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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 53

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2017, 34(3):420–422

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A 75-year-old man was admitted to our Department with fever of a week duration and pain of small joints. His past medical history included generalized lymphadenopathy, hepatosplenomegaly, hypogammaglobulinemia of 8-year duration and recurrent especially pulmonary infections, under chemotherapy with monthly courses of chlorambucil-methylprednisolone therapy. Four months ago he became anemic.

Laboratory examination revealed normochromic mild macrocytic anemia (Ht 24%, Hb 7.8 g/dL, reticulocytes 185.000/μL) and slight thrombocytopenia (98×10^9/L); direct Coombs test positive; WBC 40×10^9/L; peripheral blood smear (figures 1 to 4) and bone marrow aspiration specimens (figures 5 and 6) are shown.

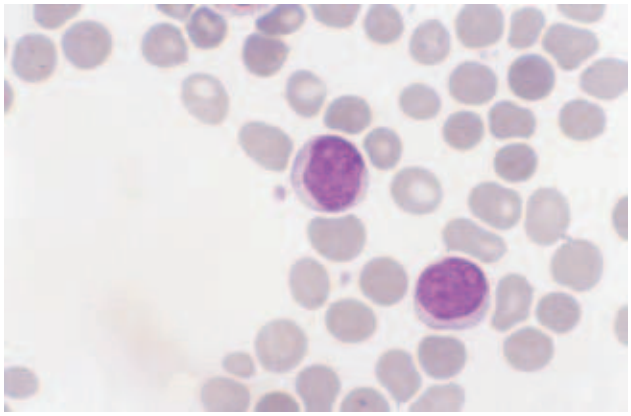

Figure 1

The erythrocyte sedimentation rate was 95 mm/h. Coagulation studies were normal. His biochemical tests were: BUN 75 mg/dL, creatinine 2.6 mg/dL, SGOT 19 IU/L, SGPT 21 IU/L, LDH 1,110 IU/L, ALP 135 IU/L, γ-GT 29 IU/L, Na^+ 141 mEq/L, K^+ 4.7 mEq/L, Ca^{++} 6.3 mg/dL, serum total proteins 6.5 g/dL (albumin 4 g/dL,

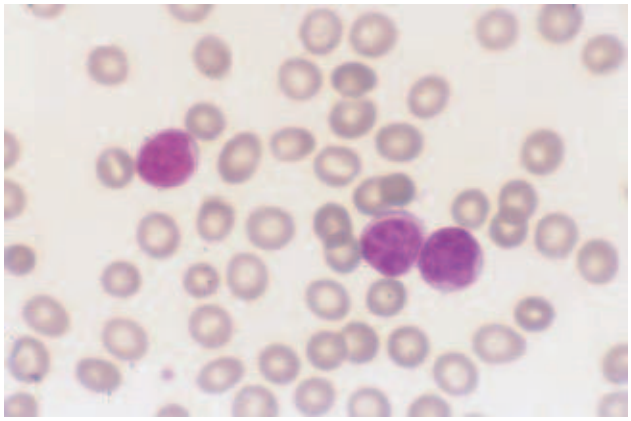

Figure 2

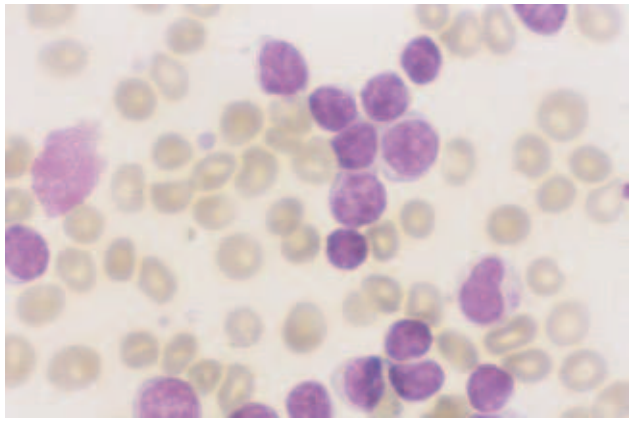

Figure 3

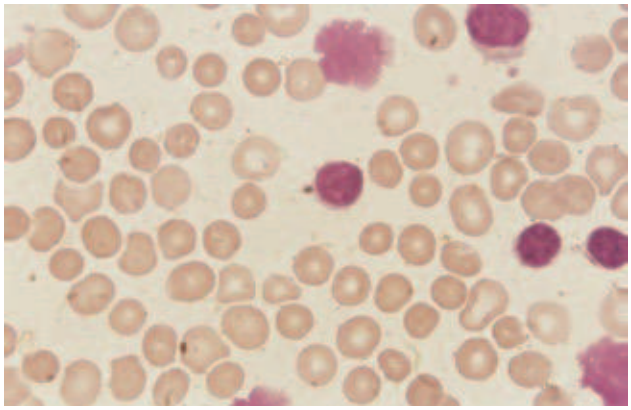

Figure 4

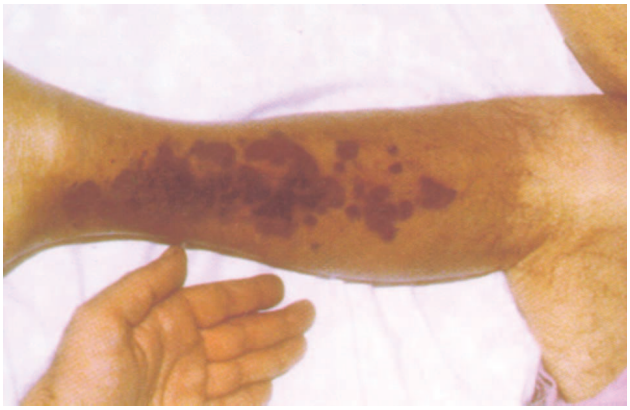

Figure 7

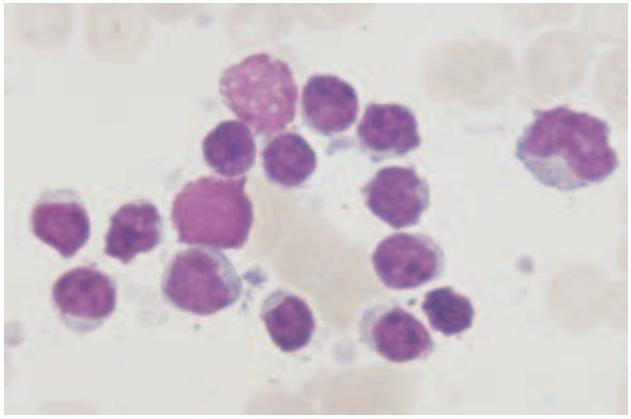

Figure 5

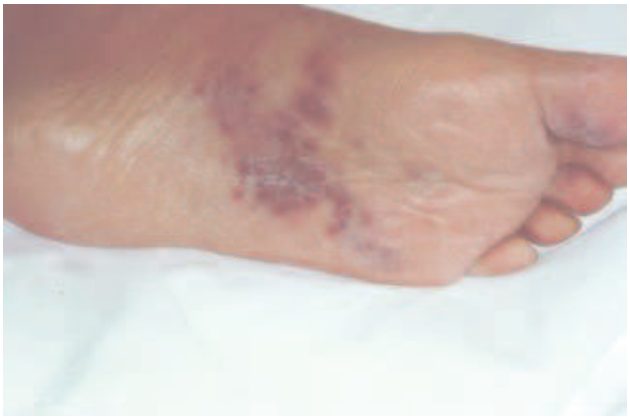

Figure 8

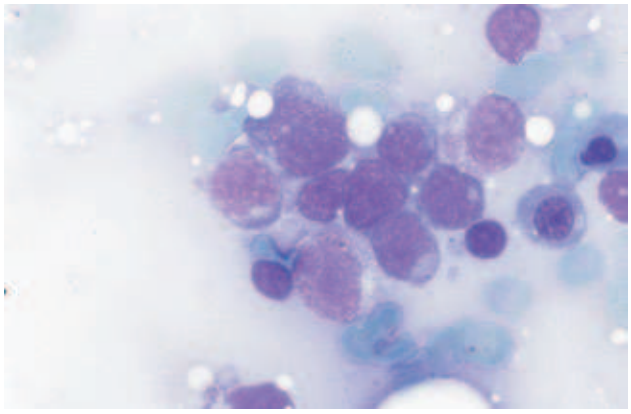

Figure 6

globulins 2.5 g/dL). The serum protein electrophoresis revealed a low spike in the area of γ-globulins. The last three months he developed a confluence palpable rash in the inferior surface of the tibia (fig. 7), and plantar area (fig. 8) (purple patches in the early lesions to red-brown-blue macules or nodules in older lesions) with rapid extension. The nodules had a large basis and were easy bleeding. The injuries was non-pruritus and painful, and the near derma was red and swollen.

Comment

This represents a lymphoid system hyperplastic disease (lymphoproliferative syndrome) because of malignant monoclonal increase of mature lymphocytes (more often B cells). These lymphocytes have a prolonged life span indicating an alteration of an apoptosis process as the main mechanism of disease pathogenicity. The disease initiation is well mild (detection usually in a context of a systematic check-up). The usual age of presentation is over 60 years of life with a male predominance.

In the hemogramme there is an absolute lymphocytosis usually more than 4.000/μL for a period of more than three months (often >50.000/μL lymphocytes). Usually the lymphocytes have a normal morphology (small size mature lymphocytes with scanty cytoplasm and round nucleus with coarse chromatin appearance) while often they present abundant smudged cells (Gumprecht cells) in the peripheral blood smear (these cells have no diagnostic value, while

they are found more often in the chronic lymphocytic leukemia [CLL] as compared to other lymphoproliferative disorders). The nuclear and cytoplasmic network is normal, while any disorder such as kidney-like nucleus or a lacy cytoplasm, in many cases, may be present. The cytoplasm is homogenous and light blue without or few granules. The nuclear cytoplasmic (N/C) ratio is usually high and the nuclear chromatin network is characteristically coarse, broken in narrow light areas without nucleoli formation. Sometimes the cells have a more abundant cytoplasm and present with nuclear network abnormalities, making the distinction of leukemic image of a nodular lymphoma difficult (immunophenotyping distinction), while rarely the cytoplasm contains crystalloid inclusions such as colorless rod-like areas in a basophilic colored cytoplasm (immunoglobulin accumulation). About 20–30% of cases contain small and large sized lymphocytes in the peripheral blood (mixed type) with a moderate amount of basophilic cytoplasm without granulation, coarse nuclear chromatin network and non-well visible nucleoli (prolymphocytes <15%), while sometimes the large lymphocytes have a fine chromatin network and well visible nucleoli (prolymphocytes from 15% to 55%). In general, cytochemical staining is not more helpful in the diagnosis (perinuclear positive PAS staining because of glycogen accumulation present in normal lymphocytes).

In the beginning of the disease the absolute neutrophil numbers are usually in normal limits and, despite the disease extension, few patients are symptomatic. In the beginning of the disease the hemoglobin level and platelet numbers are also within normal limits. The presence of anemia and or thrombocytopenia is a bad prognostic element. The disease can progress to chronic prolymphocytic leukemia or to a large cell non-Hodgkin lymphoma. The presence of spherocytosis in the peripheral blood smear indicates the existence of an autoimmune hemolytic anemia (direct Coombs test positive).

The bone marrow is hypercellular with a high lymphocytic infiltration (more than 30%). According to the infiltration severity, a satisfactory presence or decrease of other myeloid series may be present. The bone marrow biopsy is very useful when there is absence of high lymphocyte marrow infiltration. This confirms the extension and type (diffuse or nodular) of lymphocytic infiltration and the existence or absence of bone marrow fibrosis. Bone marrow biopsy is necessary for the assessment of the infiltration type (intermediate, nodular or diffuse), and for the exclusion of different types of non-Hodgkin lymphomas.

Lymph node biopsy is also helpful in the diagnosis. It usually indicates a perturbation of lymph node normal architecture and an infiltration of a monotonous small mature lymphocytic population.

The membranic indices studies indicate the monoclonal character of lymphoid hyperplasia discovering the presence of monoclonal immunoglobulin in the lymphocyte surface. The normal C cells, as well as the B cells of CLL, express pan-B antigens (CD19, CD20 και CD23), while the B CLKL lymphocytes express receptors for the rat red cells and a weak expression of surface immunoglobulins. About 95% of CLL cases the B lymphocytes are CD5 positive (T-cell antigen, found in the fetal lymphoid tissues and in lymphocytes of germinal centers periphery zone in the adults). Increased numbers of CD5+ cells in the peripheral blood are present in a patient with autoimmune diseases and after allogeneic bone marrow transplantation and it is believed that this represents an autoantibodies source (possible responsibility for the presence of autoimmune manifestations in about 20% of CLL cases). The cases of CLL with CD5 negative cells have the same clinical disease expression. There are CLL cases expressing the hairy cell, monocyte or granulocytic series type antigens.

The presence of surface immunoglobulins in B cells (more often IgM) is indicated by immunofluorescence with the use of specific antisera. It represents a monoclonal lymphocytic population, because all lymphocytes express the same heavy (more often μ) and the same light chain (more often λ). The B lymphocytes have an abnormal function. The lymphocytes of CLL represent an intermediate maturation stage between the prolymphocyte and a normal circulating lymphocyte population. Where the surface immunoglobulin is absent one can expect the T lymphocytic nature of CLL cells.

Immunologic studies indicate the existence of immunodeficiency is responsible for the frequent presence and the gravity of different infections. There is a combined perturbation of humoral and cellular immunity of patients (abnormalities of B, T and NK cells resulting in an IL-2 deficiency).

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