Abstract IgM myeloma is a rare disease, accounting for approximately 0.5% of multiple myelomas (MM). Here we report four cases of IgM multiple myeloma. Two were diagnosed in advanced clinical stages with multiple osteolytic lesions, leading to hypercalcemia in one patient. Bone marrow morphology showed a variable degree of infiltration with mainly mature plasma cells. An immunophenotypic analysis performed in one case showed expression of CD38 and monoclonal cytoplasmatic immunoglobulin. Interphase fluorescence in situ hybridization performed in one case did not reveal any aneuploidies or deletions of the retinoblastoma, P16, or P53 tumor suppressor genes. While one patient with a smoldering IgM myeloma did not need specific therapy, the others received cytotoxic treatment based on standard chemotherapy for MM. The outcomes were one stable disease, one sustained complete remission, and one progressive disease. All four patients were alive 1 year after diagnosis. One died due to progressive disease after 31 months. We conclude that IgM myeloma shares clinical and histological features with other MM rather than with Waldenström's macroglobulinemia, which is most commonly diagnosed in cases with IgM monoclonal gammopathy. Since MM and Waldenström’s macroglobulinemia differ in prognosis and treatment strategies, the two disease entities should be distinguished based on clinical criteria, bone marrow morphology, and immunophenotypic analysis.

Keywords Multiple myeloma · Waldenström’s macroglobulinemia · IgM monoclonal gammopathy · High-dose melphalan chemotherapy

Introduction

Multiple myeloma (MM) is a B-cell malignancy characterized by a clonal proliferation of abnormal plasma cells in the bone marrow [15]. It accounts for approximately 1% of malignancies and occurs most frequently in patients between the ages of 50 and 80 years [4]. Multiple myeloma is characterized by the presence of monoclonal immunoglobulin in the serum. The IgG and IgA immunoglobulins are most commonly observed, but IgM myeloma is rare, with an estimated incidence of 0.5% in patients with myeloma [8].

The cases of IgM myeloma described in the literature present with clinicopathological features typical of MM, including lytic bone lesions, hypercalcemia, renal failure, and decreased IgG and IgA levels. However, findings may also be made that are associated with Waldenström’s macroglobulinemia (WM), such as hyperviscosity symptoms, lymphadenopathy, and hepatosplenomegaly [20]. In addition to the clinical features, IgM myeloma and WM can be distinguished by bone marrow morphology, showing a lymphoplasmacytoid proliferation in WM in contrast to a plasma cell infiltrate in MM. Furthermore, immunophenotypic analysis of neoplastic cells can confirm the diagnosis [10].

Here we report clinical characteristics of four cases of IgM myeloma, one of which was confirmed by immunophenotypic and interphase fluorescence in situ hybridization data. We emphasize that it is important to distinguish IgM myeloma from WM because of the different clinical courses and treatment options of the two conditions.

Case reports

Patient 1

A 59-year-old man was admitted to the hospital for evaluation of strong back pain and deterioration in the performance status. He was orientated to all qualities but was sleepy. Otherwise, physical examination was unremarkable. Computed tomography showed
osteolytic lesions and fractures in the thoracic spine and proximal second rib. Laboratory findings at diagnosis were as follows: erythrocyte sedimentation rate 100 mm/h, hemoglobin 9.0 g/dl (reference range: 14.0–17.5), white blood cells 7.1 × 10^9 /l (reference range: 4.5–11.5), platelets 437 × 10^9 /l (reference range: 170–410), creatinine 1.2 mg/dl (reference range: –1.24), calcium 3.37 mmol/l (reference range: 2.13–2.63), protein was 94 g/l (reference range: 60–80); other routine laboratory parameters were normal. Immuno-electrophoresis revealed a highly elevated IgM of 46.1 g/l (reference range: 0.4–2.3) and immunoglobulin light chain (IgL) λ of 5.2 g/dl (reference range: 0.9–2.0), low levels of IgG with 2.3 g/l (reference range: 7.0–16.0), and IgA with 0.4 g/l (reference range: 0.7–4.0). The β2-microglobulin level was 10.5 mg/l (reference range: –2). The bone marrow aspirate showed an infiltration with 40–80% of mainly mature, sometimes undifferentiated plasma cells (Fig. 1). The immunophenotypic analysis of bone marrow cells revealed monoclonal cytoplasmatic IgL λ. The malignant cells were positive for CD38 and CD43 but did not express B-cell markers such as CD19, CD20, and FMC7 (Table 1).

Interphase fluorescence in situ hybridization was performed on bone marrow cells using DNA probes hybridizing to the centromeric regions of chromosomes 3, 7, 9, and 11, the region of 11q22, the BCL1 gene on 11q13, the CMYC gene on 8q24, and the tumor suppressor genes P16 (9p21), retinoblastoma (13q14), and P53 (17p13). No gains or losses of the analyzed loci were detected. In accordance with the described data, an IgM λ myeloma, stage IIIA according to Durie and Salmon [9] was diagnosed.

The patient was treated with bisphosphonates and four courses of oral idarubicin and dexamethasone, followed by one course of ifosfamide-epirubicin-etoposide, high-dose melphalan, MP melphalan-prednisone, VAD vincristine-doxorubicin-dexamethasone, CR complete remission, PD progressive disease, SD stable disease. 9 months after the second course of high-dose melphalan chemotherapy, the patient is in good clinical condition and in complete remission.

Table 1 Summary of clinical and laboratory data in four patients with IgM multiple myeloma

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Type of Ig</th>
<th>Stagea</th>
<th>IgM (g/l)</th>
<th>β2-Mg (mg/l)</th>
<th>Calcium (mmol/l)</th>
<th>Osteolytic lesions</th>
<th>Plasma cell infiltration (%)</th>
<th>Immunophenotype</th>
<th>Chemo- therapy</th>
<th>Response</th>
<th>Survivalb (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>59</td>
<td>IgM λ</td>
<td>IIIA</td>
<td>46.1</td>
<td>10.5</td>
<td>3.37</td>
<td>&gt;3</td>
<td>40–80</td>
<td>CD19: 7%; CD20: 6%; CD38: 75%; CD43: 93%; CyL: 10%</td>
<td>4×ID, IfoEV, HDM</td>
<td>CR</td>
<td>20+</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>54</td>
<td>IgM κ</td>
<td>IIIA</td>
<td>7.7</td>
<td>2.8</td>
<td>Normal</td>
<td>&gt;3</td>
<td>5+</td>
<td>n.d.</td>
<td>MP, 3×VAD, HDM</td>
<td>PD, death</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>70</td>
<td>IgM κ</td>
<td>IA</td>
<td>60.8</td>
<td>n. d.</td>
<td>Normal</td>
<td>None</td>
<td>13+</td>
<td>n.d.</td>
<td>4×MP</td>
<td>SD</td>
<td>16, lost to follow-up</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>52</td>
<td>Smoldering</td>
<td>7.63</td>
<td>n. d.</td>
<td>Normal</td>
<td>None</td>
<td>None</td>
<td>22/24</td>
<td>n.d.</td>
<td>None</td>
<td>SD</td>
<td>60+</td>
</tr>
</tbody>
</table>

a According to Durie and Salmon [9]  
b Survival after primary diagnosis  
Abbreviations: Ig immunoglobulin, β2-mg β2-microglobulin, CyL λ cytoplasmatic monoclonal lambda, n. d. not done, ID idarubicin-dexamethasone, IfoEV ifosfamide-epirubicin-etoposide, HDM high-dose melphalan, MP melphalan-prednisone, VAD vincristine-doxorubicin-dexamethasone, CR complete remission, PD progressive disease, SD stable disease.