. *A) Tracheal aspirate evidencing the presence of fungi; B) Blood smear showing the presence of intracellular microorganisms compatible with Histoplasma capsulatum.*

Table-I

Laboratory tests during hospital stay.

	Admission	Day 2	Day 3	Day 4	Day 5
Hb (g/dL)	10.4	-	10	9.7	10.4
Ht (%)	29.6	-	27.9	26.8	29.4
Leukocytes (cells/mm^3)	5,820	-	3,680	4,360	5,720
Platelets (cells/mm^3)	122,000	-	95,000	87,000	95,000
Ur / Cr (mg/dL)	193 / 3.9	192 / 3.5	202 / 5.0	137 / 3.5	108 / 1.9
Na/K (mEq/L)	121 / 4.4	-	129 / 3.9	137 / 3.3	135 / 4.2
Albumin (g/dL)	-	2.7	-	-	-
AST/ALT (UI/L)	28 / 04	-	68 / 11	-	-
PT (%)	-	-	35.9	-	-
LDH (UI/L)	-	988	2383	-	-
Arterial pH	7.35	-	-	7.31	7.19
HCO_3 (mEq/L)	20.0	-	-	15.6	19.0

Hb: hemoglobin, Ht: hematocrit, Ur: urea, Cr: creatinine, AST: aspartate amino transaminase, ALT: alanine amino transaminase, PT: prothrombin time, LDH: lactate dehydrogenase, HCO_3: arterial bicarbonate.

day and nifedipine 20mg/day. At physical examination he was with poor general state, febrile and dehydrated. Pulmonary auscultation evidenced diffuse decreased murmur and rales. Blood pressure was 110x70 mmHg, heart rate 108bpm and respiratory rate 24irpm, oxygen saturation 92% without supplementary O_2.

Laboratory tests are summarized in Table-I. Urinalysis showed proteinuria (1+), hemoglobinuria (1+), leukocyturia (11 cells/high power field) and granulous cylinders. The chest x-ray showed a bilateral diffuse interstitial infiltrate, mainly in the left lung (Figure 1). HIV and other viral (Epstein-Barr, cytomegalovirus and hepatitis) serologies were negative. The tracheal aspirate and the peripheral blood examination evidenced the presence of microorganisms compatible with *Histoplasma capsulatum* (Figure 2). The search for *Pneumocystis jiroveci* in the tracheal aspirate was negative.

The patient developed respiratory insufficiency, requiring mechanical ventilation, and acute kidney injury with the need of hemodialysis. He was then transferred to the intensive

care unit, where therapy with antibiotics was started (ceftriaxone, levofloxacin, thrimetropim-sulfametoxazole and amphotericin B). Despite intensive care, the patient progressed with septic shock and died five days after admission.

Discussion:

DH is an opportunistic infection commonly found in AIDS patients, but it is rarely seen in solid organ transplant recipients. DH is relatively common in our region, with several cases described in AIDS patients.[2] We reported a fatal case of DH in a kidney transplant recipient.

The disease is acquired after inhalation of conides present in the nature. Histoplasma capsulatum multiply within the cells of the macrophage/lymphocyte system, and the fungus spread from the lungs to the lymph nodes and the circulation, causing inflammatory foci in different parts of the body. Different organs can be involved in DH (liver, spleen, lymph nodes, kidney and bone marrow). The initial Th1 immune response uses to cure the primary infection, which can activate in immunosuppression states, mainly HIV infection.[4] Invasive fungal infection in kidney transplant recipients are rare, occurring in only 1-2% of all patients in developed countries.[5] The majority of these infections occur in the first six months after the transplantation due to the use of higher doses of immunosuppressive drugs.[5] In the case presented here, the patient had a five years history of transplantation and his immunosuppression regimen was not aggressive, which turns the case even more rare.

The clinical manifestations of DH in solid organ transplant recipient are unspecific. Eventually the patients present lung involvement, which can be evidenced by radiographic findings, culture or histopathologic tests.[6] The initial symptoms presented by the patient were related to the respiratory system, and a rapid progression to systemic disease was observed.

The symptoms of DH include fever, malaise, anorexia and weight loss. Physical examination can evidence hepatosplenomegaly, lymphadenopathy, pallor, petechiae and other skin and mucous lesions.[7] Severe forms of DH can present as sepsis, septic shock, disseminated intravascular coagulation, acute kidney injury and respiratory insufficiency. Chest x-ray can be normal of present diffuse interstitial infiltrate.[8]

The finding of the fungi in organic smears is not easy, even using special staining. In the present case, the exam of tracheal secretion and peripheral blood evidenced the presence of *H. capsulatum*, confirming the infection. It is reported a rate of isolation of the fungus from tracheal secretions in 60-85% of cases of pulmonary histoplasmosis. Peripheral blood examination can also allow the identification of the microorganism, mainly in the cases of DH.[9]

According to the Infectious Diseases Society of America, the treatment of DH is done with amphotericin B for severe cases or itraconazole for mild cases. The duration of therapy varies from 12 weeks for acute cases to 12 months for progressive disseminated cases.[10]

In summary, we reported a rare case of DH in a kidney transplant recipient with fatal outcome. DH should be investigated in every transplanted patient with febrile disease, mainly in those with respiratory symptoms or sepsis.

Conflict of Interest: None.

Financial Support: Elizabeth De Francesco Daher received a grant from CNPq (Brazilian Research Council) – PQ2.

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