

CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 55

A 72-year-old man presented to the Outpatient Clinic because of fever (39 °C) of 10 days duration. The patient also had a suppurative inflammation in the right hand, after a recent wound in this area. He was given ampicillin orally. The hand improved significantly; the fever initially decreased. However, 3 days later it started again with shivering and resistance to antipyretic medication. The patient simultaneously presented with jaundice with dark urine.

Physical examination revealed mild painful splenomegaly and jaundice. His hematology was as follows: Ht 28%, Hb 9.6 g/dL, reticulocytes 6.2%, WBC 12.000/μL (neutrophils 70%, lymphocytes 22%, eosinophils 5%, monocytes 3%) and platelets (PLT) 200.000/μL. The erythrocyte sedimentation rate (ESR) was 96 mm/h, LDH 890 IU/L, SGOT/SGPT 51/31 IU/L, bilirubin 4.6 mg/dL (unconjugated 3.6 mg/dL), SAP 104 IU/L, γGT 36 IU/L. Serum electrophoresis revealed polyclonal hypergammaglobulinemia. HIV antibodies were negative; HBsAg was negative. The thick blood film revealed no parasites. The patient has not often taken his anti-malaria treatment and he has not been abroad for six months.

As jaundice and anemia were aggravated the patient was admitted to the hospital. During hospitalization leukocytosis and neutrophilia increased. The thin blood films (figures 1 to 8) showed no undistorted parasites in the red cells. In spite of this, he was given anti-malaria treatment; 5 days after the fever vanished and his clinical status and laboratory findings were normal.

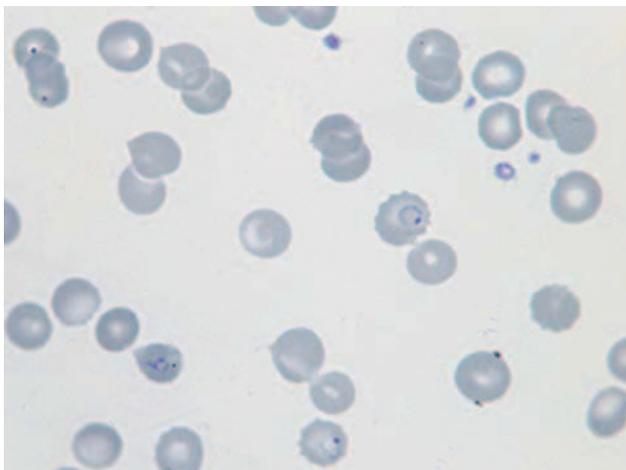


Figure 1

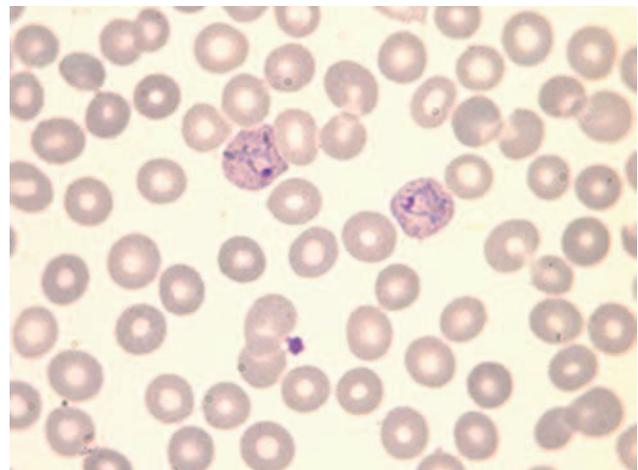


Figure 2

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2017, 34(5):712–714

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Comment

In malaria, three species are recognized in the humans namely: Plasmodium falciparum (malignant tertian), P. vivax (benign tertian) and P. malariae (quartan) malaria. In human blood, asexual and

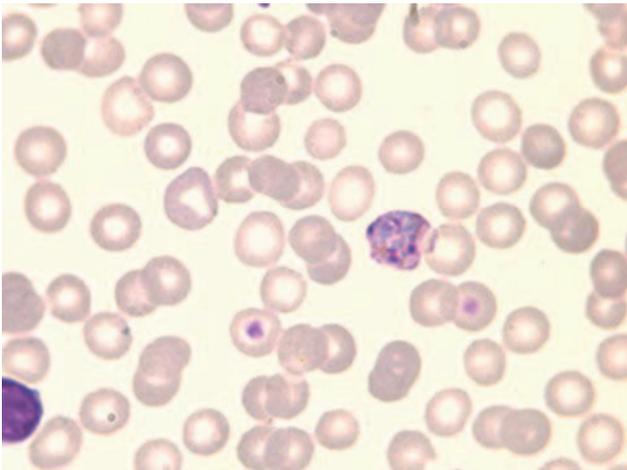


Figure 3

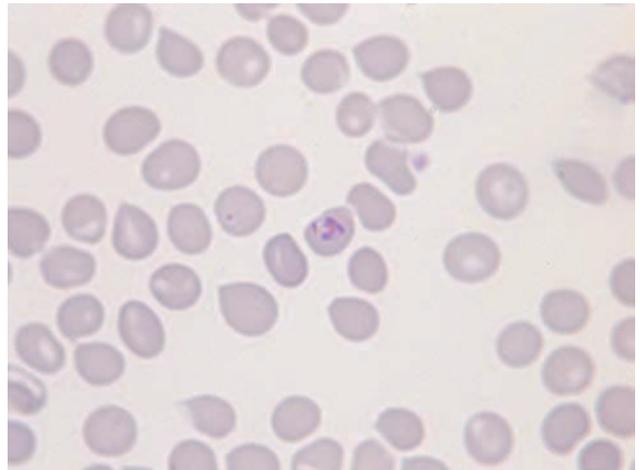


Figure 6

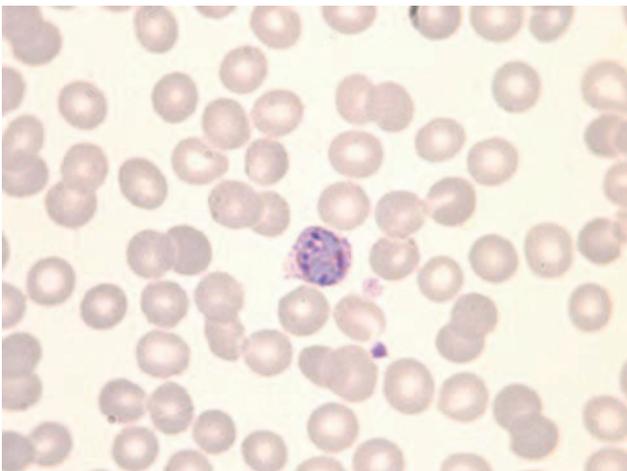


Figure 4

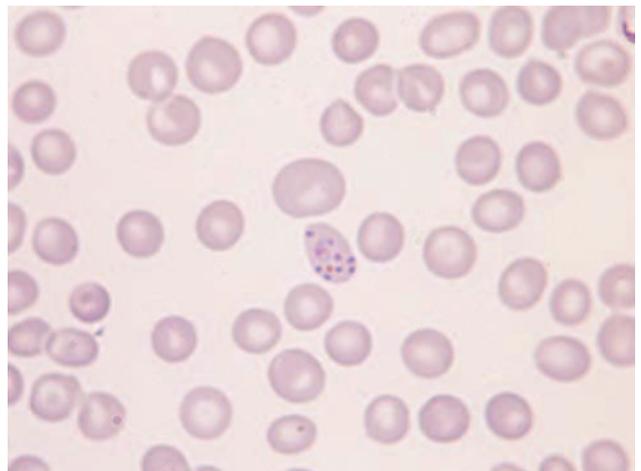


Figure 7

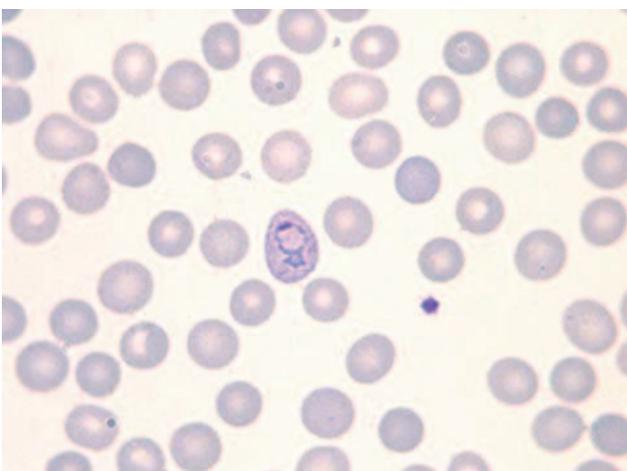


Figure 5

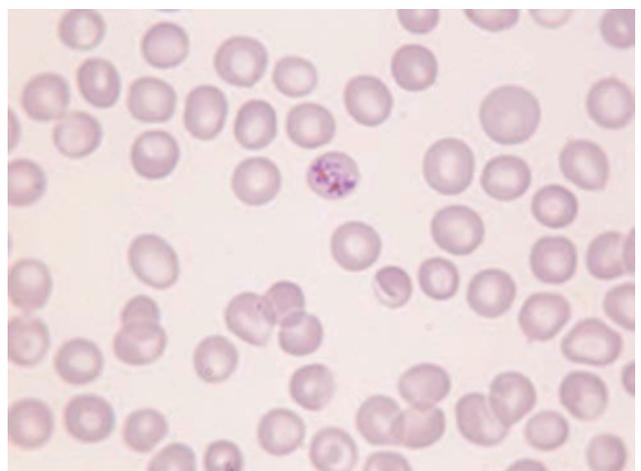


Figure 8

sexual forms can be found. The trophozoite appears as a "blue ring" formation including a red nucleus; as it develops within the erythrocyte, the latter ruptures discharging in this way the daughter merozoites into the bloodstream. These are capable of rapidly invading other red cells, thus repeating the parasite cycle. As long as the micro- and macrogametocytes (circulating sexual forms) are ingested in the blood meal of a biting mosquito, they fuse in its midgut and are finally transformed to sporozoites within its gut wall. These are inoculated to another human in the next bite. It is possible to find in the blood film early and mature ring forms, multiple erythrocyte parasitism, early trophozoites, gametocytes (male and female), division forms containing many merozoites, red cell containing plasmodium ring and surrounding Schiffner granulation etc.

The hemolytic mechanism: *P. falciparum* causes a much more intense hemolysis compared to the other species, while all of them preferably affect reticulocytes, as well as younger red cells. Many of these cells become ruptured intravascularly, as a result of the parasitic increase within them. The extent of hemolysis and the severity of anemia are greater and lower, than that caused by a single rupture of parasite, including red cells. This is attributed to the following:

Plasmodium carrying cells are destroyed (intravascular rupture, extravascular phagocytosis of the corpuscle remnant soon after the parasites are removed).

Erythroblasts and younger erythrocytes are intramedullary destroyed due to enhanced phagocytic activity, hypersplenism, as well as immune hemolysis, and

Finally, folates usually become insufficient. Red cells with parasites are phagocytosed by splenic macrophages even in non-immune hemolytic conditions. As long as the parasite is removed, the remaining red cell acquires the shape of a spherocyte (increased osmotic fragility) and is therefore, captured by the spleen.

A partial immunity is acquired however in repeated infections. On the other hand, the degree of hemolysis is greater in those cases due to erythrocytic phagocytosis within the spleen, bone marrow, liver and blood (thymus-dependent activity of macrophages). Splenic enlargement results in hypersplenism, hence a mild anemia occurs which is associated with the size of the spleen and not with the extent of parasitemia.

It has been supported that malaria facilitates immune-based hemolytic mechanisms, thus a positive direct Coombs test often exists. There are *P. falciparum* infected patients who actually produce IgG antibodies against a soluble antigen of the parasite. This antigen-antibody complex is therefore passively attached to the red cell surface. This, along with the presence of complement, makes these cells more vulnerable to phagocytosis, intensifying the degree of anemia. While an acute infection occurs, both erythroblastic hyperplasia and reticulocytosis exist, since the 9th day of parasitemia, inversely affecting, in this way, folic acid adequacy. The latter can be mainly demonstrated in cases of chronic infection or even during pregnancy. Dyserythropoiesis has also been shown in some chronic malarial cases. Iron incorporation to circulating red cells is decreased, probably due to intramedullary destruction of normoblasts and young erythrocytes. In the peripheral blood, anisocytosis, microcytosis, polychromasia, microspherocytes, red

cells with parasites or circulating gametocytes may all be observed.

In acute malaria, numerous stimulated lymphocytes or even plasma cells are seen in the peripheral blood after the 3rd day of the onset of fever (the whole hematological picture may resemble that of a lymphoid leukemia reaction). Monocytosis with monocytes acquiring vacuoles, parasitic pigments in their cytoplasm, or even phagocytized erythrocytes, may be found as well. During the first two days of infection, neutrophilia along with shift to the left of the granulocytic series is observed, whereas *P. falciparum* infection is usually characterized by the presence of neutropenia. Although their marrow ancestors are normal, the neutrophil pool is definitely decreased. On the other hand, their marginal pool is increased in the peripheral blood, while their detection by the spleen is enhanced. During recovery, leukocytosis with a shift to the left of the granulocytic series or even eosinophilia may be seen.

Acute malaria can disturb the hemostatic mechanisms in two different ways:

A moderate thrombocytopenia (capture in the spleen) along with normal or increased megakaryocytes in the bone marrow compose the picture which often exists in uncomplicated parasitemia, and

The appearance of disseminated intravascular coagulation constitutes a complication of severe acute malaria in some patients, including the whole biological spectrum of coagulation factors' disorders. An acute activity against platelets (reduction) has been found to *P. vivax*. A mild thrombocytopenia in uncomplicated malaria, does not usually cause bleeding to the patients. Purpura is also rarely present but, however, platelet values are rapidly restored as soon as therapy is instituted.

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