Aplastic Anemia

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INTRODUCTION

Aplastic anemia (AA) is characterized by bone marrow hypocellularity in association with peripheral blood cytopenias. The incidence of AA is 1 to 3 cases per million persons per year in North America and Europe, a rate which is 2 to 3 times higher in Asia. Although patients can be affected at any age, there are 2 peaks in incidence in early childhood and young adulthood. These 2 peaks in incidence are explained by the heterogeneity of AA, which encompasses both acquired forms and the less common inherited bone marrow failure syndromes. Moreover, AA overlaps with other diseases, such as the myelodysplastic syndromes (MDS) or paroxysmal nocturnal hemoglobinuria (PNH). An understanding of these issues is important to correctly diagnose patients with AA and select an appropriate course of treatment. In this review, a case is provided to illustrate the clinically relevant aspects of AA. Specifically, the differential diagnosis and workup of a patient with pancytopenia will be discussed. In addition, the available options for first-line treatment and relapsed or refractory disease will be described.

EVALUATION OF A PATIENT PRESENTING WITH PANCYTOPENIA

CASE PRESENTATION

A 25-year-old man presents to the emergency department and reports several weeks of fatigue, exertional dyspnea, and easy bruising. The patient has no significant past medical history. He is afebrile, with a blood pressure of 120/80 mm Hg, a regular heart rate of 80 bpm, and 97% oxygen saturation on room air. Physical examination is remarkable for pallor of the conjunctivae, a systolic ejection murmur at the left upper sternal border, and several ecchymoses on his upper and lower extremities. A complete blood count shows a white blood cell (WBC) count of 1.4 × 10^9/µL (4.5–11.0 × 10^9/µL), a hemoglobin level of 7.0 g/dL (normal, 13.0–17.0 g/dL), and a platelet count of 18 × 10^9/µL (normal, 150–450 × 10^9/µL). The absolute neutrophil count is 400/µL (normal, 2000–6500/µL), and the differential shows no WBC forms. Other routine laboratory studies (including electrolytes, creatinine, and liver function tests) are unremarkable.

• What is the differential diagnosis for this patient?

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for a patient presenting with pancytopenia (Table 1) can be categorized in terms of bone marrow cellularity. Pancytopenia that occurs with a hypocellular marrow suggests AA, viral infection (notably HIV infection), or direct toxic injury to the marrow (eg, radiotherapy, chemotherapy). Pancytopenia that occurs with a hypercellular marrow suggests malignant bone marrow infiltration, which is frequently hematologic in origin (eg, leukemias, lymphomas, multiple myeloma, MDS). Solid tumors can also metastasize to the bone marrow; however, pancytopenia is an unusual presenting complaint as the primary tumor or other metastatic sites are often clinically apparent by that time. Also, some hematologic malignancies can present with a hypocellular marrow, most notably hypocellular MDS. Nonmalignant causes of pancytopenia with a hypercellular marrow include infections (tuberculosis or atypical mycobacterial infections, ehrlichiosis, legionellosis, overwhelming sepsis), connective tissue diseases (eg, systemic lupus erythematosus), nutritional deficiencies (vitamin B12 or folate deficiency), sarcoidosis, Kikuchi-Fujimoto disease, and hypothyroidism.

The history, physical examination, and/or results of basic laboratory studies may aid in diagnosing a patient with pancytopenia. For example, AA is usually characterized by an absence of associated clinical findings beside those directly related to the pancytopenia. As splenomegaly is exceedingly rare in AA, its presence should strongly suggest an alternative diagnosis. Laboratory studies also may indicate that pancytopenia is caused by nutritional deficiency. If the patient has mild pancytopenia and is otherwise well, it may be possible to await the results of blood work before undertaking additional studies.

• Which additional diagnostic studies should this patient undergo?