

HOSPITAL PHYSICIAN®

HEMATOLOGY BOARD REVIEW MANUAL

STATEMENT OF EDITORIAL PURPOSE

The *Hospital Physician Hematology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in hematology. Each manual reviews a topic essential to the current practice of hematology.

PUBLISHING STAFF

PRESIDENT, GROUP PUBLISHER

Bruce M. White

EDITORIAL DIRECTOR

Debra Dreger

ASSOCIATE EDITOR

Rita E. Gould

EDITORIAL ASSISTANT

Farrowh Charles

EXECUTIVE VICE PRESIDENT

Barbara T. White

EXECUTIVE DIRECTOR OF OPERATIONS

Jean M. Gaul

PRODUCTION DIRECTOR

Suzanne S. Banish

PRODUCTION ASSOCIATE

Kathryn K. Johnson

ADVERTISING/PROJECT DIRECTOR

Patricia Payne Castle

SALES & MARKETING MANAGER

Deborah D. Chavis

NOTE FROM THE PUBLISHER:

This publication has been developed without involvement of or review by the American Board of Internal Medicine.



Endorsed by the
Association for Hospital
Medical Education

Aplastic Anemia

Series Editor:

Eric D. Jacobsen, MD

Instructor in Medicine, Harvard Medical School, Department of Medical Oncology, Brigham & Women's Hospital and Dana-Farber Cancer Institute, Boston, MA

Contributor:

Philippe Armand, MD, PhD

Instructor in Medicine, Department of Hematology and Oncology, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA

Table of Contents

Introduction	2
Evaluation of a Patient Presenting with Pancytopenia.....	2
Treatment	5
Conclusion	10
References	10

Cover Illustration by Christine Armstrong

Copyright 2007, Turner White Communications, Inc., Strafford Avenue, Suite 220, Wayne, PA 19087-3391, www.turner-white.com. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, mechanical, electronic, photocopying, recording, or otherwise, without the prior written permission of Turner White Communications. The preparation and distribution of this publication are supported by sponsorship subject to written agreements that stipulate and ensure the editorial independence of Turner White Communications. Turner White Communications retains full control over the design and production of all published materials, including selection of topics and preparation of editorial content. The authors are solely responsible for substantive content. Statements expressed reflect the views of the authors and not necessarily the opinions or policies of Turner White Communications. Turner White Communications accepts no responsibility for statements made by authors and will not be liable for any errors of omission or inaccuracies. Information contained within this publication should not be used as a substitute for clinical judgment.

Aplastic Anemia

Philippe Armand, MD, PhD

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,¹ a rate which is 2 to 3 times higher in Asia.² 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 $1.4 \times 10^3/\mu\text{L}$ ($4.5\text{--}11.0 \times 10^3/\mu\text{L}$), a hemoglobin level of 7.0 g/dL (normal, 13.0–17.0 g/dL), and a platelet count of $18 \times 10^3/\mu\text{L}$ (normal, 150–

$450 \times 10^3/\mu\text{L}$). The absolute neutrophil count is $400/\mu\text{L}$ (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?