CASE REPORT

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Invasive Aspergillosis After Kidney Transplant–Treatment Approach

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ABSTRACT

Aim: Aim of the article was to present a case of post transplantation invasive aspergillosis, successfully treated with conservative and surgical treatment. **Case report:** Patient, male, 44 years old, with second kidney transplant, required special preparation therapy, because he was sensitized, with concentration of Panel Reactive Antibody (PRA) class I 11% and PRA class II 76%. On the day of transplantation, induction was done with *anti-thymocyte globulin* (*ATG)* and glucocorticosteroids. After transplantation, plasmapheresis with ATG was performed. On the fourth day patient was anuric. Fine-needle biopsy of the graft was performed and showed positive CD4 antibodies for peritubular capillaries and humoral rejection. 14 plasmaphereses through 14 days, were negative and ATG treatment was suspended completely. Full therapeutic dosage of tacrolimus and mycophenolate mofetil were given during treatment. Four days after treatment patient was stable, but next day clinical status had worsened with dyspnea and fever. In sputum, spores of Aspergillus species were microscopically found, and radiologically by computerised tomography. Caspofungin was administered for seven days. Voriconazole therapy was given for first ten days by intravenous route and after then orally. Even with this treatment, there was no improvement in clinical picture, while CT scan of the lungs showed abscess collection in right lung. Lobectomy was performed and pus collection was found. After graft-nephroctomy, patient was treated with continous veno-venous hemodiafiltration (CV-VHDF) dialyses, with constant voriconazole therapy for the next three months (200mg two times per day). After one month of diagnosis, Galactomannan (GM) test was negative. **Conclusion:** Although highly sensitized patients, those who are on hemodialysis, in preparation for transplantation, receive intensive immunosuppressive therapy that suppress the immune system. Occurrence of secondary fungal infections especially infection by aspergillosis, is cause of high mortality of infected. Application GM test that detects existence of antibodies against Aspergillus antigens and usage of different type of immunosuppressive preparation can increase longevity of graft and patients in solid organ transplantation program. Aspergillosis is treated with voriconazole and surgery, and sometimes graft-nephrectomy if needed. Recommendation is that in all immunocompromised hosts and organ transplant recipient should have been tested with GM test.

Keywords: Aspergillosis, Kidney, Transplantation.

1. INTRODUCTION

Aim of the article was to present a case of post transplantation invasive aspergillosis (IA), successfully treated with conservative and surgical treatment, in a 44 year old male second kidney allograft recipient. IA is present in 0.7% and in up to 4% of the renal transplant recipients (although incidence is smaller in comparison to other organ transplant recipients) with mortality rate from 65% to 92% (1-8). Renal transplant-specific risk factors have not been defined (1).

2. CASE REPORT

Patient R.S., 44 years old was admitted to Intensive Care Unit, Clinic for Anesthesiology and reanimation, Clinical Centre, University of Tuzla with second kidney transplant, required special preparation therapy, because he was sensitized, with concentration of Panel Reactive Antibody (PRA) class I 11% and PRA class II 76%. In human leukocyte antigen (HLA) profile donor specific antibody (DSA) was in traces. First cross-match was positive, after which special desensitizing treatment was performed. After admission of rituximab, four plasmaphereses were performed. On the day of transplantation, induction was done with anti-thymocyte globulin (ATG) and glucocorticosteroids. After transplantation, plasmapheresis with ATG was performed. Furthermore, plasmapheresis were performed on the first and second day after trans-

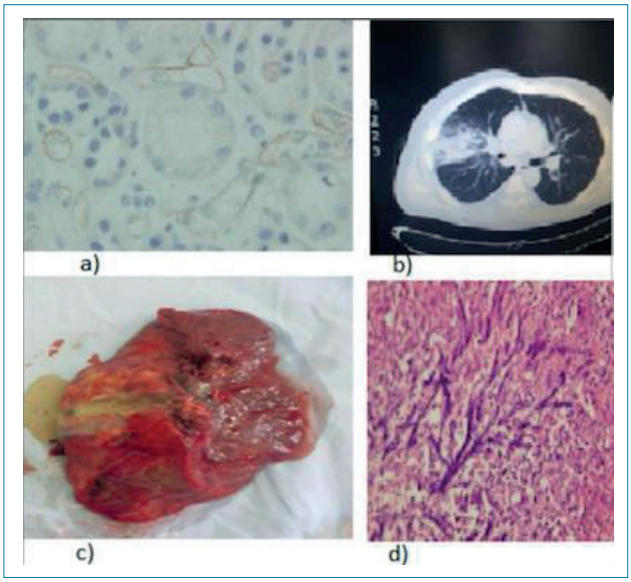

Figure 1. Diagnostic findings in patient a) fine needle biopsy showed positive CD4 antibodies (humoral rejection), b) CT showed cavernous finding, c) pyogenic macroscopic finding after lobectomy d) pathognomonic microscopic Aspergillus finding.

plantation. Patient had diuresis on the first day after transplantation, which gradually declined on second and third day. On the fourth day patient was anuric. Fine-needle biopsy of the graft was performed and showed positive CD4 antibodies for peritubular capillaries and humoral rejection (Figure 1a). Treatment was continued with plasmapheresis, ATG, half standard dosage of tacrolimus and mycophenolate mofetil. After the fifth admission of ATG, lymphocytes decreased while thrombocytes remained stable. After 14 plasmaphereses through 14 days, were negative and ATG treatment was suspended completely. Full therapeutic dosage of tacrolimus and mycophenolate mofetil were given during treatment. Four days after treatment patient was stable, but next day clinical status had worsened with dyspnea and fever. In sputum, spores of Aspergillus species were microscopically found, and computed tomography (CT) of the chest showed typical finding of cavernous space in basal part of the right lung (Figure 1b). Caspofungin was administered for seven days (70 mg/day). Voriconazole therapy was given for first ten days by intravenous route (6 mg/kg once every 12 hours on day 1, then 4 mg/kg once every 12 hours) and after then orally 200mg two times per day. Even with this treatment, there was no improvement in clinical picture, while CT scan of the lungs showed abscess collection in right lung. Surgical treatment was indicated. Lobectomy was performed and pus collection was found (Figure 1c). Microscopic findings identified Aspergillus (Figure 1d). Besides aspergillosis, patient had Cytomegalovirus (CMV) infection (confirmed by PCR). He was treated with recommended gancyclovir for ten days (5 mg/kg/day). Therapy did not provide results, number of lymphocytes were reduced and graft nephroctomy had to be performed. After graft-nephroctomy, patient was treated with continous veno-venous hemodiafiltration (CV-VHDF) dialyses, with constant voriconazole therapy for the next three months (200mg two times per day). After one month of diagnosis, Galactomannan (GM) test was negative. Despite negative results, voriconazole therapy was continued for next two months. Dialysis treatment was performed three times per week with continuous patient monitoring who was clinically stable with adequate laboratory values.

3. DISCUSSION

Prolonged corticosteroid therapy, graft failure requiring hemodialysis, duration of dyalisis, leukopenia and potent immunosuppressive therapy present risk factors for IA after kidney transplantation (8-11). At the time of transplantation, there was no guideline for kidney transplantation which recommended usage of GM test, that detects antibodies for Aspergillus. Previously it was well documented that diagnosis of invasive aspergilosis can only be confirmed by identification of the fungus in biopsy samples. GM test is not highly sensitive (9, 10), but it provides a positive leverage in suspected patients. There is no universal strategy in treatment of IA in this type of patients. In prevention and treatment of Aspergillosis, voriconazole is more effective, less nephrotoxic and has lower mortality rate compared to amphotericin B (13). Duration of therapy with voriconazole should last two weeks after disappearance of all signs and symptoms of Aspergillosis, even some authors recommend 6 months duration of treatment with voriconazole after surgical treatment and some suggested all life prevention plan and yearly GM test control (9-12).

4. CONCLUSION

In highly sensibilized kidney allograft recipients who are treated with ATG it would be useful to do GM before the transplantation because of possible fungal and especially Aspergillus infections and the impact on patient outcome.

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.

- **Author's Contribution:** S.T., A.M , E.N. and E.B. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work, S.T., A.C., A.T.. and M.A.H. had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they are agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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REFERENCES

1. Heylen L, Maertens J, Naesens M. et al. Invasive aspergillosis after kidney transplant: case-control study. Clin Infect Dis. 2015 May 15; 60(10): 1505-1511.

2. Morgan J, Wannemuehler KA, Marr KA. et al. Incidence of in- vasive aspergillosis following hematopoietic stem cell and solid organ transplantation: Interim results of a prospective multi- center surveillance program. Med Mycol. 2005; 43(Suppl 1): S49-S58.
3. Paterson DL, Singh N. Invasive aspergillosis in transplant recipients. Medicine (Baltimore). 1999; 78: 123-138.
4. Brown RS, Jr., Lake JR, Katzman BA. et al. Incidence and significance of Aspergillus cultures following liver and kidney transplantation. Transplantation. 1996; 61: 666-669.
5. Altiparmak MR, Apaydin S, Trablus S. et al. Systemic fungal infections after renal transplantation. Scand J Infect Dis. 2002; 34: 284-288.
6. Kasper EM, Bartek J, Johnson S, Kasper BS, Pavlakis M, Wong M. Post-transplant aspergillosis and the role of combined neurosurgical and antifungal therapies under belatacept immunosuppression. Surgical Neurology International. 2011; 2: 75. doi:10.4103/2152-7806.81969.
7. Marr KA, Carter RA, Boeckh M, Martin P, Corey L. Invasive aspergillosis in allogeneic stem cell transplant recipients: Changes in epidemiology and risk factors. Blood. 2002; 100: 4358-4366.
8. Singh N, Husain S. Aspergillosis in solid organ transplantation. Am J Transplant. 2013 Mar; 13 Suppl 4: 228-241.
9. Tonelli M, Wiebe N, Knoll G. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant. 2011 Oct; 11(10): 2093-2109.
10. Patterson TF, Thompson GR, Denning DW. et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016; 63(4): e1-e60.
11. Baddley JW, Andes DR, Marr KA. et al. Factors associated with mortality in transplant patients with invasive aspergillosis. Clin Infect Dis. 2010; 50(12): 1559-1567.
12. Lin SJ, Schranz J, Teutsch SM. Aspergillosis case-fatality rate: systematic review of the literature. Clin Infect Dis. 2001; 32(3): 358-366.
13. Herbrecht R, Denning DW, Patterson TF. et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med. 2002 Aug 8; 347(6): 408-415.