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Case Report

Skin: mirror of marrow- case of POEMS syndrome

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ABSTRACT

Monoclonal gammopathy is clonal proliferation and accumulation of immunoglobulin producing B-cells. A variety of skin disorders are associated with an increased level of monoclonal immunoglobulin proteins. Synonyms such as monoclonal gammopathies, paraproteinemias, plasma cell dyscrasias and dysproteinemias are used to designate gammaglobinopathies. Here in we report a case of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) syndrome presenting with sclerodermoid features.

Keywords: POEMS syndrome, Hypergammaglobulinopathies, Skin disorder

INTRODUCTION

Hypergammaglobulinemia, or pathological increase in gamma globulin, can be monoclonal or polyclonal. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome is rare multisystem disease that occurs due to plasma cell dyscrasia.

CASE REPORT

A 79 year old male patient, presented with generalized thickening and tightening of skin all over body (Figure 1), with restricted mouth opening since three years. He also had itchy non healing ulcers in flexural areas (Figure 2) since three months. He gave history of sensory loss on extremities, weight loss and anorexia. Due to diffuse thickening of skin patient had difficulty in flexing of elbows and knees and clenching fist (Figure 3). Patient experienced proximal muscle weakness of upper and lower limbs, but did not report any difficulty in deglutition or Raynaud's phenomenon. Detailed dermatological examination revealed diffuse hide bound skin all over body involving trunk, face and bilateral extremities. Multiple punched out ulcers, with raised margins were noted in axillae, antecubital and popliteal fossae surrounded by firm erythematous to violaceous waxy papules. He had drawn mask-like face with a positive Ingram's sign. The modified Rodnan Skin score was calculated to be 40. Above findings led to differential diagnosis of scleredema, scleroderma, dermatomyositis, and paraneoplastic dermatosis. Routine baseline investigations like liver function tests, renal function tests, serum electrolytes, urine routine microscopy with 24 hour urinary protein, blood sugar levels were within normal limit. Erythrocyte sedimentation rate was raised and hemogram showed increased platelet counts. Chest x-ray was unremarkable but X- ray skull and spine demonstrated lytic bone lesions. Antinuclear antibody profile (including ds DNA and Scl70) was negative. Skin histopathological examination was almost normal except for a single small focus of thin band of collagen near dermo-epidermal junction. Hence above differentials were ruled out and possibility of hypergammaglobulinopathy was considered. On performing special staining with Congo red, which was negative, amyloidosis was ruled out. On further investigation,

fundoscopy revealed papilledema. Further search for gammaglobulinopathy revealed slight reversal of Albumin: Globulin ratio (0.81) but Bence Jones proteins were negative. Serum immunoglobulin's level were performed which disclosed increased levels of serum IgA and IgM (1277 gm/dl and 63.07 mg/dl respectively) and HbA1c showed prediabetic state. In view of his neurological symptoms, nerve conduction velocity was done which revealed demyelinating axonal sensory-motor polyradiculopathy, more in lower limbs as compared to upper limbs. Above investigations were pointing towards diagnosis of POEMS syndrome. For confirming POEMS syndrome bone marrow aspiration was performed revealing hypercellularity with markedly increased plasma cells.Thus, final diagnosis of POEMS syndrome was established according to the criteria (Table 1).

Table 1: Criteria for POEMS syndrome.

Major criteria	**Polyneuropathy**
	Monoclonal plasmaproliferative disorder
Minor criteria	Sclerotic bone lesions*
	Castleman disease*
	Organomegaly(splenomegaly, Hepatomegaly or lymphadenopathy)
	Oedema (edema, pleural effusion or ascities)
	Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic)
	Skin changes(hyper-pigmentation, hypertrichosis, plethora,hemangioma, white nails)
	Papilledema
Known associations	Clubbing
	Weight loss
	Thrombocytosis
	Polycythemia
	Hyperhydrosis
Possible associations	Pulmonary hypertension
	Restrictive lung disease
	Thrombotic diatheses
	Arthralgia
	Cardiomyopathy
	Low vitamin B12 levels
	Fever
	Diarrhea

Two major and at least one minor criteria are required for diagnosis of POEMS syndrome.

Patient is currently on treatment with intravenous dexamethaxone 40 mg pulse therapy monthly for 3 days along with oral thalidomide daily 100 mg since last 2 months with significant improvement in terms of mobility and regression in Modified Rodnan Score to 32.

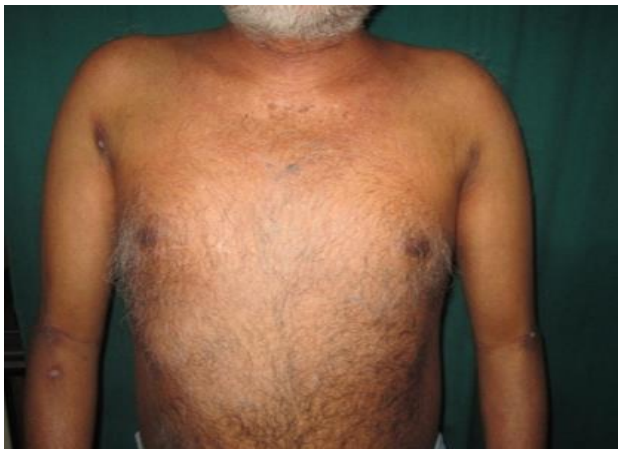

Figure1: Diffuse thickening of skin.

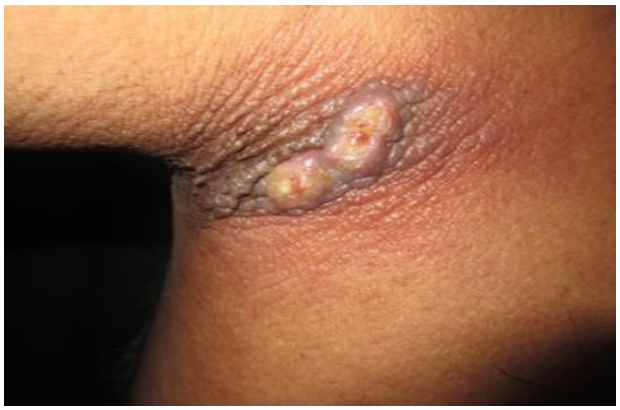

Figure 2: Punched out ulcer.

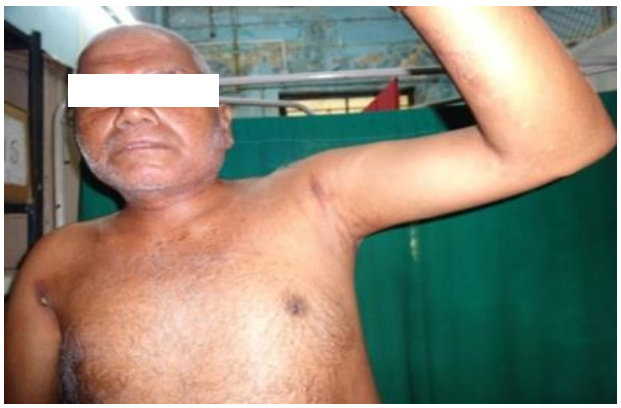

Figure 3: Patient unable to extend upper limb.

DISCUSSION

A variety of skin disorders are associated with monoclonal gammopathy, which are divided into 2 groups. The first represents a direct consequence of plasma cell proliferation with colonization of the plasma cell clone in the dermis expressed as a deposition of

proteins related to the M component (AL amyloidosis, cryoglobulins). The second group represents skin disorders associated with an M component (scleromyxedema and Schnitzler syndrome**)**

POEMS Syndrome is a Paraneoplastic syndrome associated with underlying plasma cell neoplasm. It is also known as Takatsuki syndrome or Crowe-Fukase syndrome. The acronym was coined by Bardwick (1980).[2] It is a rare multisystem disorder with slight male preponderance (male: female = 2.5:1) without any specific racial association. The exact incidence of POEMS is not known. There are few case studies of 99 and 68 patients by Dispenzeri et al and Driedger et al Cytokines have been implicated in the pathogenesis of POEMS.[1,3] It appears to be mediated by an imbalance of pro-inflammatory cytokines like Interleukin-1(IL-1), IL-6, and tumour necrosis factor.[1] Vascular endothelial growth factor is an excellent marker as a pathogenic factor which induces a rapid and reversible increase in vascular permeability and causes angiogenesis. Skin changes present in POEMS syndrome are hyperpigmentation (most common), acrocyanosis and plethora, glomeruloid hemangioma, telangectasia, sclerodermoid changes/ thickening and hypertrichosis. Of these our patient had only diffuse thickening of skin. According to Dispenzeri et al skin thickening is a rare skin presentation seen only in 5% patients.[1] Peripheral neuropathy is the dominant clinical feature of this disorder. The neuropathy is symmetrical and ascending, with either an insidious or rapidly progressing onset. In most patients, it is the presenting symptom. The neuropathy is seldom painful, and autonomic involvement is rare. It is typically a chronic, large fibre sensorimotor neuropathy. Organomegaly (hepatomegaly, splenomegaly, lymphadenopathy) is not seen classically in all patients of POEMS syndrome and was absent in our case. Endocrine abnormality is one of the defining features of POEMS. Of all the above mentioned criteria and associated features, our patient had monoclonal gamopathy and peripheral neuropathy as major criteria while minor criteria like skin involvement, sclerotic bone changes along with papilledema were present.For treatment, radiation and chemotherapy are the most useful. There is insufficient evidence regarding the treatment options available for POEMS syndrome.[1] It requires a multi-disciplinary care. Radiotherapy and chemotherapy (Melphalan, corticosteroids, cyclophos-phamide) and autologous stem cell transplantation are commonly used. The benefit of anti-VEGF antibodies (Bortezomib) is conflicting. The median survival of patients with POEMS syndrome is poor, about 12 to 33 months.[4,5]

CONCLUSION

Therefore, just as skin acts as mirror of internal disease, it also reflects the condition of marrow. High index of suspicion with thorough investigations is necessary for accurate diagnosis of dyscrasias presenting with cutaneous features mimicking other common conditions.

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