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Miliary tuberculosis in a renal transplant patient

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ABSTRACT

Various complications are common after renal transplantation as also the recipients are at a high risk of opportunistic infections. One of the leading infections following renal transplantation is tuberculosis. As it is relatively frequent among renal transplant patients, it is known to present with a wide variety of clinical manifestations, often involving various organs and may be potentially fatal. The authors of this study overview the case report of a 47-year-old patient, who suffers from a miliary tuberculosis involving pulmonary and gastrointestinal organs. The patient is a recipient of deceased kidney and was admitted to the hospital with a mind fever and fatigue. This case report illustrates how unpredictable can a case of post-transplant ailment get and how difficult it is to diagnose such serious illness as tuberculosis. Also the review of literature on miliary tuberculosis and its clinical presentation is reported.

Keywords: nephrology, renal transplantation, miliary tuberculosis.

Introduction

Tuberculosis (TB) is the predominant infectious cause of morbidity and mortality worldwide and in 2016 infecting 10.4 million people who were sick with TB, and there were 1.7 million TB – related deaths worldwide [1]. *Mycobacterium tuberculosis* is a common infection among the recipients, especially after the renal transplantation. In transplanted patients the incidence rate of this opportunistic agent is frequent, related with 512 cases/100.000 inhabitants/year and it is often linked with adverse outcomes [2-3]. Because of the immunosuppressive therapy, recipients are predisposed to the primary infections and also at risk for reactivating latent infections acquired before the transplantation. Despite that, the clinical diagnosis of any infection, especially TB, may be difficult as in most cases the clinical manifestation of the disease is atypical and as it is also misleading to believe that TB involves mainly the lungs. Unlike general population, renal transplant (RT) patients have higher incidence rate of extra-pulmonary TB, as 15% of TB-related cases present with miliary TB affecting gastrointestinal or urogenital system organs [4]. In this case report the authors present how difficult can a TB-related illness be to diagnose and how important is it to suspect and treat an immunosuppressed patient without the usual clinical manifestation and symptoms of the disease.

Case report

The 47-year-old male patient, who underwent the deceased renal transplantation 12-years prior because of the chronic kidney disease caused by chronic glomerulonephritis. The treatment after transplant involved immunosuppressive therapy with cyclosporine, mycophenolate and methylprednisolone as also the antihypertensive substances. The patient was admitted to the hospital due to fever up to 39.5 °C, nausea, diarrhea and general weakness. Two weeks prior to the hospitalization patient complaint of diarrhea and the valganciclovir was administered due to suspected cytomegalovirus (CMV) infection, but the patient declined it due to the worsening diarrhea. Patient had no recent travel history or

known TB exposure. On admission the blood pressure was 120/70 mmHg, heart rate 80 beats/min. No other complaints were documented. Analytical study revealed elevated C-reactive protein (CRP=74.5 mg/l), there were no leukocytosis, anemia with a hemoglobin of 94 g/l. Urea on admission was 9.0 mmol/l and elevated to 15.7 mmol/l. Creatinine level of 194 μmol/l. The preliminary diagnosis of unspecified fever and CMV was documented. The dosage of immunosuppressive medication was lowered, empiric antibiotic therapy of amoxicillin and clavulanic acid was administered and valganciclovir therapy was reapplied. During the first week of hospitalization the CRP levels were fluctuating (CRP=74.5 → 64.7 → 150.1 → 188.6 mg/l), the creatinine stabilized from 261 to 130 μmol/l, anemia was at stable ± 95 g/l, and other blood, urine analyses were within normal ranges. CMV DNR in blood and stool samples were negative and there were no viruses detected during the nasopharyngeal culture testing. Valganciclovir was removed from treatment plan. All other tests including chest x-ray, abdominal ultrasound showed no pathology. Any other infectious processes were rejected. The general state of patient was worsening and during this period of time the antibacterial treatment was changed from amoxicillin with clavulanic acid (after four days) to piperacillin with tazobactam (for seven more days) to meropenem. Empiric treatment with vancomycin and metronidazole was also administered and immunosuppressive treatment changed to hydrocortisone. After few more days of treatment, the D-dimer results elevated to 1470 mg/l, the chest computed tomography was indicated – the pulmonary artery thromboembolism was diagnosed. Treatment with warfarin and heparin was prescribed. On the 10th day of hospitalization the sudden pain in the abdomen appeared. Urgent consultations with general and vascular surgeons were arranged and the abdominal CT angiography was performed – it showed pneumoperitoneum with no visible perforations. Urgent laparotomy was indicated, multiple ileac erosions with perforations were found, the resection of ileum with mesentery

was performed and the jejunostomy was created. The biopsy of the resected area revealed abdominal tuberculosis and following bronchoscopy showed the growth of mycobacterium tuberculosis in the lungs which summed up the diagnosis to be the miliary tuberculosis after the renal transplantation. The patient was then transferred to the tuberculosis specific hospital for the TB treatment.

Discussion

As previously described, the renal transplant patients are at a high risk of developing any opportunistic infections and TB being the one with the most adverse related outcomes is a serious problem in today's medical world. In some research papers, the incidence rate of tuberculosis among RT is approximately 10-20 times higher than in the general population [5-6]. Nevertheless, more than 30% of cases, the TB after transplant is disseminated (miliary) or occur at extra-pulmonary sites [7]. In this case study, the authors report a unique patient who presented with non-specific clinical manifestation which ended up to be the miliary TB, disseminated to the abdomen and pulmonary organs. Gastro-intestinal TB is an infrequent form of TB and usually related with unfavorable outcomes, but being such a unique case, the reviewed patient had a TB occurring even 12 years after the RT, which may be due to a delayed diagnosis as there were no specific symptoms or clinical manifestation of the disease [8]. Tuberculosis of the lungs and abdominal organs usually presents with abdominal pain, fatigue, fever, general discomfort and weight loss. Patients with subacute or chronic disease may present with fever of unknown origin and/or dysfunction of one or more organ systems [9]. Laboratory findings in miliary tuberculosis is uncommon, as only in one third of patients the hematologic abnormalities, such as normocytic, normochromic anemia or pancytopenia, is seen. The diagnosis of miliary tuberculosis should be suspected in patients with relevant clinical manifestations such as fever and/or organ dysfunction, but the diagnosis can be established only by identifying the biopsy sample or the culture from different organ systems. The tuberculosis itself is difficult to diagnose, as the clinical signs are poor for

diagnostic purposes. In addition, radiographic imaging in TB-related cases are important, but as there are no illness-related findings, imaging of the patient may be misleading. For example, the classic appearance of the lungs in miliary TB cases is related with faint, reticulonodular infiltrate distributed fairly throughout the lungs, but this finding is significant only when the nodules are large enough, which means that the TB is already chronic, as only the 50 % of cases of these findings, with nodules greater than 3mm in diameter, can be identified as TB-related [10]. On the other hand, the chest computed tomography is more sensitive than plain chest x-ray for miliary TB, but findings of numerous nodules is not necessarily specific for miliary TB. Disseminated nodules can also be found in many other infections, even in PATE, as also just more than 50 % of cases of miliary tuberculosis can be identified with CT [11]. For diagnostic purposes, in immunosuppressed patients, the universal diagnostic criteria are bronchoscopy and organ tissue biopsy. Also the PCR (polymerase chain reaction) may also be used to identify miliary TB in blood, urine, stool cultures or tissue samples [12-13]. However, this test is expensive and may not differentiate between an active infection and a latent disseminated tuberculosis [14]. Finally, as the clinical outcomes of miliary tuberculosis have improved in recent years, the studies show that the mortality rate is still high, but with a longer duration of therapy, especially for immunosuppressed patients, the disease itself can be controlled. This sums up the necessity of diagnosing the tuberculosis in time and the authors believe that this case report gives a chance to see how difficult and unpredictable can a standard deceased renal transplant get, even 12 years after.

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