28.6. Monitoring patients with AL amyloidosis

“The introduction of the serum immunoglobulin free light chain assay has revolutionized our ability to assess hematological responses in patients with low tumor burden.”


“Introduction of the Freelite serum free light chain assay represents a landmark advance in the management of AL amyloidosis.”

Wechalekar AD, Hawkins PN, Gillmore JD. Br J Haem 2008 [2].

The aim of therapy in AL amyloidosis is to suppress the monoclonal plasma cell clone that produces the amyloidogenic FLC, and to support and preserve organ function. Treatment regimens for AL amyloidosis have essentially been modified from those developed in MM. Patients must be monitored closely, since the toxicity of chemotherapy may be substantially greater than in MM due to reduced organ function and poor performance status.

Amyloid deposits exist in a state of dynamic turnover. When the supply of amyloid-forming protein is reduced by effective chemotherapy, the balance between amyloid deposition and clearance may be favourably altered. Although complete suppression of clonal plasma cells is desirable, reduction in the amyloidogenic sFLC concentrations is often sufficient to stabilise or reduce amyloid deposits [3].

Traditionally, haematological response assessment in AL amyloidosis followed the same guidelines as MM, i.e., using serial measurement of monoclonal protein, with measurable disease defined as >10 g/L [4]. However, this approach has limited utility in AL amyloidosis as the proportion of patients with measurable monoclonal immunoglobulin is very low; typically between 15 and 20% [5]. In contrast, nearly 90% of patients have measurable disease as assessed by sFLCs (defined as dFLC >50 mg/L at diagnosis, Section 28.7.2) [5][6], and a recent survey of haematologists/oncologists found that sFLCs are the most consistently monitored biomarker in AL amyloidosis [7].

Due to their short serum half-life, sFLCs are usually the most effective marker for evaluating the early effects of chemotherapy in AL amyloidosis (Chapter 3). In a study evaluating the combination of bortezomib and dexamethasone treatment in patients with AL amyloidosis, sFLCs were assessed before each cycle of therapy [8]. Rapid haematological responses were observed, with a 50% reduction in the involved sFLC concentration in all responding patients within two courses of treatment (Figure 28.9). The authors concluded that therapy may be discontinued after two cycles if there is no sFLC response and that an alternative treatment could be considered. Similar findings were reported by Kaufman et al. [9] and Jaccard et al. [10] who demonstrated very rapid dFLC responses to daratumumab monotherapy. Kaufman et al. [9] also studied the prognostic value of dFLC reductions following the first treatment cycle; patients who demonstrated a dFLC reduction of at least 50% were more likely to experience a deep haematological response with further daratumumab therapy.
28.7. Guidelines for monitoring AL amyloidosis

28.5 AL amyloidosis patients with distinct clinical features

Figures

Figure 28.9. Monitoring response to bortezomib/dexamethasone with sFLCs.

Analysis of sFLCs was performed before each cycle of treatment. (Obtained from Haematologica Journal website: haematologica.org).

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References


