Multiple myeloma and secondary plasma cell leukemia

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Abstract

Plasma cell leukemia is very rare condition characterized by malignant proliferation of plasma cells in blood and bone marrow, which is aggressive and has a short survival even with conventional treatment. This ominous entity may be primary, or develops secondarily during the course of multiple myeloma. A 53-year-old Brazilian woman with multiple myeloma is described with bone marrow evaluation revealing 25% plasma cells. The quantification of plasma cell infiltration in bone marrow aspirate and immunohistochemistry study revealed consistent features of myeloma and plasma cell leukemia, and lambda light chain expression. Worthy of note was the absence of CD56 expression and the expression of CD20; moreover, 23% of circulating plasma cells were detected in peripheral blood smears. Therefore, the diagnosis of plasma cell leukemia was characterized and therapeutic schedules with dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide were utilized. With significant clinical improvement, the patient is currently waiting for bone marrow transplant.

Keywords: multiple myeloma, plasma cell leukemia, diagnosis, immunophenotyping.

Introduction

Plasma cell leukemia (PCL) is a rare and aggressive entity characterized by malignant proliferation of plasma cells (PCs) in blood and bone marrow, which often has a survival of less than one year [1–5]. The diagnosis of PCL is based on circulating PCs>2000/mm³ and >20% of total leukocytes [1–5]. There are two types of this severe neoplasm: primary, usually presenting with infiltration in internal organs, brain, muscles, and rarely in the skin; and secondary to late-stage of multiple myeloma [1–5].

We present the case of a 53-year-old Brazilian woman with secondary PCL. She underwent chemotherapy using dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide. Currently, she is asymptomatic, in good general status, and waiting for bone marrow transplantation. The aim of this case study is describe an uncommon clinical entity that has very ominous outcome.

Case presentation

A 53-year-old woman was admitted in November 2015 with asthenia, lack of appetite, loss of weight, and intense epigastric pain in colic for approximately two months, without improvement by medicines; additionally, there was nausea, vomiting and constipation. Ten months ago, she started with pain on the neck and was utilizing non-steroidal anti-inflammatory drugs (NSAIDs) daily, with no significant relief. She denied comorbidities and alcohol abuse, but smoked 3–6 cigarettes daily during 29 years. On physical examination, she was in regular status of health, with pale mucosa (+++) and dehydrated (+); epigastric pain elicited by superficial and profound palpation but no signs of peritonitis; absence of hepatosplenomegaly or lymphadenopathy. There was pain during mobilization of the cervical vertebrae, in absence of meningeal signs. Radiographic studies of skeleton showed symmetric bilateral changes of bone pattern at upper half of humeral diaphysis, with multiple radiotransparent areas of speckled pattern (Figure 1); normal aspect of the rest of bones and joints of extremities, as well as of surrounding soft tissues.

Figure 1 – Radiograph study showing bilateral areas of speckled pattern at humeral diaphysis (arrows).

Laboratory tests (Table 1) revealed elevated levels of urea and creatinine, hypercalcemia and anemia. Electrophoresis of proteins showed albumin 3.3 g/dL, globulins 4.0 g/dL, and gamma-globulin 2.1 g/dL; tests showed low levels of IgA 41.5 (70–400) mg/dL, IgG 547 (700–1600) mg/dL and IgM 16.8 (40–230) mg/dL. Negative serological tests included B and C viral hepatitis, human immunodeficiency virus (HIV), venereal disease research laboratory (VDRL), cytomegalovirus (CMV), and Epstein–Barr virus. Bone marrow smears showed features consistent with the diagnosis of multiple myeloma (MM).
Flow cytometry done in sample of bone marrow showed: erythroblasts 4.88%; granulocytes 55.74%; monocytes 3.23%; lymphocytes 10.17% and 85% T-cells (CD4/CD8: 1.64); evidenced increased PCs rate (25%) expressing CD20 (partial), CD38 (strong), CD117 (weak), CD138 and lambda light chain restriction, without expressing CD19, CD45, and CD56. The loss of CD56 expression was considered indicative with PCL, and peripheral blood smears revealed high rate (23%) of plasma cells, often appearing with dysplastic features (Figure 3).

Therefore, the diagnosis of PCL secondary to multiple myeloma was characterized and the patient underwent DTPACE, which is a chemotherapy regimen including dexamethasone, thalidomide and a four-day continuous intravenously infusion of cisplatin, doxorubicin, cyclophosphamide, and etoposide. After three cycles, there was significant improvement; currently, she is waiting for bone marrow transplant.

### Table 1 – Blood determinations of a woman with multiple myeloma and plasma cell leukemia

<table>
<thead>
<tr>
<th>Parameters (normal values)</th>
<th>D1</th>
<th>D3</th>
<th>D5</th>
<th>D9</th>
<th>D17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (11.7–15.7 g/dL)</td>
<td>8.6</td>
<td>8.5</td>
<td>8.1</td>
<td>6.6</td>
<td>7.7</td>
</tr>
<tr>
<td>Hematocrit (35–47%)</td>
<td>26.4</td>
<td>26.1</td>
<td>25.4</td>
<td>19.8</td>
<td>23.0</td>
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<tr>
<td>Leukocytes (4–10×10^9/L)</td>
<td>8.2</td>
<td>7.0</td>
<td>7.3</td>
<td>11.3</td>
<td>11.1</td>
</tr>
<tr>
<td>Neutrophils (40–70%)</td>
<td>42</td>
<td>47</td>
<td>53</td>
<td>69</td>
<td>71</td>
</tr>
<tr>
<td>Plasma cells count ×10^9/L</td>
<td>1.9</td>
<td>1.6</td>
<td>1.7</td>
<td>2.6</td>
<td>2.5</td>
</tr>
<tr>
<td>Platelets (140–450×10^9/L)</td>
<td>139</td>
<td>130</td>
<td>118</td>
<td>128</td>
<td>176</td>
</tr>
<tr>
<td>ESR (&lt;15 mm/first hour)</td>
<td>140</td>
<td>39</td>
<td>140</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sodium (136–145 mmol/L)</td>
<td>13.1</td>
<td>13.0</td>
<td>12.4</td>
<td>6.9</td>
<td>7.2</td>
</tr>
<tr>
<td>Potassium (3.5–5.1 mmol/L)</td>
<td>3.8</td>
<td>3.5</td>
<td>3.4</td>
<td>4.4</td>
<td>4.9</td>
</tr>
<tr>
<td>Calcium (8.6–10.2 mg/dL)</td>
<td>30.3</td>
<td>37.4</td>
<td>45.9</td>
<td>65.8</td>
<td>50.2</td>
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<tr>
<td>Urea (16.6–48.5 mg/dL)</td>
<td>2.2</td>
<td>3.0</td>
<td>3.2</td>
<td>2.3</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Abnormal values are in bold.**

**Discussion**

Plasma cell malignancies include four entities: classic MM, extramedullary plasmacytoma without MM, solitary plasmacytoma of bone, and PCL [1, 5]. PCL represents between 2 and 4% of this group of patients [1, 5], and 0.3% of acute leukemias [3]. PCL is a very rare and aggressive lymphoproliferative malignancy of PCs both in bone marrow and blood, which can be characterized by peripheral PCs>2000/mm^3 and >20% of blood leukocytes [1–5]. Differing from PCL secondary to MM, extramedullary involvement is common in primary PCL, which represents 60 to 70% of cases [1–5]. The diagnosis of secondary PCL herein reported was characterized by clinical, biochemical, and imaging data, in addition to hematological criteria of bone marrow and peripheral blood smears [1–5].

The 53-year-old Brazilian woman had elevated levels of urea and creatinine, hypercalcemia and anemia; and osteolytic humeral lesions, in absence of liver, spleen or lymph node enlargement. Bone marrow smears showed 25% of PCs, expressing CD20 (partial), CD38 (strong), CD117 (weak), CD138 and lambda light chain restriction, without expression of CD19, CD45, and CD56, consistent with MM. Peripheral blood smears revealed up to 2600 PCs/μL (23%), numerous of them with dysplastic pattern. One must highlight the role of immunophenotype plus peripheral count of PCs to establish diagnosis; solely phenotypic differences may not discriminate PCL from MM, but explain different survival [5]. Normal PCs express high CD40 levels; CD28 is negative in chronic phase of MM and normal PCs, and is expressed in 63% of MM accelerated phases [6]. Immunophenotypic expression is similar in PCL and MM for CD38, CD138, CD2, CD3, CD16, CD10, CD13
and CD15. PCLs often do not express CD56 antigen, but express CD20, which is usually absent in PCs of patients with MM [1, 5, 7]. Additional concern could be about anomalies in the cytoplasm of PCs due to stored immunoglobulins mimicking hairy cell leukemia (HCL) [8], as rarely described [3, 9]. Indeed, plasmacytoid “flare-cells” and PCs with eccentric nuclei and cytoplasm like “fried-egg” and hair-like projections were seen [2, 8]. However, immunophenotyping of hairy cells shows CD19, CD20, CD103, CD25 and CD11c (100%), CD79b (93.7%), kappa light chain (60%) and lambda (40%); CD10 and CD23 (20% and 12% of cases, respectively) [8, 10]. In addition to HCL, patients with atypical PCL, or pleomorphic PCL with lymphocytosis, may give rise to diagnostic challenges [11, 12].

Worthy of note in this report is the diagnosis of secondary PCL in a woman with unsuspected MM; hence, the diagnoses of MM and of secondary PCL were concomitant, a phenomenon rarely described. Therefore, she had not utilized previous chemotherapy for myeloma as usually reported. Drugs of combination chemotherapy for PCL include bortezomib, thalidomide, dexamethasone, cyclophosphamide, adriamycin, lenalidomide, melphalan, prednisone, bendamustine, doxorubicin, vincristine, etoposide, and pomalidomide [1, 3–5, 9, 11]. After her diagnosis of secondary PCL, the patient underwent chemotherapy with dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide, and is currently waiting for bone marrow transplant.

Conclusions

PCL has been scarcely reported due to very low frequency; therefore, therapy remains not consensual. The secondary type of PCL is frequently resistant to chemotherapy including agents used for MM; primary PCL also has poor prognosis in spite of multiple drug regimens, and needs stem cell rescue. Significant results of novel therapeutic tools will depend on studies including large number of patients. Because of the rarity of PCL, case studies should be described aiming to enhance the suspicion index about this severe disorder among primary care workers and no specialists in hematology and oncology.

Conflict of interests

The authors declare that they have no conflict of interests.

References