# Ophthalmoscopy in the early diagnosis of opportunistic tuberculosis following renal transplant

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Chronic renal failure is a common sequel of renal inflammatory disease or diabetes mellitus. As a result of the immunosuppression that is induced by uremia, hemodialysis or posttransplant immunosuppressive medication, these patients are at a higher risk of opportunistic infections. Various viral, bacterial and mycobacterial infections have been reported. Tuberculosis is a common systemic opportunistic infection but reports of ocular involvement with pulmonary or disseminated tuberculosis are rare. We report the systemic and ocular findings in two postrenal-transplant patients with pulmonary or disseminated tuberculosis in whom detection of choroidal tubercles led to confirmation of the diagnosis in both patients and was the only specific premortem finding in one. Fundoscopy in this group of patients may help in the diagnosis of opportunistic tuberculosis, its earlier treatment and the consequent reduction of morbidity and mortality.

**Key words:** Ocular, opportunistic, renal allograft, tuberculosis

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Chronic renal failure (CRF) is a common cause of morbidity with hemodialysis being a common short-term treatment modality and renal allograft transplantation a long-term modality. Hemodialysis and transplantation adds to the risk of opportunistic viral, bacterial or mycobacterial infection.[1] In India, there is a markedly higher incidence of tuberculosis in this group (10 to 15%).[2] As the manifestations are often varied or subtle and as clinical/ laboratory findings may be atypical, diagnosis is often difficult. We describe two cases of posttransplant disseminated tuberculosis and the role of ocular evaluation.

## Case Reports

### Case 1

A 33-year-old female was evaluated as part of an assessment for a 10-day pyrexia of unknown origin (PUO). She had undergone a successful renal transplant three years earlier and was on systemic immunosuppressants (cyclosporine and oral prednisolone) to prevent an organ rejection. Systemically she was febrile (102° F) but there were no other

clinically significant findings. A routine chest X-ray showed nonspecific consolidation in both lung fields, which led to a differential diagnosis of tuberculosis, bacterial or viral pneumonia. Routine hematological and biochemical tests were noncontributory.

On examination, her visual acuity was 20/30 in the right eye and 20/20 in the left eye. Examination of the anterior segment was normal in either eye. Dilated fundoscopy of the right eye revealed multiple choroidal tubercles scattered throughout the postequatorial retina with one cluster along the superotemporal vessels and another in the perifoveal area [Fig. 1]. The left eye showed two similar lesions in the macular area and three or four lesions in the inferior postequatorial retina [Fig. 2].

She was started on four-drug antitubercular therapy (isoniazid 300 mg/day, ethambutol 800 mg/day, pyrazinamide 1gm/day and rifampicin 600 mg/day) with resolution of her pyrexia and radiological evidence of healing within seven days. At this time partial resolution of tubercles was noted.

**Case 2**

A 62-year-old male patient was admitted with a two-day history of an acute onset high-grade fever with chills and rigors. He had undergone an uncomplicated renal allograft transplant for diabetic nephropathy one and a half years back. In the period prior to this illness he was taking mycophenolate mofetil (500 mg thrice daily) and cyclosporine A (125 mg twice daily) towards preventing an organ rejection.

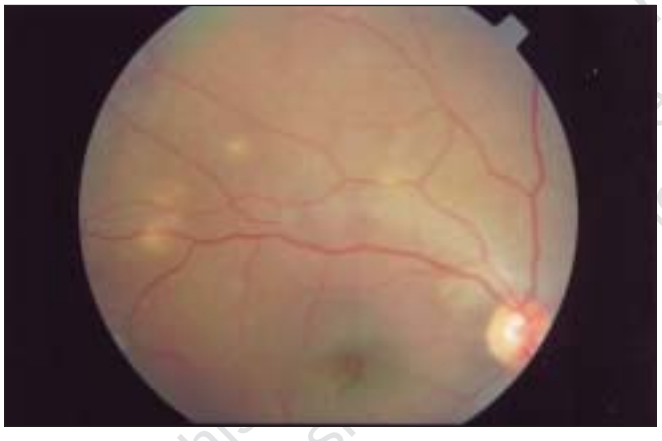

**Figure 1:** A photograph of the right fundus of Case 1 showing multiple tubercles along the superotemporal vessels and in the macula

**Figure 2:** A photograph of the left fundus of Case 1 showing tubercles in the posterior pole

At the time of admission he was highly febrile, disoriented and prostrate. Routine hemogram revealed mild anemia (9.3 g/dl), leucopenia (4000/mm$^3$) and a high erythrocyte sedimentation rate of 71 mm at one hour. His serum creatinine was elevated at 4.53 g/dl.

A chest X-ray showed ill-defined haziness in the right upper and midzones. A high-resolution chest tomogram (HRCT) scan performed the following day, revealed patchy scattered areas of consolidation and ground glass appearance in both lung fields. There was evidence of pretracheal and precarinal lymphadenopathy. The radiological findings suggested a differential diagnosis of tuberculosis, pneumocystis cariini pneumonia or a viral pneumonitis. The results of investigations for cytomegalovirus infection (IgG, IgM), malaria (peripheral smear) and typhoid (Widal test) were negative. An erythematous maculopapular rash was detected in his lower extremities, which was sent for biopsy.

Fundoscopy showed evidence of bilateral panretinal photocoagulation. The discs in either eye were pale. There were yellow-white choroidal lesions measuring 1/3 to 1/4 Disc diameter in the posterior pole of either eye (two in the right and one in the left) consistent with choroidal tubercles.

His condition rapidly deteriorated despite antitubercular therapy (isoniazid 300 mg/day, ethambutol 800 mg/day, pyrazinamide 1 gm/day and rifampicin 600 mg/day) and he died on the seventh day post admission. A histopathological examination of the skin biopsy revealed a large number of acid-fast bacilli consistent with *Mycobacterium tuberculosis* within the tissue.

## Discussion

Chronic renal failure produces a state of immunosuppression due to uremia-induced changes in leukocyte function that reduce both acute and delayed inflammatory responses. Patients on hemodialysis have disturbed leukocyte function due to the effects of the many bioincompatible dialysis membranes. The passage of blood through these membranes causes an inappropriate activation of complement and cytokine cascades with consequent defective immune responses.[3] The use of potent immunosuppressives (such as mycophenolate mofetil, cyclosporine A, azathioprine and glucocorticoids) in posttransplant groups adds to the immunosuppression.

The absence of fever or suspicious symptoms ("silent" fashion) presents a diagnostic dilemma. Anergy to the Mantoux test is common (32 to 40%).[4,5] Sputum microscopy and culture have low positive yields (11.1% cultures and 33.3% following polymerase chain reaction[6]). Additional invasive tests including bronchoalveolar lavage and analysis of pleural aspirate, gastric or peritoneal fluids and bone marrow specimens are often necessary. Lattes *et al*. performed an invasive diagnostic procedure in 13 of 14 patients with posttransplant tuberculosis.[7] Apart from the cost and the surgical risk of these procedures, specimen analysis is often time-consuming. Lui *et al*. noted a mean time from the onset of symptoms to a specific diagnosis (culture-based) of 27 ± 12 days.[8] The delay in diagnosis may have therapeutic implications. Patients with greater than five days of

delay in identification of the cause of the pulmonary infiltrates had a three-fold greater risk of death than controls.[9]

Several groups[10,11] have suggested the use of composite indices consisting of lymphocyte subsets, T-cell proliferative responses in response to mitogens, neutrophil phagocytic capacity and reactive oxygen species (ROS) generation that denote the degree of immunosuppression and consequent risk of infection. The use of these indices remains an area of future study.

In a MEDLINE search we could identify only a single previous report[12] suggesting the rarity of fundus examination rather than a low prevalence. Both patients had pyrexia following an earlier allograft (18 and 36 months respectively) with an ambiguous radiological and clinical picture. The detection of tubercles via the simple, noninvasive technique of fundoscopy confirmed diagnosis of systemic tuberculosis. The Mantoux test was deferred in our patients due to severe underlying illness and the likelihood of pharmacological immunosuppression with consequent negative readings. In Case 2, identification of the tubercles was the only premortem specific finding suggestive of disseminated tuberculosis. Fundoscopy may help in early diagnosis and permit earlier specific treatment.

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