Combined pulmonary and meningeal cryptococcosis in renal allograft recipient

Dear Editor,

The most frequently encountered clinical manifestation invasive cryptococcosis is cryptococcal meningoencephalitis (CM) which may be easily missed because of varying clinical presentations. One-year mortality is estimated at 20% to 30% even with long-term consolidation antifungal therapy.[1] We wish to highlight a case of combined pulmonary and cryptococcal meningitis in a renal allograft recipient.

A 38-year-old male patient who had a kidney transplant 4 years back was admitted to the hospital due to generalized weakness and a single episode of fever (39.2°C) with chills. He had stable kidney function. Immune suppression consisted of tacrolimus 2 mg, Mycophenolate mofetil 720 mg and prednisolone 10 mg daily.

On admission, he was conscious and hemodynamically stable. Physical examination revealed no pathological findings, the temperature was 36.4°C. Blood test results were within normal limits.

CT scan of thorax revealed bilateral nodular lesions and one nodule in the right lower lobe showed internal necrosis suggestive of infective pathology [Figure 1]. A CT-guided biopsy was requested and empirical liposomal amphotericin B was added to the treatment regimen. The biopsy report was suggestive of pulmonary cryptococcosis [Figure 2] and the dose of liposomal amphotericin B was increased to 3 mg/kg. On day 7, he complained of double vision so MRI brain and fundoscopy was done. Contrast-enhanced MRI brain showed no evidence of meningeal enhancement. Fundoscopy was not suggestive of papilledema. A lumbar puncture was performed. The opening pressure was normal (10 cm H$_2$O) but the cell count in the cerebral spinal fluid (CSF) of $64 \times 10^6$/L (70% mononuclear), glucose (24 mg/dL), and protein (86.9 mg/dL) levels were elevated. The bacterial culture showed no growth but India ink staining revealed a high quantity of encapsulated yeast forms in the CSF [Figure 3]. In addition, cryptococcal antigen tests in both CSF and blood were positive. Cryptococcus neoformans grew in cultures from CSF, leading to a diagnosis of cryptococcal meningitis.

The patient received induction therapy with liposomal amphotericin B and fluconazole for 3 weeks, a subsequent lumbar

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**Figure 1:** CT Report: Few nodular lesions in both lungs, one nodule in RLL showed internal necrosis

**Figure 2:** (a) Lung Biopsy H&E Stain, Light microscopy alveoli filled with cryptococcal yeast forms, (b) Lung Biopsy Chromic Silver methamine Haematoxylin-Eosin Stain, highlighting the cryptococcal yeast forms

**Figure 3:** CSF culture. India ink preparation showing negative staining of cryptococcal yeast forms
puncture detected no fungal growth. Consolidation therapy followed, with fluconazole only. The dose of tacrolimus was reduced to 1 mg/day, prednisolone was continued at 10 mg/day and mycophenolate mofetil was stopped. At the last follow-up (3 months after the episode), the patient was in good health.

Infection with *C. neoformans* in solid organ transplant recipients usually occurs in the late posttransplantation period (>6 months after transplantation). [2]

*C. neoformans* can invade various organs. The lungs are the main portal of entry. Generally, pulmonary Cryptococcosis patients are asymptomatic or show mild symptoms. The imaging findings are nonspecific. [3] Pathological diagnosis is the main approach for the diagnosis of pulmonary cryptococcosis. A high index of suspicion led us to do a CSF study. *C. neoformans* was cultured from the CSF and Cryptola LA antigen was also positive in CSF.

Transplant patients often present with mild and atypical symptoms. In this case, the radiological findings in the chest, biopsy, and the CSF sample were the key to the diagnosis. We suggest that for transplant patients with a lung mass or nodular lesions, the possibility of Cryptococcosis should be considered, and they should be aggressively investigated. Early lung biopsy is the key to accurate diagnosis of PC. A high index of suspicion for CM should be applied for solid organ transplant patients, even with apparently normal imaging, minor symptoms, and normal laboratory results.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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