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POEMS SYNDROME IN A WOMAN WITH MULTIPLE CUTANEOUS ANGIOMAS

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ABSTRACT
POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes) is a rare systemic pathology of paraneoplastic origin that is associated with plasma cell dyscrasia. It occurs between the fifth and sixth decades of life and affects men 2 times more than women. We report the occurrence of this disease in a woman with generalized eruptive angiomas as a rare skin manifestation of this syndrome and which was the key of the diagnosis in our patient.

KEYWORDS: Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes.

INTRODUCTION

POEMS syndrome also known in the literature as Crow-Fukase or Takatsuki syndrome, is an extremely rare multi-systemic disorder often associated with osteosclerotic myeloma, a variant of plasma cell dyscrasia[1] that affects men 2 times more than women.[2] It is characterized by the presence of sensorimotor polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes, and other systemic manifestations.

The pathogenesis of the syndrome is unknown but over-production of vascular endothelial growth factor and other cytokines is probably responsible for most of the characteristic symptoms.[3]

Cutaneous alterations were considered frequent and important for the diagnosis of this syndrome , especially hyperpigmentation, hypertrichosis, acrocyanosis, plethora,[4] and cutaneous thickening, but the occurrence of cutaneous angiomas in this syndrome is rarely described.

We report a rare case of this Syndrome in a woman with multiple cutaneous angiomas.

Observation: This is the case of a 49-years-old female, with antecedents of diabetes mellitus type 2 and followed in the department of endocrinology for acromegaly, who was hospitalized in the department of pulmonology for acute respiratory distress of unknown origin with intense fatigue, general malaise, paresthesia and cramps at the rest of the limbs. Our medical advice was asked for skin lesions on the trunk, the medical examination showed multiple cherry angiomas on the trunk , the back and buttocks with a skin thickening in the pubis, macro cheilitis and macro glossia.
The neurological examination had found a painful and proprioceptive hypoesthesia with a motor deficit on limbs with a reduction in bilateral tendon reflexes. The rest of the clinical examination didn't find any abnormalities.

Blood analysis had discovered thrombocytosis, acceleration of the sedimentation rate; hyperproteinemia and the electrophoresis of serum proteins with immunofixation had found a monoclonal hypergammaglobulinemia (IgA type with lambda light chain) with positive proteinuria of Bence-Jones. Other blood explorations especially the hormonal study and vitamin B 12 were without abnormalities.

Both a radiography and a scan of the chest were done in addition to echocardiography and DLCO (Diffusing capacity for carbon monoxide), which substantiated the presence of cardiomegaly, pulmonary hypertension, bilateral pleural effusion and a decreased DLCO which had led to respiratory failure at the beginning of her hospitalization. Also, bone radiographs of the skeleton were performed and had found lithic lesions with sclerotic borders in the pelvis bones.

Moreover, a neurophysical examination was performed, which confirmed the existence of sensorimotor-predominant demyelinating polyneuropathy.

Once the diagnosis of POEMS syndrome had been established based on the criterias described by Dispenzieri et al, the patient was referred to the department of internal medicine for appropriate management of her disease where a bone marrow biopsy

was performed and was reactive, so the patient was put under radiotherapy because of the strong suspicion of plasmocytoma and the limited areas of lithic lesions.

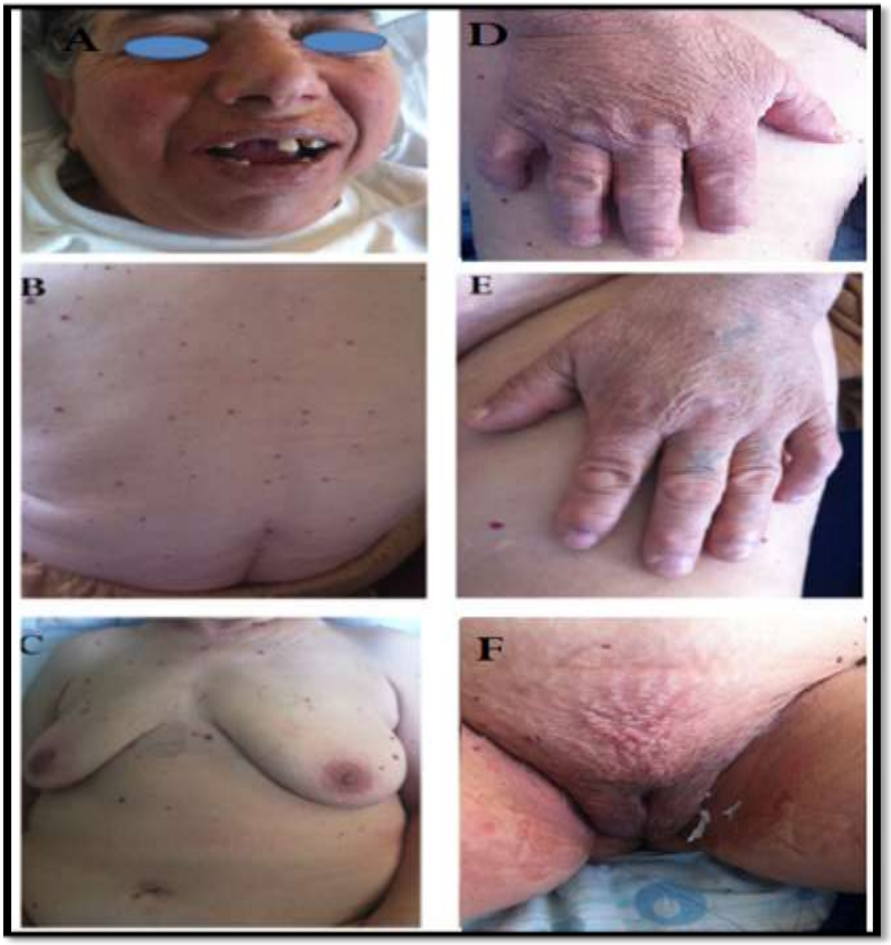

Figure 1: Clinical Images showing multiple cherry angiomas on the trunk , the back and buttocks with a skin thickening in the pubis , dental anomalies , enlarged hands , macro cheilitis and macro glossia.

DISCUSSION

POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammapathy and Skin changes) syndrome is a rare systemic pathology of paraneoplastic origin that is associated with plasma cell dyscrasia, this acronym was first described by Bardwick in 1980 ,but similar manifestations were noticed before in 1938 by Scheinker in the case of a 39-years-old man with plasmocytoma, sensorimotor polyneuropathy and cutaneous hyperpigmentation and also, in 1956, Crow reported two patients with osteosclerotic plasmocytoma, peripheral neuropathy, cutaneous pigmentation, leukonychia, lymphadenopathy and edema of the ankles, designated as Crow-Fukase syndrome.[5]

It occurs between the fifth and sixth decades of life and affects men 2 times more than women, and at first it was believed to be more common in Japanese progeny,[6] Yet, with the growing knowledge of the entity it was also observed in European, African, Hispanic and Asian descendants.[7]

The pathogenesis of the syndrome is still not well known but some theories were proposed and it's considered the result of a rare proliferative monoclonal disease of systemic plasmocyte attack with an indolent course[4], where there is an increased production of cytokines, such as interleukin-1β (IL-1β), IL-6 and tumor necrosis factor α (TNF-α), in addition to vascular endothelial growth factor (VEGF) which are responsible of all the manifestations of this syndrome.[5]

On the other hand, clinical and Para clinical manifestations of the disease are very varied and diversified: peripheral neuropathy which is usually the first clinical manifestation to appear and the key criterion for the diagnosis and is a bilateral, symmetric and ascending sensorimotor, demyelinating polyneuropathy,[3-6-8-9] which affects the lower limbs and begins as sensory symptoms followed by motor involvement,[4] with a gradual proximal spread. Severe weakness occurs in more than half of patients and results in an inability to ambulate.[10] Our case presented similarly typical clinical and electrophysiological findings.

Besides, the presence of a monoclonal plasma cell disorder is important for the diagnosis of this syndrome, the monoclonal component is usually of immunoglobulin (Ig) type A, almost always with lambda lightchain restriction, differentiating the syndrome from multiple myeloma, in which light chains are of the kappa type.[3] In addition, Cutaneous alterations in this disease are numerous, heterogeneous and nonspecific[6], they were found in about 68 % of patients in one publication and were even more observed in the largest study reported in the literature (90%).[11] The most common findings are hyperpigmentation (diffuse or localized), hypertrichosis, acrocyanosis, plethora and hemangiomas.[5] Other manifestations include hyperhidrosis, leukonychia, necrotizing vasculitis, hypertrichosis , calciphylaxis and cutaneous thickening of sclerodermiform type. The Occurrence of multiple cutaneous angiomas was considered rare[12-13], they appear during the course of the disease with firm papular lesions and an erythematous or violet coloration, on the trunk and in the proximal region of the limbs[5] as the case of our patient. It is present in only 3% of cases in one study and can precede the remaining signs and symptoms of the syndrome, allowing an early diagnosis.[14]

These cutaneous changes were also significantly associated with abnormal pulmonary function tests ($P < 0.001$) in one study; which is the same of our case and which shows the value of dermatologic evaluation in the diagnosis of this syndrome.[11]

Bone lesions are present in most of the individuals and are usually painless, they may be of the sclerotic, lithic (less frequent) or mixed (lithic with sclerotic borders) type. There is a preference for involvement of the spine, pelvis bones, ribs and proximal portion of the extremities.[4-15] In our patient , the standard radiographs of the skeleton had found mixed bone lesions in the pelvis bones . this bone affectation is highly significant because its spread determines the therapeutic approach.[3] Pulmonary morbidity includes restriction, decreased diffusing capacity for carbon monoxide (DLCO), respiratory muscle weakness, abnormal imaging, and pulmonary hypertension[16], these pulmonary manifestation may increase the risk of cardiorespiratory failure which is the most common cause of death in patients having this syndrome.[16]

Other manifestations of POEMS syndrome is thrombocytosis and endocrine disorders such as hypogonadism, hyperestrogenemia, hypothyroidism, hypoparathyroidism, adrenal insufficiency and diabetes.[17]

The presence of all related manifestations is not mandatory for the diagnosis of the disease, and no single laboratory evidence can be considered as pathognomonic. Dispenzieri et al.[18] in 2003 had proposed a criteria system for the diagnosis of POEMS syndrome based on the frequency and the relevance of the clinical and laboratory findings, they divided them into major criteria which are polyneuropathy and monoclonal plasmaproliferative alterations and minor criteria which are sclerotic bone lesions, Castleman's disease, organomegaly , endocrinopathy (adrenal, thyroid, hypophyseal, gonadal, parathyroid, pancreatic), extravascular volume overload (edema, pleural effusion, or ascites), skin disorders and papillary edema, thrombocytosis and polycythemia. The primary pulmonary arterial hypertension, obstructive pulmonary disease, thrombosis, arthralgias, cardiomyopathy, fever, diarrhea and B12 hypovitaminosis may also be observed. Establishing the diagnosis of POEMS syndrome requires the presence of two major criterias and at least one minor criterion.

In our patient, two Major criterias were present, which were the polyneuropathy and the monoclonal plasma cell-proliferative disorder in addition to organomegaly (acromegaly, cardiomegaly), endocrinopathy (acromegaly, Diabetes), skin changes, thrombocytosis and pulmonary morbidity. Also, the diagnosis of POEMS syndrome was evocated thanks to the presence of cutaneous manifestations, which prove again the crucial role of these cutaneous manifestations in the diagnosis of this rare and underestimated disease.

Treatment of POEMS syndrome is not well established, the mode of therapy is based on whether the patient has limited or widespread sclerotic bone lesions. Radiotherapy is the treatment of choice in cases of single sclerotic bone lesions or whenever the syndrome occurs within a limited area, as the case of our patient.

In the case of widespread lesions, chemotherapy regimens based on alkylating agents (cyclophosphamide or melphalan) have been used alone or in combination with corticosteroids, which achieve clinical improvement in about 40% of patients.[3] Autologous bone marrow transplantation can be used in young patients with disseminated osteosclerotic disease[4, 19, 20] and in patients with rapidly progressive neuropathy.[21] Monoclonal blocking antibodies for the VEGF receptor (bevacizumab) were employed successfully according to some reports.[4, 22]

CONCLUSION

The originality of our observation is the occurrence of this syndrome in a woman with generalized eruptive angiomas as a rare skin manifestation of the disease.

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