Primary Systemic Amyloidosis – A Great Mimicker

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Abstract

A 40 year old female patient presented with myalgia and both knee joint pain for 3 years and raised skin lesions over both eyelids for 1 year. General examination and systemic examination were normal and vitals were stable. Dermatological examination showed multiple well defined erythematous smooth plaques over both eyelids, waxy papules over upper lips, microstomia, macroglossia, sclerodactyly, nodules over both suprascapular region, fixed flexion contracture of index and middle finger present. Routine investigations were normal. Serum protein electrophoresis showed band in gamma globulin region. Histopathology showed homogenous eosinophilic material in papillary dermis and dense fibrocollagenous tissue in reticular dermis. Congo red stain was positive. Hence diagnosis of primary systemic amyloidosis was made.

Keywords: Sclerodactyly, macroglossia, systemic amyloidosis

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Introduction

Amyloidosis is a generic term, originally coined by Rudolf Virchow in 1854, which denotes extracellular deposition of proteinaceous substance, composed of family of biochemically unrelated proteins(1). Amyloidosis can be classified as systemic and cutaneous amyloidosis. Systemic further into primary and secondary(2). Primary systemic amyloidosis is a rare disorder. Wilksin 1856, was the first to describe it(3). Primary maybe idiopathic or myeloma associated. It is characterized by fibrils composed of protein AL and appears to be a consequence of plasma cell dyscrasia. We report a case of primary systemic amyloidosis with classical cutaneous findings.

Case Report

48 years old female patient, presented with chief complaints of myalgia and pain over both knee joints of 3 years duration, intermittent initially and then became continuous and also pain radiating from gluteal region to lower leg. She also complained of pain & stiffness of both hands. She also had raised skin lesions over both upper and lower eyelids, around mouth of 1 year duration. Patient also had thickening & hardening of skin of both forearms, enlargement of tongue and difficulty in opening mouth. There were no other systemic complaints or any chronic illnesses in the past.

General examination was normal except for pallor. Vital signs were normal. Systemic examination, normal. Multiple well defined waxy soft, smooth papules/ plaques of size 0.3*0.5cm to 1*3cm over upper & lower eyelids. Multiple well defined skin coloured waxy papules & plaques over upper lip & angle of mouth. Macroglossia (Fig. 1), grade II microstomia, angular stomatitis, chelitis were present. Sclerodactyly(Fig. 2), sclerosis extending upto wrist joint & lower legs, fixed flexion contracture of both middle & index fingers, xerosis of UL, LL. Glove & Stocking anaesthesia was present. Shoulder pad sign was positive(Fig. 3). Oral, genital, conjunctival mucosa was normal. Nails, scalp and hair also normal.

Routine investigations- Normal except for anaemia. ESR raised, CRP positive. Peripheral smear study-normal. Urine BJP- negative. Lipid profile & thyroid assay normal. ASO, RF, ANA- negative. Chest and cardiac evaluation normal. USG Abd& KUB- normal. UGI Scopynormal. NCS showed B/L sensorimotor asymmetrical axonal neuropathy. Serum immunoelectrophoresis-band in gamma region (Fig. 7)

Histopathology –Irregular acanthosis, homogenous eosinophilic material (Fig. 4) in papillary dermis, dense fibro collagenous tissue in reticular dermis. Congo red(Fig. 6) showed brick-red color of amyloid under ordinary light and areas of apple-green biref ring enceunder polarized light microscopy

Neurologist opined as? Small fibre neuropathy? CTD and advised T.Methylcobalamin 1-0-1 and T.Amitryptyline 25mg 0-0-1.

Medical oncologist started with cycle 1 chemotherapy with Inj. Dexa 40mg in 250 ml of NS over 1 hr, Inj.

Borteozomib 1.3 mg/m² iv bolus, Inj. Vit B12 2cc im after giving prophylaxis for P.jiroverci/herpes and advice skeletal survey/ BMA. Patient is at regular follow up at medical oncology department and there is no deterioration in patient's condition.

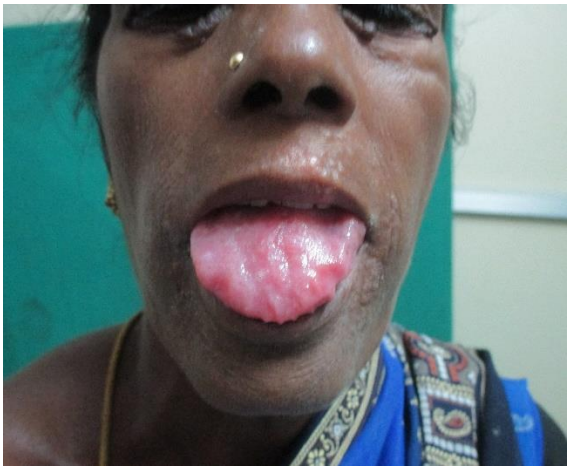

Fig. 1: Macroglossia

Fig. 2: Sclerodactyly

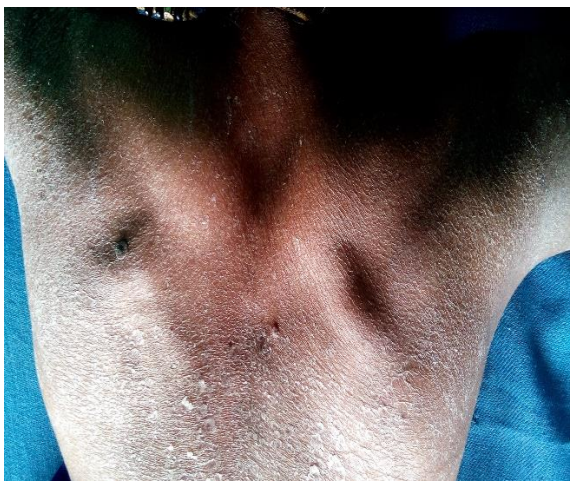

Fig. 3: Shoulder pad sign

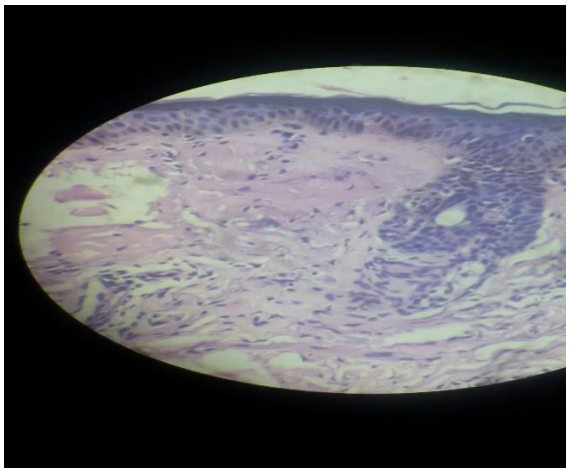

Fig. 4: HPE showing hyaline deposits

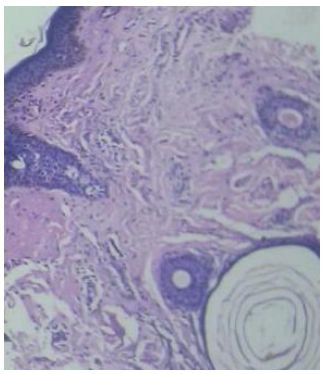

Fig. 5: Perivascular infiltrates

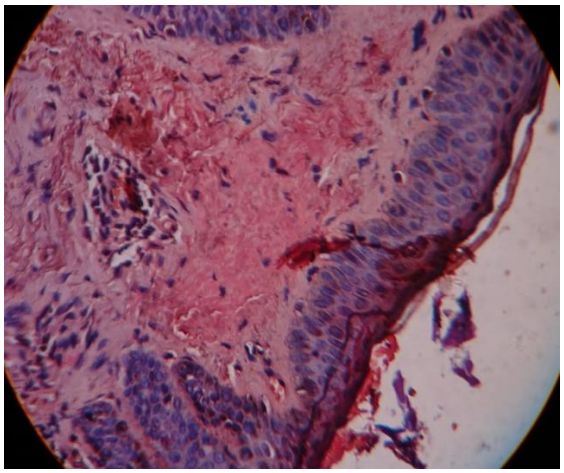

Fig. 6: Congo red positive

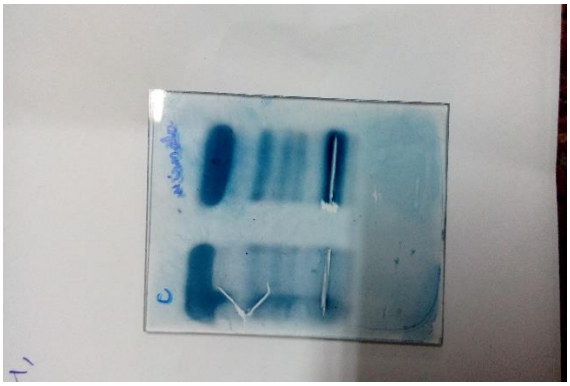

Fig. 7: M spike in serum electrophoresis

Discussion

Primary amyloidosis is a multi-system disease involving renal, cardiovascular, gastrointestinal, musculoskeletal and nervous system. It is characterized by presence of abnormal light chain of lambda class in serum or urine. Idiopathic in 85% cases. Associated with myeloma in 15% cases. Multiple myeloma associated - precursor light chains of immunoglobulin (Bence Jones protein). Mean age of onset – 65 yearswith slight male preponderance.

Cutaneous Features

Deposition in superficial dermis- shiny waxy translucent papules[5]. Common sites - eyelids, retroauricularareas, neck, and axillae. Deposition in deep reticular dermis and subcutis- nodules and tumefactions. Infiltration of blood vessel walls- capillary wall fragility leading to purpuramosly in periorbitalarea[1]. Diffuse infiltration of scalp- enlargement of skin which is thrown into longitudinal folds resembling cutis verticis gyrate. Infiltration of nail matrix by amyloid- ridging, splitting, and brittleness of nail plate. Diffuse infiltration of large area of skin - simulate scleroderma. Amyloid deposition in tongue- macroglossia, permanent tooth indentation on the lateral borders of the tongue[4].

Systemic Involvement:

Hepatomegaly occurs in 50% of patients. Congestive cardiac failure[9], and nephrotic syndrome[8] in 30%. Splenomegaly occurs in about 10%. Carpal tunnel syndrome is seen in up to 25%. Peripheral neuropathy in 10-35%. Malabsorption in 5% cases. Autonomic dysfunction. Muscle weakness, lymphadenopathy, Sjogren's syndrome, amyloid deposition around joints.

Investigations:

Monoclonal protein or light chains detected in 90% of patients by immunofixation of serum or urine. Lambda: kappa- 2-3:1. Skeletal survey reveal lytic bone lesions. Bone marrow aspiration show lymphoplasmacytosis(>25%). EMG shows signs of active denervation. Distal median motor latencies prolonged in patients with carpal tunnel syndrome. Nerve conduction studies- changes of axonal neuropathy with low amplitude or absent SNAPs and low amplititude CMAPS but preserved motor conduction velocities.

Although different types of amyloidosis are associated with distinct clinical pictures, all amyloids have certain common features[10]:

- Amorphous eosinophilic appearance on light microscopy in H and E staining.
- Bright-green fluorescence observed under polarized light after Congo red staining.
- Beta-pleated structure on X-ray crystallography

Diagnostic values of various biopsies

Amyloid demonstrated in normal forearm skin biopsy – 50%. Rectal mucosal biopsies- 80% (gastric> rectal). Abdominal fat aspirates- 88%. Hepatic biopsy- 96%. Jejunal biopsy- 65%. Gingival and tongue biopsies – 19%[9]. Combined muscle and sural nerve biopsy provides confirmation in 90%. BMA- 45%

Prognosis and Treatment:

Prognosis in AL amyloidosis is poor and major causes of death are cardiac and renal failure. Median survival – 40-50 months. 5 year survival of 31.6%. High dose melphalan, prednisolone, colchicine are currently being used. Autologous peripheral stem-cell, tandem transplants and thalidomide and its derivatives are used with success. Borteozomib – proteosome inhibitor used in myeloma associated has given promising results.

Conclusion

This case is reported for its rare presentation. This condition mimicked peripheral neuropathy initially

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