Impaired splenic function in systemic amyloidosis

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Summary: In four cases of biopsy proven amyloidosis there was evidence of impaired splenic function. All had absent or grossly reduced splenic uptake on colloid isotope scans and three had haematological changes consistent with hyposplenism. Poor splenic function with a normal sized or enlarged spleen may be a clue to underlying amyloid.

Introduction

Poor splenic function is now an accepted finding in a wide range of systemic disorders including coeliac disease, ulcerative colitis, Crohn's disease, sickle cell disease, primary thrombocythaemia and systemic lupus erythematosus. Recently attention has been drawn to hyposplenism in systemic amyloidosis,^{1,2} a disease in which the spleen is frequently enlarged. We describe four patients in which hyposplenic features provided useful clues as to the underlying diagnosis.

Patients

The characteristic histological appearances of acellular congophilic birefringent deposits of amyloid were demonstrated by biopsy in all four cases. Table I summarizes the clinical, laboratory and radiological features.

Case reports

Case 1

A 61 year old housewife was found to have gross hepatomegaly and heavy proteinuria. A liver biopsy demonstrated diffuse parenchymal infiltration with amyloid. Four months later she was readmitted to hospital with increasing breathlessness and oedema due to a restrictive cardiomyopathy. A blood film showed haemoglobin (Hb) 13.3 g/dl, white cell count (WCC) $7.8 \times 10^9/l$, platelets $573 \times 10^9/l$; Howell-Jolly bodies, target cells and schistocytes were present. A ⁹⁹Tc liver scan confirmed hepatomegaly but showed no

splenic uptake. Ultrasound examination showed the spleen to be enlarged.

Bed rest and diuretic therapy improved her condition and she was discharged home; two months later she was readmitted in a shocked state and died within an hour of admission.

A post-mortem examination confirmed generalized amyloidosis. The spleen weighed 400 g.

Case 2

A retired 80 year old man was admitted with a 6-month history of right upper abdominal ache, weight loss and constipation.

Physical examination revealed hepatomegaly but no stigmata of chronic liver disease and no splenomegaly. He had peripheral oedema and gross proteinuria. A percutaneous liver biopsy demonstrated parenchymal amyloid. A ⁹⁹Tc liver scan confirmed hepatomegaly but showed no splenic uptake though the spleen was enlarged on ultrasound scanning. The peripheral blood film was normal. The serum contained a monoclonal protein of IgG K type but no excess of light chains was detected in the urine. There was no immune paresis and a radiological skeletal survey was normal.

His health deteriorated steadily until his death two months later. Post-mortem examination was not performed.

Case 3

A 56 year old decorator presented in August 1979 with diarrhoea, weight loss and proteinuria. Investigations over the subsequent months, including gastrointestinal radiology and a rectal biopsy, were unhelpful. His symptoms persisted and in June 1982 he developed a nephrotic syndrome with a serum albumin of 18 g/l and a 24 hour urinary protein excretion of 6.4 g. A

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Accepted: 27 October 1986

Table 1 Clinical, laboratory and radiological features of patients

<i>Age/Sex</i>	<i>Clinical features</i>	<i>Immunology</i>	<i>Histologically demonstrated amyloid</i>	<i>Peripheral blood film</i>	<i>Spleen imaging</i>
61 years Female	Hepatosplenomegaly, Restrictive cardiomyopathy	Not available	Liver parenchyma on biopsy. Post-mortem amyloid infiltration of heart, renal glomeruli and splenic parenchyma	Howell-Jolly bodies Target cells Schistocytes Thrombocytosis	Splenomegaly on ultrasound No splenic uptake on isotope scan
80 years Male	Hepatomegaly	IgG κ monoclonal protein (14 g/l) No free light chains in urine	Liver parenchyma	Normal	Spleen enlarged on ultrasound No splenic uptake on isotope scan
62 years Male	Nephrotic syndrome Malabsorption and diarrhoea	IgG λ monoclonal protein (3 g/l) No free light chains in urine	Renal glomeruli	Target cells	Normal sized spleen present on plain abdominal radiograph No splenic uptake on isotope scan
60 years Male	Hepatomegaly Dysphonia Proteinuria	IgG λ monoclonal protein (8.5 g/l) No free light chains in urine	Liver parenchyma	Howell-Jolly bodies Target cells	Spleen normal on ultrasound. No splenic activity on isotope scan

renal biopsy demonstrated glomerular and vascular amyloid. A bone marrow showed 9% of plasma cells but was not diagnostic of myelomatosis. The serum contained a monoclonal protein of IgG type but there was no immune paresis. A skeletal survey was normal. His diarrhoea has persisted with attacks of vomiting and the radiological suggestion of gastric outlet obstruction. However, upper gastrointestinal endoscopies with multiple biopsies have been normal. His immunological changes have remained stable for the last 4 years.

Throughout this period his peripheral blood count has been normal but target cells have been detected regularly. A ^{99}Tc liver scan showed no splenic uptake but the spleen was clearly present on plain radiographs of the abdomen.

Case 4

A fit 60 year old coal miner was referred for investigation as possibly suffering coeliac disease following features of hyposplenism on a routine blood film.

Examination revealed mild hepatomegaly and proteinuria. He has impaired renal function with a creatinine of $236\ \mu\text{mol/l}$. Liver function tests were abnormal and liver biopsy demonstrated parenchymal amyloid. Small intestinal biopsy was normal, excluding coeliac disease. A monoclonal protein of IgG λ type was present in the blood and urine. A ^{99}Tc liver scan (Figure 1) showed no splenic uptake but the spleen was of normal size on ultrasound scanning.

Discussion

The spleen is commonly and extensively involved in cases of systemic amyloidosis.^{3,4} This involvement is commonly of the sheathed arteries and of the reticulum of the Malpighian bodies when it would not be expected to affect spleen function appreciably. However, involvement of the reticulum of the pulp and of the venous sinuses by amyloid would be expected to impair spleen function and this indeed has been reported.² This latter type of involvement produces the diffuse waxy spleen which is usually enlarged. Most clinical reviews of patients with amyloidosis rarely consider the role of the spleen except to mention splenomegaly and the rare complication of spontaneous splenic rupture.⁴

Three of our four patients had peripheral blood film changes of hyposplenism of varying degree with intrerythrocyte inclusions and abnormally shaped erythrocytes. One case actually presented with classical hyposplenic changes suggesting to the haematologist a diagnosis of occult coeliac disease. These blood film appearances are due to defective 'pitting' and 'culling' function of the spleen.⁶ Presumably amyloid tissue in

Figure 1 ^{99}Tc isotope liver-spleen scan in Case 4 demonstrating negligible radioactivity in the region of the spleen.

the pulp produces blockade of the reticulo-endothelial tissue to interfere with 'culling' and causes some narrowing or rigidity of the sinusoidal clefts to interfere with 'pitting'.

All four patients had grossly reduced or absent splenic uptake on conventional ^{99}Tc liver/spleen scans which are dependent on phagocytic clearance of colloid for effective imaging. It is likely that scans which depend on organ blood flow for imaging will demonstrate the spleen normally in amyloid. In coeliac disease the phagocytic impairment whilst causing blood film abnormalities may not be severe enough to affect colloid scans and these patients, at least in remission, have normal liver-spleen Tc-colloid scans.⁵ Hyposplenism due to repeated infarcts as in monozygous sickle cell disease results in a small spleen on scanning.⁷ Amyloidosis, with the possible exception of sarcoidosis,⁸ is the only example of hyposplenism occurring with an enlarged spleen.

Reviews of amyloidosis suggest that infection is an identified cause of death in about 10% of cases. It may be even higher as sudden death is often ascribed a cardiac aetiology but with underlying hyposplenism there may be cases of fulminant sepsis, the equivalent of overwhelming septicaemia seen following splenectomy.⁹

Acknowledgements

We thank Dr C.J. Hawkey for permission to report Case 4.

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