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Research article

POEMS syndrome misdiagnosed as CIDP: A case report

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Abstract: POEMS syndrome is a paraneoplastic disorder manifested by peripheral neuropathy and monoclonal plasma cell dyscrasia. Due to its clinical and electrophysiological aspect, POEMS syndrome is often mistaken as a chronic inflammatory demyelinating polyneuropathy (CIDP) [1]. Its acronym is derived from its principal characteristics: polyneuropathy, organomegaly, endocrinopathy, M proteins, and skin changes [2]. The purpose of this paper is to present the case of a patient who was lately diagnosed with POEMS syndrome after he was mistreated for CIDP in order to show the importance of a complete physical examination.

Keywords: POEMS syndrome, demyelinating polyneuropathy, monoclonal plasma cell disorder, skin changes, vascular endothelial growth factor.

1. Introduction

POEMS syndrome is a rare multisystem disorder manifested by polyneuropathy, organomegaly, endocrinopathy, a monoclonal plasma cell disorder and typical skin changes. The initial symptom is often polyneuropathy, which can hide other features of the disease in the first years of onset [3]. This manuscript presents a case of a patient who was misdiagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP) and treated with immunomodulatory medication, with minimal clinical response. A proper diagnosis and management of POEMS can be made with a high clinical suspicion and recognition of the electrodiagnostic results, even if the patient presents only with polyneuropathy [4]. The nerve conduction study (NCS) and electromyography (EMG) attributes might differentiate POEMS from CIDP and lead to earlier therapeutic intervention [5].

The importance of a full clinical and neurological examination is crucial for diagnosing POEMS, due to the heterogenous aspect of its presentation. Tardive or delayed diagnosis leads to clinical deterioration and a delayed appropriate treatment [6].

2. Case study

We present a case of a 37-year-old male who presented numbness, progressive bilateral lower limb weakness and inability to walk. Nine months prior to his admission he developed paresthesia in his feet, described as prickling sensation, which progressed to ascending muscle weakness of lower limbs, having difficulty in climbing stairs and unsteady gait. He also had numbness at both upper limbs. He reported a weight loss of 22 kg in the last year and erectile dysfunction.

Throughout his multiple hospitalizations, he was investigated for polyneuropathy: Magnetic resonance imaging (MRI) of the spine showed no signs of tumor or radicular compression. Autoantibodies for vasculitides and serologic tests for infectious diseases were negative, cerebrospinal fluid analysis revealed an increased protein level at 227,78 mg/dl. NCS revealed a pattern which was consistent with CIDP. He was treated with a 3-day course of intravenous immunoglobulin (IVIG), with no significant clinical response. He also followed physical therapy with minimal improvement of symptoms.

On his actual admission, upon physical examination, he had skin changes such as hyperpigmentation with areas of depigmentation, hypertrichosis, papilloma, acrocyanosis at extremities of upper and lower limbs, white nails and bilateral pretibial edema (Fig. 1). Blood cells count revealed thrombocytosis. Blood biochemistry analysis showed low albumin and globulin. Fibrinogen, C-reactive protein and erythrocyte sedimentation rate were elevated. Serum immunoglobulin levels were within normal. Vitamin B12 and folate levels were low. Tumoral marker CA-125 was elevated. The abdominal ultrasonography showed hepatomegaly and splenomegaly.

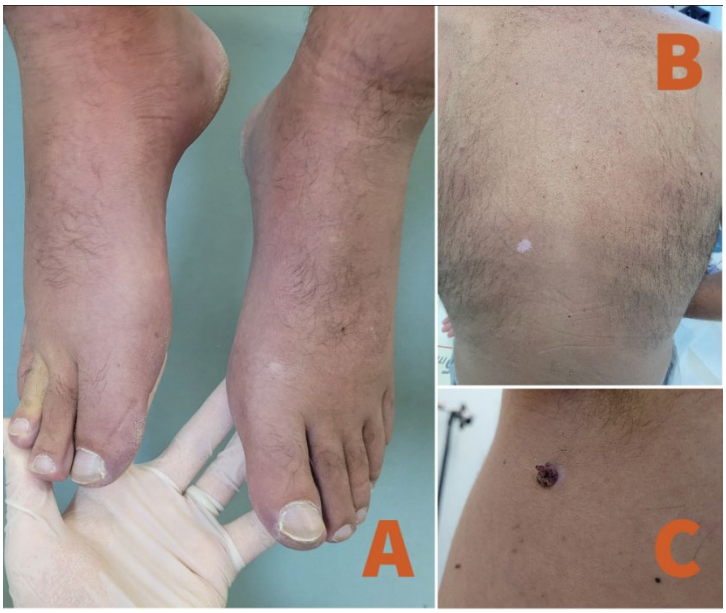

Figure 1. Skin changes: acrocyanosis at extremities of lower limbs (A), hypertrichosis and lesions of depigmentation (B), papilloma (C).

Motor examination revealed lower limbs strength MRC=3/5 proximally and MRC=0/5 distally; upper extremities MRC=4/5. Reflexes were absent. Also was noted reduced sensation to temperature, light touch and pain up to knee level for both lower limbs (in stocking distribution pattern) and reduced sense of vibration to the level of the knees (0/8); downgoing planter responses. Examination of the cranial nerves was normal. In our neurophysiology laboratory, electroneurography showed a typical aspect of demyelination in the upper limbs, represented by decreased motor and sensory nerves velocities, prolonged distal motor latency and prolonged F wave (Fig. 2). In addition, sensory and motor NCS were not obtained in the lower limbs and needle EMG showed a chronic denervation pattern in the tibialis anterior muscle.

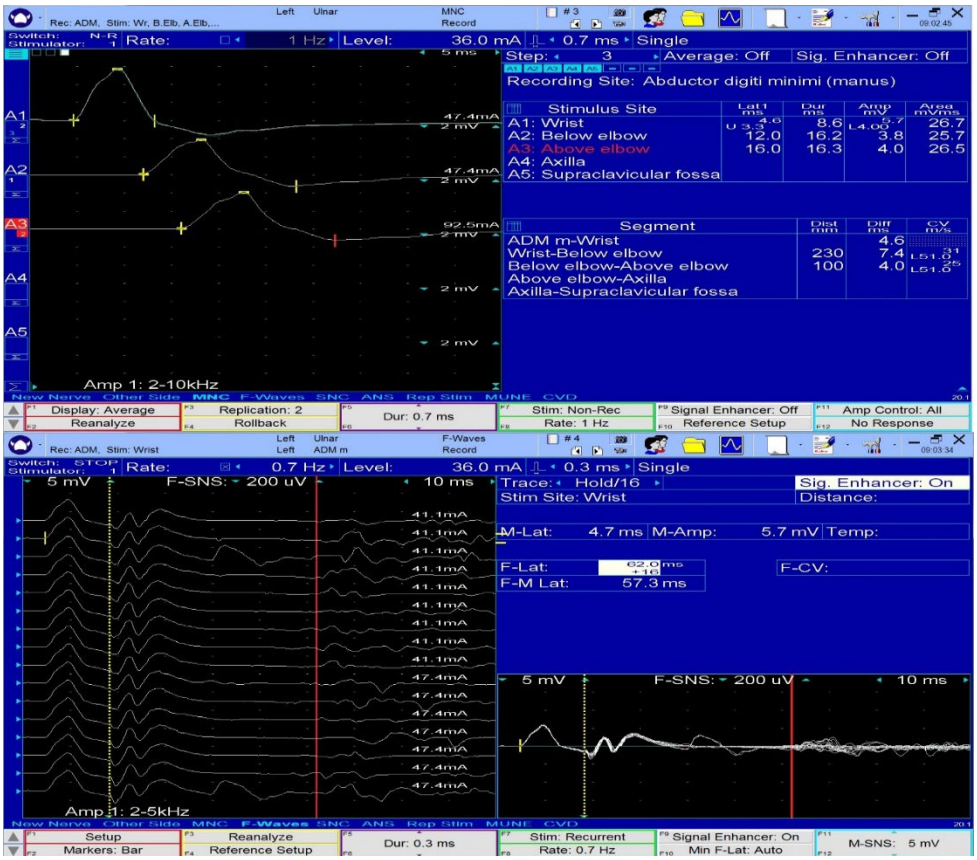

Figure 2. Homogeneous slowing of motor nerve conduction associated with prolonged F wave on the left ulnar nerve

In view of no significant neurological improvement, despite getting the standard therapy and given the clinical aspect and the electrophysiological pattern, a diagnosis of POEMS syndrome was suspected, and investigations were completed with a malignancy screening. Whole body computed tomography (CT) revealed the presence of multiple osteolytic masses, bilateral pleuritis, ascites, and pelvic adenopathy. Serum protein electrophoresis revealed monoclonal immunoglobulin G-lambda (IgG-λ) paraprotein. Repeated serum protein electrophoresis with immunofixation confirmed a monoclonal spike IgG lambda (0.64 μg/dL). Vascular Endothelial growth Factor (VEGF) level was found elevated; JK2 was normal. Bone marrow examination showed 15 % plasmacytes suggesting a multiple myeloma with IgG lambda chains. The patient was treated with Bortezomib, a proteasome inhibitor, 2.6 mg, four doses, with minimal clinical improvement.

3. Discussions

Diagnosis of POEMS syndrome in the early stage is difficult. The differential diagnoses include Guillain-Barré syndrome, CIDP, vasculitic neuropathy, infectious diseases complicated with polyneuropathies, metabolic deficits, paraneoplastic polyneuropathies such as paraprotein-associated neuropathy (multiple myeloma, Waldenström's macroglobulinemia, primary amyloidosis, cryoglobulinemia, and lymphoma) [7].

In order to set a diagnosis of POEMS most authors proposed that the presence of two major criteria, including polyneuropathy and monoclonal plasma cell proliferative disorder and the existence of one minor criterion, is sufficient for diagnosis. Minor criteria include organomegaly, endocrinopathy, skin changes, thrombocytosis, polycythemia [8]. Our patient filled the diagnosis criteria of POEMS having polyneuropathy, a monoclonal plasma proliferative protein, skin changes, endocrinopathy, organomegaly and sclerotic bone lesion. In addition, he had high level of VEGF, which is considered by some authors a major criterion for the diagnosis, and persistent thrombocytosis.

POEMS syndrome can be often misdiagnosed with inflammatory polyneuropathy due to its clinical presentation and nerve conduction findings. The pathogenesis of POEMS syndrome is thought to be related to the production of various inflammatory cytokines, such as interleukins (IL-1 and IL-6) and VEGF. High levels of VEGF were found in patients' serum. In CIDP or Guillan-Barré syndrome there was not observed increasing level of VEGF, hence the rise of VEGF may have a diagnostic role. Studies showed that nerve biopsy in POEMS revealed higher rates of axonal degeneration comparing with CIDP, diffuse myelinated nerve fiber loss, opened tight junctions between endothelial cells, pinocytic vesicles adjacent to cell membranes [9].

Regarding the treatment, radiotherapy is recommended in localized disease, while widespread osteosclerotic lesions should beneficiate by chemotherapy. Recovery from POEMS neuropathy depends on the early diagnosis and prompt therapy. The standard therapies used for CIDP such as IVIG are ineffective in POEMS and may delay appropriate management. Treatment for POEMS targets the plasma cell clone and is dependent on the degree of plasma cell infiltration into bone marrow [10].

4. Conclusions

POEMS syndrome is often undiagnosed or misdiagnosed, having similar symptoms with other disorders. Due to its rapidly progressive course, any misdiagnosis as CIDP or delay in appropriate diagnosis may result in disease progression and additional complications. This case showed the importance of an appropriate examination, which includes a complete general examination of patients who have CIDP symptoms, before declaring the case an idiopathic CIDP, and for those with refractory neuropathy, making a serum and urine electrophoresis completed with immunofixation should be taken into consideration [11].

5. Conflict of interest

There is no conflict of interest for any of the authors regarding this article.

6. Informed consent

The informed consent was obtained from the patient.

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