Autonomic Failure in Primary Amyloidosis

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Abstract
Amyloidosis is an uncommon plasma cell dyscrasia affecting Multisystem, characterized by deposition of amyloid proteins in extracellular spaces and the tissues. Reported incidence of amyloidosis is 8 cases per million per year. Deposition of amyloid fibrils occurs in peripheral nerves in 20% of the cases in Primary Amyloidosis. Though, polyneuropathy is one of the presenting manifestations in cases of Primary Amyloidosis, pure autonomic failure without involving peripheral nerves is not a documented entity. Here, we present a case of Primary Amyloidosis presenting as Pure Autonomic Failure (Dysautonomia).

INTRODUCTION
Amyloidosis is a rare multisystem disorder, characterized by extracellular deposition of abnormal proteins. Six types of amyloidosis have been described in literature – primary, secondary, haemodialysis-related, hereditary, senile and localized. Primary amyloidosis (AL) is associated with monoclonal light chains in serum/urine with 15% of patients having multiple myeloma. Secondary amyloidosis (AA) is associated with inflammatory, infectious, and neoplastic causes. As the symptoms like fatigue, shortness of breath, edema, paraesthesias and weight loss, remain vague most of the times, the diagnosis is difficult to reach. However, patients may present as nephrotic range proteinuria with or without renal insufficiency, cardiomyopathy, hepatomegaly, symptomatic peripheral neuropathy, and autonomic failure. Autonomic failure is always a part of symmetric peripheral neuropathy in reported cases of primary amyloidosis. Here, we report a case of Pure Autonomic Failure without involving peripheral nerves in case of Primary Amyloidosis.

CASE REPORT
Mr. ABS, 50 years old previously healthy male presented with history of giddiness for 1 and ½ years, especially while getting up from lying down position and when beginning to start walking. It was associated with feeling of blackout sensation which used to get relieved on sitting down. The giddiness progressively increased from initial 2-4 episodes per week to present 2-4 episodes per day. There is no history of increase in giddiness on movement of neck. There is no history of rotation of surroundings, diplopia, tinnitus or ear discharge.

There is no history of headache, weakness in limbs, dysarthria, dysphagia, change of speech, paraesthesias or dysaesthesias, imbalance of gait, falls, tendency to fall backwards, tremors or seizures. There is no history of chest pain or palpitations. There is no history of bladder involvement, hyper- or hypohydrosis. No history of drug intake or toxins could be elicited. No history suggestive of abnormal pigmentation was noted. Patient denied history of Diabetes Mellitus and alcoholism.

Patient gave history of impotency for the same duration – inability to get erection and ejaculation, no early morning tumulescence and loss of libido associated with increased frequency of stools.

There are no family members suffering from similar symptoms.

Examination revealed severe orthostatic hypotension (BP supine – 100/70 mm Hg and BP standing – 62/50 mm Hg). His general and systemic examination was unremarkable. Central nervous system (CNS) examination didn’t reveal any involvement of pupils, cerebellar system or peripheral nerves. All sensations were intact without any thickening of peripheral nerves. ENT examination was normal. Patient was evaluated in detail for cardiac autonomic neuropathy as follows:

Sympathetic:
1. Postural hypotension – BP supine – 100/70 mm Hg and BP standing 62/50 mm Hg (abnormal)
2. Sustained hand grip response – DBP 60 mm Hg initially and DBP 64 mm Hg at the end of the test (abnormal)

Parasympathetic:
3. Valsalva manoeuvre : RR/rr ratio – 1.0 (abnormal)
4. Heart rate response to standing : 30/15 RR ratio – 1.065 (abnormal)
5. Heart rate response to deep breathing – RR max – RR

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min – 1.0 (abnormal)

He underwent Head Tilt Test – positive with reproduction of symptoms – heart rate accelerated to 102 bpm and BP dropped to 60mm Hg systolic.

His hematological and biochemical reports were normal except severe dyslipidaemia (Total Cholesterol – 341 mg%, Triglycerides – 247 mg%, LDL Cholesterol – 262.3 mg% and HDL Cholesterol – 29.3 mg%). His urine examination revealed 3+ proteinuria with normal microscopy and 24 hours urinary proteins were 5.0 Gms. His ECG, 2-D Echo, and Holter monitoring were normal. His MR Brain and 4-vessel MR Angio were normal. His NCV/EMG studies were normal. His serum cortisol, aldosterone and thyroid hormones were normal. Serum immunoelectrophoresis report revealed light chain gammopathy (IgA lambda isotype).

Patient was subjected for renal biopsy which revealed mesangial deposits, positive for Congo Red stain with green fluorescence on UV light, confirming the diagnosis of Primary Amyloidosis (Light Chain – AL).

**DISCUSSION**

A wide variety of medical conditions can present as autonomic disorders – Primary conditions like Shy-Drager syndrome, the Riley-Day syndrome, the Bradbury-Eggleston syndrome or Secondary due to Diabetes, Alcoholism, Nutritional deficiency, Toxins, drugs, paraneoplastic, amyloidosis and others. Light-chain (AL) amyloidosis is the most common form of systemic amyloidosis. Peripheral neuropathy and autonomic neuropathy is one of the presenting manifestations of Primary Amyloidosis. Autonomic neuropathies are inherited or acquired (as in amyloidosis) in which the autonomic nerve fibers are selectively or disproportionately affected. Several familial cases of amyloidotic polyneuropathy (FAP) have been reported in literature. A case has also been reported with primary amyloidosis with progressive hypotension. However, intensive search has not revealed a single case of Autonomic Failure without involvement of peripheral nerves due to primary amyloidosis. Our case emphasizes the need of good clinical history and examination with full investigational work up which revealed autonomic neuropathy as the cause of orthostatic hypotension. His neurological work up ruled other causes of primary autonomic failure and his renal profile confirmed the diagnosis of Primary Amyloidosis and the likely cause of his pure autonomic failure. Chemotherapy with Thalidomide is contemplated in the case.

**CONCLUSION**

Primary amyloidosis is a rare disease. Though peripheral neuropathy with autonomic neuropathy is common manifestation of primary amyloidosis, pure autonomic failure in a case of primary amyloidosis is an unreported entity.

**REFERENCES**