

Primary Systemic Amyloidosis: A Case Report

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ABSTRACT

Primary systemic amyloidosis is a rare entity. We report a case of primary systemic primary amyloidosis, an elderly male presented with generalized weakness since 6 months. Clinical examination revealed typical waxy lesions in the periorbital area with macroglossia. Serum electrophoresis was normal, however, bone marrow examination showed increased plasma cell with a good number of both binucleated and immature plasma cells. Diagnosis was confirmed by skin biopsy using haemotoxylin & eosin staining and congo red staining. Polarised microscopy was not done because of unavailability. We present the myriad manifestations of this uncommon disease entity.

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Introduction

Primary systemic amyloidosis (AL amyloidosis) is a rare disease with an age-adjusted incidence of 5.1 to 12.8 per million person-years.^[1] It is a plasma cell dyscrasia of unknown etiology with production of monoclonal chains.^[2] Immunoglobulin light chains, or fragments of light chains, produced by these plasma cell clones form extracellular amyloid fibrils which are deposited in the organs.^[3] Most frequently organ involved are heart, smooth and skeletal muscle, and other soft tissues, kidney, liver and spleen.^[2] It's the disease of elderly.

Case Report

A 61 years old male patient was presented to skin department with chief complaints of pigmentation around the eyes since 1 year and generalized weakness since 6 month. There were no other systemic complaints or any chronic illnesses in the past.

On examination waxy papules, purpura and ecchymoses were seen in the periorbital region [Figure 1A] with macroglossia [Figure 1B]. Per abdomen examination and Neurological examination was unremarkable

On investigations, he had hemoglobin of 10.4 g/dl with neutrophilic leucocytosis. Urine examination was normal. 24 hrs urine examination negative of albumin and urinary Bence Jones proteins were absent. Liver and kidney function tests were normal. Serum protein electrophoresis was normal (serum albumin-3.60, serum α 1 globulin- 0.23, serum α 2 globulin-0.55, γ globulin-1.50, No M band was seen.

Skin biopsy showed flattened epidermis with eosinophilic material deposition in the papillary dermis [Figure 2A]. Skin appendages appeared normal. Congo red stain was positive [Figure 2B]. Polarised microscopy was not done.

Bone marrow examination showed normoblastic normocellular marrow with plasmacytosis (10%). There were good number of both mature and immature plasma cells. Few of the plasma cells are binucleated [Figure 2C].

No other biopsies or aspirate were performed to demonstrate the amyloid.

Discussion

Amyloid is a pathologic proteinaceous substance deposited in the extracellular space in various tissues and organs of the body.^[5]

In light microscope and H & E stains, amyloid appears as an amorphous, hyaline, eosinophilic, extracellular substance which encroaches on and produces pressure atrophy of adjacent cells.^[5] The Congo red stain result in a brick red staining reaction. It gives green birefringence in polarizing microscopy. These staining characteristics result from the cross beta-pleated sheet conformation of the polypeptide backbone of the amyloid fibrils. These fibrils are ultrastructurally continuous, nonbranching with diameter of 8 to 12 nm and of indeterminate length.^[2, 5]

Systemic amyloidosis can be classified as follows: (1) Primary systemic amyloidosis, usually with no evidence of preceding or coexisting disease, plasma cell dyscrasia or paraproteinemia, amyloid is derived from monoclonal immunoglobulin light chain and is called as AL amyloid; (2) Amyloidosis associated with multiple myeloma; or (3) Secondary systemic amyloidosis with evidence of coexisting previous chronic inflammatory or infectious conditions.^[3,6,7] Amyloid fibrils in secondary systemic amyloidosis are derived from cleavage fragment of the circulating acute phase reactant serum amyloid A protein. This serum amyloid A protein is synthesized in liver during inflammation.^[3, 8]



Figure 1A: Showing waxy papules, purpura and ecchymoses in the periorbital region., (1B): Macroglossia with ecchymosis on hard palate (arrow).

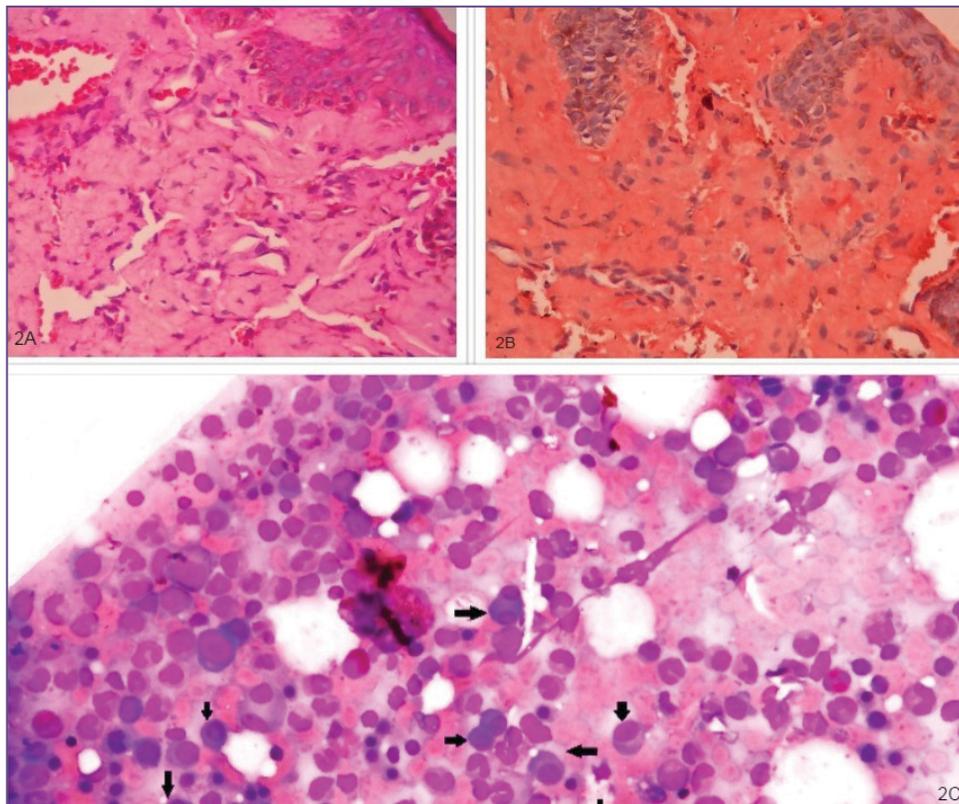


Fig. 2A: Skin biopsy showed flattened epidermis with eosinophilic material deposition in the papillary dermis (400X)., **(2B) :** Congo red showing brick red staining reaction in the dermis.(400X)., **(2C):** Bone marrow aspiration (wright stain) showing increase in plasma cells (arrow).(1000X)

Historically, the distinction between Primary systemic amyloidosis (AL amyloidosis) and Secondary systemic amyloidosis (AA amyloidosis) was made utilizing the latter's sensitivity to permanganate.^[2] Loss of Congo red staining after treatment with potassium permanganate is a property of AA amyloid that can distinguish it from other types.^[2] In our case, congo stain was retained after the potassium permanganate treatment.

Amyloidosis confined to the skin is known as *primary localized cutaneous amyloidosis*. Amyloid in these cases are derived from keratin released from apoptotic keratinocytes.^[2, 3] Different forms of primary localized cutaneous amyloidosis are lichen amyloidosis, macular amyloidosis and nodular amyloidosis.^[2] They all differ in their clinical presentation. **Lichen amyloidosis** is the most common form of primary localized cutaneous amyloidosis, it present as multiple pruritic, red/brown, scaly papule which can coalesce to thickened verrucous surfaces. It usually, occurs in male, aged 50-60 years and most common site are shins, thighs, feet, and forearms.^[2] **Macular amyloidosis** present over upper back in early

adult life, as pruritic macules showing pigmentation with a reticulated pattern.^[2] **Nodular amyloidosis** is the rarest form, it occurs on the trunk, limbs, extremities, face, and genitals as single or multiple nodules.^[2] Whereas **primary systemic amyloidosis** present as petechiae , ecchymoses, waxy papules, nodules or plaques around the eyelids, neck, groin and anogenital area.^[2]

In multiple myeloma associated AL amyloidosis, neoplastic plasma cell clone produces precursor light chains of immunoglobulin (Bence Jones protein) which can be detected in serum or urine electrophoresis.^[3] Systemic amyloidosis is found in 5-15% of multiple myeloma patients but majority of the patient with AL amyloidosis don't have obvious B cell or plasma cell neoplasm i.e. idiopathic, however these patients have underlying B cell dyscrasia in which production of abnormal protein and increased plasma cell population on the bone marrow examination rather than tumour masses is the predominant manifestation.^[2,3]

Amyloid can be deposited in any tissues which lead to distortion of tissue architecture and organomegaly and organ dysfunction.

Mucocutaneous involvement is seen in 30-40% of AL amyloidosis patients.^[7] The most common cutaneous lesions are petechiae and ecchymoses.^[2] They are the result of deposition of amyloid in vessel wall causing capillary wall fragility which can rupture even from minor trauma, it is also called as “pinch purpura”.^[2] Periorbital area is most common site of purpura formation. Senile purpura also is due to capillary fragility but it is rarely seen on face.^[3]

Amyloid deposition in superficial dermis produces shiny waxy papules and commonest sites are eyelids, face, flexor surface and the buccal mucosa. When it is deposited around pilosebaceous unit, it leads to destruction of hair leading to alopecia. Direct infiltration of skin can result in scleroderma.^[4] Infiltration in nail matrix results in whitening of nails, banding, brittleness and onycholysis. Amyloid deposition in tongue leads to macroglossia. Macroglossia is reported in 19% of patients with primary systemic amyloidosis.^[7] Carpel tunnel syndrome is seen 25% cases of primary systemic amyloidosis.^[2,3]

Infiltration to peripheral nerves causes peripheral neuropathy.^[2,3] Cardiac involvement leads to conduction defects, arrhythmias and congestive cardiac failure.^[2,3] The major cause of death in primary systemic amyloidosis is cardiac failure and renal failure.^[3]

The median survival of patient with myeloma associated AL amyloidosis is 5 months to 2.1 years.^[7]

Treatment aim is to reduce the precursor protein by decreasing the proliferation of plasma cells, by cytotoxic agents, immunosuppressants, .Anti neoplastic drugs can be used to slow down the renal impairment by inhibiting polymerization of amyloid fibrils.

Conclusion

Primary systemic amyloidosis is a rare condition with poor prognosis. Its timely recognition has important implication for management and prognostication in order to reduce morbidity and mortality. This case is presented, due to

rarity of the condition and also to increase awareness of its characteristic features and help in diagnosis.

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Competing Interests

None declared

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