Case Report

Multidrug resistant malaria in splenectomized patient

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Abstract

Malaria is a dangerous infection in splenectomized individuals. In endemic areas, managing malaria in such individuals is a clinical challenge. In the tropics, death from malaria after splenectomy has been reported, but no formal study has been undertaken. Here we discuss a case of multidrug resistant malaria in a splenectomized patient, managed by antimalarial drugs and exchange transfusion with a successful outcome.

Key words: Malaria, multidrug resistant malaria, splenectomy

Introduction

Malaria is a dangerous infection in splenectomized individuals. In endemic areas, managing malaria in such individuals is a clinical challenge. In the tropics, death from malaria after splenectomy has been reported, but no formal study has been undertaken.[1] Clinical features, therapeutic response, parasitic clearance and outcome are likely to differ in splenectomized individuals.[2] Definite guidelines to manage malaria in splenectomized individuals in different circumstances is not available.[1,3] Here we report such a case managed successfully.

Case Report

A 24-year-old-male patient underwent emergency splenectomy for traumatic rupture of spleen following road traffic accident on November 7, 2005. Four units of O positive blood was transfused intra and postoperatively. Postoperatively he was also vaccinated with pneumococcal vaccine. On the seventh postoperative day, the patient developed fever which was intermittent and of high grade. He was investigated for malaria which was negative initially. Blood culture was negative, total count was normal, abdominal ultrasonography did not reveal any septic focus and the chest X-ray was normal. Patient was treated with broad spectrum antibiotics and other supportive measures. On the 12th day, repeat malarial parasite (MP) test was positive for both plasmodium vivax and falciparum. Considering the splenectomized state and associated falciparum malaria, patient was started on Injection Arteether intramuscularly once daily for three days. Simultaneously sulphadoxine and pyrimethamine combination was administered internally. Even after three days, the patient continued to have spiking temperature and repeat MP (FT) was positive for *P. vivax* and Falciparum (4+). Hence the patient was started on Tab. Quinine 600 mg three times a day and Tab. Doxycycline 100 mg two times a day. But the patient continued to have high fever, headache, and malaise. However renal function test, liver function test and platelet counts remained normal. Even after five days of quinine and doxycycline, smear remained positive for malaria. As the situation was suggestive of R3 drug resistance, patient was given mefloquine 1,250 mg stat. On the 10th day of diagnosis and treatment with various antimalarials, the patient's general condition worsened; he developed persistent vomiting and showed evidence of mild renal and hepatic dysfunction. Patient was shifted

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Table 1: Investigation profile of the patient

Investigations	Dates						
	7-11-05	**12-11-05**	**19-11-05**	**22-11-05**	**28-11-05**	**30-11-05**	**8-12-05**
Hemoglobin (gm%)	10	12.2	-	-	-	10.3	10.5
TC (Cells/ cmm)	10200	11200	-	15600	-	20500	11200
DC (%)	N-65 L-34 E-1	N-76 L-20 E-4	-	-	-	N-45 L-54 E-4	-
ESR (mm/1st hour)	20	24	-	-	-	74	34
Urine analysis	-	Normal	-	-	-	-	-
MP (FT)	-	Negative	Positive for *P. falciparum* (++) and *vivax*	Positive for *P. falciparum* (4+) and *vivax* (4+)	Positive for (4+) *P. falciparum* (4+) and *vivax*	-	Negative
Blood culture	-	No growth	-	No growth	-	No growth	-
Chest X-ray	-	Normal	-	-	-	-	Normal
USG abdomen	-	No septic Focus	-	-	-	Grade 1 renal parenchymal changes with hepatomegaly	Mild Heepatomegaly
Epatomegaly	-	-	20	24	-	85	48
Serum creatinine (mg%)	-	-	1.1	1.2	-	5.5	1.2
Serum bilirubin (mg%)	-	-	1.2	1.2	-	1.9 Unconjugated-0.9 Conjugated-1	0.7
Serum potassium (meq/lt	-	-	-	-	-	6.5	3.8
Widal test	-	-	-	Negative	-	-	-
Parasite index (No.of parasite/ high power field)	-	-	-	-	-	360	0
Echo cardiogram	-	-	-	-	-	Normal study	-
Platelet count (lakhs)	-	-	-	2.2	-	1.76	-

to ICU care. As the patient failed to respond to most of the antimalarials and had evidence of organ dysfunction, the last option left to us was exchange transfusion. At this point of time, the case was discussed with the infectious disease specialists. Patient was started on higher antibiotics and injection artesuanate 2 mg/kg / body weight twice daily on first day and 1 mg/kg body weight for subsequent six days. Meanwhile exchange transfusion was done with two units of fresh blood on each day for five days. The patient was symptomatically better on the second day and parasite index decreased gradually. On the fifth day of postexchange transfusion patient became a febrile and the smear became negative for malaria.

Discussion

Antimalarial immunity involves humoral (IgG and IgM antibodies) and cellular (essentially involving the spleen) immune responses.[2] The role of spleen in the removal of intraerythrocytic parasites is a well documented fact.[1] The spleen may contribute to protection against human malaria by mediating humoral or cellular immune responses or by clearing both rheologically and immunologically altered host erythrocytes. Conversely, little is known about the effect of splenectomy on human malaria.[1,2] On the basis of four Thai case reports, Looareesuwan *et al* concluded that spleen may not be essential for the processes leading to parasite clearance in partially immune patients.[1] Malaria in splenectomized individuals is difficult to manage. Clinical manifestations, complications and response to treatment are difficult to predict.

Development of malaria after splenectomy is either mosquito-borne or through blood transfusion. The interval between splenectomy and acquisition of malaria seems to be important. Body's immune system and alternative reticuloendothelial system in the liver takes some time to take the charge of spleen. So, if the patient develops malaria during the immediate postoperative period, it is likely that the incubation period will be short and the outcome fatal. Along with the antimalarial drugs, it is body's immune system that is essential for parasite clearance.[2]

Although laboratory experiments using animal models have confirmed the importance of the spleen in the host's defense against Plasmodium, the exact mechanisms of

its protective effect remain unclear. Interactions between parasite antigens on the surface of the infected erythrocytes and receptor molecules on endothelial cells, allow parasitized red blood cells (PRBCs) to adhere to capillary and postcapillary venular endothelial cells. This parasite sequestration phenomenon usually limits the observable parasitemia to ring forms and gametocytes. This is not found in splenectomized primates, suggesting that the spleen removes mature *P. falciparum* stages from the peripheral blood by modulating the surface antigens involved in cytoadhesion and thus parasite sequestration.[4] Furthermore, the spleen enhances the removal of infected red cells with reduced deformability such as PRBCs and those coated with antibodies.[5] However the role of spleen in cytoadhesion and parasite clearance in acute human malarial infection depends on the immune status.[1,2] The absence of a spleen may slow down the clearance of infected red blood cells sensitized with IgG antibodies.[5] Thus, PRBCs displaying IgG on their surface membranes were actively and intensively phagocytosed by monocytes and neutrophils in the peripheral blood from patients, with a high proportion of pigment containing leukocytes.

Practically monitoring therapeutic response in malaria in splenectomized individuals is difficult as parasite clearance is reduced. Smear is likely to remain positive for a prolonged period. In this situation, whether the WHO classification of the drug resistance is applicable or not is unclear.[6] Technically, because of reduced parasite clearance, fluorescent technique may even identify the dead parasites and reports are likely to be misinterpreted.[2] So, ideally in splenectomized individuals, smear examination and parasite index has to be done by a qualified pathologist to avoid misinterpretation.

Drug treatment in these patients is not different from routine malarial treatment. As more complications are anticipated, patient needs to be monitored for organ dysfunction and parasite index daily.[2] Evidence of organ dysfunction or increase in the parasitic index is an indication for exchange transfusion along with intravenous antimalarial drugs and other organ supportive measures.

Looareesuwan *et al*.[1] reported four cases of malaria in splenectomized patients, in one nonimmune and three partially immune Thai adults. The clinical course was uncomplicated for all four patients and parasite clearance was delayed only in the nonimmune patient. Demar *et al*.[2] suggested that regardless of immune status, clinical and parasitologic aspects in asplenic humans may be the result of a complex combination of host factors such as host susceptibility and /or virulence of the strain. Only the patient who died had the merozoite surface protein 1 (msp-1) allele B-K 1 and the var D gene genotype, which is considered to be a probable parasite virulence factor. It is currently difficult to know whether these atypical parasitologic features were due to host susceptibility or to the virulence of the strain.

The largest series has been reported by Boone *et al*.[3] from Papua New Guinea. In this series (excluding cases lost to follow-up) 17 surgically asplenic patients and 33 patients who retained their spleens after splenic trauma were reviewed between one and 10 years after intervention. All 17 asplenic patients reported that they had malaria, compared with 18 of the 33 patients managed with splenic conservation and 23 of 50 in a control group. Bridgewater *et al*.[7] reported two cases of postsplenectomy malaria in civilian patients, managed successfully.

As human malaria in splenectomized individuals is likely to be severe, to prevent fatal outcome, patients living in endemic areas should continue to take antimalarial prophylaxis for life in addition to pneumococcal vaccination and Penicillin prophylaxis. Those living in the tropics, but outside malario (above 5000 feet),require prophylaxis when they travel into an endemic zone.[3,7]

Even though malaria in the immediate postoperative period in splenectomized patients is highly fatal, we could manage this patient with mixed malaria successfully using antimalarial drugs and exchange transfusion. Considering this case, we conclude that it is advisable to follow all mosquito bite preventive measures and chemo prophylaxis following splenectomy in endemic areas to prevent probable fatal outcome.

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