HYPOSPLENISM IN GASTRO-INTESTINAL DISEASE

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Keywords: *Hyposplenism, Inflammatory Bowel Disease, Coeliac Disease, Liver Disease, Sepsis*

INTRODUCTION

The hazards of living without a spleen were recognised by the paediatricians in the early 1960's when they focussed attention on the syndrome of fulminant sepsis, often due to pneumococcal infection, occurring in young children within the first two years of splenectomy [1]. A child, well at breakfast, might be febrile by lunch, comatose by evening and dead by the following morning. We now recognise that this danger of post-splenectomy sepsis (PSS) extends into adult life and splenectomised patients remain at risk 10, 20 and even 30 years after the operation [2].

Problems following splenectomy may just be the tip of the iceberg. What is now clear is that many other diseases are associated with impaired splenic function in the presence of intact spleens (Table I). These patients with functional hyposplenism are, like the splenectomised, also vulnerable to the syndrome of PSS. In some of these patients with diseases such as sickle cell disease and thrombocythaemia, where there is infarction of splenic tissue, the cause of the hyposplenism is obvious. It is also easy to understand the mechanics involved in infiltrative diseases such as sarcoidosis or amyloidosis. However in the gastro-intestinal disorders, including inflammatory bowel disease and coeliac disease, the reasons for the hyposplenism are obscure. To this group must now be added alcoholic liver disease in which impaired splenic function appears to be yet another factor in the known vulnerability of the alcoholic to infection [3].

INVESTIGATORY TECHNIQUES

Early studies to define those patients with hyposplenism in gastrointestinal disease relied on simple haematological markers such as the presence of Howell-Jolly bodies, acanthocytes and target cells. It soon became apparent that these methods were not sufficiently sensitive to pick up lesser degrees of hyposplenism. The Hammersmith group in London solved this problem by measuring the clearance of isotopically labelled heated erythrocytes [4]. This test is based on the fact that red cells damaged by heat become mildly spherocytic and are preferentially cleared by the spleen when re-injected. In this way they behave in a similar way to erythrocytes in hereditary spherocytosis. Impaired clearance of such labelled cells has been shown to be a reliable index of hyposplenism.

While the clearance of heated red cells proved a useful experimental tool it was time consuming and needed careful calibration. A simpler method was required and this was provided by Gino Corazza who was able to exploit some earlier observations on erythrocytes from splenectomised patients [5,6]. If such erythrocytes are viewed by differential interference contrast microscopy, (which gives a three dimensional view), pits or craters are seen (Figure I). The number of pits or craters can be counted in a simple and reproducible way. In health less than 2% of erythrocytes contain pits whereas after splenectomy up to 50% of cells show pits. This therefore gives a method of assessing splenic function which correlates well with the more complex methods. The true nature of these pits remains uncertain but electron microscopy suggests that they are really vacuoles containing intra-cellular debris of ferritin, haemoglobin and cell membranes [6]. This method supplemented with ultrasonic measurements of spleen size provides, therefore, a relatively easy method to assess splenic size and function.

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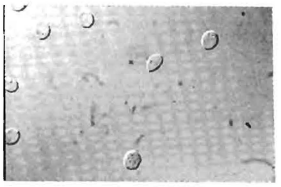

FIGURE I - *Erythrocytes from Splenectomised patient*

COELIAC DISEASE

One of the first gastrointestinal diseases shown to be associated with hyposplenism was coeliac disease [7] and several groups using the clearance of isotopically labelled erythrocytes or pitted cell counts have confirmed that from 25% to 75% of patients with coeliac disease have hyposplenism. Much depends, of course, on the sensitivity of the methods used. The severity of the hyposplenism increases with age at diagnosis and the duration of exposure to gluten [7,8]. Although in most patients hyposplenism improves with gluten withdrawal, some investigators have shown it to progress inspite of apparently strict dietary control [9]. The dreaded complication of gut lymphoma does not seem to be influenced by whether or not hyposplenism is present [10].

No single mechanism has been put forward to explain the hyposplenism of coeliac disease. In some patients the hyposplenism is associated with generalised lymph node atrophy and it has been suggested that this is all part of a more widespread atrophy of the lympho-reticular system. Increased levels of circulating immune complexes have been found in untreated coeliac disease [11] and it is possible that this could lead to functional blockage of the splenic reticulo-endothelial system. However, very high levels of immune complexes in childhood are insufficient to induce splenic hypofunction in childhood coeliac disease [12].

Interestingly patients with dermatitis herpetiformis, a disease linked closely to coeliac disease, may also show evidence of impaired splenic function.

TABLE I

Haematological	Sickle Cell Disease
	Thrombocythaemia
Auto-Immune	Systemic Lupus Erythematosus
	Thyroid Disease
Gastrointestinal	Coeliac Disease
	Ulcerative Colitis
	Crohn's Disease
	Whipple's Disease
	Idiopathic Ulcerative Enteritis
	Tropical Sprue
	Intestinal Lymphangiectasia
	Alcoholic Cirrhosis
Miscellaneous	Sarcoidosis
	Amyloidosis
	Old Age
	Long Term Parenteral Nutrition

CHRONIC INFLAMMATORY BOWEL DISEASE

Preston, a haemotologist in Sheffield, was one of the first to notice changes of hyposplenism in the peripheral blood of patients with active ulcerative colitis. Subsequent formal investigation of patients with inflammatory bowel disease using the heated red cell clearance method showed significant degrees of hyposplenism in both ulcerative colitis and Crohn's disease. The relationship with disease activity seems much clearer with ulcerative colitis where both medical and surgical treatment improves the hyposplenism which is dependent on the extent of the disease [13-15]. Pereira et al[16] using the simple measure of spleen length at laparotomy noted that patients with ulcerative colitis and Crohn's disease shown to have small spleens had more severe disease and more complications such as perforation, fistulae, abscesses, bleeding and toxic megacolon. Disseminated intravascular coagulation was also shown in hyposplenic patients with inflammatory bowel disease[15], a complication noted previously in asplenic subjects. The association between Crohn's and hyposplenism is less well defined[17] and there are suggestions that it is colonic Crohn's disease where the link is strongest.

The mechanisms, as with coeliac disease, are poorly understood but the profound enteric loss of lymphocytes in inflammatory bowel disease might contribute to the splenic hypofunction.

CHRONIC LIVER DISEASE

The spleen in liver disease sometimes plays a dual role in that it may contribute to haematological hypersplenism concurrently with immunological hyposplenism. Earlier suggestions of immunological hyposplenism in

immune chronic active hepatitis and primary biliary cirrhosis have not been confirmed [18] but there are now clear indications that immunological hyposplenism frequently complicates alcoholic cirrhosis [3]. The alcohol itself seems to be more important than the cirrhosis since abstinence reverts the hyposplenic changes.

MISCELLANEOUS GASTROENTEROLOGICAL CONDITIONS

Hyposplenism has been described in several other gut diseases though they have been less extensively investigated. Low spleen weights, between 5 and 75 g, have been reported from autopsies in tropical sprue though no formal studies of splenic function have been undertaken[19]. Splenic atrophy and/or Howell-Jolly bodies are often features of chronic idiopathic ulcerative enteritis though of course these findings may be primarily related to the pre-existing gluten enteropathy. Increased pitted cell counts with other confirmatory evidence of hyposplenism have been noted in Whipple's disease [20] and intestinal lymphangiectasia [21].

IS HYPOSPLENISM IMPORTANT IN GASTROINTESTINAL DISEASE?

Recent arguments have been put forward that the risks of PSS have been over-stressed[22]. Nevertheless, the majority of paediatricians, haematologists and physicians regard PSS as a very real and much feared entity. The Sheffield group have reported high rates of post-operative infections after surgery for ulcerative colitis in patients with defective splenic function [13-15] and overwhelming pneumococcal septicaemia has been reported in both ulcerative colitis and coeliac disease[23,24]. Wyke[25] has offered several explanations why alcoholics get infections which include impaired humoral and cellular host defences and defective reticulo-endothelial phagocytic function. Now hyposplenism must be added to this list.

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