SUNTEXT REVIEWS

SunText Review of Neuroscience & Psychology
ISSN: 2766-4503

Open Access
Case Report
Volume 2:2

POEMS Syndrome Without "M"- Could It Be Possible? – A Case Report

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Received date: 29 July 2021; **Accepted date:** 03 August 2021; **Published date:** 10 August 2021

Citation: Bianchi da Silva E, Mestrinelli Carrilho PE, Reck de Oliveira BC, Silva Schran L, Lazzarin Silva TAA, Carvalho CC, et al. (2021). POEMS Syndrome Without "M"- Could It Be Possible? – A Case Report. SunText Rev Neurosci Psychol 2(2): 133.

DOI: https://doi.org/10.51737/2766-4503.2021.033

Abstract

Introduction: POEMS syndrome is a rare disease characterized by polyneuropathy, organomegaly, endocrinopathy, "M-protein" disorder and skin changes. The purpose of this article is to report a case of a patient with progressive polyneuropathy without M protein and plasma cells disorder, one of the mandatory criteria diagnosis.

Case: A 43 year-old man of Japanese origin with three months of weight loss, painful feet paresthesias and reduction of muscle strength in the lower limbs. At physical examination he presented distal motor deficit in legs, global absence of profound reflexes, feet amyotrophy, hepatosplenomegaly, gynecomastia, papilledema, axilar lymph node enlargement and a cyanosis of extremities. Myelogram and bone marrow biopsy discarded myeloma or plasma cell neoplasy. Protein electrophoresis and immunofixation electrophoresis not detected "M-spike". After a clinical worsening, new diagnosis investigation was made and a vascular endothelial growth factor dosage was available (2812 pg/ml –normal range: 31-86pg/ml).

Discussion: Polyneuropathy and plasma cells disorder are both mandatory diagnosis criteria for POEMS syndrome. However, we present a case without plasma cells disorder and "M-protein spike", with the diagnosis confirmed with the combination of characteristic clinical manifestations and elevated vascular endothelial growth factor. We highlight that in some situations the diagnose can be made with auxiliaries exams to avoid delay in starting treatment.

Keywords: POEMS syndrome; Hepatosplenomegaly, Gynecomastia, Papilledema

Introduction

POEMS syndrome, also known as Crow-Fukase syndrome or Takatsuki syndrome, is a rare systemic disease, characterized by polyneuropathy, organomegaly, endocrinopathy, plasma cells disorder (or "M-protein") and skin changes. These five characteristics form the acronym that gives name to the syndrome. Other manifestations like sclerotic bone lesions, pleural effusion, ascites, edema, lymphadenopathy, Castleman disease, low fever, papilledema, clubbing, hyperhidrosis and hematological disorders (thrombocytosis, polycythemia) are also commons [1].

Most cases occur at the fifth and sixth decades of life. It is more common in man and among Japanese people. Although the etiology of the syndrome remains unknown, an association with Herpes Virus HHV8 infection and an increased production of cytokines (IL-1β, IL6, TNF-α e VEGF) [2] is observed. Polyneuropathy and monoclonal plasma cell disorder are both considered mandatory for the diagnose of POEMS syndrome [3,4]. However, in rare occasions, "M-protein" spike or an identifiable plasma cell disorder cannot both be easily defined by usual methods [5,6]. In such cases, other clinical features and other laboratory markers should be equally considered with the aim do avoid delays in the diagnose and treatment [3]. The

purpose of this article is to report a case of a patient with progressive polyneuropathy without "M-protein" and plasma cells disorder.

Methods

It is a case report study based on review of medical record. The data presented here were collected and presented after the patient previous authorization allowing the use of his health data with scientific purpose.

Case Report

A 43 year-old man of Japanese origin and severe smoker was evaluated in neurology service with a 3 months history of weight loss, painful feet paresthesias and reduction of muscle strength in the lower limbs. Neurologic exam disclosed an important distal motor deficit in legs, with global absence of profound reflexes and presence of feet amyotrophy. Hepatosplenomegaly, gynecomastia, papilledema, axilar lymph node enlargement and a cyanosis of extremities were also recorded (Figure 1).

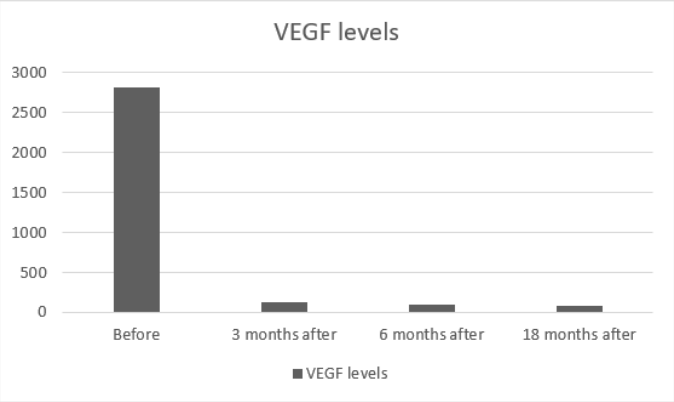

Figure 1: *VEGF levels before and after autologous bone marrow/stem cell transplantation.*

Complementary investigation showed discrete polyglobulia, hypothyoidism and thrombocytosis. Electroneuromyography of lower limbs demonstrated mixed demyelinating-axonal polyradiculoneuropathy pattern. Bone x-ray screening for plasma cell lesions showed small osteolythic and non-sclerotic lesions in the ribs and ilium bones. Positron emission tomography do not showed neoplasic lesions. Axilar lymph node biopsy demonstraded Castleman disease. Myelogram and bone marrow biopsy no evidenced myeloma or plasma cell neoplasy. Protein electrophoresis and immunofixation electrophoresis not detected "M-spike" and Urinary Bence-Jones protein was absent.

Patient condition worsed and therapy for a chronic inflammatory demyelinating polyneuropathy with prednisone (1 mg/kg/day) was started, with some initial subjective and objective improvement. After sixty days, a new deterioration of polyneuropathy occurred. It was decided to initiate intravenous immunoglobulin (five days of 400 mg/kg/day). No benefit was obtained.

A new diagnosis investigation was made and the vascular endothelial growth factor (VEGF) was measured, the result was 2.812 pg/ml (normal range: 31-96 pg/ml). So that, a POEMS "incomplete" syndrome, because the absent of "M-protein" was considered to be the target of our efforts. A proper therapy was started with a sequence of cyclophosphamide plus methylprednisolone. It was followed by melphalan plus prednisone, both without improvements. A course of bortezumib was attempted and also a localized radiotherapy of suspected bone lesions but they had both failed to bring some amelioration in his clinical condition.

The patient was referred to autologous bone marrow/stem cell transplantation. After two months his clinical situation started to improve, with progressive weight regain, disappearance of visceromegalias, lymph nodes enlargements, papilledema. After two years of the transplantation patient presented continuous improvement, but slow, of his motor and sensory symptoms. A relentless decline of VEGF levels was also observed soon after transplantation (see graphic).

Discussion

POEMS syndrome is a paraneoplastic syndrome with predominance in Japanese men and average incidence at fifty years-old [7]. The patient of the study was a man of Japanese origin and with 43 years-old at the moment of onset of the disease.

The diagnosis of the syndrome is made based on Mayo clinic criteria. It is confirmed when both mandatory major criteria (polyneuropathy and monoclonal plasma cells disorder), at least one of the major criteria (Castleman disease, sclerotic bone lesions and elevated vascular endothelial growth factor) and one of the minor criteria (organomegaly, endocrinopathy, skin changes, extravascular volume overload, papilledema and thrombocytosis) are present [7]. Our patient presented polyneuropathy, Castleman disease, bone lesions, elevated VEGF, organomegaly (hepatosplenomegaly and lymphadenopathy), endocrinopathy (gynecomastia, hypothyroidism), papilledema and thrombocytosis, but the plasma cells disorder was absent.

Establish the diagnosis of POEMS syndrome is a challenge because of the rarity and the complexity of the disease. However, a good clinical history and physical examination with bones X-rays, VEGF dosage, detection of "M-protein" and bone marrow biopsy, make possible the differentiation between the syndrome and another disorders of plasma cells or peripheral neuropathy [3,8]. But, the evidence of "M-protein" or plasma cell disorder is essential for the diagnosis, therefore the importance of this case.

Castleman disease can promote a "POEMS-like" polyneuropathy, but usually, a sensory painless neuropathy is far more frequently

observed in this disease, and not a severe polyradiculoneuropathy with prominent demyelinating features [3,9] as noticed in the present case. However, every Castleman's with POEMS-like disorder, without evidence of "M-protein" or plasma cell disease, cannot be defined as "real POEMS syndrome", according to recently defined clinical criteria [3,9]. So that, the patient presented here could be in the clinical spectrum of "Castleman disease associated neuropathy" [9]. Nevertheless, all his clinical features were strongly suggestive of a polyradiculoneuropathy associated with a POEMS syndrome with almost all major and minor criteria, with the crucial exception of a well-defined M-protein disorder.

The course of POEMS syndrome is chronic and progressive and the time of survival is about ten years [7]. Based on that, the early diagnosis is very important for reduce morbidity and enhance survival of the patients. Therefore, we advocate that in cases similar to ours, with the presence of a proper clinical syndrome, even with no clear-cut or well-identified plasma cell disorder, VEGF can be not only a real laboratory POEMS marker, but it can be considered a kind of "monitor index", closely related to the diagnosis and the treatment evolution.

Abbreviation List

IL- 1β = interleukin - 1β; IL-6 = interleukin – 6; TNF-α = tumor necrosis fator – α; VEGF = vascular endothelial growth factor

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