Primary Idiopathic Amyloidosis Misdiagnosed: A case report in North India (Kashmir)

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Abstract

Introduction: Amyloidosis is an infiltrative systemic disorder with an unknown etiology. There **i**s an extracellular deposition of abnormal amyloid protein in various tissues of the body, hence variant clinical presentation. **Case presentation:** Herein a case of primary idiopathic amyloidosis initially mistaken as para proteinemia was investigated without taking clinical features into consideration. This case illustrates that high index of suspicion is required for proper diagnosis and management of this rare disease. **Conclusion:** Owing to the rarity of these cases in the clinics and the lack of suspicion on the part of physicians, many cases of amyloidosis leading to sudden deaths remain undiagnosed.

Key words: Primary idiopathic amyloidosis, paraproteinemia, restrictive cardiomyopathy

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Introduction

Amyloidosis is a heterogeneous group of systemic disorders, which result due to extra cellular deposition of an insoluble, amorphous, eosinophilic, substance known as amyloid [(1,2)]. Twenty-six different amyloid precursor proteins have been identified in various human amyloidosis and the disorders have been classified according to the nature of the precursor. Although it is usually seen in a systemic form, 10-20% of cases can be localized [(3)]. Primary systemic amyloidosis (AL) involves the deposition of insoluble monoclonal immunoglobulin (Ig) light (L) chains or L-chain fragments in various tissues, including smooth and striated muscles, connective tissues, blood vessel walls, and peripheral nerves [(4)]. The disease associated with the AA amyloid is called secondary amyloidosis [(5)]. In both primary and secondary amyloidosis, the most commonly involved organ system is

the gastrointestinal system, with the colon being the most frequently involved organ [6]. Case series have described AL amyloidosis as being more prevalent in males and as occurring at a younger age than transthyretin-related amyloidosis [7, 8].

The major organs commonly involved in AL amyloidosis are kidney (usually presenting as heavy proteinuria), heart, nerve (peripheral and autonomic neuropathy), gastrointestinal (weight loss, disturbance of bowel movements), and liver (elevated alkaline phosphatase with normal transaminase, rarely associated with jaundice) [9]. The pathologic examination of amyloid infiltrated tissues has generally failed to reveal any of the conventional hallmarks of inflammation. In some experimental models of AA, however, there appears to be considerable mononuclear activation. Some have interpreted this as reflecting an attempt to clear the deposits [10]. Here we report a case of the primary idiopathic amyloidosis misdiagnosed initially as paraproteinemia.

Case presentation

A 43year old young male from remote tribal area of Kashmir province was referred to our outpatient department with chief complaints of fatigue and breathlessness on exertion for last 9 months. He had previously got admitted in hospital with the provisional diagnosis of congested heart failure with underlying restrictive cardiomyopathy. Since his arrival at our tertiary hospital, immunocyte dyscrasias was made with impression of heavy chain disease. There was no family history of amyloidosis. On physical examination clinical findings were thin built, pallor, macroglossia (Figure1), hepatospleenomegaly (Figure 2) and abnormality in sensory sensation.

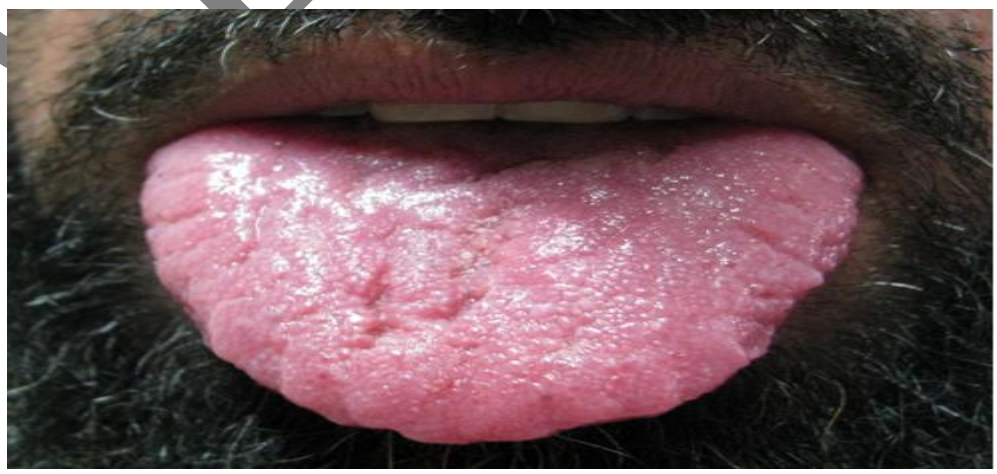

Figure 1: Macroglossia in a patient with Primary Idiopathic Amyloidosis.

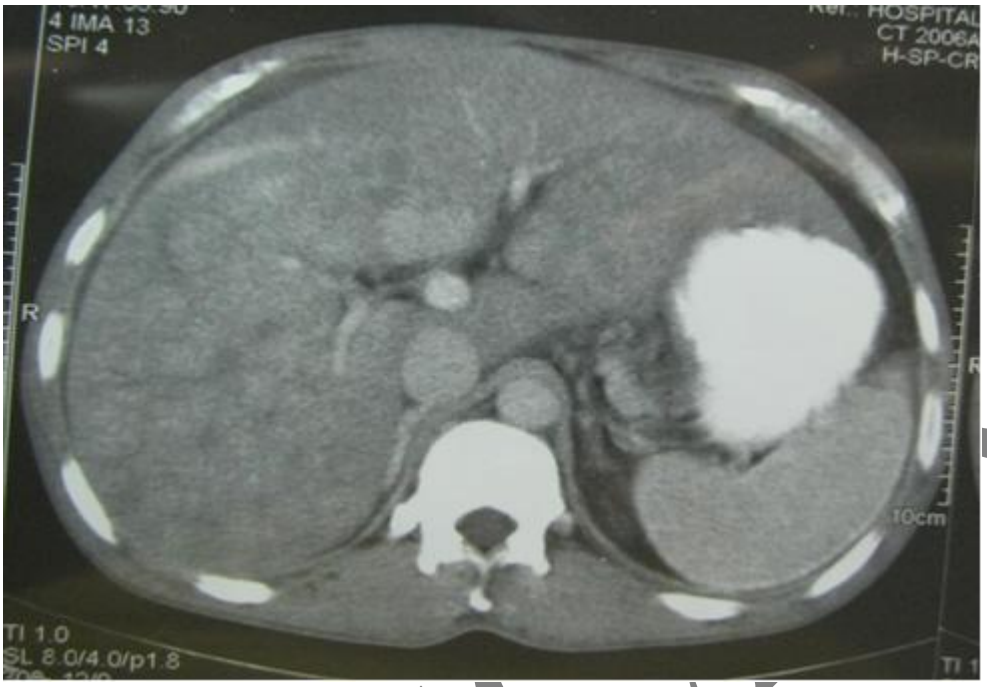

Figure 2: CT abdomen of patient depicting hepatospleenomegaly.

Laboratory findings were normocytic normochromic anemia, isolated high ALP, ECG showing low voltage QRS complex. NCV showed bilateral radial and sural nerves sensory neuropathy. On imaging, echocardiography showed restrictive physiology, CT abdomen depicted organomegaly (Figure 2), cardiac MRI showed thickened septa and ventricle walls with delayed gadolinium contrast filling of sub endocardium (Figure 3).

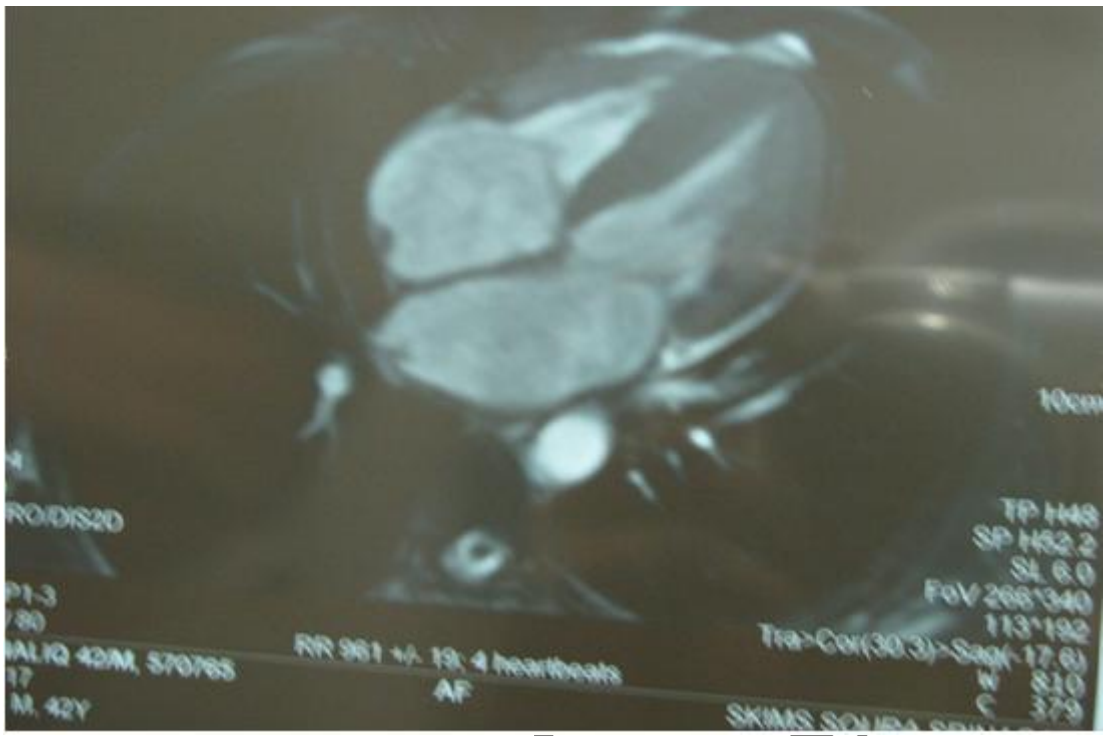

Figure 3: Cardiac MRI showing thickened septa and ventricle walls.

Biopsy of subcutaneous abdomen fat was positive for congo red stain, bone marrow showed <5% of plasma cell with no specific staining to kappa & lambda light chains. Immunophoretic fixation was done for urine and serum, but no immunoglobulin light chain and heavy chain fragments were detected.

Rectal biopsy was consistent with amyloidosis which showed scattered foamy histiocytes with eosinophilic hyaline material (Figure 4). Immunohistochemistry revealed no specific staining of amyloid protein viz; Amyloid A, Transthyretin. Moreover, blood was sent for detection of ATTR, Apo AI, Apo AII, Fibrinogen, Lysozyme and Gelsolin mutation, all of these were found normal.

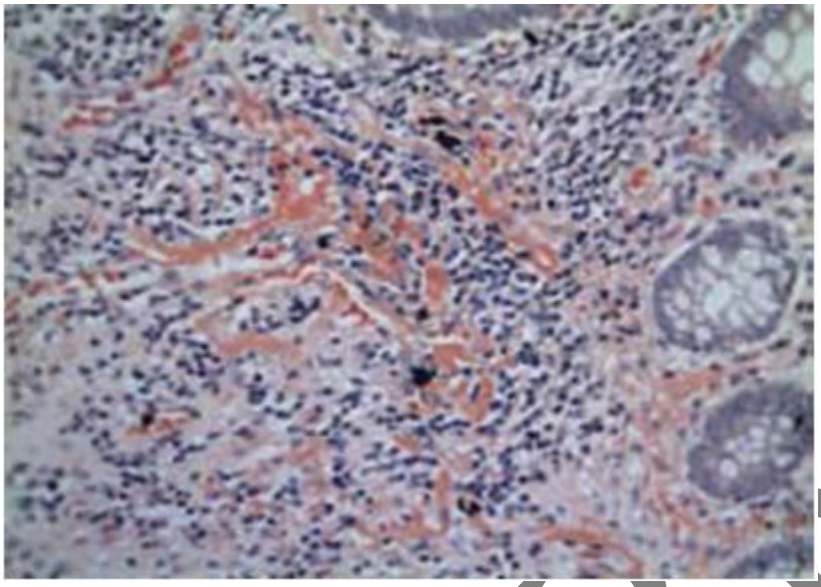

Figure 4: Rectal mucosal biopsy: Scattered foamy histiocytes with patchy pale eosinophilic hyaline material seen in rectal mucosa and Congo red stain for amyloid is positive.

Patient was finally diagnosed as a case of primary idiopathic amyloidosis with systemic involvement. Patient was discharged on colchicine and diuretics. Unfortunately, after a period of three months of his follow up he developed ventricular tachycardia and died of cardiac arrest.

Discussion

Progressive deposition of amyloid compresses and replaces normal tissue, and this leads to organ dysfunction and a wide variety of clinical syndromes, some of which have severe pathophysiological consequences [(11)]. Both the clinical and imaging presentations of amyloidosis are usually varied and non-specific, which may cause a delay in diagnosis and appropriate treatment changes. A biopsy is nearly always required for a proper diagnosis [(12)]. In both primary and secondary amyloidosis, the most commonly involved organ system is the gastrointestinal system, with the colon being the most frequently involved organ (6). Cardiac MRI showed thickened septa and ventricle walls with delayed gadolinium contrast filling of sub endocardium which is typical of cardiac amyloidosis. Serum and urine immunofixation will reveal an abnormal monoclonal band in close to 90% of cases [(9)] but didn't reveal any band in our case. Bone marrow biopsy and immunofixation staining for light chains (lambda & kappa)

and heavy chain fragments were absent, hence ruling out the possibility of light & heavy chain disease (AL & AH). In our case as there was no familial history of amyloidosis and no history of chronic diseases such as tuberculosis, osteomyelitis, rheumatoid arthritis and inflammatory bowel disease thereby ruling out the possibility of ATTR & AA which was also substantiated by the negative immunohistochemical staining of rectal biopsy. Since the mutation profile of the other amyloid variants were found normal, our case was confirmed to be idiopathic. Unfortunately, the patient developed ventricular tachycardia and died of cardiac arrest before the correct diagnosis was made. Thus, early diagnosis is critical because patients with advanced disease are usually too ill for intensive chemotherapy.

Conclusion

Owing to the rarity of these cases in the clinics and the lack of suspicion on the part of physicians, many cases of amyloidosis leading to sudden deaths remain undiagnosed. Thus, the clinician awareness of the various forms of amyloidosis and the potential for lab error is a key to ensuring an accurate diagnosis and timely intervention. This carries significant implication for treatment and potential impact for healthy wellbeing of patients.

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