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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 76

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2026, 43(6):860–863

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A 46-year-old man was admitted to the hospital because of fever of four weeks' duration. Five years previously, he had received a diagnosis of HIV infection treated with highly active antiretroviral therapy (HAART). His latest CD4 count was 299 cells/μL and HIV plasma RNA was undetectable (<50 copies/mL). On examination, the patient was intermittently confused and disorientated. He was found to have pancytopenia, massive splenomegaly, jaundice, abnormal liver function tests, hyperferritinemia, hypertriglyceridemia, enlarged para-aortic lymph nodes (2–3 cm), and polyclonal hypergammaglobulinemia.

Cultures of blood, urine, sputum, and cerebrospinal fluid were negative and a chest radiograph showed no opacities. A polymerase chain reaction (PCR) assay of the peripheral blood for cytomegalovirus, serum aspergillus antigen (galactomannan), and a QuantiFERON-tuberculosis (TB) test were negative. For diagnostic evaluation of pancytopenia, he underwent bone marrow aspiration, and the results are shown in the following photographs (figures 1–9).

Comment

Perhaps no other infection has more impact on hematopoiesis than HIV infection. Anemia, leukopenia, thrombocytopenia, or a combination of types of cytopenia are common presenting manifestations. In particular, the severity of anemia increases with disease progression. Patients with HIV and pancytopenia may have a variety of bone-marrow abnormalities. Hypercellularity and morphologic dysplasia are typical, reactive plasmacytosis, antiretroviral therapy induced megaloblastoid changes and infiltration of the marrow by

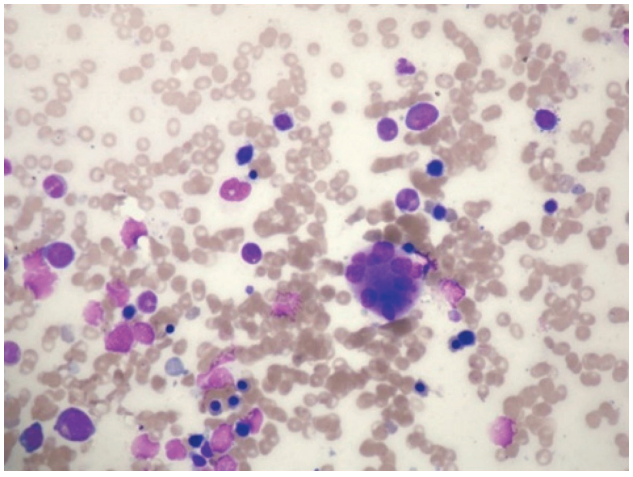


Figure 1.

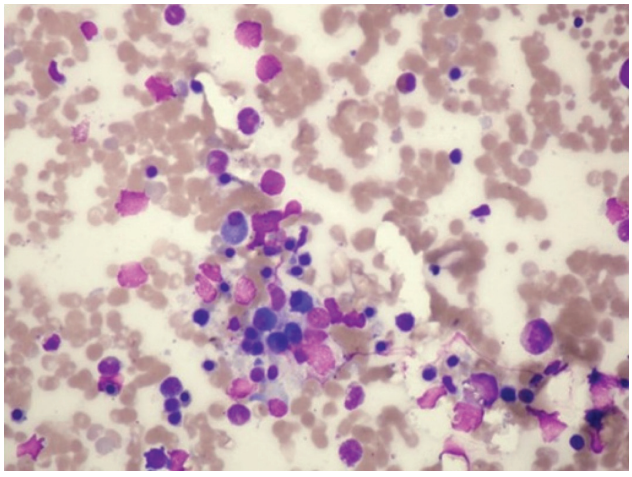
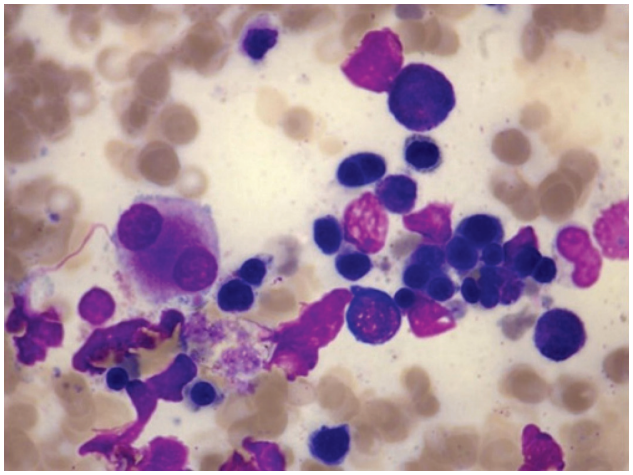


Figure 2



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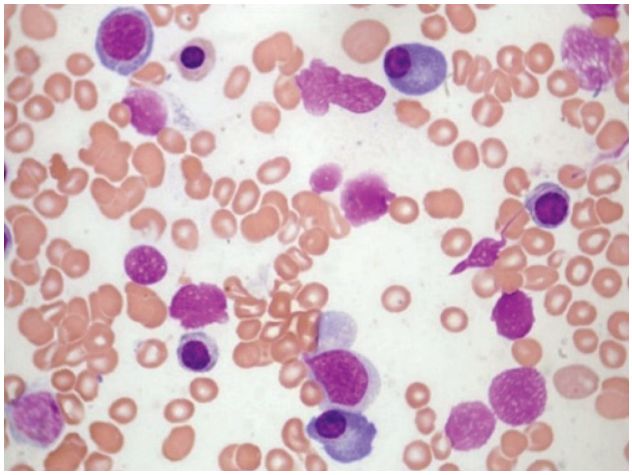

Figure 6

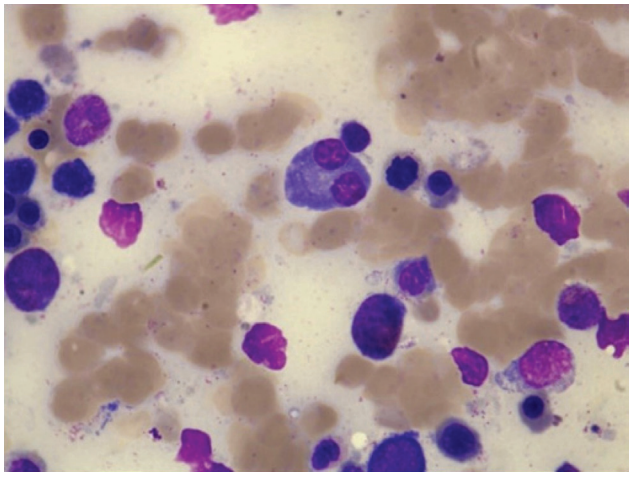

Figure 4

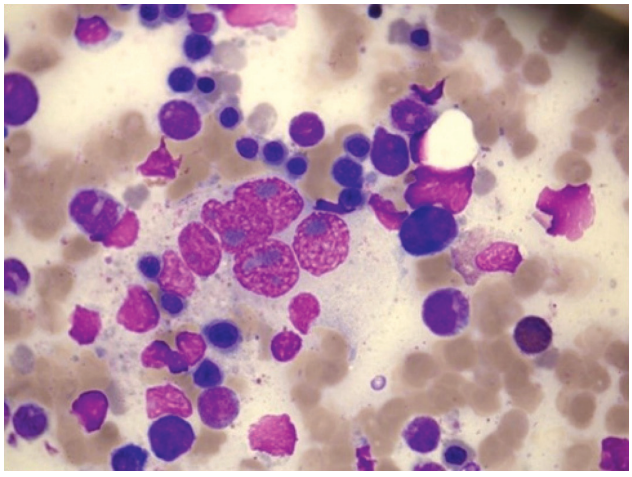

Figure 7

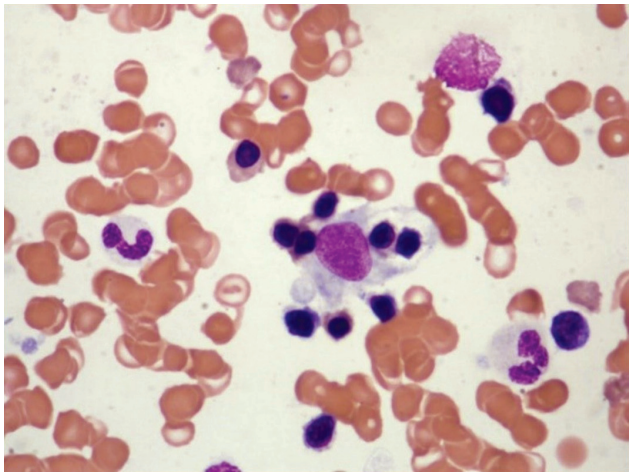

Figure 5

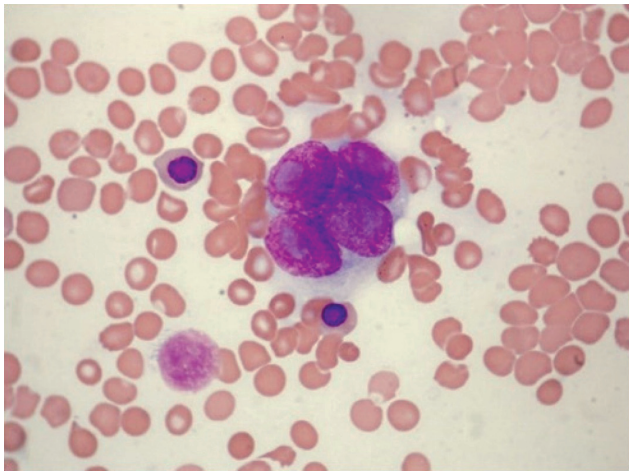

Figure 8

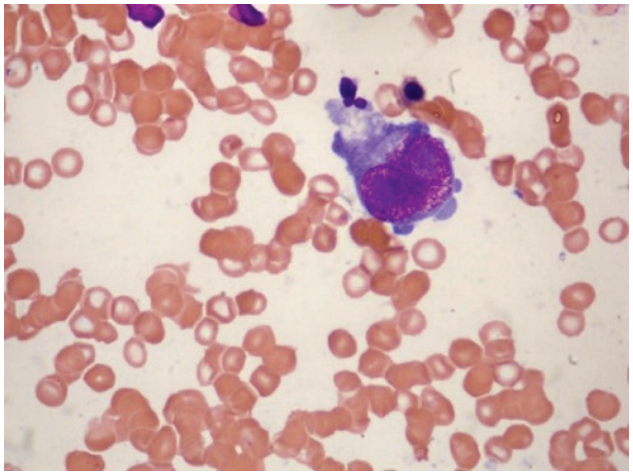

Figure 9

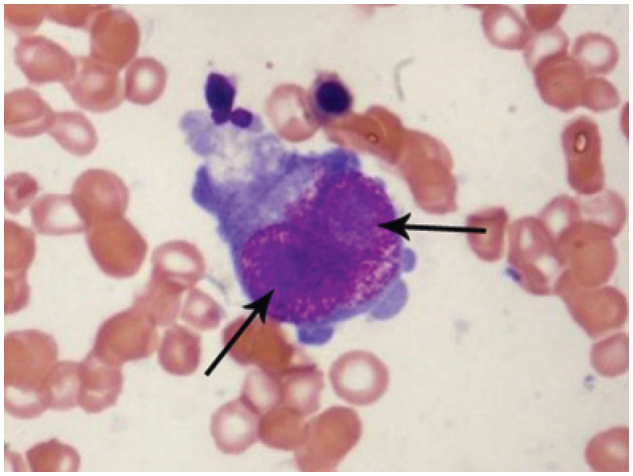

Figure 10

malignant cells or pathogens are also common, and in cases of advanced infection the bone marrow is hypocellular with serious atrophy. Even major dysplastic changes such as presence of dysplastic megakaryocytes (figures 1 and 3), dysplastic erythropoiesis, and Pelger-Huët neutrophils have been reported in HIV infection.

The following changes may be seen in the bone marrow of HIV infected patients with cytopenia: hypercellularity; dysplastic changes e.g. dyserythropoiesis and micromegakaryocytes; iron stain consistent with anemia of inflammation (i.e. storage iron plentiful with reduced number of sideroblasts); reactive plasmacytosis, binucleate multinucleate (as in fig. 4), or even plasma cells; increased macrophages and hemophagocytes (as in fig. 5); nonspecific granulomas and lymphoid aggregates; reticulin fibrosis; antiretroviral drug toxicity e.g. megaloblastic change or hypocellularity; gelatinous transformation (in advanced HIV infection); and infiltration by malignant cells, e.g. diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma and Hodgkin's lymphoma or opportunistic pathogens, e.g. visceral leishmaniasis, M. avium intracellulare complex, and H. capsulatum.

As seen in figures 2, 4 and 6, the bone marrow is infiltrated by many plasma cells. Reactive bone marrow plasmacytosis (≥5% of the total bone-marrow cell count) should raise a suspicion for multicentric Castleman's disease, angioimmunoblastic T-cell lymphoma, Hodgkin's lymphoma, and infectious diseases, in particular, visceral leishmaniasis, Kaposi's sarcoma-associated herpesvirus (KSHV), inflammatory cytokine syndrome (KICS), and HIV infection. Unlike plasma cell dyscrasias, nuclear immaturity (i.e. nucleoli) and plasmablasts are uncommon in reactive plasmacytosis. Binucleate or even multinucleate plasma cells and morula cells of Mott (Mott cells) may be seen in reactive plasmacytosis.

The bone marrow in this patient was negative for mycobacteria, parasites and fungi, but revealed the presence of large abnormal cells with abundant cytoplasm, multilobular nuclei, and one or more large blue nucleoli, as shown in figures 7, 8, 9, and 10 (arrows).

These large blue nucleoli ("owl's eyes") are characteristic of Reed-Sternberg cells (figure 11 illustrates a Reed-Sternberg cell with characteristic giant blue nucleoli in a lymph-node aspirate smear of another patient with Hodgkin's lymphoma). Bone-marrow infiltration with Hodgkin's lymphoma was confirmed by bone-marrow biopsy.

Hodgkin's lymphoma is most common in immunocompromised patients, and especially in patients with HIV infection in whom the relative risk is >50 times higher than the general population. Immunodeficiency-associated Hodgkin's lymphoma is almost always positive for Epstein-Barr virus (EBV). The cells express a type II EBV latency pattern in which expression of EBV-encoded genes is limited to EBNA1 and latent membrane proteins (LMP1 and LMP2). Both these proteins have oncogenic potential, including the activation of the NF-kappaB pathway. In HIV-related Hodgkin's lymphoma, there may be decreased CD4+ T cells and lack of CD4+ rosetting around Hodgkin/Reed-Sternberg cells. Even in the era of highly active antiretroviral therapy (HAART), the disease still has a much higher incidence compared to the general population suggesting

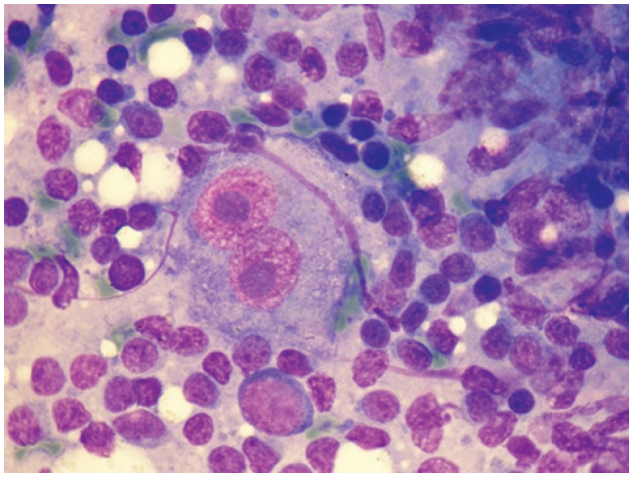

Figure 11

that HAART does not provide protection from developing Hodgkin's lymphoma. In HIV-positive patients, Hodgkin's lymphoma typically manifests with advanced stage disease and half of the patients have bone marrow involvement. Liver involvement is also common. In the era before HAART, most cases were of the mixed-cellularity or lymphocyte-depleted subtypes. Likely due to improved immunity with anti-HIV therapy, nodular sclerosis now accounts for nearly 50% of cases. The characteristics of HIV-associated Hodgkin's lymphoma, as compared with non-HIV-associated Hodgkin' lymphoma, are shown in table 1. Hodgkin's lymphoma, unlike diffuse large-B-cell lymphoma and Burkitt's lymphoma, is not considered an AIDS-defining condition.

Table 1. Clinical characteristics of patients with classic Hodgkin's lymphoma.

	Number (%)
HIV-infected patients with Hodgkin's lymphoma	
Median age *(years)*	38.5
No of men/no of women	66.7/33.3
B class symptoms	77
Bone-marrow infiltration	55
Median hemoglobin, g/L	97
Median white-cell count, $\times 10^9$/L	3.85
Known HIV infection prior to Hodgkin's lymphoma	109
Median time between HIV and Hodgkin's lymphoma, months	93.67
AIDS before Hodgkin's lymphoma	55
Mean CD4-cell count/μL (±SD)	185±147
CD4 cells <100/μL	33
Undetectable HIV-1 viral load	45
Non-HIV-infected patients with advanced Hodgkin's lymphoma	
Median age *(years)*	31
B class symptoms	69
Bone marrow infiltration	21
Median hemoglobin (g/L)	120
Median white-cell count ($\times 10^9$/L)	9

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