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BRIEF REPORT

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Isolated zygomycosis in a bought living unrelated kidney transplant

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Abstract We report the first case of zygomycosis by *Absidia corymbifera*, only localized in an unrelated living donor kidney that was bought and transplanted in India. Zygomycosis was diagnosed 2.5 months post-transplantation, in the clinical setting of rapid transplant failure, following an episode of cytomegalovirus (CMV) colitis, CMV nephritis, and acute rejection. Treatment consisted of transplantectomy. One year later, the patient is doing well, without clinical or serological evidence of persistent mycotic or virological infections. We speculate that this isolated mycotic infection originated with the donor or was due to the poor hygienic conditions in the operating theater or surgical ward. Another possibility is that this isolated renal involvement resulted from a subclinical pulmonary infection with hematogenous dissemination to the kidney in a manner comparable to renal tuberculosis. The patient received no amphotericin and was cured with transplantectomy alone.

Key words Kidney transplantation, zygomycosis · Zygomycosis, kidney transplantation · Living nonrelated kidney, infection

Introduction

Zygomycosis (mucormycosis) is an uncommon infection mostly affecting patients with diabetes mellitus and ketoacidosis, hematological malignancies, burns, or severe trauma, as well as organ transplant recipients. Depending on the port of entry, the major anatomical sites involved are rhinocerebral, pulmonary, gastrointestinal, and cutaneous; it may also be widely disseminated. In kidney transplant recipients, all kinds of clinical manifestations of zygomycosis have been reported. Isolated renal zygomycosis is extremely rare. We report the first case of zygomycosis only localized in the transplanted kidney itself.

Case report

A 51-year-old man of Asian origin living in Belgium for more than 20 years was hemodialysed in our department since October 1991 for end-stage renal disease due to Henoch-Schönlein nephritis. Although the patient was on our waiting list for a cadaver kidney, he decided to go to India where he bought a living unrelated donor

kidney that was implanted at the end of November 1993. His native kidneys were left in place. Preoperative and postoperative follow-up was done in Singapore. Immunosuppressive therapy consisted of prednisolone (30 mg/day), cyclosporin (375 mg/day), and azathioprine (100 mg/day). Apart from a urinary tract infection and a herpes genitalis infection, the initial evolution was uneventful and renal function improved (best serum creatinine on day 11 was 1.5 mg/dl), as did the patient's general condition.

On day 45 post-transplantation the patient developed fever, midabdominal pain, and oliguria. Bacteriological work-up revealed pyuria and a positive urine culture for *E. coli*, which was treated with ceftriaxone. Fever persisted in spite of negativation of urine culture. Therefore, a quinolone was added and immunosuppressive therapy reduced.

On day 49 the patient developed a bloody diarrhea. Colonoscopy revealed a hemorraghic colitis of CMV origin, as evidenced by the presence of CMV inclusion bodies. The CMV colitis was treated with ganciclovir. Azathioprine was discontinued and prednisolone was replaced by hydrocortisone, 200 mg/day. The diarrhea gradually improved.

On day 53 serum creatinine started to rise (day 53, 2 mg/dl; day 62, 3.1 mg/dl). A first renal biopsy on day 62 showed mild, nonspecific changes, but CMV inclusion bodies were found, mainly in the endothelial cells. A second needle biopsy performed on day 67 showed signs of acute rejection. In view of the persistence of CMV infection, antirejection therapy was not started. Renal function further deteriorated and hemodialysis was restarted on day 72 post-transplantation.

Two days later, the patient was transferred from Singapore to our department. Physical examination on admission revealed diffuse edema, a raised central venous pressure and bilateral dorsobasal pulmonary crepitations, a tender right fossa iliaca (implantation site), but no fever. Laboratory findings disclosed the following values: hemoglobin 9.8 g/dl; white blood cell count (WBC) 11.4. $\times 10^9$/l with 91 % polymorphonuclear leukocytes, 5 % lymphocytes, 4 % monocytes, 0 % eosinophils, and an erythrocyte sedimentation rate (ESR) of 88 mm after 1 h; serum creatinine 7.33 mg/dl; and serum urea 194 mg/dl. HIV serology was negative. On day 74 a percutaneous renal biopsy was performed. Frozen sections suggested acute rejection. CMV inclusion bodies could not be found. CMV early antigen was negative in buffy coat, urine, and throat smear. As we had no evidence of ongoing CMV infection, we started antirejection therapy on day 74 with high-dose prednisolone (200 mg/day). Cyclosporin was continued in a dose of 375 mg/day).

The patient's general condition worsened. He was subfebrile and he developed a new episode of bloody diarrhea. A colonoscopy showed colitis, most prominent in the right colon, with multiple deep ulcerations. While awaiting for the results of the colon biopsies, ganciclovir and hyperimmune gamma globulins were started because of the previous history of CMV colitis. Gradually, the diarrhea improved.

After immunohistochemical and PAS staining of the transplant biopsy, the pathologist found irregular structures suggestive of hyphae, as seen in zygomycosis or other fungal disease. Rejection could not be excluded. A surgical wedge biopsy performed 85 days post-transplantation showed massive fungal infection with infarction and abscess formation of the kidney by mucormycosis. The fungus was microbiologically identified as *Absidia corymbifera*. The colon biopsies showed no specific abnormalities, but were compatible with ischemic colitis. There was no evidence of mucormycosis or CMV infection on the colon biopsies. CMV early antigen in buffy coat was still negative. Immunosuppressive therapy was stopped and transplantectomy was carried out on day 87. Again, *Absidia corymbifera* was isolated. A CT scan of the sinuses and the chest did not disclose infectious lesions. As there was no evidence of other localizations of mycotic infection, no treatment with amphotericin B was given.

After transplantectomy, the patient's condition gradually improved. To date, he has developed no new mycotic lesions, and he is considered to be cured from infection. He is now again waiting for a cadaveric renal graft. Revision of the renal biopsies performed in Singapore showed acute rejection and CMV nephritis, but mycotic lesions could not be found.

Discussion

We report the first case of an isolated zygomycosis by *Absidia corymbifera* in a bought, living unrelated kidney transplant.

Zygomycosis refers to a rare mycotic disease caused by fungi in the class Zygomycetes, which has two orders: Entomophthorales and Mucorales. Mucormycosis is often used as a synonym for zygomycosis. These opportunistic organisms are ubiquitously found in soil, air, and decaying organic matter [8]. Patients with diabetes mellitus and ketoacidosis, hematological malignancies, burns, and severe trauma, as well as organ transplant recipients, are most susceptible. Mucormycosis became known to nephrologists in the West after reports were published indicating a high incidence of mucormycosis in patients treated with deferoxamine for aluminium toxicity [2]. Depending on the port of entry, the major anatomical sites involved are rhinocerebral, pulmonary, gastrointestinal, and cutaneous; it may also be widely disseminated. In kidney transplant recipients, all kinds of clinical manifestations of zygomycosis have been reported [3].

Isolated renal zygomycosis is extremely rare [4, 6]. Kidney involvement usually occurs within the spectrum of disseminated zygomycosis and can be the cause of acute renal failure [7]. Recently, however, several cases of isolated renal mucormycosis have been reported in patients infected with HIV [9].

In the absence of any other identifiable focus, the occurrence of isolated renal involvement can only be speculated to result from a subclinical pulmonary infection with hematogenous dissemination to kidneys in a manner comparable to renal tuberculosis [4]. Alternatively, the infection might take an ascending route from the lower urinary tract. In a transplanted kidney, the infection may be of donor origin or it may be the result of contamination of the preservation fluid (in the case of cadaveric renal transplantation), or of inoculation of the wound during surgery or later on at the ward as case to case transmission [1].

In our patient, no focus other than the transplanted kidney was found, not at the time of the transplantectomy when the surgeon inspected the wound, nor 1 year later when the patient was doing well on hemodialysis. Thus, we speculate that this isolated kidney transplant zygomycosis was of donor origin.

Zygomycosis is generally an acute, rapidly developing and spreading infection [8]. In our patient, about 2.5 months passed between transplantation and diagnosis, and the infection was limited to the transplanted kidney. An acute rejection and its treatment make a patient more prone to the development of zygomycosis [7]. One report [1] speculates on the role of CMV infection and its immunosuppressive effect as the trigger for the clinical manifestation of zygomycosis. Our patient was reported to suffer from both CMV colitis and CMV nephritis.

The treatment advocated for this mostly fatal disease consists of controlling the underlying disease, surgical debridement of infected tissues and, if required, amphotericin B [8]. In our case, the only radical treatment option was transplantectomy, which proved to be sufficient, possibly because immunosuppressive therapy was discontinued at the same time.

Among recipients of bought, living unrelated donor kidneys, mortality and morbidity are high, especially when the kidney is bought in a third world country like India [5, 10, 11]. The main cause of death is infection – bacterial or fungal – most probably due to poor hygienic and sanitary conditions in this tropical environment and to insufficient donor selection criteria.

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