Abstract:
Renal transplant recipients are prone to infectious, metabolic and neoplastic complications, which is the trade off for low incidence of rejection with potent immunosuppressive drugs. Malignancy is the third common cause of death after transplantation. Normal immunological surveillance is impaired in transplant recipients due to the immunosuppressive drugs. Our patient was a 50 year lady, who had normal graft function until 9 years post transplant, presented with disseminated colon carcinoma.

Keyword: Renal transplantation, immunosuppression, colon carcinoma

Introduction: Transplantation is an effective form of renal replacement therapy for end stage kidney disease patient. The long term survival of patients undergoing transplant is increasing with the availability of potent immunosuppressive therapy which decreases the incidence of rejection. But, there is increased incidence of infectious, metabolic and malignant complications\(^1\). In the early post transplant period there is a risk of Kaposi sarcoma and post transplant lymphoproliferative disorder\(^2\). The incidence of colon carcinoma is mildly increased in the late post transplant period.

Case report: Mrs. A, 50 year old lady underwent live related donor renal transplant in March 2002. She was started on triple immunosuppression cyclosporine, azathioprine and prednisolone. After one year cyclosporine was gradually tapered and stopped. She was continued on azathioprine and prednisolone from September 2003. She maintained normal graft function till 9 years post transplant. In April 2012, she was admitted with acute dysentery. She responded to metronidazole. One month later she presented with colicky abdominal pain, vomiting, abdominal distension and mucoid stools. On examination, she had no pallor, but had pedal oedema. Her abdomen was distended with diffuse tenderness and sluggish bowel sounds. She had minimal ascites. She was diagnosed as intestinal obstruction and managed with nil per oral and intravenous fluids.
Her investigations revealed, haemoglobin-12g/dl, total count-8700, urea-24mg/dl, serum creatinine-1mg/dl, bilirubin-0.8mg/dl, AST-24IU/L, ALT-21IU/l and serum albumin-3.4g/dl. Ascitic fluid analysis- sugar 85mg/dl, albumin 1.4gm/dl, and serum ascites albumin gradient SAAG 2.0. Oral contrast enhanced CT abdomen revealed ascites, omental thickening, peritoneal thickening, and matted bowel loops in the right lumbar area. She underwent colonoscopy which showed nodular lesion in the rectosigmoid junction 18 cm from the anal verge, which was biopsied. Biopsy showed adenocarcinomatous deposits.

Haematoxylin and eosin stain of colon biopsy specimen showing poorly differentiated adenocarcinomatous deposits. MRI abdomen showed liver nodules, peritoneal thickening and ascites. She was diagnosed as a case of metastatic adenocarcinoma of colon and was advised chemotherapy. She was not willing for chemotherapy. She was discharged at request.

DISCUSSION:
The incidence of malignancy after renal transplant is 3 to 5 times higher when compared to general population. In the late post transplant period, the relative and absolute frequency of malignancy increases. The most frequent type of tumours are post transplant Lymphoproliferative disorders and non melanoma skin cancers, according to Cincinnati transplant tumour registry.

Risk factors for the development of malignancy in the post transplant period include, impaired immune surveillance secondary to immunosuppression, conventional risk factors like smoking, analgesic abuse and advanced age, genetic predisposition to cancer, presence of oncogenic viral infection, history of treatment with cytotoxic drugs and prolonged dialysis. The intensity and duration of immunosuppressive therapy by dampening anti-viral immunity and disruption of immune surveillance predisposes to malignancy. Proliferation signal inhibitors by angiogenesis inhibition and PI3K- mTOR pathway blockade inhibit tumour growth.

Malignancy can develop in three different ways- De novo occurrence in the recipient, transmission of malignancy from the donor and recurrent malignancy in the recipient. The standardized incidence ratio is the ratio of the observed number of tumours to the expected number in transplant recipients, compared with age and sex matched controls in the same geographical area.

Malignancy incidence Un- De-increased (SIR) creased

Squamous cell carcinoma of the skin Lung

Non-Hodgkins lymphoma (10.2) Prostate breast

Kaposi sarcoma (26.4) Uterus

Cervix (6.6), vulva, perineum (45.6) Ovary
Management include reduction and/or conversion to mTOR inhibitor when standardized incidence ratio (SIR>3), in addition to the specific therapies for the particular tumour type. Screening for cancer include physical examination to exclude disseminated organ involvement every 3 months during the first year after transplantation, then at yearly intervals for PTLD, skin examination by dermatologist yearly, USG or CT scan of the native kidney yearly, gynaecologic examination, including PAP smear and ultrasonography of female reproductive organs yearly, faecal occult blood testing (age >50 yr) at yearly intervals and in carriers of hepatitis B or C, abdominal ultrasound and serum -fetoprotein levels at yearly.

For non-skin cancers, KDIGO guidelines recommend solely reinforcement of the regular cancer screenings performed in the general population. The SIR of colon carcinoma is 1.24, so incidence is only slightly increased in the post transplant setting. When SIR is less than 1.5 reduction of immunosuppression is not necessary. But, reducing immunosuppressive medications may reduce complications of cancer chemotherapy. Colon carcinoma presents at an earlier age in renal transplant recipient and tend to be more aggressive, and their five year survival rate was also significantly lower than for immunocompetent patients with colorectal cancer.

Our patient presented with metastatic colon malignancy with large bowel obstruction. There is increased risk of operative morbidity and mortality associated with resection of obstructing colon carcinoma. Initial management in her would be faecal diversion by creation of proximal colostomy, to relieve obstruction. The next step would be medical therapy based on combination of biological agent bevacizumab and fluorouracil. When there is no response to first line therapy, oxaliplatin, fluorouracil, and leucovorin based second line combination therapy with bevacizumab may be tried.

The incidence of side effect like neutropenia and neuropathy is more with second line drugs. Bevacizumab is a humanized monoclonal antibody to vascular endothelial growth factor (VEGF). The risk of death was reduced by 19% for those who received bevacizumab in combination with standard chemotherapy in both the first- and second-line compared to those who received chemotherapy alone. She may be continued on her routine immunosuppression during chemotherapy with close monitoring for bone marrow suppression during therapy.

This case is presented to highlight the malignant complication of renal transplant recipient, which is one of the causes for death with the functioning graft, reducing patient survival. High index of suspicion is needed to diagnose post transplant malignancy early, as the progression is rapid with dissemination in a short span, making management difficult.

References:


