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# Amyloidosis as a Manifestation of POEMS Syndrome: Report of a Clinical Case

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## Abstract

POEMS syndrome was first established in 1980 by Bardwick, referring to the presence of polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes, as part of a manifestation of an underlying plasma cell neoplasm. To our knowledge there are few reports with cardiac involvement in POEMS syndrome, where chemotherapy has shown to reverse such involvement. We report a clinical case with cardiac amyloidosis and POEMS syndrome. On the other hand, amyloidosis turns out to be an infrequent entity that is the product of the deposit of an abnormal protein (Amyloid), which interferes with the functioning of the affected organ by producing deposit. The patient we present is of particular interest because he has the presence of both pathologies, we consider that the discussion in this clinical case implies a probable better prognosis of amyloidosis if it is associated with POEMS syndrome.

**Keywords: Amyloidosis; Paraneoplasic; POEMS syndrome**

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## Introduction

POEMS syndrome was first established in 1980 by Bardwick, referring to the presence of Polyneuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes (POEMS), as part of a manifestation of an underlying plasma cell neoplasm [1]. POEMS syndrome has evolved, redefining its diagnosis criteria which includes mandatory criteria, major criteria and minor criteria. Mandatory criteria include polyneuropathy, usually demyelinating, and monoclonal plasma cell-proliferative disorder. Major criteria, includes Castleman's disease, sclerotic bone lesions, vascular endothelial growth factor elevation, at least one is required. Minor criteria include organomegaly, extravascular volume overload, endocrinopathy (other than hypothyroidism), skin changes, papilledema, thrombocytosis/polycythemia, along with other symptoms which are none specific clubbing, weight loss, hyperhidrosis, pulmonary hypertension, thrombotic diatheses, diarrhea, low vitamin B12 values [2]. Ten-year survival is 79% which can vary [3], in a Mayo Clinic series during 2003, overall median survival was of 13.7 years, being a bit lower in patients with clubbing or extravascular volume overload having a median survival of 2.6 and 6.6 years [4,5]. The relationship between amyloidosis with cardiac involvement and POEMS syndrome has not been well established in terms of prognosis, considering POEMs syndrome has a good prognosis with adequate treatment compared to those patients with cardiac amyloidosis, for this reason we would like to share the following clinical case.

## Case Presentation

We present the case of a 65-year-old male patient who came to our hospital starting his condition 2 years prior to his visit with hair loss, constipation, dry skin, fatigue, and difficulty speaking; being valued by various doctors without reaching a diagnosis. Six months after the onset of the symptoms of the previous ones, the patient presented dysphonia, and dysphagia to solid foods, weight loss of 3 kg (unintended), paresthesias and dysesthesias in the lower extremities; therefore, a diagnostic protocol was started. Physical examination reveals macroglosia (Figure 1), left cervical lymph node movable and painless 2 cm around area IV of the neck, maculopapular hyperpigmented skin lesions in thorax, holosystolic tricuspid murmur 4/6, ungeal lesion with trachyonychia on both hands (Figure 2), and lower extremities with pitting edema accompanied with decreased vibratory sensation. Contemplating the manifestations amyloidosis was suspected and periumbilical biopsy

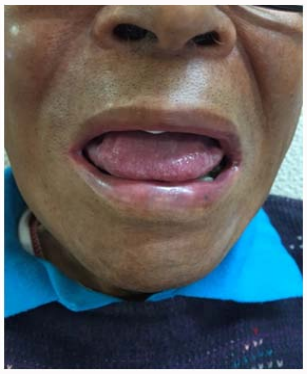

**Figure 1:** Macroglosia in patient with POEMS syndrome.

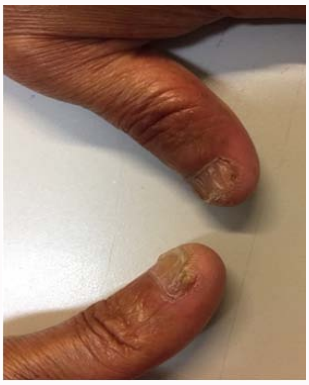

**Figure 2:** Trachyonychia: Rough, longitudinally ridged on both nails.

was done reporting collagenous homogenous fiber interlaced with fibroblasts staining orange red with red Congo stain making the diagnosis of amyloidosis. Laboratory evaluation revealed a light chain in urine with kappa spike predominance of 290.94 mg/L (0.01 mg/dL to 33 mg/dL), lambda of 10.89 mg/L (0.45 mg/dL to 4.9 mg/dL), a kappa/Lambda relation of 26.7, a beta 2 microglobulin of 2195 ng/mL (609 ng/mL to 2366 ng/mL), a vascular endothelial grow factor of 310.6 pg/mL (31 pg/mL to 86 pg/mL) and N-terminal cerebral natriuretic pro-peptide of 4686 pg/mL. Although hypothyroidism is common in amyloidosis and a thyrotropin (TSH) blood test was obtained reporting TSH of 8.3 IU/mL, rest of profile was normal diagnosing subclinic hypothyroidism. A complete hormonal profile was requested that report hypogonadism with total testosterone of 101 ng/dL (181 ng/dL to 772 ng/dL), a dehydroepiandrosterone of 12.1 µg/dL (228 µg/dL to 283 µg/dL); what allowed us to integrate POEMS syndrome. Due to the data found in the histopathological study of the periumbilical fat, an echocardiogram was performed that reported infiltrative myocardiopathy in racemic grapefruit pattern suggestive of Amyloid infiltration, ventricular hypertrophy, systolic ejection fraction 50%, diastolic dysfunction with restricted pattern, moderate mitral insufficiency, severe tricuspid insufficiency, moderate pulmonary hypertension PSAP 60 mmHg, biatrial dilatation without thrombi. After these findings N-terminal cerebral natriuretic pro-peptide (NT-Pro-BNP) was obtained reporting a value of 4,686 pg/mL (<900 pg/mL), confirming poor prognosis associated with cardiac involvement. Due to the symptoms that the patient reported in the extremities and the alterations found in the physical examination, an electromyography was performed that reported mixed predominance polyneuropathy with axonal demyelinating damage. And due to the gastrointestinal symptoms, an endoscopy was obtained with a report of chronic esophagitis, alterations in motility due to amyloidosis and chronic duodenitis. Finally, as part of the diagnostic protocol, a complete bone series that did not have osteosclerotic changes, ruling out damage at this level.

## Discussion

Since amyloidosis or POEMS syndrome are treated in a similar manner, identifying coexistence between these two entities doesn't see of significant importance and it basically speaks of the presence of a chronic inflammatory process generated mainly by interleukin-6 that has been detected present in the germinal centers of the lymph nodes. For the above the treatment is usually started with melphalan plus dexamethasone o bortezomib when there is a monoclonal peak, which is accompanied by the presence of remission of polyneuropathy, macroglossia and skin lesions [6]. In the case of our patient with cardiac amyloidosis and POEM syndrome, we asked ourselves whether the coexistence of both pathologies had an association linked to a better prognosis, finding only that the survival reported in these cases is usually 79% at 10 years [3]. In POEMS syndrome, skin findings (hyperpigmentation, hemangiomas, hypertrichosis, redness, acrocyanosis, white nails, facial atrophy or clubbing) are frequent, so there should be a thorough examination when this entity is suspected, as in the case presented [2]. A Mayo Clinic prognostic model involving NT-pro-BNP plus cardiac troponin has been established in patients with cardiac amyloidosis, where a 5-year survival rate ranges from 8% to 28% [7] compared to a rate of 13.7-year overall survival in patients with POEMS Syndrome; however, in the case of our patient, the elevated levels of NT-pro-BNP in isolation confer a poor prognosis of cardiac function [4,5]. Cardiac involvement is rarely seen in POEMS syndrome, but it is seen more frequently in the development of amyloidosis, although the most affected organ is the kidney; it usually presents as a restrictive heart disease with predominantly septal concentric ventricular hypertrophy, as reported in the echocardiogram of our patient, and arrhythmias are usually present in up to 30% [8,9]. Some authors have suggested cardiomyopathy as a manifestation of organomegaly [10-12], which should raise the argument in designing new therapeutic strategies. Tanus T and Miller HJ reported a case of POEMS syndrome and cardiac involvement showing resolution of cardiomyopathy after chemotherapy [13]. This result implies a change in prognosis among patients with cardiac amylosis and POEMS syndrome. It is possible to infer that those patients with POEMS syndrome along with cardiac involvement due to amyloidosis may have a better prognosis compared with amyloidosis without POEMS syndrome [14-16]. A case series could further clarify this prognosis, probably changing the panorama. A series of cases could further clarify this prognosis, probably changing the panorama, without forgetting that by modifying the inflammatory state of the organism, the presence of Amyloid tends to decrease. In our patient's case, the fact that he does not present sclerotic lesions or disseminated bone marrow is a good prognostic data, although in the literature they are described as one of the most characteristic findings of POEMS syndrome.

## Conclusion

We consider that the case presented is representative of the affectation of both pathologies, in a patient who began with very general symptoms where the physical examination was a fundamental pillar for the suspicion of the entities involved, which was corroborated by the complementary studies; in the case of the patient, the presence of both pathologies could be demonstrated, on

the one hand, with myocardial infiltration and positive Congo red staining, and on the other, meeting the diagnostic criteria, which represented a benefit for patient follow-up.

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