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Malarial Hepatits in Non Endemic Area

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ABSTRACT

Kashmir valley is a non endemic area for malaria due to its high altitude. However, globalization and increased human travel has led to an increased incidence of malaria here. Further malaria can have varied presentation; therefore, a high index of suspicion is necessary especially in non endemic area. We present our experience of six patients with documented malarial infection who presented with typical clinical features of hepatitis and hence a diagnostic challenge since malaria is regarded rare in Kashmir and index of suspicion is low.

Key words:- *Malaria ,malarial hepatitis, renal failure, plasmodium falciparum*

INTRODUCTION

Malaria is a protozoal disease transmitted by the bite of an infected female *Anopheles* mosquito. Malaria not only presents as acute febrile illness but can present in the form of serious complications like cerebral malaria, acute renal failure (ARF), severe anaemia, jaundice, acidosis ,acute respiratory distress syndrome (ARDS).These complications are usually seen with plasmodium *falciparum* malaria.

Malaria is an endemic disease in 109 countries with half of world population at risk of malaria. There were 247 million cases of malaria in 2006 and nearly 1 million deaths, mostly in children under five years of age(1). Globalization and increased human travel has led to increased incidence of malaria in non endemic areas. Although liver is the first organ to be infected by malarial parasite, it is considered to be a rare cause of hepatitis. In the last decade increasing number of cases of acute malarial hepatitis are being reported from many countries especially from South East Asian Countries (2-7).]. Malaria is one of the major public health problems in India.

Around 1.5 million confirmed cases are reported annually by the National Vector Borne Disease Control Programme (NVBDCP) of India, of which 40–50% are due to *falciparum* (8).

Hepatitis in malaria occurs in around 20% of cases and it is characterised by elevated serum transaminases, particularly alanine aminotransferase Jaundice secondary to malarial hepatitis affects 5% to 20% of patients with severe *Plasmodium falciparum* malaria. Severe malaria due to *P.falciparum* may appear as fulminant hepatic failure (FHF), hepatomegaly with normal prothrombin time helps us to make the distinction between FHF due to malaria and viral FHF (9).

It is important to distinguish between acute malarial hepatitis and acute hepatitis due to other causes especially when hepatitis is severe because the response to treatment and hence prognosis is much better in the former. However, it may produce a diagnostic challenge in a non endemic area due to low index of suspicion. The aim of our study is to share our experience with malarial hepatits, how they are diagnosed and managed .

METHOD AND RESULTS

This was a prospectictive study conducted in department of gastroenterology at Sheri Kashmir institute of medical sciences soura Srinagar Kashmir, a northern state of India over a period of 2 years from Jan 2010 to Dec 211. Over a period of two years we diagnosed 6 cases of malarial hepatits who were managed at our institute.

All six patients were males with average age of 32 years (range 22-45 years), four patients were paramilitary personals posted in Kashmir and were residents of other states and two patients were residents of Kashmir. All patients gave history of travel to outside state in recent past (15 days to 2 months). All patients presented with fever and jaundice for 3-7 days. On examination, all six patients had fever, jaundice and mild to moderate hepato splenomegaly. Two patients had

grade-ll encephalopathy and two patients had grade-l encephalopathy. Laboratory investigations revealed mild to moderate anemia with average heamoglobin of 9.5 mg/dl (range 7.8-11.9 mg/dl), transaminitis with average aspartate transferase (ALT) of 581 IU/L (range 148-1540 IU/L) & average amino transferase (AST) of 620 IU/L (range 164-1630 IU/L) . Two patients had azotemia, serum creatinine 3.4 & 6.5 mg/dl. However, even in presence of severe transaminitis coagulogram and serum albumin were normal. Table 1 shows base line parameters of 6 patiens. Malaria was suspected on the basis of history & clinical presentation and exclusion of other common causes of hepatitis i.e, Hepatits A,B,C,D and Hepatits E virus infeions, Herpes simplex virus(HSV), Ebestin bar virus(EBV). Cytomegalo virus(CMV) infections and Weils disease. Septic screen was sterile.Brain imaging was normal in patients with encephalopathy. Peripheral blood film(PBF) for P. falciparam was positive in four patients and negative in two patients. Presumptive rapid antigen test (RAT) was positive in those two patients and revealed mixed infection with P. vivax and P. falciparam in one and P. falciparam in other. These smear negative cases were having severe malaria with multi organ dysfunction. All patients were treated as complicated malaria as per WHO guidelines with parentral artesunate and other supportive measures. Parenteral artesunate was given as 2.4mg/kg at 0,12 and 24 hrs then once daily. average duration of treatment was 7 days (range 5-9days).

One patient needed two sessions of hemodialysis for severe azotemia (sr. creatinine 6.5 mg/dl) and hyperkalemia (Sr. potassium 7.6 meq/l). All patients were discharged within a period of 8-14 days. All patients were diacharged on Tablet of Primaquine 15 mg OD for 14 days after ruling out gulcoss 6 phosphate dehydrogenase deficiency(G6PD) . All biochemical parameters normalized within 3 weeks. Table 2

Table 1: showing base line clinical, biochemical and hematological parameters of the patients.

	CASE-1	CASE-2	CASE-3	CASE-4	CASE-5	CASE-6
AGE (YEARS)	35	40	25	22	28	45
GENDER	MALE	MALE	MALE	MALE	MALE	MALE
PLASMODIUM SPECIES	P. FALCIPARUM PBF +	P. FALCIPARUM PBF +	P. FALCIPARUM RAT +	P. FALCIPARUM PBF +	P. FALCIPARUM PBF +	P. FALCIPARUM P.VIVAX RAT+
BILIRUBIN (mg/dl)	5.2	4.0	10.5	5.6	6.9	8.7
ALT (IU/L)	184	154	1210	250	148	1540
AST (IU/L)	190	164	1260	287	190	1630
ALBUMIN (mg/dl)	3.5	3.6	4.5	3.9	4.2	3.8
PT (seconds)	13	12	12	14	13	12
INR	1.1	1.0	1.0	1.1	1.1	1.0
HB (mg/dl)	9.6	8.8	7.8	11.9	10.6	8.0
TLC($x10^3/mm^{3)}$	5.6	4.5	5.2	6.0	3.9	5.8
PLATELETS($x10^3/mm^{3)}$	150	093	073	131	104	107
CREATININE (mg/dl)	1.2	1.1	3.4	1.2	1..4	6.5

Table 2: showing biochemical and hematological parameters of the patients on follow up

	CASE-1	CASE-2	CASE-3	CASE-4	CASE-5	CASE-6
BILIRUBIN (mg/dl)	1..0	0.8	1.4	1..2	1.1	1.9
ALT (IU/L)	48	39	45	50	45	35
AST (IU/L)	35	60	65	45	38	70
ALBUMIN (mg/dl)	3.9	3.6	4.2	4.0	4.1	3.9
PT (seconds)	13 12	12 12	12 13	14 12	13 12	12 13
INR	1.0	1..0	1..0	1..0	1..0	1..1
HB (mg/dl)	12.0	11.3	10.9	12.3	12.6	11.6
TLC ($x10^3/mm^{3)}$	5.2	4.2	4.8	5.2	4.2	4.9
PLATELETS($x10^3/mm^{3)}$	139	135	119	125	168	155
CREATININE (mg/dl)	1..0	1..1	1..2	1..0	0.9	1..2

DISCUSSION

Malaria is an uncommon cause of acute hepatitis. According to WHO, other than jaundice, signs of liver dysfunction are unusual and clinical signs of liver failure are rare unless there is concomitant viral hepatitis (10). In recent years increasing number of cases of malarial hepatitis (both falciparum and vivax) including fulminant hepatic failure are being reported from all over the world especially from South East Asian countries like India (2-7).

Malarial hepatitis refers to hepatocyte dysfunction that occurs in severe and complicated malaria and is characterized by a rise in serum bilirubin along with rise in serum transaminases to more than three times the upper limit of the normal level (11,12) . Histopathological features of severe malarial hepatitis are swollen hepatocytes, malarial pigment deposition, kupffer cell

hyperplasia and inflammatory infiltrate. The bridging necrosis and cenntrilobular necrosis, seen in fulminant hepatic failure due to other causes, is usually not seen in malarial hepatitis, hence some authors have suggested the term "acute malarial hepatopathy" instead of "acute malarial hepatitis"(11).The diagnosis of malarial hepatitis is made by demonstrating plasmodium infection, presence of at least 3 fold increase in ALT, absence of serological evidence of viral hepatitis and rapid response to antimalarials or evidence of disseminated malarial infection on autopsy (11).

Severe malarial hepatitis may simulate other causes of acute fulminant hepatitis like viral hepatitis, leptospirosis, septicemia etc. It is important to differentiate between these conditions because the prognosis of acute liver injury due to malaria is better (9) .Clinically malarial hepatitis can be differentiated from acute fulminant hepatic failure due to other causes. The features suggesting malarial etiology include persistent fever, disproportionate anemia, normal or increased liver span and normal coagulation profile even in presence of severe transaminitis (7, 9).

Devarbhavi H. et al compared 25 patients with FHF with 25 patients with severe malarial hepatopathy simulating as FHF and found no statistical difference in duration of jaundice and altered sensorium but hepatomegaly was more common in malarial hepatitis and abnormal prothrombin time was more common in FHF (9). Therefore, hepatomegaly and normal prothrombin time in the setting of FHF are highly suggestive of malarial hepatitis whereas reduced liver span and prolonged prothrombin time is suggestive of viral hepatitis. In all our patients liver span was normal or increased and prothrombin time was normal. However, D.K. Kochar et al observed that jaundice resolves much more quickly in malarial hepatitis (1-2 weeks) as compared to that of viral hepatitis (6-8 weeks) and suggested that if jaundice does not resolve in 1-2 weeks time in a patient of suspected malarial hepatitis serious consideration for presence of other concomitant disease like viral hepatitis should be made (13). The mechanism suggested to explain liver insult in malaria is ischemia, resulting from adherence of infected RBCs to endothelial cells blocking sinusoids. Hepatic dysfunction in malaria is reversible. Early recognition and prompt treatment leads to rapid reversal of liver abnormalities. No residual defect has been documented in survivors (14). Serum transaminase level starts regressing within 72 hours and normalizes over a period of 2-3 weeks. In our series jaundice improved within 2 weeks while as complete biochemical recovery took 3 weeks. Shivaraj et al reported two cases of Malarial hepatitis with renal failure due to. *P.malariae* and *P.falciparum who were managed conservatively with anti malarial treatment, we also saw two patients with* of Malarial hepatitis with renal failure who respond to anti malarial treatment, one of our patient needed hemodialysis to correct renal failure and hyperkalemia. (15)

CONCLUSION

Malarial hepatitis is a well recognized entity and should be considered in the differential diagnosis

of viral hepatitis even in non endemic areas, including Kashmir Valley. Hepatomegaly and normal prothrombin time in the setting of FHF are highly suggestive of malarial hepatitis. Early recognition and prompt treatment leads to rapid clinical improvement and complete recovery in all cases otherwise it caries high mortality.

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