Effect of Malaria on Renal Transplant Recipient

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Malaria is widespread in India. Transplanted patients are at a higher risk of getting malaria which can severely compromise graft function and at times can cause graft loss or pose serious threat to life of the patient. Chloroquine prophylaxis can reduce the incidence of malaria in transplanted patients.

Introduction

Malaria is the most common and widespread infectious disease all over the world. Presently some 90 territories in the world are considered malarious. In middle and South Asia over 2.5 million recorded cases of malaria occur per year. In India nearly 65% of malaria is caused by Plasmodium vivax and 35% by Plasmodium falciparum. Protective immunity to malaria develops according to the level and the duration of exposure to malaria parasite by the individual. Tcell system is essential for manifestations and maintenance of immunity from malaria. Malaria affects kidneys commonly leading to tubulo-interstitial damage often presenting as acute renal failure. Mahakur reported 2.5% of all medical admissions to be due to Malaria; out of which 1.08% were associated with acute renal failure. Approximately 1% of Plasmodium falciparum infected patients suffer from acute renal failure due to acute tubular necrosis.

Considering this, it is clear that immuno-compromised patients such as recipients of renal transplantation could be more susceptible to malaria. The incidence of malaria in Gujarat State is shown in Table 1. Our institution is situated in a small town of Nadiad in South Gujarat, which is endemic for malaria and epidemics happen every year.

Our experience in renal transplantation & malaria

We first became aware of malaria leading to severe graft damage in 1987. One of our renal transplant recipient from one haplo-type match live donor, developed severe oligo-anuria on the 13th post operative day. He had achieved near normal graft function prior to this. Mild fever (peak 99.4°F) preceded the oligo-anuria by 24 hours. Renal biopsy showed extensive cortical necrosis. The peripheral blood smear on second day of oligo-anuria showed the presence of Plasmodium falciparum infection.

We had seen patients with malaria and renal transplantation prior to this as well, but as their renal functions were stable no serious note of the problem was taken. It is at this time, that study of malaria affecting renal transplantation

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Fig. 1: Graft Biopsy : Giemsa x 1000 : Shows schizonts of Plasmodium in glomerular arterioles (arrows) (See inside back cover for this microphotograph in colour).
was undertaken. 107 episodes of malaria were diagnosed at our hospital, from January 1988 to June 1992. During the same period 467 transplantations were done. Compared to this, 797 episodes of malaria were diagnosed in 14006 patients who were not transplanted. We found that transplanted patients suffer significantly more from malaria compared to Non-transplanted patients (P<0.001); also chance of getting Plasmodium falciparum infection compared to vivax is significantly higher (p<0.05) among transplanted individuals, Table No. II.

Transmission of malaria

Apart from the vector borne infection which remains same as in the community in endemic areas; there is evidence that malaria may be transmitted with blood transfusion and with organ grafts. Thus, transmission of Plasmodium with kidney grafts was reported by; Lefavour8 1980, Johnston 1981, Holzer 1985, Yenen 1994, Lee 1994 and by Hung 1994. Transmission with bone marrow was reported by Dharmasena 1986, Lefere 1996, Salutari 1996, O’Donnell 1998 and by Tran 1998. Transmission by heart was reported by Babinet 1991. Transmission with liver graft was reported by Crafa 1991 and by Talabiska 1996.

Clinical features & laboratory diagnosis

High index of suspicion is needed for diagnosis. Peripheral blood smears, both thick & thin stained with Giemsa stain should be examined repeatedly. This should be seen by a person experienced to look for malaria parasite and should be done everytime whenever there is fever and/or increase in serum creatinine in a transplanted patient, specially in endemic area and also for the patient who may have visited an endemic area.

Fig. 2: Same as figure 1 x 1600 (See inside back cover for this microphotograph in colour).
Prevention & treatment

There are no guidelines or well designed clinical trials to my knowledge in transplanted patients for preventing and treating malaria. Considering the damage malaria can do to the renal graft it is prudent to make every effort to prevent malaria. In our unit we screen all potential blood donors as well as kidney donors for malarial parasite. If malaria is detected in any blood donor or kidney donor, the person is treated with Chloroquine as per the standard WHO recommendations. They are then screened for G 6 PD deficiency and if found negative Primaquine is given orally in the dose of 7.5mg twice a day for 2 weeks. Both the recipient and the donor receive prophylaxis with chloroquine 300 mg base once a week for at least 2 weeks pre-transplantation even if blood smears are negative for malaria. The prophylaxis to the recipient following transplantation is also with chloroquine 300 mg base given twice a week indefinitely till the patient continuous to remain in endemic region. Since June 1992 till December 1995 with this regime for prophylaxis; we had 39 episodes of malaria in our transplanted patients. (Thus, 107 episodes in 54 months compared to 39 episodes in 42 months: P<0.001).

As far as treatment of malaria in transplanted patient in our centre is concerned; our first line therapy is Chloroquine in standard doses orally or intramuscular, if the renal function is unchanged. We use quinine intravenously in case chloroquine resistance is detected or in case there is associated reduction in graft function. Dose of quinine used by us is 600mg in 300ml 10% Dextrose given 12 hourly if serum creatinine is below 2mg/dl and once a day if creatinine is more than 2mg/dl. Doxycycline 100mg daily orally is added, if only partial response is seen within 48 hours of Quinine therapy.

Respiratory manifestations are common in malaria. However in our patient examination of sputum did not show any bacteria on direct smear and it was sterile on culture. Direct smear of the sputum showed presence of eosinophils.

In our unit 34 graft biopsies were performed for patients who had rise in serum creatinine and had peripheral blood smear positive for malaria. Commonest lesion on light microscopy in these biopsies was acute tubular necrosis in 16 (47.05%) patients. 11 (32.35%) biopsies did not show any abnormality. It is important to note that 4 (11.76%) biopsies showed cortical necrosis; two of these were diffuse whereas two had patchy lesion (Figure 3 & 4). Three (8.82%) biopsies showed acute interstitial nephritis without any features of tubulitis or vasculitis. The cellular infiltrate showed many eosinophils. Associated acute cellular rejection was seen in 8 (23.52%) of these biopsies.
as seen by examination of blood smear; we use mefloquine in case of quinine toxicity in the dose of 750 mg given orally stat followed by 500 mg after 6 hours and 250 mg after another 6 hours. During IV quinine therapy blood glucose is monitored daily along with ECG monitoring. On satisfactory response to initial IV therapy with quinine; it is switched over to oral quinine. We have recently used Artesunate in a case of chloroquine resistant *Plasmodium falciparum* who could not tolerate quinine and also had cerebral involvement; with excellent results. The dose used was 60 mg IV daily for 5 days.

### Outcome

Malaria poses serious hazard to the renal graft function. We lost 2 grafts and there was incomplete recovery of renal function in 6 out of 107 episodes of malaria. We have not had mortality due to malaria in our hospital; however the possibility is always real, particularly if diagnosed late and parasitemia is heavy leading to multi-organ system failure.

### Summary

Malaria is widespread in India. Transplanted patients are at a higher risk of getting malaria particularly by the falciparum species. Malaria seriously affects the graft function sometimes with loss of the graft and poses serious threat to life of the patient. Well designed studies are needed to determine pathophysiology, prevention and to ascertain ideal treatment for these transplanted patients. Prophylaxis with chloroquine to recipient and to donors seems to reduce the incidence of malaria in transplanted patients.

### References

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