ASPERGILLOSIS FOLLOWING CYTOMEGALOVIRUS DISEASE IN A KIDNEY TRANSPLANT PATIENT

Sh. Ameri[1] and B. Broumand[2]

1) Department of Infectious Diseases, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2) Department of Nephrology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Abstract- A 32-year-old end stage renal disease (ESRD) woman was scheduled for transplantation. Also, she has had fever of unknown origin (FUO), rise of ESR and PPD> 22 mm. Therefore treatment with isoniazid and rifampin was started three months prior to transplantation. She developed allograft dysfunction one week after transplantation. She received a few course pulse therapy (methyl prednisolone), antilymphocyte globulin (ALG), hemodialysis and because of low blood level of cyclosporine, isoniazid and rifampin were stopped. She was seen because of unilateral decreased vision, fever, cough and in physical examination, chorioretinitis and bilateral infiltration in both lungs were seen three weeks later. Severe cytomegalovirus (CMV) antigenemia was detected and she responded rapidly to gancyclovir. One month later, she complained of fever and productive cough again. In chest X-ray (CXR), cavitary lesions were shown and with transthoracic biopsy, invasive aspergillosis was detected. In spite of amphotericin B therapy, she developed CNS involvement. Unfortunately she expired six months post transplantation. This is an interesting case of aspergillosis following CMV infection most likely because of an excess of immunosuppression.

Acta Medica Iranica, 41(2): 122-125; 2003

Key Words: CMV, aspergillosis, transplantation, kidney

INTRODUCTION

Use of potent immunosuppressive agents for renal rejection will cause the opportunistic infections to increase in the future (1).

One of this infections, is CMV which is a cofactor for the other infections (1,3). Here, we are presenting a case with aspergillosis following CMV infection in a kidney transplant patient.

Case report

A 32-year-old woman with undetermined end stage renal disease (ESRD) etiology and history of two years maintenance hemodialysis, was candidated for renal transplantation. One year prior to the transplantation, she had fever of unknown origin (FUO), ESR >100 and occasional leukocytosis without any definite diagnosis. Regarding a PPD of more than 22mm, a three months course treatment with isoniazid and rifampin was started. She was candidated for kidney transplantation subsequently. The renal transplantation from living unrelated donor was performed. Both donor and recipient were seropositive for CMV. Immunosuppressive regimen was triple therapy with cyclosporine, prednisolone and azathioprine. The patient gradually complained of fever and a decrease of urine volume in the first week. Also as the serum creatinine raised to 7 mg/dl, needle biopsy was performed which revealed acute cellular rejection (stage II A banff). She received two courses of three days pulse therapy (methylprednisolone), two courses of ALG and hemodialysis.

INH and rifampin were discontinued due to low level of cyclosporine. She was discharged from hospital with a serum creatinine of 2.2 mg/dl two months after admission. A prophylactic course of intravenous gancyclovir was prescribed and then change to oral acyclovir (200 mg/TDS), because of ALG treatment.

She was admitted because of unilateral decreased vision, fever and cough, three weeks later (3 months after transplantation). In physical. exam, sever chorioretinitis and fine rales in lungs were detected. In chest X-ray, bilateral interstitial infiltraties, especially in the base of lungs were noted.

Received: 24 January 2002, accepted: 19 February 2003

Corresponding Author:
Sh. Ameri, Department of Infectious Diseases, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 8740242 , Fax: +98 21 3921320
E-mail: R.Ameri_2000@yahoo.com

Bronchoalveolar lavage for B.K, Pneumocystis carinii and Nocardia was negative. Sever antigenemia (CMV Ag- PP65=500 from 50000 PMN with Immuno-cytochemistry) was detected. Treatment with gancyclovir was started and the dose of immunosuppressive agents was decreased due to probable CMV disease (chorioretinitis and pneumonia). She responded rapidly to gancyclovir. However, one month later, she complained of fever, productive cough and chest pain again. In CXR, multiple cavitary lesions in the lungs were noted (Fig. 1).

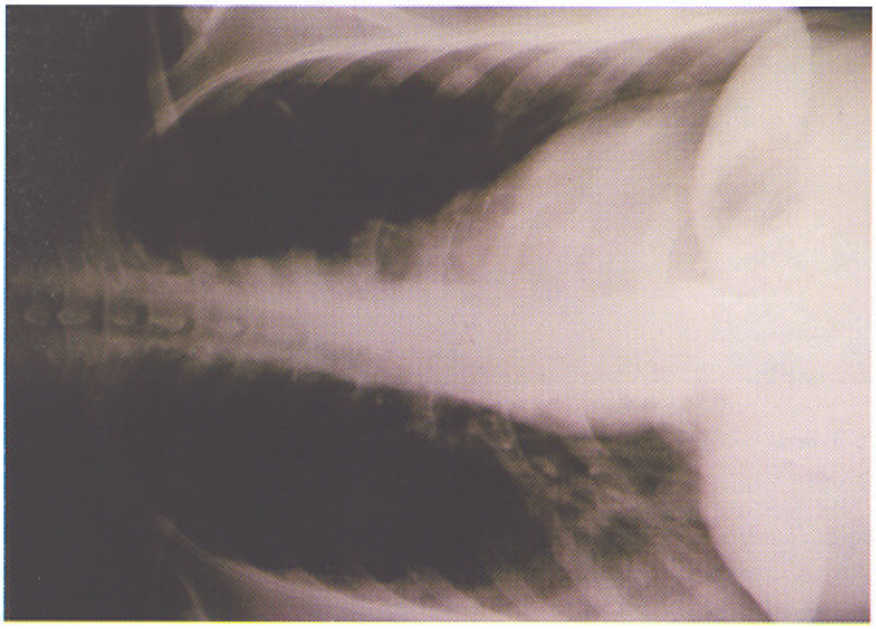

Fig. 1. Multiple cavitary lesions in lungs, 4 months after transplantation

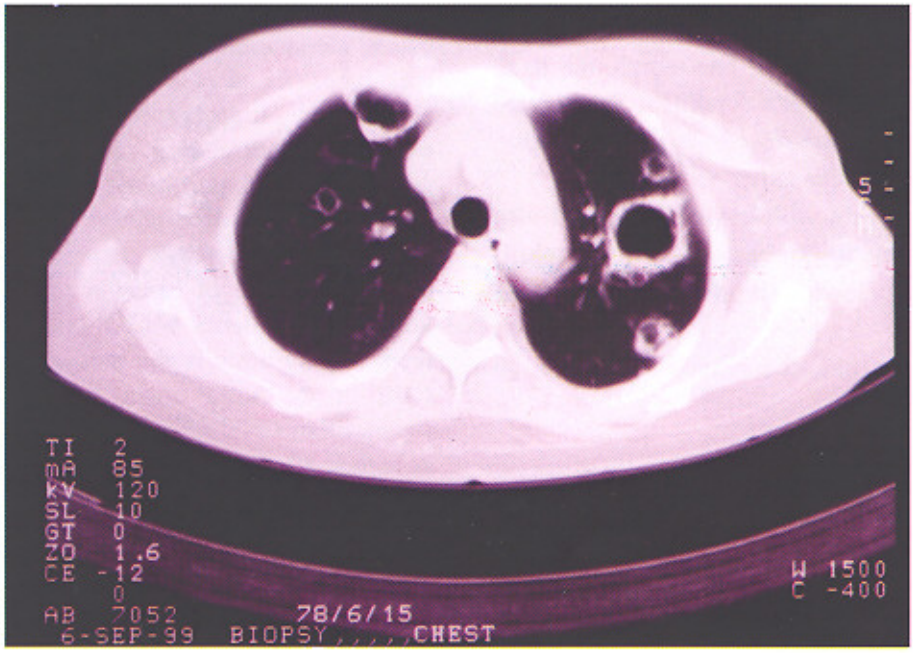

Fig. 2. Pulmonary aspergillus was isolated in transthorasic biopsy under chest CT Scan-guided

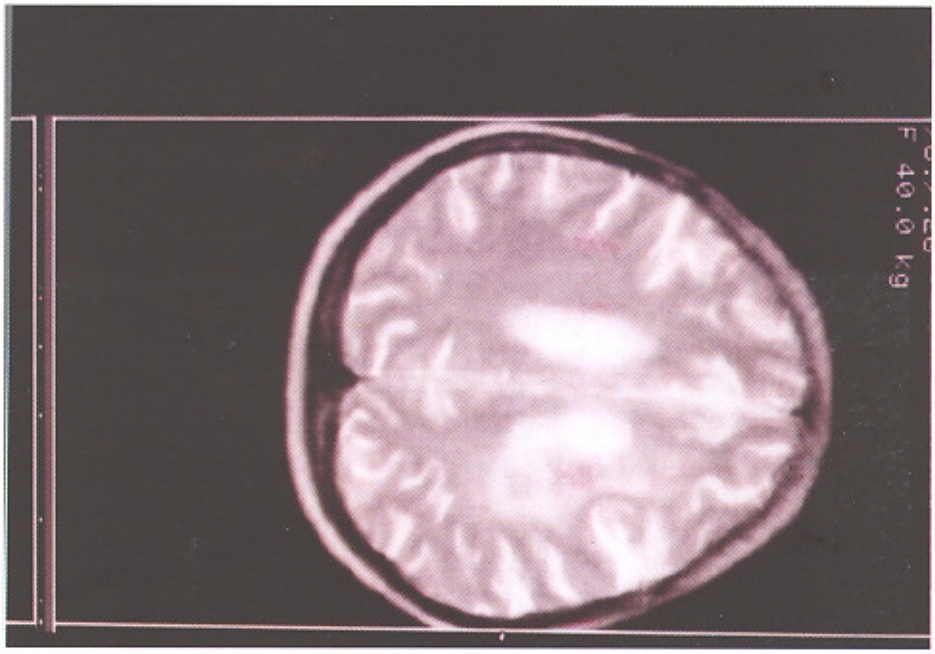

Fig. 3. Brain CT Scan revealed focal hypo and hyperdense-lesions in left fronto-parietal lobe

In Bronchoalveolar lavage, aspergillosis was detected and in transthoracic biopsy, tissue invasion of aspergillosis was confirmed (Fig. 2).

She was treated with intravenous amphotericin B. As the creatinine raised to 3 mg/dl it was replaced by itraconazole three weeks later. The patient complained about headache, vomiting and confusion four days later. Brain CT Scan revealed focal hypo and hyperdense lesions in left fronto-parietal lobe with edema (Fig. 3).

Therefore, treatment with amphotericin B was again started and continued for one month, but there was no change in the patient's condition. She became gradually aphasic and comatosed. The brain biopsy, could not be performed due to her poor condition.

In spite of treatment with amphotericin and also wide spectrum antibiotics for bacterial, toxoplasmosis, and Nocardial brain lesion, she died 6 months after transplantation.

Unfortunately the patient's relatives didn't let an autopsy to be carried out.

DISCUSSION

Diagnosis and management of transplant infections have many problems in developing countries. However, rate of transplantation is on the rise increase in all of the world. Management of this case has some problems. In the first step, it could be asked why a patient without a proven problem has been candidated for transplant program. It is a well known issue that in these patients, due to the effect of rifampin and INH, the allograft has the higher chance of being rejected and the infectious consequences of potent anti-rejection therapy is expected (1,2). In spite of aspergillus isolation in bronchoalveolar lavage and cavitary lesions in imaging, transthoracic biopsy was needed for definit diagnosis.

Another problem in the management of this patient is changing amphotericin B to itraconazole after the patient's condition improved, because of rising serum creatinine.

Although itraconazole has been approved for pulmonary aspergillosis, however due to lack of penetration to blood brain barrier, it will not be effective for CNS aspergillosis (1,4).

Diagnosis of CNS aspergillosis was mostly probable because of isolation of aspergillosis of the lung and coincidence of CNS involvement at the same time. Aspergillosis is the most probable infection of CNS in the solid organ transplantation (1). The prognosis of CNS aspergillosis is poor with mortality as high as 80-100%.

To have a definite diagnosis of brain lesions, biopsy was needed. Neurosurgeons did not agree with brain biopsy because of poor patient's condition. In general it seems that the brain lesions of the patient could be due to aspergillosis, because the form of CNS involvement and lung was similar.

Generally, kidney transplantation is associated with the lowest incidence of fungal infection among all solid argan transplantations (1,3,7,9). Fungi account for 5% of all infections in renal transplant recipients. However aspergillus infection has the highest mortality in this population (6). In fact, the overall mortality from aspergillus infection of CNS has been 100% in large series of solid organ transplant recipients (1,6). The source of inhalation of Aspergillus for her at the discharge time, was the construction work in her neighbourhood. Coincidence of potent immunosuppressive treat-ments and an immunomodulating infection like CMV, could explain such a fetal course. Due to lack of liposomal amphotericin in Iran, treatment with high dose of amphotericin (because of nephrotoxicity) for transplant kidney was not possible. Perhaps if higher does of liposomal amphotericin could be used even with loss of kidney, the patient would have had a more favorable outcome (8,10).

This is an interesting case of aspergillosis following CMV infection, most likely in the excess of immunosuppression, in review literature such a coincidence is very well known (7,3,11).

REFERENCES

1. Bowden RA. Infection in Renal Transplantation. Transplant infections. First edition Lippincott company 1998; 178-221.

2. Risko H, Gronhagen R. Tuberculosis in renal allograft transplantation. Transplant Proc 1987; 19: 4096-4097.

3. Dummer JS. Infections in solid organ transplant recipients. In: Mandell GL, Bennett's JE, Dolin R (eds) principles and practice of infectious disease. Fifth edition -2000- Churchill livingstone company p: 3148-3159.

4. Houston SH. Infections in transplantation in: Reese RE, Betts RF. A practical approach to infectious diseases-Fourth edition-Little and Brown company 1996; p: 785-812.

5. Gustafson TL, Schaffner W, et al. Invasive aspergillosis in renal transplant recipients: correlation with corticosteroid therapy. J Infect Dis 1983; 148: 220-238.

6. Chush KS, et al. High mortality in systemic fungal infections following renal transplantation in third-world countries. Nephrol dial transplant 1993; 8: 168-172.

7. Weiland D, et al. Aspergillosis in 25 renal transplant patients: epidemiology, clinical presentation, diagnosis and management. Ann Surg 1983; 198: 622-629.

8. While MH, et al. Amphotericin B colloidal dispersion vs. Amphotericin B as therapy for invasive aspergillosis. Clin Infect Dis 1997; 24: 635-642.

9. Boden MD, Dummer JS. Infections after organ transplantation. J Intensive Care Med 1997; 12: 166.

10. Peterson PK, Anderson RC. Infection in renal transplant recipients: Current approaches to diagnosis, therapy, and prevention. Am J Med 1988; 81:2

11. Suwansirikul S, Rao N, Dowling JN, HOM. Primary and secondary cytomegalovirus infection. Arch Intern Med1990; 137: 1026