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Research Paper

Multi Drug Resistant Mixed Malaria in A Splenectomized Patient- A Case Report

Bio-medical

KEYWORDS : Multi drug resistant malaria, Splenectomy

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ABSTRACT

Malaria is an endemic disease in Mangalore. Malaria resistant to chloroquine and artesunate is seen in endemic areas. We present a case of a 58-year old resident of Ullal (Mangalore Taluk) who had mixed malaria (vivax and falciparum) resistant to chloroquine, artesunate, arteether, mefloquine, quinine, clindamycin and doxycycline. The patient had undergone splenectomy some years earlier due to hereditary spherocytosis. Despite appropriate multi-drug regimen, parasitemia persisted. Parasite clearance was delayed and he eventually succumbed to the overwhelming disease.

INTRODUCTION:

Treating malaria in splenectomized patients is difficult because of the decreased parasite clearance. Very few cases of malaria in splenectomized case have been reported. There are no specific guidelines for treatment of mixed malaria in splenectomized patients. This case report describes a splenectomised patient who had multi drug resistant malaria. Splenectomy was done in him when he was diagnosed with hereditary spherocytosis.

CASE VIGNETTE:

A 58-year old male patient, belonging to the local fishing community, presented with the complaints of low grade intermittent fever with chills since 3 weeks.

Before coming to us, the patient had a fluorescent antibody test done from a local laboratory which showed Plasmodium vivax trophozoites & gametes ++++.

Patient was diagnosed hereditary spherocytosis and had undergone elective splenectomy in 2009. Three weeks back, the patient was prescribed Tab. Diethylcarbamazine (DEC) 100 mg TID for mild hypereosinophilia. He had also received Tab Albendazole 400 mg then.

The physical examination revealed normal vitals except for mild fever (99.6^{0}F)

Except for the splenectomy scar in the left subcostal region, all systems were unremarkable. The repeat malaria fluorescent antibody test was positive as was the peripheral smear. The blood component cell counts were within normal limits.

Course in the hospital:

Patient was admitted and started on arteether, chloroquine and a combination of pyrimethamine and sulphamethoxazole. Other symptomatic treatment was started. DEC was discontinued .

Parasitemia persisted even after the adequate course of chloroquine and and arteether was given. Soon after this clindamycin was started and continued for ten days.

A full course of artesunate and doxycycline were also started.

The patient received primaquine 45 mg stat and then 15 mg daily.

Since the patient continued to be febrile and the fluorescent antibody test persisted to be positive, quinine was started and continued for 10 days. On day 28 after admission, mefloquine and artesunate were given for the next 3 days.

On the day mefloquine was started, the patient had loose stools and developed hypotension. The blood pressure did not pick up even after fluids were initiated, hence ionotropic support was started.

In view of impending sepsis the patient was started on piperacilin and tazobactum. Patient's liver enzymes and later serum creatinine increasedand hence the piperacilin/tazobactam dose was reduced.

He had convulsions on day 30, due to hypocalcemia which was corrected immediately. Next the coagulation profile was deranged patient was bleeding from the oral cavity bicarbonate correction was also initiated.

In view of his deranged coagulation profile and thrombocytopenia FFP, platelets and whole blood were transfused.

For serially worsening GFR dialysis was started on 30/7/12 and since parasitemia persisted patient had undergone 2 liters plasma exchange and then hemodylasis was done on 1-8-12.

Inspite of the treatment received patient succumbed to the illness on 2-8-12.

BIRDS EYE VIEW OF THE INVESTIGATIONS:

	2-7-12	6-7-12	18-7-12	22-7-12	28-7-12	29-7-12	30-7-12	31-7-12	1-8-12
Hb gm/dl	13.6			12.1	10.7	10.5		10	7
TC	7900			11600	1600	1500		8900	8500
Platelets Lakhs/cc	4.57			5.70	1.10	0.62		0.14	0.30
MPFT	PVTG ++++	PVTG ++++	PVTG ++++	PVTG ++++		PVTG ++++		PVTG +++	PVTG +++
S. creatinine mg/dl	0.6				2.6	4.0		6.7	6.6
APTT								71.7	42
INR								1.59	2.21
Blood culture	No growth				No growth				
Dengue Ab					Negative				
Leptospira Ab					Negative				
S. calcium mg/dl								5.8	7.8
T. bil mg/dl					2.0		5.7		
SGOT mg/dl					32		1060		
SGPT mg/dl					10		758		
Widal test	Negative								

P. Smear- leukocytosis with thrombocytosis

USG abdomen- spleen not visualized. No other sonological abnormality

DISCUSSION:

The spleen removes infected RBC by Fc receptor mediated immune mechanism and by recognition of reduced deformability filtration mechanism. The splenic threshold for filtration and Fc receptor mediated phagocytosis is lowered in malaria.

The spleen helps in cytoadhereance. This has been shown in Saimiri monkeys infected with plasmodium falciparum.

Due to this function spleen prevents development of severe malaria and helps in parasite clearance.

Spleen is capable of removing damaged intraerythrocytic parasites and returning the once infected red cells to circulation (pitting). This is an important contribution to parasite clearance following anti malarial drug treatment especially with artemisinin derivatives. The role of the spleen in controlling parasitemia and in the immune response is only realized in situations like this when its absence significantly contributes to the mortality (1).

The main mechanism of parasite clearance after artemesinin derivative is by the removal of the malarial parasite which are intraerythrocytic, without the destruction of the RBC. This study done by Chotivanich e.tal shows the central role of spleen in malarial parsite clearance. The spleen plays a major role in monitoring the RBC in circulation and removing RBCs that are coated with antibody or have reduced deformability and extracting intracytoplasmic particulate material, such as nuclear remnants (Howell Jolly bodies) or oxidized hemoglobin (Heinz bodies). The function of splenic clearance is increased during malariainfection. In the absence of a functioning spleen, RBC inclusions, such as dead or dying malaria parasites are found in the circulation (2).

Treatment of malaria is in splenectomised patients is controversial with no standard guidelines.

The efficacy of exchange transfusion as an adjunct treatment for severe falciparum malaria is controversial.

No sufficiently powered, randomized, controlled study has been reported**.** Exchange transfusion as an adjunct treatment for the most-severe cases was introduced in 1974, it reduces the parasite load, remove toxic substances, reduce microcirculatory sludging, and increase the oxygen-carrying capacity of the blood(3-5)

Riddle Mark S etal suggests a greater benefit from adjunct exchange transfusion in patients in Asia, compared with patients in Africa, although this factor had less effect on survival than did the subject's malaria-immunity status(6).

However, some investigators are completely opposed to the recommendation of exchange transfusion, citing successful treatment with chemotherapy alone of patients with high-grade parasitemia of up to 81%(7-9)

Boctor F.N studied 3 patients who had drug resistant malaria. He used red blood cell exchange transfusion to treat multi drug resistant malaria in 3 pediatric patients. The parasitized red blood cells were replaced by citrate phosphate dextrose adenine anticoagulant-preservative solution, leukoreduced, sickle cell-negative, red blood cells and E, C, and K antigen-negative, matching red blood cells. One-blood volume exchanges were performed once, and the fluid balance was maintained at 100% (10).

Exchanges of 1 to 2 blood volumes were recommended by some investigators (11, 12).

White NJ suggested plasma exchange to remove toxic substances and cytokines because plasma exchange is safer compared to RBC exchange (13).

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