IJNU Case Report

Int J Nephrol Urol, 2010; 2(1): 273 - 277

Ulcerative Colitis Remission after Renal Transplantation: Two Case Reports

Zohreh Rostami[1*], Seyed-Moayed Alavian[2], Behzad Einollahi[1]

[1]Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, I.R.Iran

[2]Research Center for Gastroenterology and Liver Disease, Baqiyatallah University of Medical Sciences, Tehran, I.R.Iran

Abstract

Background and Aims: The combination of ulcerative colitis (UC) and end stage renal disease (ESRD) is uncommon. Immunosuppressive drugs that are used after kidney transplantation are considered as effective therapeutic alternatives for UC. We report two renal transplant recipients with long term refractory UC prior to kidney transplantation and confirmed by histological examination, cured following transplantation. Clinical remission occurred immediately after kidney transplantation, and they had no symptoms of UC during 3 and 8 years of follow up periods. Their immunosuppression regimens were cyclosporine, mycophenolate mofetil / azathioprine and prednisone. In conclusion, kidney transplantation with immunosuppression leads to clinical remission in patients with the inflammatory bowel diseases and ESRD.

Keywords: Inflammatory Bowel Disease, Renal Transplantation, Recipients, Ulcerative Colitis, Remission

Introduction

Ulcerative colitis (UC) is an idiopathic disease with a T cell driven inflammatory condition of the gastrointestinal track that is characterized by a life-long chronic course with remissions and exacerbations (1-3).

Considerable controversy exists regarding the inflammatory bowel disease (IBD) activity after organ transplantation (4). Some authors have reported no significant change in IBD activity. On the contrary, others have demonstrated improvement in IBD symptoms, while some reports revealed the worsening of the disease activity (1, 5, 6). In addition, there are no specific reports of UC remission after renal transplantation, whereas overall full spectrum of de novo and new onset of IBD can be rarely present after solid organ transplantation (4, 7, 8).

In non transplant patients, refractory IBD can remit by immunosuppressive agents such as cyclosporine (CsA), tacrolimus (Tac), mycophenolate mofetil (MMF) and azathioprine (AZA). However, MMF, sirolimus and Tac are the risk factors for IBD exacerbation in transplant recipients (1, 5).

Herein, we describe two cases of refractory UC who were clinically cured after renal transplantation. Further studies on such patients could shed light on

*Correspondence:
Zohreh Rostami, MD
Nephrology and Urology Research Center,
Baqiyatallah University of Medical Sciences,
Molla Sadra St. Vanak Sq. Tehran,I.R. Iran.
E-mail: rostami@inu.ir
Received: 20 Apr 2009
Accepted: 10 May 2009

the exact pathogenesis of IBD.

Case 1:

A 28-year-old Caucasian woman with history of two years symptomatic UC introduced to our center for renal replacement therapy (RRT). Hemodialysis modality (3 times weekly) was initiated for unknown etiology of end stage renal disease (ESRD) in 2000. The patient received a kidney from a living unrelated donor after 3 months. Fortunately, she tolerated surgery well with no complications. The patient was initially treated with CsA (6 mg/kg/day), AZA (2 mg/kg/day) and prednisone (2 mg/kg/day), which were gradually tapered to 0.15 mg/kg/day within three months after transplantation. The clinical course of the patient was followed for 9 years. No episode of acute rejection or graft dysfunction was seen and therefore monoclonal and polyclonal antibodies and steroid pulse were not used.

Two years prior to renal transplantation, she was suffering from weight loss, intermittent mucoid stool and bloody diarrhea, recurrent abdominal pain, nausea, vomiting and sometimes low grade fever. Her family history was negative for IBD, other autoimmune disorder and renal disease. At the presentation, her cardiovascular, abdominal and pulmonary examinations were normal. No peripheral edema, arthritis and skin lesions were noted on physical examination. In laboratory findings, a hypochromic microcytic anemia (hemoglobin 7.6 g/dl) has been associated with decreased transferin saturation (12%), increased amount of serum ferritin (1402 g/L) and normal LDH level. The serum albumin concentration had fallen by 2.1 g/dl. Moreover, antinuclear antibody (ANA) and rheumatoid factor (RF) were negative, but perinuclear antineutrophil cytoplasmic antibody (P-ANCA) titer was high (1:140).

Liver enzymes levels (AST=15 IU/L, ALT=18 IU/L) and alkaline phosphatase (202 IU/L) were also normal. All serum electrolytes values except for plasma potassium (2.8 meq/l) were within normal limits. Barium enema study illustrated mucosal granularity in rectosigmoid and thickened haustral fold with superficial ulcerations in transverse colon as well as “lead pipe” appearance of colon were found, which were suggestive of UC. A clean base ulcer in duodenum (D1) was displayed in upper gastrointestinal endoscopy. Colonoscopic evaluation showed large ulcers in mid-transverse colon and the edematous mucosa with impending bleeding. Stool and colonic samples were negative for acid fast bacilli, cytomegalovirus, fungi and Clostridium difficile (C. difficile). UC was confirmed by a pathologic examination of bowel mucosa, exhibited inflammation (acute and chronic inflammatory cells) in the lamina propria and distortion of crypt architecture and crypt abscesses. Three pathologists examined the tissue samples and had a consensus on UC. Treatment was started with prednisone and sulfasalazine. Wax and wane pattern in her symptoms were observed within 2 years of follow up period before transplantation. Malnutrition and progressive anemia developed and she became refractory to treatment.

Lymphoproliferative disorder was ruled out with mediastinal and abdominopelvic CT scan. Unfortunately, serum creatinine level gradually increased with unknown etiology and progressive deterioration of renal function that continued despite treatment and eventually she went on hemodialysis.

Following renal transplantion, she had no evidence for blood or mucus in stool, and other symptoms of UC such as abdominal pain were completely cured. Her immunosuppression was maintained with the triple agents and no symptoms of UC were seen within 9 years of follow up after transplantation, and her allograft renal function remained stable as well.

Case2:

A 22 year-old Caucasian man with history of three years symptomatic UC, confirmed by histological examination, who underwent living-unrelated

donor renal transplantation. Moreover, the etiology of ESRD was uncertain and he was on hemodialysis thrice a week from 1st year before operation. In the first presentation, he had a history of weight loss, poor appetite, episodic abdominal cramping and chronic diarrhea, occasionally associated with blood-streaked stools. The patient had about 5 times bowel movements per day and about 2 to 3 times during the night. No fever or chills were reported at initial presentation. He had a pale and malnourished appearance. Lymphadenopathy and abnormal finding were not detected in chest, abdomen, pelvic, extremity and rectal exam. His medications were only vitamins and ibuprofen for intermittent migratory arthritis. He had no history of recent travel. Family history was unremarkable. No evidences of mucus, leukocytes, blood, ova parasites or pathological organisms and C. difficile toxin were detected in stool examination.

Laboratory data were notable for a normocytic normochromic anemia (Hb=8.5 g/dl), hypoalbuminemia (2.9 g/dl), hypokalemia (3.5 meq/l), hypophosphatemia (2 mg/dl) and hypocalcemia (6.8 mg/dl). His liver enzymes levels and LDH were within normal limits with an increased alkaline phosphatase (605 IU/L). His C-reactive protein (CRP) was raised and ANA and P-ANCA were negative. Serum ferritin was elevated to 1202 g/L with a transferrin saturation of 10%. Upper gastrointestinal endoscopy appeared normal while on colonoscopic evaluation, rectosigmoid mucosa was found diffusely erythematous with severe mucosal ulceration and friability.

Therefore, biopsy was performed from macroscopically intact mucosa of colon and diagnosed as proctocolitis with mononuclear inflammatory cells infiltration in the lamina propria, distortion of crypts, goblet cell depletion and crypt abscesses.

There was no evidence of granulomata, amebic protozoa or viral inclusion bodies. A barium enema revealed a featureless appearance in transverse and descending colon. UC was confirmed by two expert pathologists. Treatment was begun with prednisone and sulfasalazine. He had repeatedly experienced remission and exacerbation episodes, and then was planned to take mesalamine, oral sulfasalazine, 3 g/day. His symptoms relatively improved. However, his renal function was impaired insidiously and renal function did not resolve with discontinuation of drugs. Unfortunately, he had several recurrent UC episodes within 2 years before start of hemodialysis.

He was given prednisone 5 mg per day, CsA 50 mg twice daily and MMF 1gr twice a day as a maintenance therapy within 3 years follow up after transplantation and fortunately no flare up of UC has occurred.

Discussion

The IBD exacerbation is influenced by two factors, the immune tolerance and treatment modality (7). There are two common protocols for post-transplant immunosuppression regimens which include of CsA or Tac in combination with AZA/MMF and prednisone, which all of them will be gradually tapered (1, 4). On the other hand, the choice of appropriate medical treatment in patients who have refractory IBD to steroid is immunosuppressive agents such as AZA, CsA and MMF (9-11).

There are various studies that show AZA and MMF can result in remission of disease but Tac may cause exacerbation of IBD (7), conversely some reports demonstrated that MMF may lead to exacerbation of post-transplantation erosive enterocolitis, Crohn's colitis and refractory UC to intravenous steroid (12).

As illustrated by our experience, refractory UC can be improved in context of post renal transplant immunosuppressive therapy. Consequently, we have investigated why such paradox happens.

1-A recent onset of IBD before organ transplantation, active disease at the time of surgery, acute CMV infection and using of Tac are risk factors for IBD

worsening after transplantion (2); however, refractory UC in our patients were lasted more than 2 years. In addition, there was no evidence of UC exacerbation at the time of operation and none of them had received Tac.

2- Both UC and organ allograft are associated with expression of HLA class II (13), subsequently, low amount expression of such material to the immune system gradually produces an immune tolerance.

3- Immunosuppressive agents are not only used to prevent allograft rejection in long term (1), but also it may lead to self tolerance in IBD following transplant. Moreover, combination of immunosuppressive drugs can be effective in inhibition of other proinflamatory cytokines which participant in IBD exacerbation and allograft rejection, such as tumor necrosis factor (TNF-α), nuclear factor κ B (NFκB) and interleukin-12, which are not suppressed by CsA and Tac (1).

4- Some authors have shown that MMF may lead to exacerbation of post-transplant IBD by histological alteration of colonic mucosa (2, 4). However, small amounts of MMF can only reach GI tract, which may not induce IBD exacerbation (12).

5- Post organ transplant IBD have been predominantly observed with orthotopic liver transplant (OLT) than other solid organ transplants that were associated with other autoimmune conditions such as autoimmune hepatitis and primary sclerosing cholangitis. There is some proposition that autoimmune disorder and biliary stasis affect on IBD presentation after OLT (1, 2, 5). On the other hand, prednisone is often discontinued early after OLT in many centers and this can influence IBD activity (6).

Conclusions

The improvement of UC in our patients can be attributed to use of the immunosuppressive drugs that have become the mainstay of therapy for the IBD. Previous studies have suggested that CsA and AZA are effective in active corticosteroid-refractory UC. We conclude that the renal transplantation can be a safe and effective therapeutic option in patients with steroid refractory UC.

Conflict of Interest

None declared.

References

1. Ramji A, Owen DA, Erb SR, Scudamore CH, Yoshida EM. Post-liver transplant crohn's disease graft tolerance but not self-tolerance? Dig Dis Sci. 2002;47:522-7.
2. Hampton DD, Poleski MH, Onken JE. Inflammatory bowel disease following solid organ transplantation. Clin Immunol. 2008;128:287-93.
3. Rodriguez-Moranta F, Soriano-Izquierdo A, Guardiola J. [Current status of treatment of inflammatory bowel disease]. Cir Esp. 2007;82:254-9.
4. Haagsma EB, Van Den Berg AP, Kleibeuker JH, Slooff MJ, Dijkstra G. Inflammatory bowel disease after liver transplantation: the effect of different immunosuppressive regimens. Aliment Pharmacol Ther. 2003;18:33-44.
5. Riley TR, Schoen RE, Lee RG, Rakela J. A case series of transplant recipients who despite immunosuppression developed inflammatory bowel disease. Am J Gastroenterol. 1997;92:279-82.
6. Papatheodoridis GV, Hamilton M, Mistry PK, Davidson B, Rolles K, Burroughs AK. Ulcerative colitis has an aggressive course after orthotopic liver transplantation for primary sclerosing cholangitis. Gut. 1998;43:639-44.
7. Halim MA, Said T, Nair P, et al. De novo Crohn's disease in a renal transplant recipient. Transplant Proc. 2007;39:1278-9.
8. Halim MA, Al-Otaibi T, Elsisi A, et al. De-novo [corrected] post renal transplantation inflammatory bowel disease. Saudi J Kidney Dis Transpl.

2008;19:624-6.

9. Miehsler W, Reinisch W, Moser G, Gangl A, Vogelsang H. Is Mycophenolate Mofetil an Effective Alternative in Azathioprine-Intolerant PatientsWith Chronic Active Crohn's Disease? Am J Gastroenterol. 2001;96:782-7.
10. Domenech E, Garcia-Planella E, Bernal I, et al. Azathioprine without oral ciclosporin in the long-term maintenance of remission induced by intravenous ciclosporin in severe, steroid-refractory ulcerative colitis. Aliment Pharmacol Ther. 2002;16:2061-5.
11. Weber A, Fein F, Koch S, et al. Treatment of ulcerative colitis refractory to steroid therapy by oral microemulsion cyclosporine (Neoral). Inflamm Bowel Dis. 2006;12:1131-5.
12. Dalle IJ, Maes BD, Geboes KP, Lemahieu W, Geboes K. Crohn's-like changes in the colon due to mycophenolate? Colorectal Dis. 2005;7:27-34.
13. Hibbs AM, Bznik-Cizman B, Guttenberg M, Goldberg B, Meyers K. Ulcerative colitis in a renal transplant patient with previous Goodpasture disease. Pediatr Nephrol. 2001;16:543-6.