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Images in hematology-oncology

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CLINICAL HISTORY

A 43-year-old woman was admitted to hospital with fever and hematemesis. Laboratory studies showed hemoglobin (Hb) of 8.9 g/dL, WBC of $0.7x10^3/\mu L$, and a platelet count of $11.0x10^3/\mu L$. Differential count showed 47.1% neutrophils, 48.6% lymphocytes, 3.4% monocytes. Peripheral blood smear examination revealed anisocytosis and abnormally granulated cells.

PATHOLOGY

Bone marrow aspirate and trephine biopsy were performed. The aspirate was used for morphologic and immunophenotypic studies. Cell-suspension immunophenotypic studies were performed using the following antibodies: CD2, CD3, CD5, CD7, CD10, CD13, CD14, CD15, CD19, CD20, CD22, CD33, CD34, CD41, CD42a, CD45, CD117, MPO, CD64, TdT and HLA-DR. Flow cytometric studies showed that majority of the abnormal cells expressed CD33, MPO, and CD117 and lack of HLA-DR. Bone marrow aspirate was stained with May-Grünwald-Giemsa (MGG) and the marrow trephine biopsy with hematoxylin-eosin. The biopsy was hypercellular with marked infiltration by immature cells with abundant eosinophilic cytoplasm. The granules were not evident on the hematoxylin-eosin stain. However, occasional cells on the PAS stain contained large inclusions. The marrow aspirate was markedly hypercellular, with predominance of hypergranular promyelocytes. Many contained Auer rods, with some of them in bundles.

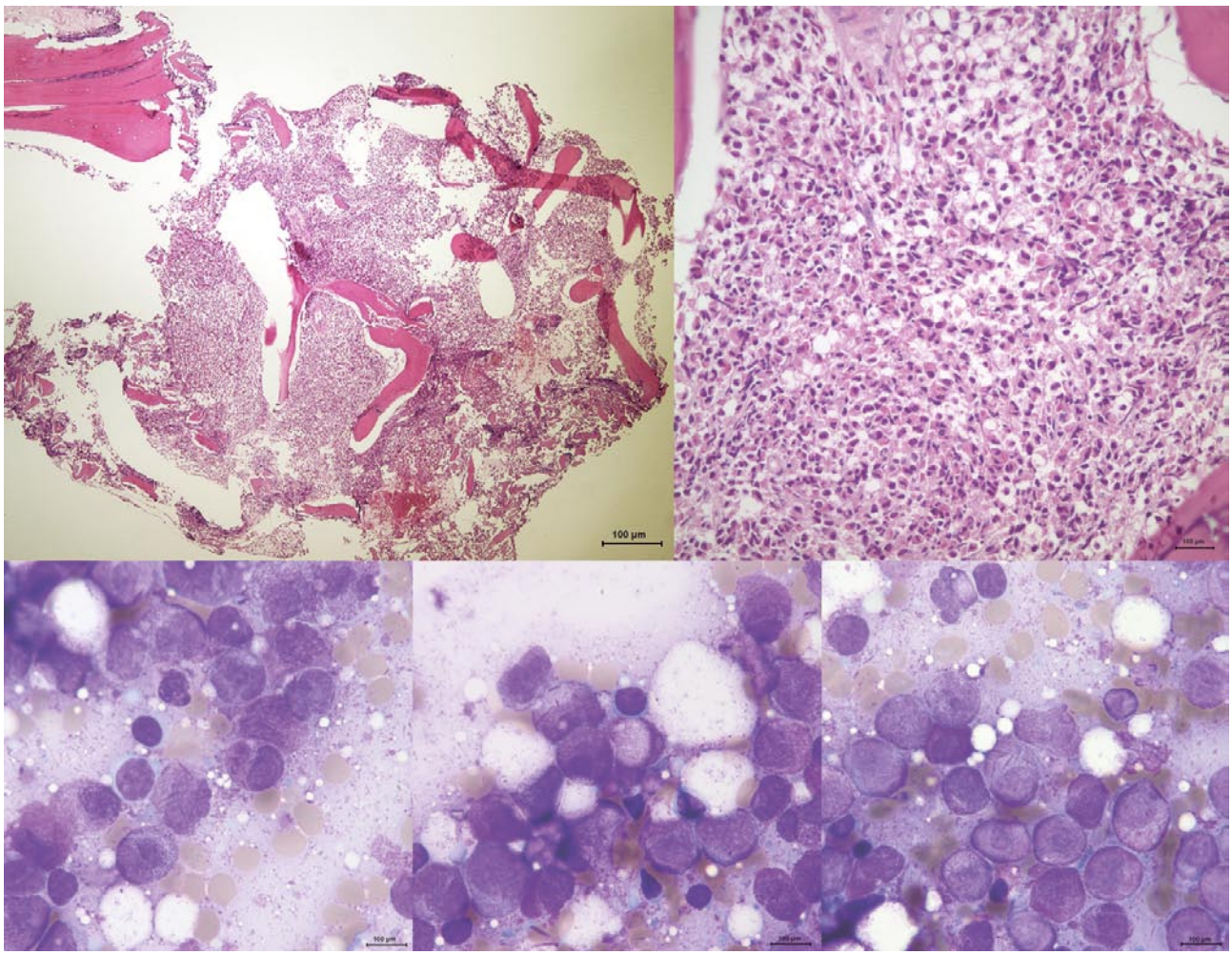
What is your diagnosis?

PATHOLOGIC DIAGNOSIS

Acute promyelocytic leukemia

DISCUSSION

APL is one of the most distinctive subtypes of AML with regard to morphologic, clinical, and cytogenetic features. In most patients, the morphologic diagnosis is straightforward, with the marrow being replaced by immature cells that resemble abnormal, unusually heavily granulated progranulocytes. The nuclei are round, usually with obvious nucleoli, and the cytoplasm is filled with multiple, large, and often coalesced, azurophilic granules. Auer rods are usually seen, and multiple Auer rods seen in sheaves (faggot cells) are frequently noted. Class II HLA antigens (HLA-DR), which are found on all hematopoietic precursors, are usually not detected or expressed. Patients with APL tend to be younger, with a median age of 30 to 40 years. APL accounts for approximately 10% of AML. APL is almost uniformly characterized by hypofibrinogenemia, variable depletion of other coagulation factors, elevated levels of fibrin degradation products, and accelerated consumption of endogenous and transfused platelets. The granular contents have been shown to contain potent procoagulants, and DIC is generally accelerated following lysis of blasts by chemotherapy, often with increased bleeding. Cytogenetic studies have demonstrated that almost all patients with APL have a characteristic translocation involving chromosomes 15 and 17 [t(15;17)(q22;q12)]; involving the retinoic acid receptor-alpha gene on chromosome 17 (RARα) and promyelocytic leukemia gene (PML) on chromosome 15. Four other gene rearrangements have been described in



APL fusing RARα to promyelocytic leukemia zinc finger (PLZF), nucleophosmin (NPM), nuclear matrix associated (NUMA), or signal transducer and activator of transcription 5b (STAT5B) genes. The resultant fusion proteins disrupt the function of RARα which blocks the normal maturation of granulocytes. Although the chromosomal translocation involving RARα is believed to be the initiating event, additional mutations are required for the development of leukemia.

References

1. Vitoux D, Nasr R, de The H. Acute promyelocytic leukemia: new issues on pathogenesis and treatment response. Int J Biochem Cell Biol 2007;39:1063-70. Epub 2007 Mar 21.
2. Di Noto R, Mirabelli P, Del Vecchio L, et al. Flow cytometry analysis of acute promyelocytic leukemia: the power of 'surface hematology'. Leukemia 2007;21:4-8.
3. Warner JK, Wang JC, Hope KJ, et al. Concepts of human leukemic development. Oncogene 2004;23:7164-77.
4. Grimwade D, Enver T. Acute promyelocytic leukemia: where does it stem from? Leukemia 2004;18:375-84.
5. Foucar K, editor. Bone Marrow Pathology. 2nd ed. Chicago, IL: ASCP Press, 2001;439-83.
6. Jaffe ES, Harris NL, Stein H, et al., editors. WHO Classification of Tumors: Tumors of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press, 2001.