Initial Evaluation of the Patient with Waldenström Macroglobulinemia

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KEYWORDS

• Waldenström macroglobulinemia • Bone marrow aspiration • Anemia
• Hyperviscosity • Cryoglobulinemia • Peripheral neuropathy • Bing-Neel syndrome
• Amyloidosis

KEY POINTS

- The initial evaluation of the patient with Waldenström macroglobulinemia can be challenging.
- Not only is Waldenström macroglobulinemia a rare disease, but the clinical features of patients with Waldenström macroglobulinemia can vary greatly from patient to patient.
- The authors provide concise and practical recommendations for the initial evaluation of patients with Waldenström macroglobulinemia, specifically regarding history taking, physical examination, laboratory testing, bone marrow aspiration and biopsy evaluation, and imaging studies.
- The authors review the most common special clinical situations seen in patients with Waldenström macroglobulinemia, especially anemia, hyperviscosity, cryoglobulinemia, peripheral neuropathy, extramedullary disease, Bing-Neel syndrome, and amyloidosis.

INTRODUCTION

Given its rarity and a highly variable clinical presentation, the initial evaluation of the patient with a clinicopathologic diagnosis of Waldenström macroglobulinemia (WM) can be challenging. The clinical manifestations of WM can be associated with infiltration of the bone marrow and other organs by malignant lymphoplasmacytic cells and/or the properties of the monoclonal IgM paraproteinemia, and include anemia, hyperviscosity, extramedullary disease, peripheral neuropathy, cryoglobulinemia, cold agglutinemia, and coagulopathy, among others. It is important to note, however, that a substantial number of patients with WM can be asymptomatic at diagnosis.

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Hematol Oncol Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.hoc.2018.05.008 **hemonc.theclinics.com**

It is paramount to appropriately evaluate patients with WM to better inform the need for further evaluation, appropriateness of treatment initiation, and treatment options. The objective of this review was to succinctly summarize current recommendations with regard to initial evaluation of patients with WM. The recommendations provided herein are in line with those from the International Workshop for Waldenström macroglobulinemia and the National Comprehensive Cancer Network.

ESSENTIAL EVALUATION

The essential evaluation of the patient with a diagnosis of WM must include a history and physical examination, laboratory studies, bone marrow aspiration and biopsy, and computed tomography (CT) scans of the chest, abdomen, and pelvis with intravenous contrast.[1] It is important to note that there is no sign or symptom pathognomonic of WM. However, the presence of particular clinical findings can help to direct additional evaluation. Additionally, other causes of any sign, symptom, or laboratory or imaging finding should be further investigated to determine the likelihood of its relation to WM.

HISTORY

A careful and systematic history taking can provide information not only on the presence of constitutional symptoms such as fevers, night sweats, or unintentional weight loss, but also for potential alternative causes for these symptoms. Symptoms associated with anemia are very common in patients with WM, and include fatigue, malaise, and shortness of breath. Symptomatic hyperviscosity can induce recurrent episodes of spontaneous epistaxis, new-onset headaches, and blurred vision.[2] WM-related neuropathy is typically sensory and affects the feet more than the hands in a bilateral and symmetric pattern. If advanced and prolonged, it can manifest as muscle weakness and muscle wasting.[3] A history of skin color changes induced by exposure to cold temperatures may indicate the presence of cryoglobulins. Recurrent episodes of urticarial rash might be associated with Schnitzler syndrome.[4] Increased bruising or mucosal bleeding can be due to thrombocytopenia or acquired von Willebrand disease. Finally, recurrent upper respiratory infections might indicate secondary hypogammaglobulinemia.

PHYSICAL EXAMINATION

The physical examination can reveal lymphadenopathy and/or hepatosplenomegaly. Raynaud phenomenon or ulcers in the lower extremities or tip of the nose and ears can be manifestations of cryoglobulinemia.[2] Darkening of the urine after exposure to cold might be a manifestation of cold agglutinemia.[5] Skin examination might reveal urticarial rash, lymphomatous lesions, purpura, or bruising. A neurologic examination can reveal sensory or motor deficits in upper and lower extremities and can indicate peripheral neuropathy. Cranial nerve deficits can be a manifestation of Bing-Neel syndrome (BNS).[6] A funduscopic examination can reveal engorgement, increased tortuosity or “sausaging” of retinal vessels or retinal hemorrhages in patients with hyperviscosity.

LABORATORY STUDIES

Essential laboratory studies include a complete blood count, peripheral blood smear evaluation, complete metabolic panel, quantitative serum immunoglobulins (IgA, IgG, and IgM), serum and urine protein electrophoresis with immunofixation and beta-2-microglobulin level. The complete blood count can identify patients with WM with