



Primary systemic amyloidosis with peripheral and autonomic neuropathy presenting as recurrent presyncope: A case report

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General Note



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ABSTRACT

Amyloidosis may occur as a familial disorder with dominant inheritance or as non-familial variant. Non familial amyloidosis is further divided into primary amyloidosis, which occurs in the absence of other disorders but usually associated with multiple myeloma; and secondary amyloidosis in association with disorders such as chronic infections and rheumatologic diseases. Only primary and familial

amyloidosis is commonly associated with a polyneuropathy. We present a case of a fifty-one year old female who presented with recurrent pre syncopal attacks and neuropathy, and later on diagnosed as primary systemic amyloidosis.

Keywords: amyloidosis, familial, rheumatologic, polyneuropathy, infections

1. INTRODUCTION

Primary systemic amyloidosis is a rare disorder with a prevalence of 0.9 per 100 000 population. According to epidemiological data the median age of development of primary systemic amyloidosis is sixty-five years with a male to female ratio of 2:1, suggesting a male preponderance. This multisystem disorder is characterized by extracellular deposition of fibrillar proteins arranged in a β -pleated sheet conformation throughout organs and tissues. As far as the symptomatology is concerned; the initial symptoms are usually fatigue and weight loss, which is later followed by features of different organ system involvement, chiefly renal disease (48%), cardiac involvement (21%) and peripheral neuropathy (9%), (Kyle et al., 1997; Kyle et al., 1989).

Peripheral neuropathy is a one of the common neurologic manifestations of the systemic amyloidosis. Amyloid neuropathy is usually a form of axonal neuropathy that preferentially involves the small myelinated and unmyelinated fibers. The pathogenesis of the axonal degeneration in amyloid neuropathy is unknown, but; it is mostly due to insoluble protein aggregates (amyloid) deposition within the nerve (Vernino et al., 2007). Sporadic primary amyloidosis is known to cause peripheral neuropathy and autonomic failure (Vernino et al., 2007).

2. CASE REPORT

A fifty- one year old female presented with tingling and weakness of both lower limb along with recurrent presyncope since one year. She was apparently all right 1 year back when initial complaint started with darkening of vision when she suddenly used to acquire upright posture from supine. She also started having tingling sensation in both lower limbs, which gradually increased up to the knees over this 1 year duration. She also noticed weakness in lower limbs initially affection the distal muscles which progressed to involve proximal muscles as she was unable to climb stairs and had difficulty getting up from squatting position. Family history was unremarkable. On asking leading questions she complained of alteration in speech and heavy sensation in tongue. There was no history was diabetic mellitus, hypertension.

General examination

Pulse 110/ min (resting tachycardia), BP on supine right arm 110/70 mm Hg standing after 3 min was 80/50 mmHg (postural hypotension present), JVP was not raised. Pallor, clubbing, icterus, lymphadenopathy was absent. There were no hypopigmented patches on the body. Skin was dry especially on the fingers and toes. Examination of tongue revealed macroglossia. Cutaneous ecchymotic rash was over eye lids and neck (fig 1-a, b, c).



Figure 1 a) magroglossia. b) macroglossia and Cutaneous ecchymoses particularly around the eyes and c) Neck

Central nervous system examination: Higher functions and cranial nerves were normal. Motor system examination revealed distal leg muscle atrophy. Power was 4/5 in proximal and 3/5 in distal muscles of lower extremities. DTR: absent Knee and ankle jerks. In sensory examination vibration sensation was absent at the toes. Temperature and pain sensation was decreased up to the knee bilaterally. Position sense and sense of passive movements were preserved. His gait was wide-based and cautious. On palpation non-tender nerve thickening is present.

Blood investigations

Complete blood count, MCV, kidney functions test, liver function tests, hemoglobin A1C, vitamin B12 level, ANA, ds DNA, c-ANCA, p-ANCA, ESR, serum electrophoresis for M spike, CT thorax and abdomen and thyroid function tests were within normal limits. NCV Study revealed reduced motor responses and absent sensory responses in the lower extremity. 2D Echo was normal.

In view of macroglossia, echymotic rash, Peripheral and autonomic neuropathy with palpable nerves a possibility of Amyloidosis was entertained and tongue biopsy was done.

Tongue biopsy

H & E stained slide 10 X view showing myocytes with intervening stroma showing homogenous extracellular hyaline material compressing the surrounding myocytes (Fig 2a): 40 x view slide with special stain Congo red showing amyloid deposition between the myocytes (Fig 2b).

He was treated with Fludrocortisone and Midodrine for postural hypotension, and gabapentin for the sensory symptoms.

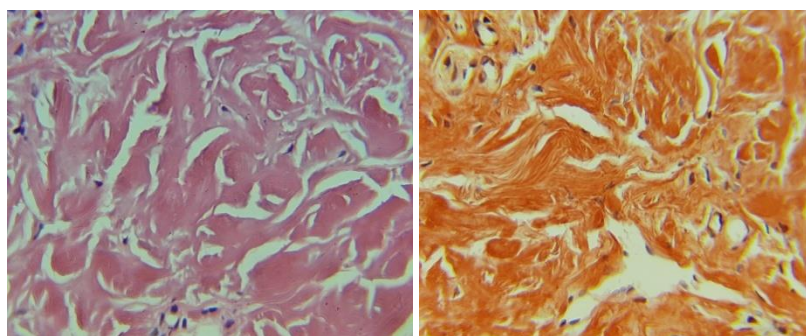


Figure 2 a) H & E stained slide 10 X view showing myocytes with intervening stroma showing homogenous extracellular hyaline material compressing the surrounding myocytes. b) 40 x view slide with special stain Congo red showing amyloid deposition between the myocytes.

3. DISCUSSION

Amyloid neuropathy is characterized by deposition of insoluble protein aggregates (amyloid) in nerves. Sporadic primary systemic amyloidosis and familial amyloidosis are invariably associated with peripheral neuropathy and autonomic failure (Xu et al., 2015). Familial amyloid neuropathy occurs due to mutations of three proteins: TTR (transthyretin), apolipoprotein A1, and gelsolin (Xu et al., 2015). As far as primary systemic amyloidosis is concerned; peripheral neuropathy occurs in 17% of cases with AL amyloidosis. Most common variants are sensorimotor polyneuropathy, which is characterized by symptoms of neuropathic pain, numbness, and in advanced cases weakness in distal extremities. The most common pattern of neuropathy is sensory-motor axonal polyneuropathy and carpal tunnel syndrome. Symptoms typically begin with painful paresthesia in the feet resembling small fibre neuropathy. Later as the disease progresses large fibers are also affected leading to areflexia, motor weakness and loss of proprioception and most cases (65%) would develop autonomic failure (Vernino et al., 2007).

Once autonomic failure sets in then the symptoms and signs are; blurred vision or problems with glare resulting from impaired parasympathetic pupillary activity, dry eyes or dry mouth resulting from impaired cholinergic sympathetic innervation, abnormal sudomotor features (gustatory sweating and heat intolerance), abnormal vasomotor features (cold hands and feet with cyanotic hue because of peripheral adrenergic sympathetic dysfunction), orthostatic intolerance leading to light-headedness, dizziness which can be demonstrated by postural fall of blood pressure on standing. Gastrointestinal symptoms are of nausea, vomiting, bloating, early satiety, abdominal colic, alternating diarrhea and constipation). Genitourinary symptoms may manifest as urinary frequency and urgency, incontinence, and finally sexual dysfunction may manifest in form of difficulty with erection and ejaculation (Low et al., 1997).

Patients may present with having either peripheral neuropathy or isolated small-fiber neuropathy. Small-fiber neuropathy presents with symptoms of prominent pain and burning in the feet and/or hands, with distal loss of pain and temperature sensation and relative preservation of distal vibration sensation and reflexes on examination, and; large fibre neuropathy presents with loss of proprioceptive responses (Stewart et al., 1992). Other causes of polyneuropathy like alcohol abuse, drugs, toxins, chronic renal failure, liver failure, hypothyroidism, multiple myeloma should be ruled out. Occurrence of an M monoclonal protein in the blood or urine is the most common association seen in around 89% of cases of primary amyloidosis, often missed by routine serum and urinary electrophoresis. In our case electrophoresis was negative. Pathological confirmation of amyloid deposition is the gold standard and we confirmed it in tongue biopsy.

4. CONCLUSION

Primary systemic amyloidosis is a multisystem disorder characterized by extracellular deposition of fibrillar proteins in organs and tissues of the body. The symptoms usually start with fatigue and weight loss. Cardiac involvement presents with features of restrictive cardiomyopathy with heart failure, renal involvement presents with renal failure. The most common neurodeficit is peripheral neuropathy. Amyloid neuropathy should be considered in patients presenting with marked postural hypotension along with unexplained systemic symptoms.

Patient's Consent

Proper informed consent was taken from the patient before writing this case report.

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Conflicts of Interest: The authors declare no conflict of interest.

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