Hematology Quiz – Case 49

A 44-year-old Greek sailor presented to the outpatient department because of fever of one month’s duration, fatigue, weakness and dyspnea on slight exertion. He had been administered ampicillin initially and clarithromycin afterwards but with no effect. Fever reached 38.5 °C, often peaking twice daily. There were also chills, sweating, weakness and sometimes dry cough. His past medical history was unremarkable. Physical examination on admission revealed pallor, splenomegaly (the spleen was hard, non-tender and extended 6 cm below left costal margin), mild hepatomegaly (the liver was palpable 2 cm below right costal margin) and mild lymphadenopathy in the cervical and axillary region (the lymph nodes were smaller than 0.5 cm in diameter, firm, mobile and non-tender). The body temperature was 37.8 °C, pulse rate was 105/min and blood pressure was 130/75 mmHg. His hematological tests showed a normochromic and normocytic anemia (Ht 29.8%, Hb 9.8 g/dL), leukopenia (white blood cells 2.2×10^9/L; differential count: neutrophils 29%, lymphocytes 44%, monocytes 26% and eosinophils 1%) and a mild thrombocytopenia with large and bizarre platelets (98×10^9/L) although MPV was within normal range. The erythrocyte sedimentation rate was 98 mm/1h and coagulation studies were normal. Serum biochemistry was as follows: SGOT 49 IU/L, SGPT 54 IU/L, LDH 776 IU/L, GGT 59 IU/L, ALP 162 IU/L, total bilirubin 1.17 mg/dL. Serum protein electrophoresis revealed diffuse hypergammaglobulinemia (total proteins 9.8 g/dL, albumin 4.1 g/dL, and gamma-globulins 5.7 g/dL), serum electrophoresis revealed a polyclonal hypergammaglobulinemia (IgG 3,920 mg/dL, IgA 1,070 mg/dL and IgM 768 mg/dL). The tests for rheumatoid factor, antinuclear antibodies, LE cells and cryoglobulins were negative. IgM antibodies titers for EBV, CMV, HCV and VZV were not elevated while IgM antibodies for HSV were positive (titer: 1/480). Antibodies against Brucella were not detected. Blood and urine cultures revealed no bacteria. No malaria parasites were present in the peripheral blood smears. Tuberculin skin test was negative. Stool examination for ova and parasites was negative. The abdominal ultrasound showed hepatosplenomegaly (diameter of the spleen: 17 cm) without any lymphadenopathy. The bone marrow aspirate was hypercellular with an erythroid hyperplasia and megaloblastoid changes. A mild shift of the myeloid series to the left at the myelocytes stage was also present. There was a focal increase of small mature lymphocytes, plasma cells and macrophages (fig. 1). The marrow cultures for bacteria were negative. Although no bacteria were detected cefotaxime, gentamycin and metronidazole were initially administered; however, fever was not controlled and vancomycin and amphotericin were added.
The fever persisted and five days after admission small grouped vesicles on an erythematous base appeared on the abdomen (fig. 2). The rash improved dramatically, with acyclovir administration, but fever continued. A second bone marrow aspiration was decided 3 weeks after the first marrow was diagnostic (figures 3–6). The administration of the appropriate therapy was effective: Fever diminished and the blood cell count normalized.

Comment

Leishmania species constitute intracellular parasites, mainly localized within the blood and various monocytes of the organs. L. donovani (visceral leishmaniasis) can be mostly found in the monocytic population of the spleen, liver, bone marrow, lymph nodes, intestine and skin. During febrile episodes, it may also appear in the peripheral blood within these cells. There is a progressive hyperplasia of macrophages and lymphocytes leading to a massive IgG production as well as liver/spleen enlargement (splenic}
depends on the duration of the infection), hence pancytopenia occurs, the severity of which is definitely associated with the spleen size. The red cell life-span (as estimated by the use of chromium) is certainly reduced, whereas the degree of anemia really aggravates as plasma volume increases. C3 increased sensitivity to complement action restraint of erythrocytic enzymes and leishmanial production of hemolysins, all compose the hemolytic mechanism.

In the early stages of leishmaniasis leucocytosis along with a shift to the left of the granulocytic series may occur as soon as the disease is further established; however, a severe neutropenia, even descending to agranulocytosis, can take place. This is due to a poor marrow reservoir, reduced life-span of circulating neutrophils or an increase of their marginal pool, although their function is not disturbed. Reduced numbers of eosinophils, whereas increased monocytes and lymphocytes, even exceeding to leukemoid reactions, may be observed in the peripheral blood. Because of their rupture by the spleen and their life-span reduction, platelets also appear to be diminished in number. This might, anyhow, lead to epistaxis or mucosal bleeding accompanying serious platelet decreases, but is “rarely” the cause of purpura. Fibrinogen is reduced as well, and there is a marked fibrinolytic activity in the plasma. Liver disturbances, seen in the chronic phase of the disease, are followed by hypoprothrombinemia, low albumins and a prolongation of both bleeding and coagulation times.

In general the bone marrow seems hyperplastic, containing increased populations of lymphocytes, plasma cells and macrophages, many of which include the infectious organism. Neutrophils are overproduced and there is an erythroblastic hyperplasia usually acquiring megaloblastic characteristics due to folic deficiency. The bone marrow iron stores might be absent, resulting in the presence of secondary hypochromic anemia and the presence of marrow sideroblasts, but dyserythropoiesis however seems, unlikely to occur in the majority of patients, since the iron incorporation on the erythroid series cells is normal. Its reduction can be explained by taking into account the fact that reticulocytes are destroyed early within the spleen. Fetal hemoglobin appears increased as compared with red cell hyperplasia. On the other hand, marrow hyperplasia, fibrosis along with a reduced production of all cell series constitute a characteristic of only few selected cases of long-lasting chronic infections.

References


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