Chapter 6
Bone Marrow Examination in Systemic Disorders

ABSTRACT

Systemic disorders can induce several bone marrow abnormalities; most are nonspecific, and some morphologic clues can help diagnose them. Examination of the bone marrow is critical in specific clinical scenarios, such as uncertain etiology for cytopenia, newly developed disease complications, and detecting diagnostic criteria. Cytopenia of one or more blood elements is common in many systemic diseases and may require deep investigations, including bone marrow examination, to explain, e.g., chronic kidney and liver diseases. Other conditions with a profound effect on hemopoiesis may resemble primary hemopoietic disorders like dysplastic changes, e.g., severe infections and chronic inflammatory diseases. In addition, bone marrow examination is integral to investigating specific systemic conditions by confirming a particular etiology and pathogenesis, e.g., fever of undermined origin and systemic amyloidosis. This chapter discusses disease examples in each clinical group, their etiological and pathogenic factors, and their essential diagnostic features.

INTRODUCTION

Reactive bone marrow describes a polyclonal bone marrow response to various local or systemic 'insults,' often inflammatory, which can induce a broad spectrum of morphologic changes. *(McGraw-Hill, 2002*).

Many systemic disorders are associated with inflammatory or metabolic changes involving several tissues, including the hemopoietic system. However, these changes are seldom severe or unexplained to warrant bone marrow examination. A few clinical contexts may require bone marrow evaluation in patients with systemic disorders. Notable clinical examples include a newly developed clinical or laboratory finding unexplainable by the underlying disease mechanism, known sequelae or complication of the disease warranting bone marrow examination, or when bone marrow examination is an integral diagnostic step of a suspected systemic disorder. *(Spivak, 2005).*

A common example of the first clinical situation is the development of treatment-resistant, unexplained anemia in chronic liver or kidney disease. Individuals with stable systemic diseases such as autoimmune disorders or chronic infections may develop an alarming clinical or laboratory abnormality such as signs of a bone marrow hypofunction or fibrosis. Fever of Unknown Origin (FUO) or recurrent

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fever with severe neutropenia exemplify cases requiring a comprehensive diagnostic workup integrating bone marrow evaluation. (*Hasserjian, 2008&Spivak, 2005).*

In all these conditions, diagnostic evaluation of the bone marrow is challenging and often requires specific ancillary investigations.

This chapter aims to raise alertness to the specific indications for bone marrow examination in patients with benign systemic disorders. The schematic workup of bone marrow examination and its particular diagnostic value in these situations are emphasized.

Systemic Disorders With Unexplained Abnormal Finding

Overview

Inflammatory mechanisms in many systemic disorders could disturb growth factors and cytokine release or reduce the circulating blood cells' lifespan, inducing hematologic abnormalities. In a few instances, abnormalities may be unexpected or exaggerated. *(Wanitpongpun et al., 2012).*

Common examples include chronic renal and liver diseases. (Spivak, 2005).

Chronic Kidney Disease

Indications for Bone Marrow Examination

1. Unexplained anemia and EPO resistance are the most typical indications for bone marrow examination in chronic kidney diseases, and can also reveal an unexpected cause, such as pure red cell aplasia (PRCA) or hyperparathyroidism. *(Santos et al., 2020).*
2. A bone biopsy is the gold standard for diagnosing specific types of renal osteodystrophy

Mechanisms and Pathogenesis of Hematologic Abnormalities

Unexplained Anemia and EPO Resistance

Anemia in renal diseases is often proportional to the degree of renal impairment with a hemoglobin reduction of about two g/dl with every ten mmol/l rises in the blood urea and a gradual decline of MCV. The anemia may become resistant to erythropoietin (EPO) due to increased phosphatidylserine expression. The EPO reduction will also affect the megakaryocyte colony-stimulating factors (CSF), acetyl-hydrolase, and paraoxonase. *(Latif et al., 2017)*

In advanced stages, the anemia becomes disproportionate to the disease severity, and bone marrow examination is warranted.

Thrombocytopenia

Thrombocytopenia is a late-developing complication related to deranged platelet kinetics induced by hemodialysis, progressive vascular damage, intermittent use of heparin, and clotting in the dialyzer enhancing platelet consumption. *(Horina et al., 1991).*