Primary Diffuse Large B-Cell Lymphoma with Features Simulating POEMS Syndrome: Case Report and Review Of The Literature

Ahmed Mili1*, Salma Naija1, Asma Nasr1, Manel Ben Halima1, Anis Hassine1, Sana Ben Amor1, Nesrine Ben Sayed2, Yosra Ben Youssef2, Abderrahim Khelif2, Dorra Chiba3, Badreddine Sriha3, Moncef Mokni3

1Department of Neurology, Hospital Sahloul of Sousse, Sousse, Tunisia
2Department of Hematology, Hospital Farhat Hached of Sousse, Sousse, Tunisia
3Department of Anatomopathology, Hospital Farhat Hached of Sousse, Sousse, Tunisia

*Corresponding author: Ahmed Mili. Department of Neurology, Hospital Sahloul of Sousse, Sousse, Tunisia, Tel: + 21655612902; E-mail: miliahmed@hotmail.com

Received date: June 17, 2020; Accepted date: August 21, 2020; Published date: August 28, 2020


Abstract

POEMS syndrome is a rare systemic affection of paraneoplastic origins. The main manifestations include polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes. This disease is commonly associated with plasma cell dyscrasia or Castleman disease. A 51-year-old-man presented with a four-month history of gait impairment, four-limb sensorimotor deficit, general areflexia and facial diplegia. The diagnosis of chronic polyradiculoneuritis was made based on Cerebrospinal fluid (CSF) analysis and electromyography study (EMG). At the time of initial evaluation, physical examination displayed enlarged lymph nodes, hepatosplenomegaly, endocrinopathy and skin changes. Complete Blood Count did not reveal significant monoclonal plasma cell proliferative disorder. The biopsy of the adenopathy identified a large B-cell lymphoma. We concluded a POEMS-like syndrome due to the lack of monoclonal plasma cell proliferative disorder. To our knowledge, this is the third reported case of B-cell Lymphoma associated with POEMS features. Our findings may suggest that POEMS syndrome has an unusual presentation in patients with diffuse large B-cell lymphoma even in the absence of monoclonal plasma cell proliferative disorder considered as the essential criterion.

Keywords: POEMS syndrome; B-cell lymphoma; Monoclonal Gammopathy of Undetermined Significance; Polyneuropathy.

Introduction

POEMS syndrome is a rare systemic affection of paraneoplastic origins. The main manifestations include polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes. This disease is commonly associated with plasma cell dyscrasia or Castleman disease [1]. According to the World Health Organization (WHO), diffuse large B-cell lymphomas are classified as a distinct lymphoma entity and present the most frequent group of non-Hodgkin’s lymphomas (NHL) in adults including various groups of lymphoid neoplasms with heterogeneous clinical, histological, immunophenotypic, cytogenetic and molecular features[2]. The association of POEMS syndrome with diffuse large B-cell lymphoma is rare and we found two cases of association between primary cutaneous large B-cell lymphoma and POEMS. We report a rare case of an atypical POEMS syndrome with diffuse large B-cell non-Hodgkin’s lymphoma, through which we highlight unusual features that may be considered in future diagnostic criteria.

Case Report

A 51-year-old man developed facial diplegia, numbness and weakness of 4 limbs and gait impairment. Two weeks later, he developed rapidly progressive bilateral swelling in the cervical, axillary and inguinal regions with gradually worsening instability when walking. He was therefore admitted to our hospital.

Physical examination revealed bilateral, painless lymphadenopathy in the retro auricular, cervical, occipital, axillary and inguinal regions with hepatosplenomegaly. Neurological examination found tetraparesis (3/5 according to the manual muscle testing), general areflexia, symmetric facial diplegia and loss of proprioception in lower limbs. Hyperpigmentation was noted in the left lower limb associated to an oval-shaped nodular lesion with a purple smooth surface and a firm consistency on the right shoulder (Figure 1).

Results

LAB analysis revealed the following results: blood cell count (CBC): white blood cells= 6.12 × 109.L-1[69.9% neutrophils,
14.2% lymphocytes; hemoglobin= 143 g.L⁻¹; platelet = 189 × 10⁹ elm.L⁻¹; sodium= 125 mmol.L⁻¹; calcium= 2.32 mmol.L⁻¹; total protein= 70 g L⁻¹; creatinine= 51 µmol.L⁻¹; albumin= 37.2 g L⁻¹; LDH = 372 IU L⁻¹; CRP= 17 mg.L⁻¹.

Figure 1: Patient’s cutaneous manifestation: (A) Clinical observation of the hyperpigmentation in the left lower limb. (B) Clinical observation of the nodular lesion on the right shoulder.

Endocrine investigations showed hypothyroidism: TSH=5.432; T4=0.7. Protein electrophoresis revealed an increase in Beta-2 Globulin with a monoclonal immunoglobulin M kappa (IgMκ) paraprotein spike (6.6 g.L⁻¹) (Figure 2).

Figure 2: Capillary electrophoresis and immunosubtraction of patient’s serum: arrow A shows the spike in Beta-2 Globulin fraction. Arrows B and C show the difference between the sample analyzed before and after immunosubtraction.

Bone marrow smear was infiltrated by 9% of plasma cells with few signs of dysmorphia (2% of plasmablasts).

Computed Tomography scans revealed enlarged cervical, axillary thoracic, abdominal and inguinal lymph nodes, and hepatosplenomegaly. No lytic bone lesion was found.

Nerve conduction studies (NCS) were performed using standard surface stimulation and recording techniques. Compound muscle action potentials (CMAPs) were evaluated at the bilateral peroneal (extensor digitorum brevis and Tibialis anterior), tibial (abductor hallucis), median (abductor pollicis brevis), and ulnar (adductor minimi) nerves. Motor conduction velocities (MCVs) were evaluated from the wrist to the elbow for the upper limb nerves, and from the ankle to the knee for the lower limb nerves. Sensory nerve action potentials (SNAPs) were recorded from the median and ulnar nerves via orthodromic studies and from the sural and superficial fibular nerves via antidromic studies.

The nerve conduction study showed the absence of a response in both distal peroneal stimulation (extensor digitorum brevis), great reduction in both the upper (ulnar) and lower limbs (peroneal and tibial) CMAPs, prolongation in distal motor latency in the right median and both tibial nerves, the absence of SNAPs in ulnar, median and superficial fibular nerves, normal SNAPs in radial and sural nerves and absence of conduction block. The NCS parameters are shown in Table 1 and Table 2.

Table 1: Motor Nerve conduction study findings in our patient.

<table>
<thead>
<tr>
<th>Nerve / Site</th>
<th>Latence (ms)</th>
<th>Amplitude (mv)</th>
<th>NCV(m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (right)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>4.7</td>
<td>7.4</td>
<td></td>
</tr>
<tr>
<td>Elbow</td>
<td>9.8</td>
<td>6.8</td>
<td>44.3</td>
</tr>
<tr>
<td>Ulnar (right)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>2.8</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Elbow</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Peroneal (left / Tibialis anterior)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below Fibular head</td>
<td>5.7</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Above Fibular head</td>
<td>19.7</td>
<td>0.28</td>
<td>16.4</td>
</tr>
<tr>
<td>Peroneal (right/ Tibialis anterior)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Below Fibular head</td>
<td>7.6</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Above Fibular head</td>
<td>14.1</td>
<td>0.3</td>
<td>12.3</td>
</tr>
<tr>
<td>Tibial</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ankle</td>
<td>6.8</td>
<td>1.1</td>
<td></td>
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<tr>
<td>Tibial</td>
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<tr>
<td>Ankle</td>
<td>9.1</td>
<td>0.3</td>
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</tr>
</tbody>
</table>

According to these findings, the diagnosis of a sensorimotor polyneuropathy with a pattern of diffuse axonal degeneration and demyelination was made.

A biopsy of the right neck lymph node showed loss of normal architecture with diffuse infiltration composed of large lymphoma cells with narrow cytoplasm, round vesicular nuclei with prominent nucleoli. Nuclear pleomorphism and numerous mitotic cells were observed. Immunohistochemical study revealed that the lymphoma cells were positive for CD20 and CD3, and a high expression of Ki67 (70%). Contrariwise, they were negative for CD30 (Figure 3). Biopsy of the
cutaneous lesion of the right shoulder concluded to a cutaneous localization of the large B-cell lymphoma (Figure 4).

Table 2: Sensory Nerve conduction study findings in our patient.

<table>
<thead>
<tr>
<th>Nerve / Site</th>
<th>Latence (ms)</th>
<th>Amplitude (uv)</th>
<th>NCV (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (right) 2nd digit</td>
<td>-</td>
<td>NR</td>
<td>-</td>
</tr>
<tr>
<td>Ulnar (right) 5th digit</td>
<td>-</td>
<td>NR</td>
<td>-</td>
</tr>
<tr>
<td>Radial Forearm</td>
<td>1.9</td>
<td>14.7</td>
<td>41.7</td>
</tr>
<tr>
<td>Superficial fibular-Leg</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>superficial fibular-Leg</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sural (right) Leg</td>
<td>6.8</td>
<td>9.4</td>
<td>-</td>
</tr>
<tr>
<td>Sural (left) Leg</td>
<td>9.1</td>
<td>11.2</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 3: Biopsied adenopathy. (A): large lymphoma cells with narrow cytoplasm, round vesicular nuclei with prominent nucleoli (Hematoxylin–eosin stain; original magnification x200). (B): Lymphoma cells positive for CD20 (original magnification x200). (C): Lymphoma cells positive for CD3 (original magnification x200).

Figure 4: Biopsied cutaneous shoulder lesion. (A): diffuse infiltration of dermis and subcutaneous tissue by neoplastic cells. A clear grenz zone is seen separating lymphoma cells from epidermis (Hematoxylin–eosin stain; original magnification x40). (B): large lymphoma cells with narrow cytoplasm, round vesicular nuclei with prominent nucleoli (Hematoxylin–eosin stain; original magnification x200). (C): Lymphoma cells positive for CD20 (original magnification x200). (D): Lymphoma cells positive for CD3 (original magnification x200).

Our results are consistent with a Diffuse large B-cell lymphoma (DLBCL) with cutaneous metastasis [3]. Moreover, the patient manifested many signs and symptoms characteristic of POEMS syndrome such as polyneuropathy, endocrinopathy, skin changes and organomegaly. Although monoclonal plasmacell proliferative disorder is required for the diagnosis of POEMS syndrome, the patient was instead diagnosed with POEMS-like syndrome associated to a DLBCL [1,4]. The serum paraprotein was classified as monoclonal gammopathy of undetermined significance (MGUS). After six courses of R-CHOP therapy (a regimen of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) the lymphadenopathy disappeared (Figure 5) and neurological symptoms improved markedly.

**Discussion**

The first description of POEMS syndrome was established in 1938 by Scheinker, who reported the case of a 39-year old man who had a solitary plasmacytoma with polyneuropathy and cutaneous changes [5]. Later on, more cases have been reported by Crow (1956) and Fukase (1968). It was then known as Crow-Fukase syndrome [6] or Takatsuki syndrome [7]. Acronym POEMS was proposed in 1980 by Bardwick [8]. It characterized the syndrome by the combination of polyneuropathy (P), organomegaly (O), endocrinology (E), monoclonal protein (M) and skin changes (S). Other features, not included in the acronym, may exist such as papilledema, extravascular volume overload, sclerotic bone lesions, thrombocytosis, erythrocytosis, elevated VEGF levels,
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of initiating the POEMS syndrome since they are a possible source of VEGF [21].

Another particularity of our case is the nature of the M component (IgMk). In large series, Nakanichi et al. (1984) reported IgM in one of 75 patients (1.3%) and kappa light chain in 4 (3 IgA; 1 IgG) patients (5%) [6]. Dispenzieri and colleagues (2002) reported IgM in 1 of 84 patients (1.2%) and lambda light chain in all of their patients [4]. No IgM or kappa light chain were reported in the French series [18]. In the literature, only 2 cases of IgMk associated to POEMS syndrome were reported, both of them were associated to Waldenström’s macroglobulinemia [22,23]. These cases suggested that IgM might have a role in the geneses of POEMS syndrome and that Lambda light chain was not necessary for its development.

In most of paraneoplastic syndromes, the main goal of treatment is to control the tumor. To treat our patient, we used R-CHOP combination that is the backbone of DLBCL therapy, with a 10-year progression free survival at 36.5% [24,25]. In typical POEMS syndrome, treatment protocols are based on the therapeutic arsenal of plasma cell disorders like multiple myeloma. Initial improvement is always obtained, but long-term follow-up studies have yet to be published [16].

**Conclusion**

In summary, our study reported a rare POEMS-like syndrome with DLBCL and IgM kappa. We suggested that B-Cell lymphoma might be associated to POEMS features. Therefore, monoclonal plasma cell proliferative disorder or Castleman Disease should be reconsidered as mandatory criterion in POEMS syndrome. Moreover, physicians should be aware of the possible role of B-cells and IgM-k in the geneses of this disease.

**References**


