Differentiating IgM Multiple Myeloma From Waldenstrom's Macroglobulinemia

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IgM Multiple Myeloma (MM) and Waldenstrom's Macroglobulinemia (WM) are two distinct hematologic entities with the common finding of an IgM monoclonal gammopathy. Distinguishing these two diagnoses is critical as management is significantly different for initial therapy, selection for autologous stem cell transplant and choice of long term maintenance.

Although it is apparent from clinical practice that there are overlapping features of the two diseases, it is critical to define them in such a way that they can be strictly differentiated. Furthermore, it is best to use an objective measure that is reproducible to ensure its accuracy and sustainability. As knowledge of a disease evolves, that definition may be broadened.

A recently proposed definition of IgM MM that will clearly identify patients with the disease is as follows: a symptomatic clonal plasma cell proliferative disorder characterized by an IgM monoclonal protein (regardless of size), 10% or more plasma cells on bone marrow biopsy, plus the presence of lytic bone lesions and/or translocation t(11;14). This was generated by the largest reported series in the literature by the Mayo Clinic. (see Table 1)

The use of t(11;14) is pertinent in that it is not sensitive (could not be a mandatory feature to definition) but is rather specific to IgM MM and is there valuable. Similarly, lytic bone disease is specific to myeloma, but is not a feature of WM. The lack of the inclusion of immunohistochemistry is notable and controversial; however, this is a test with variability and does not genuinely discriminate these two diseases. Other clinical features such as anemia, hypercalcemia and renal dysfunction are not specific enough to MM to be included in diagnostic criteria for IgM MM. A subset of patients without lytic lesions or t(11;14) who do not clearly meet criteria for WM require further study.

In the Mayo Clinic series, median survival of patients with this strict definition of IgM MM had a median survival of 30 months (similar to those with non IgM MM). This is shorter than would be expected for WM, further corroborating a discrete clinical condition of IgM MM that must be distinguished from WM.

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Table 1. Clinical Characteristics of Mayo Clinic Series Patients with IgM Myeloma at Time of Diagnosis*

Clinical characteristicS	Median value (range)	Percentage of patients with abnormal level
Age, years	66 (51-77)	
Lytic Lesions	__	100%
t(11;14)	__	38%
Hemoglobin, g/dL	10.2 (6.1-13.3)	95.2% (Hgb < 13.2)
Creatinine, mg/dL	1.4 (0.7-3.6)	47.6% (Cr > 1.3)
Corrected Calcium, mg/dL	10.4 (8.5-14.4)	61.9% (Ca > 10.1)
IgM, quantitative, mg/dL	4660 (160-11400)	90.5% (IgM > 300)
M-spike, mg/dL	3.1 (0.001-6.2)	47.6% (M-spike ≥ 3)
β2-macroglobulin, mcg/mL	3.61 (1.7-8.51)	92.3% (level > 1.8)
Viscosity, centipoise	4.0 (0.9-12.7)	85.0% (level ≥ 1.5)
Bone marrow plasma cell, %	50 (20-100)	100% (> 10%)

* Schuster, Mikhael et al Am J Heme 2010