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## Dose kidney transplant nephrectomy stop disease progression in plasma exchange resistant post transplant hemolytic uremic syndrome? A case report

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### ABSTRACT

**Background:** Two different case reports, which have been published previously, suggested that bilateral nephrectomy can improve sever and refractory hemolytic uremic syndrome (HUS) in adults without a history of transplantation. At this study, kidney transplant nephrectomy in a patient with sever post transplant HUS was investigated.

**Case:** Patient was a 55 years old man with a single small size kidney and end-stage renal disease (ESRD). He had received a kidney from an unrelated donor three months before admission. The patient was admitted with fever and acute renal failure. Clinical and laboratory evaluation were consistent with sever De novo hemolytic uremic syndrome (HUS). Different therapeutic regimens administered in this patient including intensive plasma exchange, plasma infusion, empirical antibiotics, and high doses of corticosteroid. Although Cyclosporine was changed to Tacrolimus. After 45 days of treatment, patient's condition did not improve and severe thrombocytopenia (10000-15000/ $\mu$ L) developed. Patient was also suffered from severe hypersensitivity reaction (fever, chills, and itching) following each plasma exchange. Kidney transplant nephrectomy was done. However, severe post operative bleeding occurred. HUS and thrombocytopenia did not improve and patient died two days after operation.

**Conclusions:** According to this experience, Kidney transplant nephrectomy may not be an effective treatment and is not recommended in the treatment of severe and refractory post transplant HUS.

### Implication for health policy/practice/research/medical education:

Kidney transplant nephrectomy is not effective and not recommended in the treatment of severe and refractory post transplant hemolytic uremic syndrome.

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## 1. Introduction

**T**hrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP-HUS) is one of the most important complications in post kidney transplant period (1,2). Similar to non transplant patients, it should be suspected in a recipient who presents with evidence of microangiopathic hemolytic anemia and thrombocytopenia without another clinically apparent cause (1, 2). It is occurred in two different conditions; First, as recurrent in patients whose primary cause of end stage renal disease (ESRD) was HUS and Second, as de novo with a different primary renal disease (3-5). Although, the reported recurrence rate of TTP-HUS after renal transplant is between 25-50 percent, De novo HUS is a rare problem among these patients. In some patients with de novo HUS, disease was localized in the kidney, while others may have abnormalities in multiple organs (3-6).

Several modalities have been used for the treatment of TTP-HUS including plasma exchange and plasma infusion. However, in kidney transplant recipients, treatment experiences, especially in severe and refractory cases, are extremely limited.

## 2. Case report

A 55 years old white man with a single small sized kidney and ESRD underwent kidney transplantation from unrelated living donor. He had been on hemodialysis three times a week for around a year prior to the transplantation. The surgery and post surgical course were uneventful. Patient had a good hospital course. Eleven days after transplantation, the patient was discharged with the following vital signs: blood pressure: 130/85mmHg, Creatinine:1.3mg/dL, WBC:13.2x103/ $\mu$ L, Hb:11.6 g/dL, Plt:239,000/ $\mu$ L. Three months after transplantation, patient was admitted because of having fever and rising

serum creatinine at our center. Patient's immunosuppression regimen was Prednisone 15 mg/daily, Mycophenolate mofetil 1 g/BD and Cyclosporine 100mg/BD. In laboratory data creatinine: 3.8mg/dL, WBC:12.8 x 10<sup>3</sup>/ $\mu$ L, Hb: 10.1g/dL, platelets:43, 000/ $\mu$ L and Cyclosporine blood level were in acceptable therapeutic range. Coagulation profile was in normal range as well. An ultrasound evaluation showed an enlarged transplant kidney with an increased resistive index (0.80), without evidence of renal artery stenosis and urinary tract obstruction. Serum lactate dehydrogenase (LDH) level elevated (1300 U/L) and evidences of microangiopathic haemolytic anaemia, fragmented red blood cells in a peripheral smear, was found. Serum cytomegalovirus studies, CMV IgG and IgM antibodies were negative. Since this patient's thrombocytopenia was associated with a drop in hemoglobin level, elevated serum LDH, evidences of microangiopathic haemolytic anaemia in peripheral smear and no evidence of renal artery stenosis or urinary tract obstruction in ultrasound, we considered HUS as the leading cause of acute renal failure (ARF). Daily plasma exchanges with two liters of fresh frozen plasma started immediately, Broad spectrum antibiotics were also administered and Cyclosporine was switched to Tacrolimus. Hemodialysis (4 times/week) was also started due to severe renal failure two weeks after admission. Because of poor response to intensive plasma exchange, high doses of corticosteroid were added four weeks later, Tacrolimus was also discontinued. Intensive plasma exchange and plasma infusion were continued; however, three weeks later, clinical and laboratory courses of HUS did not improve. Patient's condition was poor and platelets count was between 10000-15000/ $\mu$ L. Patient didn't tolerate plasma exchanges due to severe hypersensitivity reaction (fever, chills, and itching)

after each plasma infusion. Finally, kidney transplant nephrectomy was done. Severe bleeding after operation was occurred. However, HUS and thrombocytopenia did not improve and patient died two days postoperation.

### 3. Discussion

In adult patients without a history of transplantation, plasma exchange and plasma infusion are the most effective treatments available for TTP-HUS, if left untreated, it typically follows a progressive course and leading to death is a common outcome. While, prior to the use of plasma exchange, the outcome of thrombotic microangiopathy (TMA)-associated syndromes was poor in the last decades, standard plasma exchange has significantly reduced the mortality rate of TTP/HUS from 94.5% to 13%. Therefore, it is recommended that even if there is some uncertainty about the diagnosis of TTP-HUS, plasma exchange should be initiated and if an alternative diagnosis is subsequently discovered it should then be stopped (7,8).

In the development of post-transplant de novo HUS, multiple factors have been implicated including systemic viral infections, particularly cytomegalovirus, HIV and some other infections. In addition, the use of some protocols of immunosuppressive strategies have been considered (9-11). Therefore, the mainstay of the management is the removal of the inciting factors, such as treatment of cytomegalovirus, dose reduction or switching from one drug to the another and plasma infusion or exchange.

There is some evidence that calcineurin inhibitors, such as cyclosporine A (CsA) have an important role in the development of post transplant HUS (10). On the other hand, it has been reported that the switch of CsA to other calcineurin inhibitor, tacrolimus is effective in some

patients. Zarifian et al (1999), have reported that 13 of 16 renal allograft recipients, who developed TTP-HUS while taking cyclosporine, had a high rate of graft salvage after switching to tacrolimus (6), however, this modality did not improve our patient's condition.

Glucocorticoids have a controversial role in the treatment of TTP-HUS. However, it appears that in patients whose platelet counts do not rise within several days of treatment, plasma exchange, adjunctive immunosuppressive treatment with prednisone or methylprednisolone should be envisaged as a reasonable and appropriate modality (12-15). Unfortunately high doses of corticosteroid were also ineffective in our patient.

It has also been reported that, in patients with primary refractory or relapsing de novo TTP-HUS, administration of intravenous immunoglobulin, anti-CD20 antibody, rituximab, and belatacept in combination with plasma exchange may also have had some benefits in terms of improvement (16-19). These drugs were not available in our center and we do not have access to them.

In two different case reports, by Remuzzi, and Feldman et al. (1996) bilateral nephrectomy (native kidneys) has been tried in five women with severe and refractory HUS and without a history of transplantation. They found improvement in clinical course of the patients and also the disease progression has been ceased (20-21). To our best knowledge, there is no study or case report investigating kidney transplant nephrectomy in refractory post transplant recurrent of de novo TTP-HUS. However, according to above case reports and because of poor response to all available treatments, including intensive plasma exchange and plasma infusion, broad spectrum antibiotics, high dose of corticosteroid followed by discontinuation of calcineurin inhibitors, we had to remove transplanted kidney as a last modality in

our patient,. Although it was not accompanied by improvement.

#### 4. Conclusions

Recurrent and de novo TTP-HUS should be suspected in a kidney transplant patients who present with evidence of microangiopathic hemolytic anemia and thrombocytopenia and it typically follows a progressive course. The plasma exchange and plasma infusion is the most effective treatment available for the TTP-HUS.

Treatment of cytomegalovirus, withdrawal of the suspect drugs, dose reduction or discontinuation of CsA, switched from CsA to tacrolimus,adjunctive immunosuppressive treatment with glucocorticoids, rituximab, and belatacept may also have some benefit in de novo TTP-HUS. However according to our experience in this case, Kidney transplant nephrectomy is not recommended as a treatment of severe and refractory post transplant HUS.

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#### Authors' contributions

FS, SSBM and FH prepared the primary draft. MT and MBM wrote some parts of the manuscript. MBM AND AZ edited the manuscript. SSBM prepared the final manuscript.

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