**Case report**

**Development of impaired splenic function in intestinal lymphangiectasia**

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**SUMMARY** We describe a patient with intestinal lymphangiectasia who developed hyposplenism and speculate that it resulted from chronic loss of lymphocytes into the gut.

Splenic atrophy has been long recognised in association with coeliac disease and, more recently, impaired splenic function has been described in patients with ulcerative colitis and Crohn's disease. The aetiology of this hyposplenism is unknown, but by analogy with animal models it has been suggested that it results from lymphocyte depletion due to chronic loss into the gut.

Intestinal lymphangiectasia is a disease characterised by dilated lymphatics, protein-losing enteropathy, hypoalbuminaemia and oedema, and patients with this disease lose albumin, immunoglobulins, and lymphocytes into the bowel. If the development of splenic atrophy results from prolonged lymphocyte depletion, it is likely that patients with intestinal lymphangiectasia will develop abnormalities of splenic function over a period of time, although, to our knowledge, this has not been studied.

Since 1976, various tests of splenic function have been applied to one of our patients with intestinal lymphangiectasia and the results are reported below. During this time, however, the patient also developed other clinical problems.

**Case report**

A 40 year-old man presented in 1975 with a past history of vagotomy and pyloroplasty for a duodenal ulcer. He now complained of epigastric discomfort, diarrhoea, and ankle swelling. Examination confirmed pitting oedema of the ankles but there were no other abnormalities apart from the laparotomy scar. Investigation revealed a low serum albumin of 25 g/l. There was no proteinuria but polyvinylpyrrolidone excretion in the stool was increased at 6% (Normal <1%). Serum IgG and IgM were reduced (3.87 and 0.34 g/l respectively), serum IgA was normal. The absolute lymphocyte count was 1846/mm³ of peripheral blood. Dissecting microscopic and histological examination of duodenal and jejunal biopsies showed that approximately 2% of villi were distended with lipid material. A small bowel enema revealed oedematous mucosal folds and in a number of places there were round filling defects about 2 mm in diameter, consistent with a diagnosis of lymphangiectasia. A lymphangiogram showed hypoplastic lymphatics in the left leg; the right leg appeared normal but there was a paucity of vessels passing through the right iliac region. There was an increase in the cross-circulating pattern across the lumbar vertebrae with poor opacification of the glands in the right external iliac chain, but normal filling of the para-aortic nodes and pre-aortic nodes. A laparotomy, done in 1978, found chylous ascites and abnormal small bowel, particularly in the jejunum, with dilated lacteals on the surface of the intestine. A biopsy showed mostly normal villi but some with dilated lacteals. Secondary intestinal lymphangiectasia was excluded by appropriate investigations.

In September 1976 the patient, a heavy smoker, experienced sudden onset of pain in the right hand. A clinical diagnosis of radial artery occlusion was made. A right subclavian artery bruit was noted. The ESR was 40 mm/h. The platelet count was normal. Urinalysis was normal. Tests for antinuclear...
factor and DNA binding were negative. Subsequent exploration of the forearm vessels revealed atheroma and thrombus in the brachial artery, complete occlusion of the radial artery and stenosis of the ulnar artery. After thrombo-endarterectomy a brachio-ulnar artery saphenous vein bypass graft was undertaken. In 1978 the patient experienced a transient ischaemic attack affecting the territory of the left middle cerebral artery. Bilateral carotid bruits were noted. The ESR was 5 mm/h and the platelet count was normal. Lipid profile was normal and repeated tests for auto-antibodies were negative. An arch aortogram revealed relatively normal origins and bifurcations of the common carotid arteries but the right vertebral artery appeared narrowed throughout its length. After two more transient ischaemic attacks, the patient was anticoagulated with warfarin and one month later he developed cardiac tamponade because of a haemorrhagic pericardial effusion. The warfarin was stopped. Cardiac catheterisation showed no evidence of significant pericardial or cardiac disease. Six months later the patient was found to be hypertensive and a renal arteriogram revealed complete obstruction of the right renal artery; the splenic artery was normal. The platelet count was $833 \times 10^9/l$. Bone marrow examination showed normoblastic erythropoiesis and normal myelopoiesis. Megakaryocytes were slightly increased in numbers and showed active platelet budding.

Current treatment includes: a low fat diet, diuretics, $\beta$-blockers, aspirin and dipyridamole, and dietary supplements including vitamins, Triosorbon and MCT oil. His clinical condition has improved and is now stable.

ASSESSMENT OF SPLENIC FUNCTION
Peripheral blood films were scrutinised for the presence of target cells, giant platelets, acanthocytes and Howell-Jolly bodies. Pitted erythrocytes were counted by the method of Pearson et al.$^4$ in our hands, the upper limit of normal is 4%. Clearance studies were carried out by the method of Dacie and Lewis.$^5$ Briefly, autologous erythrocytes were labelled with 1-4 $\mu$Ci sodium $^{99}$Tc-pertechnetate and damaged by heating for 20 min at 50°C. After re-injection of the cells, blood samples were taken at three and 20 minutes. The radioactivity remaining in the blood at 20 minutes, expressed as a percentage of the amount of radioactivity present at three minutes, was taken as a measure of heat-damaged red cell clearnance. Our normal range is 17.5 to 46.5%. Splenic volume was computed from scintiscans obtained after injection of radio-labelled sulphur colloid. Our normal range of computed splenic volume being 158 to 577 ml.

Results
The serum albumin, absolute lymphocyte count, platelet count and pitted cell count in relation to the clinical course, are illustrated in the Figure.

ALBUMIN
Serum concentrations have been $<30$ g/l (normal 37-49 g/l) since presentation in 1975.

LYMPHOCYTE COUNT
The absolute number of lymphocytes has fluctuated, falling to concentrations of $<1000/mm^3$ during 1980 when the patient was very ill. The proportion of T-lymphocytes has tended to be low: 51.5% in 1976 and 50% in 1982 (as detected by rosetting techniques and monoclonal antibody respectively).

PLATELETS
At presentation the platelet count and bone marrow examination were normal. The 1979 the platelet count rose to $675 \times 10^9/l$, reaching a maximum of

![Figure: Lymphocyte count, serum albumin, platelet count and pitted-cell count in relation to the clinical events during 1976–82.](http://gut.bmj.com/2017-09-21-group.bmj.com)
979 × 10⁹/l in 1980 and has remained above 500 × 10⁹/l. Bone marrow examination in 1980 revealed megakaryocyte hyperplasia.

**SPLENIC FUNCTION**

This was assessed by a peripheral blood film, heat damaged red cell clearance and splenic volume (266 ml), and was normal at presentation. The first indication of impaired splenic function was the appearance of occasional acanthocytes in 1977. Three years later the peripheral blood film showed the typical features of hyposplenism: Howell-Jolly bodies, acanthocytes, target cells, and giant platelets, which persisted for at least 12 months. The pitted red cell count rose to a maximum of 29% in 1981 and a repeat scan of the spleen showed a decrease in volume (116 ml). Follow up blood film and pitted cell count in December 1982 showed a return to normal. Unfortunately, we have not been able to repeat heat damaged red cell clearance.

**Discussion**

The abnormal concentrations of albumin and immunoglobulins found in our patient were typical of intestinal lymphangiectasia: IgG showed the greatest reduction, IgM was also low and IgA levels were normal. The lymphocyte count has been very low on only one occasion, when the patient had cardiac tamponade. The relatively normal lymphocyte count was unexpected in a patient with intestinal lymphangiectasia, however similar counts in the peripheral blood have been observed in some patients with intestinal lymphangiectasia. Lymphocyte loss into the gut, if severe or chronic, depresses the blood lymphocyte count but it has been shown in animals that blood lymphocyte count can be maintained in the face of lymphocyte loss, although there is a fall in T-lymphocyte numbers. Wieden et al have suggested that there is a change in lymphocyte subpopulations as a result of lymphocyte loss in intestinal lymphangiectasia, with a reduction in the numbers of long lived recirculating cells in the peripheral blood. Our finding of low number of T-cells in the peripheral blood is in keeping with this.

Soon after the diagnosis of intestinal lymphangiectasia was made, we began to study this patient’s splenic function. In 1976, a peripheral blood film, heat damaged red cell clearance and splenic volume were normal. From 1978 to 1980 the blood films became progressively more abnormal until by 1980 there were target cells, giant platelets, acanthocytes and Howell-Jolly bodies present, features characteristic of hyposplenism. There was also an increase in the pitted red cell count which has been shown to correlate well with other estimates of splenic hypo-function. A repeat estimation of splenic volume showed a substantial decrease in size in 1981. Over the last two years, with an improvement in the patient’s clinical condition, the blood film changes have regressed and the pitted red cell count has returned to normal.

Reversibility of abnormalities of splenic function in association with improvement in the clinical condition has been described in other conditions, including coeliac disease and inflammatory bowel disease. Provided that splenic hypofunction has not progressed to fibrosis and atrophy, it seems reasonable to postulate that if the pathological mechanism causing the hypo-function improves, splenic function might also improve.

Fish et al showed that after discontinuing lymph drainage in experimental animals, the spleen re-populated with lymphocytes. Two of the patients with intestinal lymphangiectasia described by Roberts and Douglas showed an increase in the peripheral blood lymphocyte count, presumably because of a reduction in the gastrointestinal loss of lymphocytes after treatment. As our patient's clinical state improved, there was a rise in the peripheral blood lymphocyte count and the hyposplenism resolved.

Impaired splenic function has also been shown to improve with remission in rheumatoid arthritis, possibly related to a fall in levels of circulating immune complexes. The possibility that our patient’s transient hyposplenism was because of deposition and clearance of immune complexes seems unlikely as this association has been reported only in ‘inflammatory’, auto-immune disorders, for which we found no evidence in this case.

To our knowledge, the association of splenic hypofunction and intestinal lymphangiectasia has not been described. Crosby mentioned a personal observation of splenic atrophy in a patient with lymphoma and obstruction of intestinal lacerations. Ward et al found a spleen of normal weight at necropsy in their patient with intestinal lymphangiectasia and commented on a marked reduction in the size of the lymphoid follicles. In view of the patient’s preceding illness, however, including neoplasia and suppurrative peritonitis, and his treatment, including blood transfusion and abdominal radiation, it is difficult to interpret this finding.

The aetiology of the several vascular episodes in our patient is not clear but peripheral vascular disease, perhaps related to heavy smoking, and latterly the thrombocytosis, may be contributory. The persistent rise in the platelet count from 1978 is an interesting feature. Thrombocytosis is associated with anaemia but generally our patient was not
anaemic. Thrombocytosis is associated with non-specific inflammation of the bowel, as in inflammatory bowel disease\(^\text{18}\) and coeliac disease;\(^\text{19}\) in our patient there was no evidence of inflammation of the bowel. Thrombocytosis is a well recognised consequence of hyposplenism\(^\text{20}\) although the role of the spleen in maintaining the normal platelet count is not well understood. Thrombocytosis may itself be a cause of impaired splenic function. Marsh \textit{et al}\(^\text{21}\) found that some patients with essential thrombocythaemia also had splenic atrophy and Crosby\(^\text{15}\) postulated that splenic atrophy was a secondary effect due to infarction caused by sickled red cells in sickle-cell disease. Platelet hyperactivity as a consequence of hyposplenism has been described in sickle-cell disease \(^\text{1}\) and in both sickle-cell disease and essential thrombocythaemia it has been suggested that the hyposplenism and thrombocytosis may interact to further increase the platelet count.\(^\text{21,22}\) This may have occurred in our patient and although the splenic artery was shown to be normal, clogging of small arteries within the spleen cannot be excluded.

Our reason for studying splenic function in this patient was the theoretical possibility that he might develop splenic hypofunction because of lymphocyte loss into the bowel. Although the prediction was borne out in this patient, however, other mechanisms may have been operating.

**References**

Development of impaired splenic function in intestinal lymphangiectasia.
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Gut 1985 26: 861-864
doi: 10.1136/gut.26.8.861

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