14.1. Introduction

In smouldering multiple myeloma:

- sFLCs are abnormal in approximately 80% of patients.
- Abnormal $\kappa/\lambda$ sFLC ratios are associated with an increased risk of progression.
- Asymptomatic patients with an involved/uninvolved sFLC ratio $\geq 100$ and 10% clonal bone marrow plasma cells or biopsy-proven plasmacytoma have been reclassified as multiple myeloma requiring treatment.

Smouldering multiple myeloma (SMM) is an asymptomatic plasma cell disorder. In 2014, the International Myeloma Working Group (IMWG) revised their definition of SMM and a definitive diagnosis now requires two criteria to be met: 1) the presence of a serum monoclonal protein (IgG or IgA) at a concentration of $\geq 30$ g/L or a urinary monoclonal protein $\geq 500$ mg/24 hours and/or 10 - 60% clonal bone marrow plasma cells (BMPCs), and 2) the absence of myeloma defining events or amyloidosis (Section 25.2). This revised definition excludes asymptomatic patients with clonal BMPCs $\geq 60\%$, an involved/uninvolved sFLC ratio of $\geq 100$, or those with two or more focal lesions revealed by MRI, which in conjunction with a minimum of 10% clonal BMPC or biopsy-proven plasmacytoma are consistent with a diagnosis of multiple myeloma (MM, Section 25.2). In a retrospective audit of 216 SMM patients by Kastritis et al. [3], 13% of SMM patients were re-classified as MM using this definition. Similar findings were reported by Kyrtsonis et al. [3].

Prior to the 2014 revised diagnostic criteria, Dispenzieri et al. [4] noted that unlike MGUS, in which the rate of progression remains constant over time (Chapter 13), the overall risk of progression in SMM was greatly influenced by the length of time from diagnosis, with the highest rates of progression occurring in the first few years. Presumably this reflected the fact that prior to the updated criteria, patients classified as SMM were a very heterogeneous population, comprising some patients that would now be reclassified as MM, and others that were biologically more similar to MGUS. With increasing follow-up the cohort would have become enriched with low-risk patients, resulting in progressively lower rates of progression.

Risk stratification is valuable for SMM patient management. Patients identified as high-risk require close follow-up and, if possible, inclusion into clinical trials as initial studies suggest these patients benefit from therapy [5]. Early studies identified a variety of risk factors for progression, including a high percentage of BMPCs, a monoclonal protein concentration $\geq 30$ g/L, an IgA isotype and Bence Jones proteinuria [6][7][8][9]. Subsequently, monoclonal serum free light chains (sFLCs) were identified as a significant, independent risk factor, as discussed below. Preliminary evidence suggests that immunoglobulin heavy/light chain (Hevylite®, HLC) assays may also have a role in SMM prognosis (Section 14.4).

References

the definition of symptomatic myeloma: a single center experience in 216 patients with the previous diagnosis of asymptomatic disease. Blood 2015;126:4251a


