A Dilemma Solved

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Abstract:

A 63 year old female with severe symptomatic postural hypotension was treated unsuccessfully and no underlying cause was found for three years until she was noted to have hypoalbuminaemia and proteinuria. A renal biopsy led to the diagnosis of amyloidosis. Despite being an established cause for autonomic neuropathy, amyloidosis was not suspected early enough. Although a diagnosis was reached and treatment started the patient died as a complication of chemotherapy.

Case history:

A 63 year old previously fit and well female presented with recurrent episodes of collapses. These usually followed dizziness especially when standing up and lasted up to two minutes without any residual symptoms. The only significant clinical finding was postural hypotension with a blood pressure drop of up to 60mmHg.

Attempts were made to find out the cause of postural hypotension. Short synacthen test and 24 hour urinary catecholamines were within normal limits. A long ECG trace did not show any variations in heart rate with carotid message, standing or with the Valsalva manoeuvre - a working diagnosis of primary autonomic failure was therefore made.

Her postural symptoms did not show a satisfactory response despite a variety of treatments including TED stockings, fludrocortisone, tricyclic anti-depressants, caffeine citrate, midodrine and indomethacin with water loading.

The underlying pathology was suspected when she was noticed to have a serum albumin of 20g/l. Although clinically she had no peripheral swelling, 24hour urinary protein was 4.36g/l. Renal biopsy showed amyloidosis.

In the absence of any chronic illness a diagnosis of Primary Systemic Amyloidosis – now called AL amyloidosis - was made.

The patient was referred to the National Amyloidosis Centre in London where further investigations were carried out:

Whole body serum amyloid-P protein (SAP) scintigraphy showed moderate total body amyloid load with amyloid deposits in Liver, spleen and kidneys. MRI showed structurally normal intra-abdominal organs. Echocardiography showed thickened left ventricular walls but no restrictive inflow pattern. Bone marrow aspirate was morphologically normal with no evidence of amyloid deposits. A small population of lambda light chain secreting neoplastic plasma cells was detected by flow cytometry.

Chemotherapy with melphalan and dexamethasone (Meldex regimen) was started. Soon after commencing chemotherapy she developed neutropenia and died of neutropenic sepsis.

Discussion:

Our patient had systemic AL amyloidosis resulting in nephrotic range proteinuria and significant autonomic neuropathy causing postural hypotension.

AL amyloidosis is typically viewed as a rare disease and not commonly suspected. Incidence is estimated to be 5 to 12 people per million per year, although autopsy studies suggest that the incidence might be higher[1]. The disease is often difficult to recognize because of its broad range of manifestations and what often are vague symptoms. The clinical syndromes at presentation include nephrotic-range proteinuria with or without renal dysfunction, hepatomegaly, congestive cardiac failure and autonomic or sensory neuropathy[2]. It is usually

a very serious condition, which if left untreated is progressive and typically fatal within 5 years. Treatment relies on chemotherapy aimed at the underlying plasma cell clone. If the supply of amyloid fibril precursor proteins (in her case lambda light chains) be reduced this can alter the equilibrium between amyloid deposition and removal in favour of the latter with the potential for stabilization and in time regression of existing amyloid deposits[3]. The combination of melphalan and dexamethasone in one series produced haematological response in 67% in a median time of 4.5 months, with complete remission in 33% and functional improvement of the involved organs in 48%. Treatment-related mortality is 4-7% [4].

Conclusion:

- Amyloidosis should be considered in the differential diagnosis in the disease of virtually any organ.
- Treatment strategies that have evolved during the past decade are prolonging survival and preserving organ function in patients with this disease.
- Treatments do not always prove to be in the best interest of the patients.

References:

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