Plasma Cell Neoplasms, Clinicopathological Characteristics and Immunophenotype of 21 Patients

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Received August 9th, 2012; revised September 9th, 2012; accepted September 19th, 2012

ABSTRACT

Introduction: Plasma cell neoplasms are monoclonal proliferations characterized by the secretion of an immunoglobulin product known as component “M” or monoclonal. The World Health Organization (WHO 2008) defines as plasma cell neoplasms the following: plasma cell myeloma, plasmacytoma and those syndromes defined by immunoglobulin deposits and primary amyloidosis. The objective of the present work was to correlate their clinical, morphological and phenotype characteristics in 21 patients. Material and Methods: A 2-year retrospective review was performed of the files of the surgical pathology laboratory and of the hematology service of the General Hospital of Mexico, searching for patients with a diagnosis of plasma cell neoplasm. We analyzed the following variables: age, gender, clinical symptoms, evolution, localization, laboratory tests, morphology, and expression of immunohistochemical markers. Of the 21 patients, 12 (57.1%) corresponded to plasma cell myelomas and 9 (42.8%) were plasmacytomas (seven extraosseous and two solitary bone plasmacytoma); women predominated with 61.4% and age ranged between 22 and 84 years. Mass and epistaxis were observed in the patients with plasmacytomas, and symptoms of medullary compression and anemia were observed in those patients with plasma cell myeloma. The time of symptomatology varied from 3 to 12 months. Laboratory tests revealed that lactate dehydrogenase (LDH), beta 2 microglobulin, C-reactive protein were altered and that hypercalcemia and anemia were present more in the systemic form of the disease. Treatment depended on the clinical staging and laboratory data. Mature forms predominated morphologically. Immunohistochemical stain revealed a constant expression for CD 138, six patients expressed CD 56, and expression of the Kappa and Lambda light chains was while.

Keywords: Plasma Cell Neoplasms

1. Introduction

Clonal proliferations of plasmatic cells and their precursors constitute a spectrum of diseases previously known as: “plasma cell dyscrasias”. This group includes monoclonal gammopathy of indeterminate significance, which is characterized by the presence of low levels of paraprotein in the peripheral blood, with a variable time of evolution, and later on development of a plasma cells myeloma; this phenomenon is considered as a precursor lesion.

Other immunoglobulin secreting neoplasms that affect lymphoid and plasmatic cells lie within the current classification of WHO-2008 regarding hematolymphoid neoplasms, such as the lymphoplasmacytic lymphoma, Waldenström’s macroglobulinemia, and heavy chain diseases [1].

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teins and rarely becomes disseminated. The diagnosis of solitary bone plasmacytoma or extraosseous myeloma is established after extensive imaging studies, such as MRI to exclude systemic disease. The risk of local recurrence and dissemination is high in patients with solitary bone plasmacytoma accompanied by persistence of monoclonal serum protein after local radiotherapy [5].

The objective of this study is to present the clinical, morphological, and immunophenotype characteristics of 21 patients studied at the General Hospital of Mexico.

2. Material and Methods

From the archives of the Surgical Pathology and Immunohistochemistry Service of the Pathology Unit of the General Hospital of Mexico, we reviewed the slides stained with hematoxylin-eosin, periodic acid-Shiff stain and the immunohistochemical markers of 21 patients diagnosed with plasma cell neoplasms and classified them according to WHO-2008 guidelines for hematolymphoid neoplasms [1] diagnosed in a two-year period (2006 and 2007).

We identified the morphology of the plasmatic cells: mature, lymphoplasmacytic and immature or anaplastic. Strepto-avidin-biotin-peroxidase was the immunohistochemical technique used manually. The monoclonal antibodies used were: Kappa (1:1000), Lambda (1:1000), CD 138 (1:50), CD 56 (1:20), CD 20 (1:50) and CD5 (1:50) (Dako, Carpinteira, CA, USA).

Clinical information was gathered from the clinical files and we analyzed the following variables: age, gender, localization, duration of symptoms, and laboratory tests performed, anemia, lactate dehydrogenase (LDH), beta-2-microglobulin, and serum proteins. We correlated the clinical morphological variables and the immunophenotype.

3. Results

From the 21 patients with a diagnosis of plasma cell neoplasm, 12 were identified with having plasma cell myelomas (M) and 9 had plasmacytomas (7 extraosseous and 2 osseous) (P) (Figure 1).

The clinical data of the patients with plasma cell myeloma (57.7%) are depicted on Table 1. Nine (75%) were women and three (25%) were men.

The youngest patient was a 31-year-old woman, who at the time of diagnosis presented a 38-week pregnancy. The oldest was a man of 84 years. Average age was 54.2 years. The most affected sites were the skull in six (50%), spinal cord in 4 (33.3%), and less frequently affected structures were bone marrow, long bones, pelvis, clavicle, palate, lymph node, and intestine.

![Figure 1. Plasmacytoma in the antrochoanal región.](image)

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Site</th>
<th>Laboratory</th>
<th>Morphology</th>
<th>Immunohistochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>w</td>
<td>42</td>
<td>Skull and thorax</td>
<td>B-2m</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>2</td>
<td>m</td>
<td>52</td>
<td>SC T5 and T4</td>
<td>Anemia, LDH</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>3</td>
<td>w</td>
<td>59</td>
<td>Palate, skull</td>
<td>Anemia, LDH Sx viscosity ARF, Gammopathy</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>4</td>
<td>w</td>
<td>65</td>
<td>Skull Intestine</td>
<td>LN, BM, Anemia, B2-m PBJ+</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>5</td>
<td>w</td>
<td>43</td>
<td>SCT2 LN Lumbar pain</td>
<td>Anemia, IgG/K Gammopathy</td>
<td>IPC</td>
<td>CD 138/Kappa CD 56+</td>
</tr>
<tr>
<td>6</td>
<td>w</td>
<td>50</td>
<td>Thorax, clavicle Humer (PF)</td>
<td>Anemia, B-2m ARF</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>7</td>
<td>w</td>
<td>56</td>
<td>Parietal skull BM, pain in half of the face infiltrated BM</td>
<td>B-2m, FRA</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
</tr>
<tr>
<td>8</td>
<td>w</td>
<td>66</td>
<td>SC C T BM</td>
<td>PBJ+ Anemia</td>
<td>MPC</td>
<td>CD 138/Lambda CD 56+</td>
</tr>
<tr>
<td>9</td>
<td>m</td>
<td>56</td>
<td>SCT Pain, paresthesias</td>
<td>B-2m</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
</tr>
<tr>
<td>10</td>
<td>w</td>
<td>31</td>
<td>Scapula Pelvis PF</td>
<td>B-2m, FRA Preg 38WG</td>
<td>IPC</td>
<td>CD 138/Lambda</td>
</tr>
<tr>
<td>11</td>
<td>m</td>
<td>47</td>
<td>Skull and long bones</td>
<td>Anemia, PBJ+ B-2m</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
</tr>
<tr>
<td>12</td>
<td>m</td>
<td>84</td>
<td>Skull and pelvis Bone pain</td>
<td>Anemia LDH</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
</tr>
</tbody>
</table>

B-2m (Beta-2 microglobulin), LDH (Lactic dehydrogenase), ARF (Altered renal function), PBJ (Bence-Jones Protein), Preg (pregnancy) WG (weeks of gestation), MPC ( mature plasma cells), IPC (immature plasma cells), PF (pathological fracture). VC (vertebral column), BM (bone marrow), LN (lymph node).
Seven patients (58.3%) presented anemia, in six (50%) 2-beta-microglobulin of more than 3.5 mg/L was found, three patients presented monoclonal gammopathy: IgG > 3.5 g/dL, IgA > 2 g/dL, and two patients had altered renal function, one coursed with hypercalcemia and elevated LDH.

Morphologically, the neoplastic cells corresponded to mature plasmatic cells in 10 patients (83.3%) (Figure 2) and two showed immature and pleomorphic plasmatic cells (Figure 3). The determined immunohistochemical markers are summarized in Table 1, in which expression for CD138 was observed (Figure 4); 6 patients (50%) expressed light Kappa chain and 50% Lambda (Figures 5 and 6 respectively). Two patients (16%) expressed CD
56, which morphologically corresponded to mature plasma cells and the other presented immature cells (Table 1). The others markers such CD 20 and CD 5 were negative.

The Table 2 depicts the clinical data of patients with plasmacytomas (9 cases, 42.8%). Seven were extrasosseous (77.7%) and two were bone (33.3%). Four patients were men and five women, the youngest patient was a 22-year-old man without HIV antecedents and the location was in a lymph node associated to Castleman’s disease, hyaline vascular type. The oldest patient was a 79-year-old patient, and the average age was of 52 years. The sites of the extrasosseous plasmacytomas were: two in the nasal region and two more in the palate, and one in the following sites, antrocoanal, gum, and cervical lymph node. The bone plasmacytomas were found in cervical vertebra and the sternum. Morphologically, seven were constituted by mature plasma cells and two revealed the presence of lymphocytes and plasmatic cells (lymphoplasmacytic variant). Immuno histochemical patterns in five expressed Kappa and two Lambda; expression for CD 56 was observed in four (44.4%). The others markers such CD 20 and CD 5 were negative (Table 2).

4. Discussion

According to the compiled Histopathological Registry of 1997, plasma cell tumors occupied the 15th place and corresponded to less than 1% (0.4%) of the total malignant neoplasms in our country [6].

At the Instituto Nacional de Cancerología [National Cancer Institute] in Mexico, 193 new cases of plasma cells myeloma were diagnosed between 2000-2004; of these 92 were men and 101 were women, and represented 1% of all the neoplasms diagnosed at this Institute [7].

At the General Hospital of Mexico, 21 patients were diagnosed with plasma cells neoplasm in a 2-year period, of which 12 were myelomas and 9 were plasmacytomas. In the USA, plasma cells myeloma corresponds to 1% of the total of all malignant tumors and to 10% to 15% of the hematopoietic neoplasms [8,9]. Bone and extrasosseous plasmacytomas comprise 3% to 5% of plasmatic cell neoplasms in the USA [10].

The etiology is still unknown; however, they have been related with chronic antigenic stimulation due to infection, or with the exposure to specific toxic substances or radiation [11]. Ries et al. observed that plasma cells myeloma, bone and extrasosseous plasmacytoma are more common in men than in women [9]. According to Rizo et al. [7] from the Instituto Nacional de Cancerología, and our results women predominate, as can be observed in Tables 1 and 2. The average age for myelomas was of 54 years, and 52 years for plasmacytomas. In the Western literature the average age for myeloma patients is 70 years, and 55 years for plasmacytomas [1].

The clinical presentation of plasma cells myeloma varies [12] and occasionally the symptomatic diagnosis is delayed several months; the main bone symptoms are lumbar pain or fractures of the affected bones. In the present work, pain was the predominant symptom in myeloma (Table 1), renal failure results from the tubular damage caused by the proteinuria of the monoclonal light chain proteins. One patient presented altered renal function and gammapathy, and in another it was not associated with gammapathy. Fractures were found in two patients. Among the altered laboratory tests, in the systemic form of the disease, we found anemia, hypercalcemia (>12 mg/dL), hyperviscosity, monoclonal peak as revealed by protein electrophoresis, protein C reactive, and elevation of LDH. Anemia was the most frequent alteration found in both the study performed by Kyle in the Mayo Clinic with 1027 patients (67% of patients with anemia) and in this study with a similar percentage of affectionation (66.6%). The presence of anemia in patients

<table>
<thead>
<tr>
<th>Case</th>
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<th>Age</th>
<th>Site</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>m</td>
<td>49</td>
<td>gum/tumor</td>
<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>2</td>
<td>m</td>
<td>54</td>
<td>nasal/epistaxis</td>
<td>MPC</td>
<td>CD 138/Kappa CD 56</td>
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<tr>
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<td>palate/tumor</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
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<tr>
<td>4</td>
<td>w</td>
<td>63</td>
<td>nasal/epistaxis</td>
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<td>CD 138/Kappa CD 56</td>
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<tr>
<td>5</td>
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<td>MPC</td>
<td>CD 138/Kappa</td>
</tr>
<tr>
<td>6</td>
<td>w</td>
<td>79</td>
<td>palate/lymphoplasmatic infiltration</td>
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<td>CD 138/Lambda</td>
</tr>
<tr>
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<td>57</td>
<td>sternum/tumor</td>
<td>MPC</td>
<td>CD 138/Kappa CD 56</td>
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<tr>
<td>8</td>
<td>w</td>
<td>57</td>
<td>SC</td>
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<td>CD 138/Kappa CD 56</td>
</tr>
<tr>
<td>9</td>
<td>m</td>
<td>22</td>
<td>GL</td>
<td>MPC</td>
<td>CD 138/Lambda</td>
</tr>
</tbody>
</table>

MPC (mature plasmatic cells). No laboratory tests alterations were observed in any patient. CD 20 and CD 5 were negative in neoplastic plasma cells.
results first by the replacement of bone marrow by neoplastic plasma cells and/or because of renal damage resulting from the loss of erythropoietin [13]. The other laboratory alteration found in this series was the elevation of beta-2-microglobulin in serum, which is used as a survival marker, if it is higher than 5.5 mg/dL, patient’s survival is reduced to only 28 months; therefore, it is an important prognostic laboratory marker [14].

Clinical variants of plasma cells myeloma include the smoldering plasma cells myeloma, in which the patients course with stable disease for long periods of time, it presents with solitary plasmacytoma with bone abnormalities detected only through Magnetic Resonance Image (MRI) and only 10% - 20% of plasmatic cells are seen in the bone marrow [1].

Another variant is the non-secreting myeloma that corresponds to 3% of plasmatic cells myeloma. There is lack of protein M as assessed through fixation electrophoresis. [10] Leukemia of plasmatic cells is characterized by an increase in the number of clonal plasmatic cells in peripheral blood and exceeds 2 × 10/L, (2 × 10⁹/L,) or

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REFERENCES


