Protein-losing enteropathy due to gastro-intestinal amyloidosis

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Summary

A case is described of a patient who presented with severe oedema due to protein-losing enteropathy caused by amyloidosis secondary to bronchiectasis.

Introduction

Impairment of gastro-intestinal function rarely causes the predominant symptom in generalized amyloidosis and reports of protein-losing enteropathy (PLE) are particularly uncommon.

Case report

A 57-year-old male presented with a 10-day history of oedema rising to the level of the xiphisternum. Examination also revealed coarse crepitations over the left upper lung field and finger clubbing. Ten years earlier he had been treated with standard chemotherapy for pulmonary tuberculosis and subsequently developed severe bronchiectasis with persistently purulent sputum.

Investigations showed a serum total protein of 54 g/l; albumin 13 g/l; with a normal electrophoretic pattern. The ESR was persistently elevated to 120 mm (Westergren) in the first hour. Haemoglobin 11.6 g/dl, MCV 99 fl; MCHC 31.2 g/dl; with a normal white cell count. Plasma urea and electrolytes were normal. Chest X-ray showed widespread cystic changes in the left lung with fibrosis affecting the right upper lobe. Urine and sputum cultures were negative for acid and alcohol-fast bacilli.

He had a normal dietary protein intake of 110 g/day. There was no evidence of malabsorption as the serum calcium, phosphate, alkaline phosphatase, folic acid and vitamin B₁₂ levels, glucose tolerance test, 5-day faecal fat excretion and D-xylose absorption were all normal. Gastroscopy and barium meal with follow-through were normal as were his liver function tests, liver scan and hepatic angiogram.

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There was no proteinuria and two 24-hr urinary protein collections were normal at <0.03 g/day.

⁵¹Cr-labelled albumin studies (normal ranges in parentheses) demonstrated a mean daily clearance of albumin into the gastro-intestinal tract equivalent to that of 63 ml of plasma (5-25 ml/day) or 2.4% of the plasma volume (<1%). Barium enema, ascending lymphangiogram, sigmoidoscopy, right heart catheterization and inferior vena-cavogram with hepatic venogram were normal. Laparoscopy and finally laparotomy revealed only mild hepatomegaly. Biopsies of the liver, stomach, jejunum and ileum were reported as normal.

His oedema cleared on treatment with diuretics and salt-poor albumin. He was maintained on a low salt/high protein diet and his serum albumin remained constant at 22 g/l. Six months after discharge he defaulted and 10 months later was readmitted with a 2-week history of increasing oedema. He had proteinuria, a blood urea of 33.6 mmol/l and he died in renal failure.

At post-mortem the main macroscopic finding was severe bronchiectasis. However, microscopy revealed amyloid infiltration of the walls of small blood vessels throughout the body including those of the small bowel and renal glomeruli. This had produced no gross abnormality apart from some pallor of the kidneys and thyroid which were the only organs to have amyloid deposited outside the walls of the blood vessels. The small bowel showed normal lymphatics and villous architecture and amyloid infiltration (Fig. 1). The original liver and jejunal biopsies were re-stained with Congo Red and traces of amyloid were found in the same pattern as at post-mortem.

Discussion

Hypoproteinaemia in amyloidosis is most likely to result from proteinuria or, less frequently, from hepatic involvement or from malabsorption. Initial investigations in the patient showed normal renal

FIG. 1. Post-mortem section of small bowel. Blood vessel walls in submucosa (thick arrows) and lamina propria (thin arrows) are thickened by material which showed the typical green bi-refringence of amyloid when viewed with polarized light. Congo Red $\times 160$.

and hepatic function and no evidence of mal-absorption. ^{51}Cr -labelled albumin studies revealed a PLE.

Amyloidosis as a cause of PLE is very rare. None of the 236 cases of amyloidosis reviewed by Kyle and Bayrd (1975) showed evidence of PLE. Waldman (1966) did not include amyloidosis in an extensive list of disorders recognized as being associated with PLE.

Only 4 cases of PLE resulting from amyloidosis have been reported in the literature (Jarnum, 1965; Dawson, 1965; Barandun *et al.*, 1960). These differed from the present patient in that all had renal impairment at the time of diagnosis and one case also developed malabsorption (Jarnum, 1965).

A further unusual finding in this case was the histological pattern of gastro-intestinal involvement. In most cases, amyloid is not confined to vessel walls but also involves other structures in the bowel wall (Gilat, Revach and Sohar, 1969).

It is tempting to attribute all the functional abnormalities in this case to amyloid induced alteration in vascular permeability. However in a reported case (Pittman *et al.*, 1969) of amyloid infiltration of the gastro-intestinal tract producing diarrhoea, there were ultra-structural changes in the microvilli of otherwise normal epithelial cells as well as amyloid fibrils in areas not visible by light microscopy. This suggests that electron microscopy might be a useful aid to the diagnosis of gastro-intestinal amyloid, as it is in renal involvement, when light microscopic appearances are doubtful.

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