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A RARE PRESENTATION OF CYTOMEGALOVIRUS INFECTION IN A RENAL TRANSPLANT RECIPIENT: PNEUMONIA ACCOMPANIED BY AORTIC ANEURYSM INFECTION/DISSECTION

BÖBREK NAKLİ ALICISINDA SİTOMEGALOVİRÜS ENFEKSİYONUN NADİR BİR PREZENTEASYONU: PNÖMONİ VE EŞLİK EDEN AORT ANEVRİZMA ENFEKSİYONU/ DİSEKSİYONU

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ABSTRACT

Cytomegalovirus (CMV) infection is an important cause of morbidity and mortality among kidney transplant recipients. Generally it is presented with a clinical picture called CMV syndrome, but it may cause invasive tissue involvement as well. The most frequently infected tissues are lung and gastrointestinal system tissues. Cardiovascular involvement is rare and generally associated with atherosclerosis and transplant artery stenosis. In this paper, we present the case of a renal transplant recipient with aortic aneurysm infection/dissection and pneumonia associated with CMV infection.

Keywords: CMV, pneumonia, aortic aneurysm infection, dissection, renal transplantation

ÖZET

Sitomegalovirüs (CMV) enfeksiyonu, böbrek nakli alıcıları için önemli bir morbidite ve mortalite nedeni olabilmektedir. Genellikle CMV sendromu olarak adlandırılan bir klinik tabloya yol açmakla birlikte, invaziv doku tutulumuna da yol açabilmektedir. En çok tutulan organlar akciğerler ve gastrointestinal sistemdir. Kardiyovasküler tutulum ise nadirdir ve sıklıkla ateroskleroz ve transplant arter stenozu ile birliktedir. Bu yazıda; böbrek nakli alıcısında CMV enfeksiyonu ile ilişkili aort anevrizması enfeksiyonu/diseksiyonu ve eşlik eden pnömoni nedeniyle takip ettiğimiz nadir bir olguyu sunmayı amaçladık.

Anahtar Kelimeler: CMV, pnömoni, aort anevrizması enfeksiyonu, diseksiyon, böbrek nakli

INTRODUCTION

Cytomegalovirus (CMV) infection is a major cause of morbidity and mortality in renal transplant recipients (1). Major risk factors include the serologic status of the donor and recipient, unrelated donor, and recent anti-rejection therapy. CMV can emerge as a reactivation of a latent virus or as the onset of a new infection. It might present a broad clinical spectrum from signs of viral infection to life-threatening disease (2, 3). There is limited data in literature that indicate aortic involvement associated with CMV infection. In this paper, we present a rare case with aortic aneurysm infection/dissection and pneumonia associated with CMV infection.

CASE PRESENTATION

A 34-year-old male, who had a living-donor kidney transplant 9 years ago due to unspecified end-stage renal disease (ESRD), was referred to our clinic. We learned that the patient's renal function had been normal until recently and he

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had received maintenance immunosuppressive therapy including tacrolimus, mycophenolate, and prednisolone. There was no history of diabetes, cardiovascular disease, or hypertension. One month ago, an aortic aneurysm was detected by angiography at a medical center (to which he had been admitted with diarrhea) and an endovascular graft was placed into his aortic arch. He developed fever 5 days after this procedure and he was monitored for oliguric acute kidney injury, signs of septicemia, and lactic acidosis. In this period, a contrast-enhanced thoraco-abdominal CT scan revealed pneumonic consolidation with pleural effusion in the left lower pulmonary lobe, but no pathological image on the aortic graft. Afterwards, all immunosuppressive medications were discontinued due to progressive pneumonia and broad-spectrum antibiotics therapy (meropenem, vancomycin, colistin, tigecycline, anidulafungin) was used empirically. Blood and sputum cultures were negative. Multi-organ failure and disseminated intravascular coagulation (DIC) occurred in follow-up. Mechanical ventilation, hemodialysis and transfusions of erythrocyte packs and plasma were initiated. With the suspicion of viral pneumonia or an opportunistic infection with Pneumocystis jirovecii or Aspergillus, he was started on oseltamivir, trimethoprim/sulfamethoxazole and voriconazole. Then he was admitted to our clinic with a prediction of possible CMV infection.

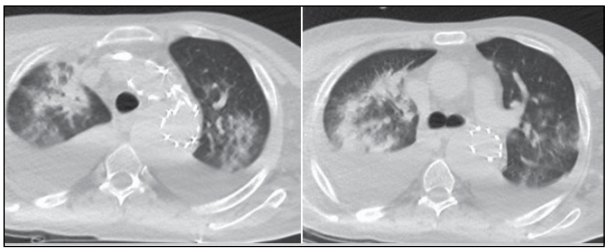

Figure 1. Thorax CT of the patient at presentation.

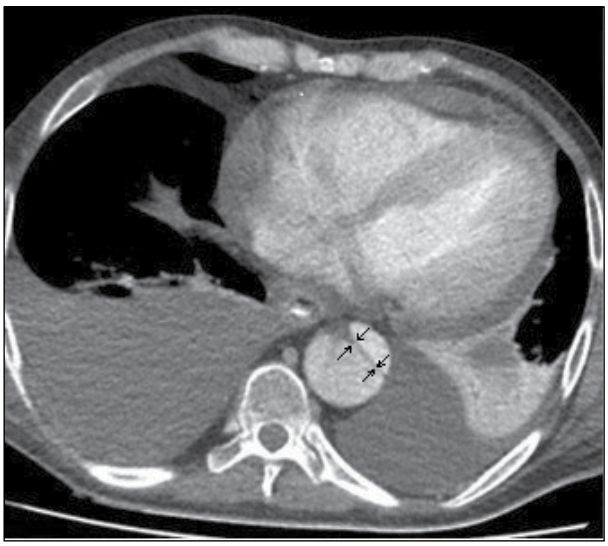

Figure 2. Double-lumen image in the thoracic aorta below the endovascular graft (CT angiography).

Upon physical examination, he was conscious. He had tachycardia (96 beat/min), and inspiratory crackles were present in the lower regions of both lungs. No pathologic feature was detected in other system examinations. The patient was oligoanuric and continued to receive hemodialysis. Blood, catheter and urine cultures were negative. Pleural fluid was transudative, and acid-resistant bacteria (ARB) was negative. A new thoracoabdominal CT scan showed bilateral pleural effusions and pulmonary parenchymal infiltrates. Moreover, there was a double lumen appearance around the endovascular graft in the aortic arch and descending aorta which was spreading to the abdominal aorta along with signs of a thrombotic and hemorrhagic lesion (Figure 1-2).

Antibodies for CMV were positive for IgG and negative for IgM. The CMV DNA level examined by PCR in a plasma sample was 41126 IU/mL (range: 0-1000). Intravenous ganciclovir was started at a dose of 2x5 mg/kg. On the 10th day of ganciclovir treatment he had a better clinical condition, CMV DNA units, and serum inflammatory markers were decreased. Laboratory values of the patient at presentation and follow-up are given in Table 1. Another thoracic CT scan revealed that pulmonary infiltrates had regressed yet pleural effusions were continu-

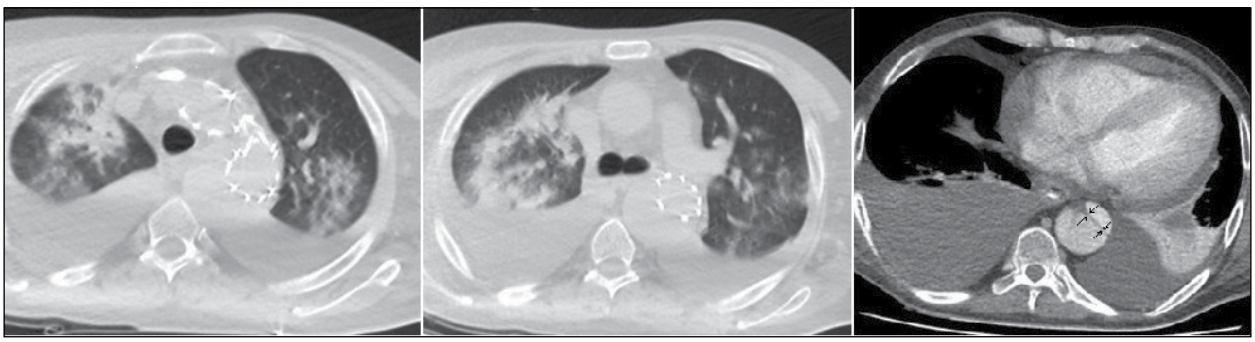

Figure 3. Regression in pulmonary infitrates on the 10th day of ganciclovir treatment.

Table 1. Serum labaratory values of the patient at presentation and follow-up

	Initial presentation	After ten days
Test (Units)	Values	Values
Haemoglobin (g/dL)	9.9	10.2
Leukocyte (/mm^3)	10.900	6200
Thrombocyte (/mm^3)	178.000	201.000
BUN (mg/dL)	76	99
Creatinine (mg/dL)	4.1	5.2
Na (mEq/L)	141	-
K (mEq/L)	4.5	-
ALT (U/L)	16	12
Albumin (gr/dL)	3.7	3.5
aPTT (sec)	22.8	-
INR	1.26	-
CRP (mg/L)	123	19
Procalcitonin (ng/mL)	2.78	1.19
CMV DNA (IU/mL)	41126	128

BUN; blood urea nitrogen, ALT; alanine aminotransferase, PTT; partial tromboplastin time, INR; international normalized ratio, CRP; C-reactive protein.

ing (Figure 3). During the following week the patient's inflammation markers rose again and he was thought to have a possible nosocomial infection. The patient gave informed consent and upon his own request, he was referred to a hospital in the city where he lived. It was learned that he died a few days later at the medical center where he had been referred.

DISCUSSION

CMV infection often manifests with a history of fever and leukopenia (known as CMV syndrome) in renal transplant recipients. However, it may lead to invasive tissue infections like gastroenteritis, hepatitis and pneumonia. Other organ involvements such as pancreatitis, meningoencephalitis, and retinitis may rarely occur (2). CMV has also been associated with various cardiovascular diseases. Pericarditis and myocarditis associated with acute CMV infection have been described, but the most common associated condition is atherosclerosis. Even so, the role of CMV in the development of atherosclerosis is not precisely defined (4, 5). Here we present a renal transplant recipient with CMV infection associated with aortic aneurysm infection/dissection and pneumonia. Atherosclerosis, hypertension, advanced age, smoking, connective tissue diseases, vasculitides and infections have been implicated in the etiology of aortic aneurysms. A previously existing aneurysm is the most important risk factor for aortic dissection that shares similar risk factors with aneurysms (6, 7). Since inflammatory aortic aneurysms may be associated with infectious agents, aortic dissection seems to be related to infection with CMV in our case.

Acute infections (brucellosis, salmonellosis, staphylococcal disease) or chronic infections (syphilisis, tuberculosis) may lead to aneurysms. CMV was demonstrated in aortic aneurysms along with lymphocyte infiltration and elastic fiber degeneration in the vessel wall (6, 8). CMV was detected in aneurysmal tissues using PCR, in situ hybridization or immunohistochemical staining (8). Additionally, CMV infection is shown to increase 5-lipoxygenase (5-LO) and leukotriene B4 in vascular smooth muscle cells. It stimulates the production of TGF-beta and other cytokines that contribute to inflammation and fibrosis (9). CMV-infected endothelial cells also facilitate the migration of leukocytes into the blood vessel wall with the expression of adhesion molecules like intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) (10). These are plausible explanations for the fact that CMV causes inflammation and cell migration on the artery wall along with smooth muscle cell proliferation and destruction of the elastic fibers.

Inflammatory aneurysms are comprised of inflammatory infiltrates and a thin fibrous intimal layer, which often contains atherosclerosis (6). Nyberg et al. (11) found no difference in CMV seropositivity rate between patients with atherosclerotic aorta aneurysm and healthy individuals. Moreover, there was no difference in CMV seropositivity rate between patients with and without aneurysm rupture. The role of CMV in these arterial lesions including atherosclerosis has not been proven.

Tanaka et al. (12) examined 60 aortic tissues (7 infected aneurysms, 37 atherosclerotic aneurysms and 16 normal) obtained during surgery. CMV mRNA transcripts were present in infected aneurysmal tissues, but were not seen in atherosclerotic aneurysmal tissues and normal aortic tissues. CMV may remain latent in many tissues as well as in myeloid cells, lymphocytes and macrophages before reactivating into its replicative phase. Yonemitsu et al. (13) showed CMV-infected macrophages, endothelial cells, fibroblasts and lymphocytes being used in in situ hybridization and PCR techniques in infected aortic aneurysmal tissues. It is clear from this data that CMV is present especially in infected aortic aneurysmal tissues and active replication seems to contribute to the inflammation of the aortic wall and elastic fiber damage.

This patient's presentation with fever after stent grafting for aortic aneurysm brought about the possibility of an aortic

graft infection. Severe infection signs and multi-organ failure that did not respond to combined antimicrobial therapy in a transplant recipient were clues suggesting a possible CMV infection. When he came to our clinic, chest computed tomography revealed bilateral diffuse infiltrates, and CMV DNA by PCR was very high in blood samples. The fact that the patient had no risk factors for developing atherosclerotic aortic aneurysm such as hypertension, smoking and advanced age could suggest that he might have had CMV aortitis from the beginning. CMV aortitis can be diagnosed with certainty by detection of CMV DNA by PCR in aortic tissue on autopsy. Dissection may be related to CMV infection or may have occured due to the progression of an intimal tear that developed during stent grafting (6). Unfortunately we did not have the chance to demonstrate CMV on tissue, in this patient. In this case, pneumonia was probably secondary to CMV. Although CMV DNA should be demonstrated in lung tissue or bronchoalveolar lavage for definitive diagnosis, DNA positivity in a kidney transplant patient with pneumonia, which does not respond to antibacterial therapy is sufficient for diagnosis.

CONCLUSION

There is a striking relationship between vascular lesions and CMV infection, and the data continues to accumulate in this regard. CMV infection should be considered and investigated in the presence of fever, leukopenia, pneumonia, and viral syndrome findings in kidney transplant patients. Besides organ involvements such as pneumonia and hepatitis, rare complications like life-threatening aortic dilatation and dissection might be associated with CMV.

Informed Consent: Written informed consent was obtained from patients' relatives who participated in this study.

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