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COMPARATIVE STUDY BETWEEN VISCERAL LEISHMANIASIS AND MALARIA FALCIPARUM IN CASES PRESENTED BY FEVER WITH ANEMIA IN THE REPUBLIC OF YEMEN

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Abstract

No doubt, both visceral leishmaniasis and malignant malaria are more or less common in many Eastern Mediterranean Countries. Both of these arthropod-borne infectious diseases have overlapping clinical presentations. This study aimed to clarify the main clinical features and laboratory diagnostic tests.

A total of forty *Plasmodium falciparum* patients and thirty visceral leishmaniasis patients were studied. Sheets were filled on each subject included, full history taking, full clinical examination, CBC, liver and renal function tests, x-ray chest and abdominal ultrasound, bone marrow aspiration..

The results showed that jaundice and liver affection tests were more common in malaria (jaundice, 55%, high ALT & AST, 60%) than in visceral leishmaniasis (high bilirubin, 30% high ALT & AST, 40%). Besides, the malaria affected the central nervous system (coma and impaired sensorium, 30%) more than visceral leishmaniasis (coma and impaired sensorium, 5%). The effect of visceral leishmaniasis on the lymphatic system (splenomegaly, 95% & hepatomegaly, 70%) was more than malaria (70% & 60% respectively). The visceral leishmaniasis markedly affected the bone marrow (anemia, 95%, thrombocytopenia, 65% & leucopenia, 70%) more than malaria (anemia, 28%, thrombocytopenia, 50% & leucopenia, 34%). Diarrhea and cough were common in visceral leishmaniasis (80% & 55% respectively) than in malaria (20% & 5% respectively) but DIC was common in malignant malaria (20%).

Key words: Malignant malaria, Visceral leishmaniasis, Clinical features, Laboratory diagnosis.

Introduction

Visceral leishmaniasis is parasitic protozoa sandfly-borne disease endemic to many temperate and tropical countries (Bucheton *et al,* 2003), including nearly all the Middle Eastern Countries (El-Bahnasawy *et al,* 2013) as well as Yemen (Al-Kamel, 2016). The vector in Yemen as well as all Arab Countries is female *Phelobemotus* species (Sundar and Chatterjee, 2006). The disease is characterized by prolonged fever, hepatosplenomegaly, pancytopenia, hypergammaglobinemia and proteinuria (Dortay and Mueller, 2010). The *Leishmania* parasite is found in the reticuloendothelial system (Pavli and Multezou, 2010). The infected macrophage disseminated infection to all parts of body especially the liver, spleen and bone marrow (Al Ani *et al,* 2012). In the liver, the Kupffer cells increased in size and number (Mohammed *et al,* 2008). Leishmanaisis is mainly T cell mediated disease so leishmanin skin test was proved to be good screening and epidemiological tool for identification clinical and subclinical cases (Al-Muhammadi *et al,* 2004). Visceral leishmaniasis parasites enter macrophages by inhibiting protein kinase and nitric oxide synthase (Al-Samarai and Al-Obaidi, 2009). Laboratory diagnosis of visceral leishmaniasis requires biopsied material mainly from the bone marrow, for stained smears examination, inoculation in hamster (Pace *et al,* 2009) as well as culture in NNN media or *Drosophila* media especially when the typing was indicated (Morsy, 2013). The diagnosis *Leishmania* parasites were done serologically using IHAT, IFAT, ELISA, PCR and coagulation tests (Mniouil e*t al*, 2018).

Malaria is transmitted by the female *Anopheles* bite, also blood transfusion and congenitally from mother to her fetus were recorded (Price *et al,* 2007) as well as via need le-stick injury (Abdel-Motagaly *et al,* 2017).

Plasmodium species mainly *vivax,* and *falciparum* were encountered in many Arab Countries particularly southern Saudi Arabia (Alshahrani *et al*, 2019) and Yemen (Atroosh *et al,* 2016). The presenting symptoms of malaria are non-specific and may include tachycardia, tachypnea, chills, fatigue, headache, and anorexia, nausea, vomiting abdominal pain, diarrhea, artheralgia, and myelgia (Breman, 2009). The majority of malaria deaths were due to complications of cerebral malaria (Wilson *et al,* 2007). Jaundice and renal failure were more commonly in patients with falciparum malaria. Jaundice result from either severs hemolysis or hepatic involvement (Devarbbavi *et al,* 2005). The rupture of red cells during the primary infestation of the red blood cell by *Plasmodium falciparum* leads to hemolysis and raised bilirubin level (Tamez *et al,* 2009). The red cells infested by plasmodium falciparum are sequestrated in the capillaries of important organ leading to organ ischemia and organ dysfunction (Rodriguez *et al,* 2007). Malaria hepatitis is characterized by arise in serum bilirubin and serum transaminase more than threefold of normal (Kochar *et al,* 2010).

The study aimed at the evaluation and differentiation between chronic malaria falciparum and chronic leishmaniasis as a cases presented by fever with anemia.

Patients and Methods

Forty male patients with malignant malaria *falciparum* and thirty patients with visceral leishmaniasis presented by fever with anemia attendant Alsalam Hospital at Saadah, Republic of Yemen from February 2014 to November 2014.

All Yemeni patients were subjected to: a- Full history taken, b- Clinical examination (general, chest, heart and abdomen), c- Peripheral blood film smears for malaria, d- CBC, renal and liver functions was done, e- X-ray film for chest and upper abdomen, f- Abdominal ultrasound examinations to evaluate liver, spleen and abdominal lymph nodes, & h- Bone marrow aspiration for staining and histo-pathological examination. Besides, critical cases were hosp-italized for evaluation and treatment.

Laboratory microscopic diagnosis: A- Malaria was laboratory diagnosed by the thick and thin blood films and stained in Giemsa stain for 45 minutes (Warhurst and Williams, 1996). B- Leishmaniasis was diagnosed in the bone marrow aspirated Giemsa stained smears for amastigotes (Rahi *et al,* 2013).

Results

There was high significant difference regarding to chills and significant difference regarding to altered level of conscious, dark urine, seizures, and jaundice as it common in malaria group and also there is significant difference regarding to bleeding and dyspnea as its common in leishmaniasis group (Tab. 1). There was significant difference between study groups regarding to sings as the fever, pallor, hepatosplenomegaly, asthenia were common in leishmaniasis but the jaundice, coma are common in malaria group (Tab. 2). Leishmaniasis mainly affected the blood, liver, spleen more than malaria but malaria affected the heart, kidney and central nervous system (Tab. 3). Malaria patients died commonly from coma, renal failure, liver failure and shock but in leishmaniasis died from recurrent infection anemia, bleeding tendency but less common from organ failure (Tabs. 4 & 5).

Leishmaniasis patients have special characters than in malaria group as darkening of skin, malnutrition, recurrent infection, abdominal pain and swelling, cough and lymphadenopathy (Tab. 6). Anemia degree was more sever in visceral leishmaniasis patients more than malaria ones but other parameters as CBCs and platelets were with-out significant difference (Tab. 7). Bone marrow examination showed hyperplasia and infiltration of chronic inflammatory cells as lymphocytes were common in leishmaniasis patients more than malaria one but the degree of marrow hyperplasia in leishmaniasis was related to parasitic infiltration of bone marrow and cells (Tabs. 8 & 9).

Table 1: Comparison between malaria and leishmaniasis patients' symptoms.

Data	Malaria	Leishmaniasis	P. value
Pallor	50%	98%	≤0.01
Jaundice	40%	6%	≤0.01
Fever	80%	98%	≤0.05
Hepatomegaly	30%	97%	≤0.01
Splenomegaly	40%	88%	≤0.01
Coma	15%	5%	≤0.05
asthenia	10%	37%	≤0.05
Meningeal sign	10%	5%	≤0.05

Table 2: Comparison between malaria and leishmaniasis patients' signs

Data	Malaria	Leishmaniasis	P. value
Fever	97%	97%	≥0.5
Chills and rigor	89%	7.5%	≤0.001
Altered consious	19%	5%	≤0.05
seizures	11%	2.5%	≤0.05
Dark urine	13%	2.5%	≤0.05
Nausea and vomiting	52%	75%	≥0.5
Diarrhea	8%	12%	≥0.5
Jaundice	28%	35%	≤0.05
Dyspnea	10%	42%	≤0.01
Bleeding	4%	11%	≤0.05

Table 3: Comparison between malaria and leishmaniasis affected organs.

Data	Malaria	Leishmaniasis	p.val.
Blood	80%	97%	≤0.05
Liver and spleen	50%	86%	≤0.01
Neurological	30%	5%	≤0.01
Renal	30%	10%	≤0.05
Cardiovascular	15%	12.5%	≥0.5

Table 4: Causes of death from malaria complications.

Causes	Malignant malaria
Myeloid hyperplasia	20%
Megaloplastic erythrpoisis	40%
Marrow hyperplasia	20%
Normal marrow	20%

Table 5: Causes death from leishmaniasis complications

Causes	%
Associated infections	72.7%
Hemorrhage	59.0%
Hepatic insufficiency	31.8%
Hemorrhage + infection	22.7%
Severe anemia	18.2%

Table 6: Characteristic signs of leishmaniasis patients.

Characteristic signs	%
Weight loss	90%
Darkening of skin	85%
Cough	80%
Abdominal swelling	75%
Abdominal pain	72%
Lymphadenopathy	20%
Edema of lower limb	7.5%
Infection	12.5%
Malnutrition	45%
Dyspnea	12.5%

Table 7: Parameters of CBC (Mean± SD) of both patients'groups.

Data	Malaria	Leishmaniasis	P. value
WBC (/mm3)	6380±3921	5636±4, 1500	≥0.5
Hemoglobin (g/dl)	9.8±2.8	7.5±2.5.	≤0.05
Platelets (103/mm3)	92000±2800	85600±30000.	≥0.5
Reticulocytes (%)	4.5±1.5	5.45±2.55	≥0.5
ESR (mm in 1 hour)	65.65±22.7	75.54±23.25	≥0.5

Table 8: Bone marrow examination of malaria patients

Parameters	Malignant malaria
Myeloid hyperplasia	20%
Megaloplastic erythrpoisis	40%
Marrow hyperplasia	20%
Normal marrow	20%

Table 9: Bone marrow pictures of leishmania Donavan.

Data	normal	increased	Decreased
Cellularity	75%	20%	5%
Erythropoiesis	65%	20%	15%
Myelopoiesis	65%	20%	15%
Megakaryocytes	60%	20%	20%
Lymphocytes	45%	35%	10%
Plasma cells	50%	40%	10%
Parasite index	5–10/100X (25%)	>10/100X (20%)	Absent (55%)

Discussion

Plasmodium falciparum malaria is one of the most common causes of anemia (Roberts *et al,* 2005). Multiple mechanisms cause anemia including hemolysis of infected and non-infected red blood cell, splenic sequestration of red cell dyserythropoiesis and bone marrow suppression (Newton *et al,* 1979). Thrombocytopenia was detected in most of the studied patients with severe malaria which may be a result of peripheral platelet destruction and consumption, also malarial antigen lead to sequestration of the injured platelet by macrophage in the spleen (Buffet *et al,* 2009). Thrombocytopenia is reversed quickly after treatment except if the case developed disseminated intravascular coagulation (Newton *et al,* 1979). Neurological manifestations were the major cause of morbidity and mortality in sever malaria but also the renal failure can cause death (Parkin *et al,* 2011). The mean hemoglobin level was higher in patients who died from malaria than the survivors (Khan *et al,* 2012).

In the present study, 30% of cases developed high BUN. This agreed with Wallar *et al.* (1995) who stated that about 17% cases developed high BUN due to acute renal failure and pre-renal azotemia due to dehydration and acute renal failure was due to acute tubular necrosis. Jaundice *falciparum* malaria was due to one or more factors including intravascular hemolysis, hepatic dysfunction and micro-angiopathic hemolysis associated with DIC. Serum bilirubin was elevated in the patients with hepatopathy (Mangistue and Diro, 2006). When liner enzymes was elevated they reached 2-3 times but may be elevated much beyond. Ultrasonography detected hepatomegaly with or without splenic enlargement. Low echogenicity suggests the diagnosis of malarial hepatomegaly. Enlarged liver with normal architecture is the commonest finding and splenomegaly is seen in most of cases but other sonographic finding as gall bladder thinking, renal enlargement and free fluid in the peritoneum was detected but not common findings (Bhalla *et al,* 2006). The altered sensorial or coma due to hypoglycemia or sever central nervous system infection was in 15% of cases and these clinical presentations may vary depending on the severity of infection and organ dysfunction. Hypoglycemia may occurs in cases of malaria due to increase glucose consumptions due to fever infection ,

aerobic glycolysis, metabolic demands of the parasites and as a side effect of quinine medication which stimulate the insulin secretion by the pancreatic B cells (Snow *et al,* 2005). Visceral leishmaniasis should be suspected in patients with unexplained fever. Cardinal feature, fever, hepatosplenomegaly, and pallor, duple peaks of temperature in 24 hours were highly suggestive of visceral leishmaniasis. Hepatomegaly and potential exposure in an endemic area or from areas from where leishmaniasis was reported in spleen enlarged progressively and also the liver enlarge in more than 75% of cases (Lathia and Joshi, 2004). The previous study was in agreement with the present study. Untreated cases of leishmaniasis led to 100% hepatomegaly and huge splenomegaly (Soomro *et al,* 2009). In this study, pancytopenia was among most cases, which agreed with Patrella *et al.* (2010) who stated that the majority of leishmaniasis cases developed anemia, leucopenia, and thrombocytopenia followed by neutropenia and lymphocytosis. Hepatomegaly, anemia, leucopenia, thrombocytopenia and lymphocytosis on peripheral blood smear had significant relationship with parasite load (Khan *et al,* 2012).

In the present study, bone marrow of leishmaniasis cases showed increase of plasma cells in Giemsa stained smears. This agreed with Pace *et al.* (2009) who found that high percentage of plasma cell provided a good indication towards the suspicion of visceral leishmaniasis. In the present study, bone marrow aspiration of malaria showed megalloplastic erythropiosis, hyper-cellular bone marrow and presence of gametocyte. This agreed with (Rathod *et al,* 2012).

Conclusion

The outcome results showed that in the areas where malignant malaria and visceral leishmaniasis are encountered the clinical diagnosis based may not be specific but the laboratory examination is indicated. This is special true as the pathogenicity, risky and treatment of both these arthropod-borne infectious diseases differ

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