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Case Report

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Patient with primary systemic amyloidosis presenting with intractable diarrhoea

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ABSTRACT

Introduction:

Primary systemic amyloidosis is the most common form of systemic amyloidosis. Clinical presentation commonly involves organs such as the kidney and heart. We report on a patient with systemic amyloidosis presenting as intractable diarrhoea. Numerous investigations had to be done before the diagnosis could be made highlighting the challenge in making a diagnosis due to the slow progression of the disease. This report is to increase awareness among physicians of this diagnosis and to emphasise the importance of identifying patients quickly.

Case Presentation:

A 63 year old male was admitted with a six months history of intractable, watery diarrhoea, anorexia and progressive renal failure. He had been investigated for proteinuria and deranged renal function prior to admission but no therapy was suggested and the diagnosis at that time was inconclusive. Extensive laboratory and radiological investigations were done. The diagnosis of systemic amyloidosis was made on serum free light chains which showed excess lambda chains and a terminal iliac and colonic biopsy which revealed eosinophilic thickening of the blood vessels with positive Congo red stain. Unfortunately the patient died prior to definitive management for the amyloidosis.

Conclusion:

This case emphasises the importance of early recognition of systemic amyloidosis so that management can be instituted.

INTRODUCTION

Primary systemic amyloidosis (AL) is a plasma cell dyscrasia characterized by fibrillar aggregates of monoclonal immunoglobulin kappa or lambda light chain type deposited extracellularly in vital organs [1]. It is the most common type of systemic amyloidosis [2].

Patients with amyloidosis usually present with a small plasma cell clone with evidence of dysfunction of one or more involved organs [3]. Typical AL amyloidosis syndromes include renal involvement (approximately 70% of patients) with nephrotic range proteinuria or renal failure in approximately 50%; cardiomyopathy in approximately 60% with thick walled heart, pericardial and pleural effusions [4]. However 30-60% of patients with amyloid also have gastrointestinal symptoms [5].

Patients with AL amyloidosis often have little intact monoclonal immunoglobulin; approximately 40% of patients have light chains only and about half the patients are missed if only serum protein electrophoresis is used for screening. Immunofixation electrophoresis to identify kappa or lambda light chains is more sensitive, and the combination of serum and urine immunofixation electrophoresis with serum free light chain (FLC) assay approaches 100% sensitivity for identifying a monoclonal protein in patients with AL amyloidosis [6]. It is also important to make every effort to characterise the immunoglobulin deposit.

AL amyloidosis should be suspected in any patient with nondiabetic nephrotic syndrome, or even non-ischemic cardiomyopathy with an echocardiogram showing concentric hypertrophy. Any patient who presents with any one of these syndromes should undergo a biopsy to detect amyloid deposits and a screening for monoclonal immunoglobulin light chains. If a monoclonal protein is present, a bone marrow examination should be performed to exclude the presence of multiple myeloma [4].

The major determinant of outcome in amyloidosis is the extent of cardiac involvement. Echocardiographic features of cardiac amyloidosis such as wall thickening, diastolic relaxation abnormalities, and reduced systolic function are associated with a poor outcome [7].

We report on a patient with intractable diarrhoea, a result of underlying AL amyloidosis in the gastro intestinal tract.

CASE REPORT

History

A 63 year old male was admitted to the Aga Khan University Hospital in May, 2011 with a six months history of intractable, watery, non mucoid and non bloody diarrhoea, anorexia and renal failure, secondary to chronic interstitial nephritis.

Progressively, the patient developed lethargy with effort intolerance (New York Heart Association [NYHA] Class 3) with associated dyspnoea on exertion, lower limb oedema and oliguria. There was no orthopnoea, paroxysmal nocturnal dyspnoea, angina or chronic respiratory symptomatology. He also reported oliguria but no dysuria or hematuria.

He had been investigated for proteinuria and deranged renal function prior to admission but no therapy was suggested and the diagnosis at that time was inconclusive.

Past Medical History

The patient had a history of ischaemic heart disease. He was not a known hypertensive or diabetic and was not on any long term medications.

Examination

The patient was underweight with mild pallor and bilateral pitting lower limb oedema. There was no lymphadenopathy or organomegaly. He had an elevated jugular venous pressure but the heart sounds were normal; there were no murmurs or pericardial effusion noted. The remaining systemic examination was within normal limits.

Laboratory Investigations

The patient underwent an extensive laboratory and radiological work-up. Pertinent investigation findings are shown in table 1 below.

Table 1: Pertinent Laboratory and Radiology Investigations

Analyte	Patient result	Reference range
BIOCHEMISTRY		
Serum protein	51.1 g/l	60 – 85g/l
Serum albumin	32.9 g/L	35 – 55g/l
Serum Creatinine	189.6 µmol/L	72 – 127 µmol/L
Blood urea nitrogen	11.4 mmol/L	2.9 – 8.2 mmol/L
Vitamin D	<4ng/mL	11.1 – 41.9 ng/mL
24 hour urinary protein	900 mg/24 hours	
Serum and urine immunofixation electrophoresis	No monoclonal protein present or kapp/lambda free light chains	
Serum Free Light chain Assay	Lambda – 387 mg/L Kappa – 29.8 mg/L Kappa : Lambda quotient - 0.08	5.71 – 26.3 mg/L 3.3 – 19.4 Mg/L 0.46 - 4
Troponin I	<0.05ng/mL	<0.5 ng/mL
HAEMATOLOGY		
Bone Marrow Aspirate	No features suggestive of a plasma cell disorder A bone marrow biopsy was not done	
MICROBIOLOGY		
Clostridium difficile antigen	Negative	
HISTOLOGY		
Terminal ileum and colonic biopsy	Eosinophilic thickening of blood vessels with positive congo red stain; consistent with amyloidosis	
Renal biopsy	Global glomerulosclerosis and patchy to diffuse chronic interstitial nephritis. No features to suggest immune-complex mediated glomerulopathy or diabetic nephropathy or amyloid deposition and no monoclonal immunoglobulin deposition disease.	
RADIOLOGY		
Barium Meal	Features consistent with malabsorption syndrome.	
ECG	ECG showed a sinus rhythm with no acute ST-T wave changes and no evidence of atrial/ventricular hypertrophy	
2D Echocardiogram	Concentric left ventricular hypertrophy with preserved left ventricular (LV) ejection fraction. LV filling pattern was consistent with restrictive LV disease. Mild to moderate mitral regurgitation, mild aortic valve sclerosis without stenosis and a nonsignificant aortic regurgitation. Right ventricular systolic pressures raised at 58.8mm Hg. This was consistent with severe LV diastolic dysfunction and mild pulmonary hypertension.	

Based on the above findings a diagnosis of primary amyloidosis was made. It is important that a bone marrow biopsy is performed for the work up of patients with amyloidosis as an aspirate alone may be insufficient to determine the plasma cell burden (our patient had only had a bone marrow aspirate).

Management

The patient was put on supportive management for his diarrhoea with octreotide. Haemodilaysis was required for the deteriorating renal function. Melphalan and Dexamathasone were considered for the amyloidosis but unfortunately the patient passed away before

they could be instituted.

This patient had been ill for six months prior to the diagnosis of amyloidosis. Although a post mortem examination was not carried out it was thought that he may have succumbed to coexistant comorbid condtions.

DISCUSSION

We describe a case of primary amyloidosis (AL) with deposition of amyloid in the terminal ileum and colon resulting in moderate malabsorption and odema of the legs.

Although in primary amyloidosis the involvement of the gastrointestinal tract is common, the clinical course and the prognosis are mainly determined by the extent of cardiac and renal amyloid deposition [8, 9].

Previous reports have shown that prominent presenting complaints in patients with gastrointestinal amyloidosis are weight loss, malabsorption, diarrhoea, steatorrhoea and hypoalbuminaemia [10]. Our patient had similar symptoms.

Diarrhea in patients with amyloidosis is often severe. It is thought to be due to a combination of autonomic neuropathy, amyloid infiltration of the submucosa resulting in malabsorption, and bacterial overgrowth [11]. Recent reports of the efficacy of somatostatin analogue in cases of refractory diarrhea suggest that a secretory mechanism may be involved [12].

Deposition of amyloid is usually greatest in the small intestine [13]. Amyloid deposition in our case was predominantly in the terminal ileum and colon. In the colon the presentation is similar to inflammatory bowel disease.

As highlighted in this case the diagnosis is usually difficult to establish primarily due to the slow progression of the disease and illustrates that awareness of diagnosis is necessary in order to identify patients quickly [14]. Numerous laboratory and radiological investigations were carried out before a definitive diagnosis was made.

Primary amyloidosis is treated with melphalan and dexamethasone, similar to the treatment of multiple myeloma. Newer agents such as bortezomib have also proven to be useful and research has shown that stem cell transplantation can offer a cure. With this therapy, median survival is prolonged [10, 15].

Our patient passed away within a few days after the diagnosis and as a result the patient was not put on any appropriate treatment.

CONCLUSION

Early diagnosis is essential for the optimal effect of treatment on patient survival and quality of life. In the future, it is hoped that clinicians will diagnose early, treat promptly, and halt the progress of an almost uniformly fatal disease [16].

CONSENT

A written informed consent was obtained from the patient's next of kin for publication of this case report.

COMPETING INTERESTS

None

AUTHORS CONTRIBUTIONS

HS, AT, MS and FJ were involved in the management of this patient. MS and RK were involved in assisting with the laboratory diagnosis. RK, FJ and MS were involved in writing of the manuscript.

All Authors read and approved the final manuscript.

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