CLINICAL RESEARCH

Blood viscosity after splenectomy

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Abstract

Blood viscosity and its contributory factors—namely, plasma viscosity, fibrinogen concentration, packed cell volume, red-cell deformability, and platelet count—were measured in 20 asymptomatic patients after splenectomy and compared with those in controls. Whole-blood viscosity was significantly increased after splenectomy and was associated with increased platelet count and, more importantly, decreased red-cell deformability. Blood viscosity was measured in six patients before and after splenectomy and in each an increase in viscosity occurred that did not occur in patients who underwent laparotomy without splenectomy.

These findings suggest that the inclusions and protein complexes within the red cell that are normally removed by the spleen decrease red-cell deformability and lead to an increase in blood viscosity. This may account for the observed increase in deaths from ischaemic heart disease many years after splenectomy.

Introduction

Whole-blood viscosity depends on many factors including red-cell deformability, which is important not only in the microcirculation, where the cell needs to squeeze through capillaries smaller than its diameter, but also in larger vessels, where constant deformation, rotation, and "tank-treading"[1] are essential to maintain the low viscosity of blood when compared with suspensions of rigid particles.[2] Abnormalities of the red cells increase whole-blood viscosity: this has been shown most clearly in sickle-cell disease[3] and hereditary spherocytosis.[4] High blood viscosity is always detrimental: it may be life threatening in the hyperviscosity syndrome complicating paraproteinaemia, leukaemia, and polycythaemia, and less distinct increases have been associated with several vascular disorders including occlusive arterial disease, venous thrombosis, and retinopathy. Many of the risk factors for arterial diseases are associated with high viscosity—for example, male sex, age, cigarette smoking, diabetes mellitus, hypertension, and hyperlipidaemia.[5] In the Framingham study[6] higher packed cell volumes, albeit still in the normal range, were associated with an increased incidence of subsequent episodes of vascular occlusion.

After splenectomy there are morphological and chemical abnormalities in red cells. Surface membrane "pits" are visible under interference phase microscopy in up to half of the red cells,[7] and high-molecular-weight proteins, normally removed by the spleen,[8] are present. There is often a high platelet count together with giant platelets. We assessed the possible importance of these abnormalities by measuring blood viscosity factors in patients who had undergone splenectomy.

Patients and methods

Twenty patients were studied after splenectomy and compared with controls matched for age, sex, and tobacco consumption. Twelve were women and eight men, with an average age of 42·9 years (range 18-70 years) and an average time since splenectomy of 5·9 years (range 6 months-37 years). Indications for splenectomy were trauma (15 patients), idiopathic thrombocytopenic purpura (four), and splenic cyst (one). Six additional patients were studied before and at intervals after splenectomy (for trauma (one patient), cyst (one), lymphoma (one), portal hypertension (one), and idiopathic thrombocytopenic purpura (two)). Controls were either healthy volunteers (10) or nonanaemic hospital inpatients with diseases not known to affect blood viscosity—for example, inguinal hernia and peptic ulcer. Controls for the serial studies were patients undergoing laparotomy but not splenectomy. Blood was obtained with minimal venous stasis and anticoagulated with solid lithium heparin for viscosity studies and ethylene diamine tetra acetic acid for haematological measurements. Whole-blood and plasma viscosity were measured at various shear stresses (0·057-1·148 N/m^2) at 37°C on a Deer rheometer within two hours of sampling. Before measurement the sample was subjected to a shear stress of 2·296 N/m^2 for two minutes to break up red-cell aggregates formed in vitro. Viscosity was plotted against shear rate over a range found during venous blood flow (10/s) and arterial blood flow (150/s).

Haemoglobin concentration, packed cell volume, and platelet count were measured on a Coulter S+ counter. Plasma fibrinogen

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concentration was measured according to the method of Ellis and Stransky[9] and red-cell deformability by a filtration method.[10] Statistical analyses were performed using Wilcoxon's rank sum test for paired data and Spearman's rank correlation.

Results

The table shows the mean values of the variables measured and the significances of the differences found. Whole-blood viscosity was significantly greater at all shear rates in the group who had undergone splenectomy ($p<0.001$) (fig 1). There was no difference between the two groups in plasma viscosity or fibrinogen concentration, but when both groups were taken as a whole there was a significant correlation between these two variables ($r=0.79$; $p<0.05$). There were no differences in haemoglobin concentration or packed cell volume between the two groups. In the control group a correlation between whole-blood viscosity and packed cell volume was noted ($r=0.68$; $p<0.05$), but no such correlation was found in the splenectomy group. Red-cell deformability was significantly decreased in the splenectomy group ($p<0.01$) and the platelet count significantly increased ($p<0.05$).

Figure 2 shows the blood viscosity and mean platelet count in the six patients studied before and at intervals after splenectomy; in each case there was a significant increase in blood viscosity. Mean blood viscosity preoperatively was 5·68 mPa s (cP) and six weeks postoperatively 6·9 mPa s at 50/s ($p<0.01$). The mean platelet count was maximum two weeks after splenectomy but fell back to high normal values eight weeks after splenectomy and bore no relation to the timing of the increase in viscosity.

Blood viscosity factors (mean values) and significances of differences found

	Splenectomy group	Controls	Significance
Platelets ($\times 10^9$/l)	462	281	$p<0.05$
Red-cell deformability (mm red cells filtered/min)	0·74	1·21	$p<0.01$
Packed cell volume (%)	41·9	41·9	NS
Haemoglobin (g/dl)	13·6	13·7	NS
Plasma viscosity (mPa s)	1·31	1·24	NS
Fibrinogen (g/l)	3·21	3·17	NS

Conversion: SI to traditional units—Plasma viscosity: 1 mPa s = 1 cP.

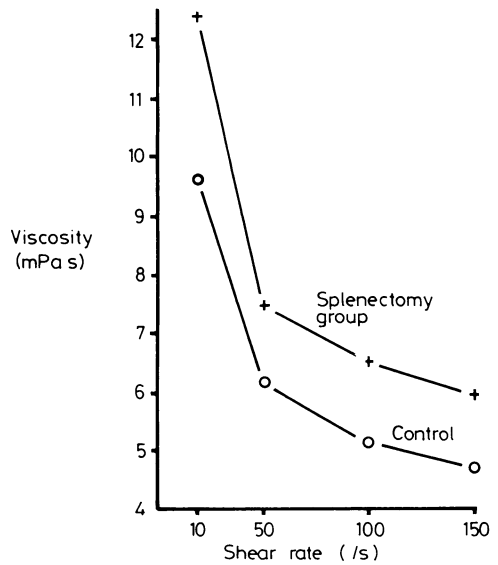

FIG 1—Mean value of whole-blood viscosity in patients who had undergone splenectomy compared with controls.
Conversion: SI to traditional units—Viscosity: 1 mPa s = 1 cP.

Discussion

Removal of the spleen is associated with a considerable mortality, principally from overwhelming pneumococcal septicaemia.[11] In their study of veterans of the 1939-45 war who underwent splenectomy Robinette and Fraumeni[12] found a significant late mortality from ischaemic heart disease, which is associated with high blood viscosity.[13]

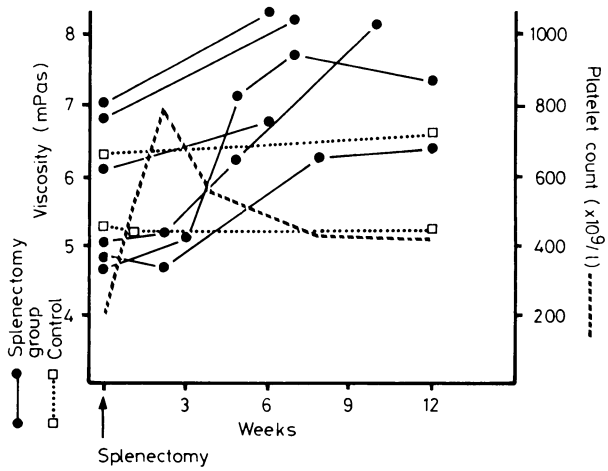

FIG 2—Whole-blood viscosity measured at 50/s before and at intervals after splenectomy, and mean platelet count.
Conversion: SI to traditional units—Viscosity: 1 mPa s = 1 cP.

We have shown that after splenectomy whole-blood viscosity is significantly increased and that this is associated with decreased red-cell deformability. Red-cell deformability is determined by properties of the cell membrane, by the viscosity of the intracellular contents, and by maintenance of the biconcave shape, which ensures the optimum ratio of surface area to volume.[14] After splenectomy all of these factors are abnormal. In the cell membrane there is cross-linking of the spectrin lattice.[8] The shape of the red cell is abnormal, with an increased ratio of surface area to volume,[15] and acanthocytes are common. "Rubbish" accumulates in the red cell after splenectomy including Howell-Jolly bodies, Heinz bodies, and siderotic granules.[16] These abnormalities may well increase the viscosity of the intracellular milieu and hence of whole blood.

The high platelet counts are not thought to be an important factor influencing whole-blood viscosity in these patients since there is no correlation between platelet count and viscosity, and in the six patients in whom serial measurements were made the platelet count increased rapidly after splenectomy then fell over several weeks to the high normal range. The increase in viscosity was delayed, but viscosity remains raised apparently indefinitely (fig 2). Although quantitative changes in the leucocyte population occur after splenectomy,[17] leucocytes are thought to contribute little to whole-blood viscosity until very high values are reached.[18]

Although highly significant, the increase in viscosity after splenectomy is small, similar to that that would be produced by an increase in packed cell volume of 2-3%. Over many years, however, such a small increase in viscosity may lead to increased mortality from occlusive vascular disease.[6] Furthermore, increased red-cell rigidity may have a direct effect on the microcirculation, causing reduced perfusion, which may be an important factor permitting overwhelming infection after splenectomy, though other reasons exist why these patients are less able to cope with serious infections.

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References

[1] Schmid-Schonbein H, Wells RE, Goldstone J. Fluid drop-like behaviour of erythrocytes—disturbance in pathology and its quantification. *Biorheology* 1971;**7**:227-34.
[2] Goldsmith HL. Microrheology of red blood cell suspension. *J Gen Physiol* 1968;**52**:55.
[3] Chien S, Usami S, Bertler JF. Abnormal rheology of oxygenated blood in sickle cell anemia. *J Clin Invest* 1970;**49**:623-34.
[4] Murphy JR. The influence of pH and temperature on some physical properties of normal erythrocytes and erythrocytes from patients with hereditary spherocytosis. *J Lab Clin Med* 1967;**69**:756-75.
[5] Dintenfass L. *Rheology of blood in diagnostic and preventive medicine.* London: Butterworths, 1976:137-42.
[6] Kannel WB, Gordon T, Wolf PA, McNamara P. Haemoglobin and the risk of cerebral infarction: the Framingham study. *Stroke* 1972;**3**: 409-20.
[7] Pearson HA, Johnston D, Smith KA, Touloukian RJ. The born-again spleen. *N Engl J Med* 1976;**25**:1389-592.
[8] Lux SE, John KM. Isolation and partial characteristics of a high molecular weight red cell membrane protein complex normally removed by the spleen. *Blood* 1977;**50**:625-41.
[9] Ellis BC, Stransky A. A quick and accurate method for the detection of fibrinogen in plasma. *J Lab Clin Med* 1961;**58**:477-88.
[10] Buchan PC. Evaluation and modification of whole blood filtration in the measurement of erythrocyte deformability in pregnancy and the newborn. *Br J Haematol* 1980;**45**:97-105.
[11] Likhite VV. Immunological impairment and susceptibility to infection after splenectomy. *JAMA* 1976;**236**:1376-7.
[12] Robinette CD, Fraumeni JF. Splenectomy and subsequent mortality in veterans of the 1939-45 war. *Lancet* 1977;ii:127-9.
[13] Mayer GA. Blood viscosity in healthy subjects and patients with coronary artery disease. *Can Med Assoc J* 1964;**91**:951-4.
[14] Anonymous. Red-cell deformability. *Lancet* 1978;ii:1348-9.
[15] Crosby WH. Splenic remodelling of red cell surfaces. *Blood* 1977;**50**: 643-5.
[16] Nathan DG. Rubbish in the red cell. *N Engl J Med* 1969;**281**:558-9.
[17] Lipson RL, Bayrd ED, Watkins CH. The post-splenectomy blood picture. *Am J Clin Pathol* 1959;**32**:526-32.
[18] Stuart S, Kenny MW. Blood rheology. *J Clin Pathol* 1980;**33**:417-29.

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Increase in drug resistance among Shigella dysenteriae, Sh flexneri, and Sh boydii

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Abstract

Two thousand three hundred and seventy strains of Shigella dysenteriae, Sh flexneri, and Sh boydii isolated in England and Wales from 1974 to 1978 were tested for resistance to 12 antimicrobial drugs. Eighty per cent of strains were resistant to one or more drugs, with sulphonamide resistance occurring most frequently. Resistance to streptomycin, tetracycline, ampicillin, and chloramphenicol increased during the period, as did the incidence of multiple resistance.

Most infections due to Sh dysenteriae, Sh flexneri, and Sh boydii are acquired abroad, and the increasing incidence of drug resistance among these organisms contrasts with the decreasing incidence of resistance among the indigenous Sh sonnei. These findings may indicate the need for better control of antibiotic use, particularly in developing countries.

Introduction

The number of *Shigella dysenteriae*, *Sh flexneri*, and *Sh boydii* isolations in England and Wales is small when compared with that of *Sh sonnei*. Nevertheless, the proportion of infections due to these subgroups increased from 2·4% of all shigella infections in 1965[1] to 16% in 1978.[2]

There is little published information on the incidence of drug resistance in *Shigella* in the United Kingdom, although the antibiotic resistance of *Sh sonnei* strains isolated in London has been documented.[3] We describe here the occurrence of resistance in *Sh dysenteriae*, *Sh flexneri*, and *Sh boydii* isolated in England and Wales from 1974 to 1978.

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Methods

Bacterial strains—Two thousand three hundred and seventy strains of *Sh dysenteriae*, *Sh flexneri*, and *Sh boydii* isolated in England and Wales from human faeces during the period 1974-8 were examined in the Division of Enteric Pathogens, Central Public Health Laboratory, London. *Sh sonnei* strains are not referred to this laboratory. All the strains were identified as members of the genus *Shigella* by the methods of Edwards and Ewing[4] and were serotyped according to the internationally accepted scheme.[5]

Drug resistance tests—The shigella strains were tested by an agar plate dilution method[6] for resistance to the following concentrations of antibacterial drugs: ampicillin (10 mg/l), cephaloridine (30 mg/l), chloramphenicol (30 mg/l), gentamicin (30 mg/l), nalidixic acid (30 mg/l), neomycin (30 mg/l), furazolidone (30 mg/l), polymixin B (100 U/ml), streptomycin (30 mg/l), sulphonamides (250 mg/l), tetracycline (10 mg/l), trimethoprim (1·25 mg/l).

Results

Of the 2370 shigella strains examined, 194 were *Sh dysenteriae*, 1867 *Sh flexneri*, and 309 *Sh boydii*. One thousand eight hundred and ninety-five strains (80%) were resistant to one or more of the antimicrobial drugs, while 782 strains (33%) were resistant to three or more drugs.

The prevalence of resistance to each drug is summarised in table I. Resistance to sulphonamides was most common (75·7%), followed by resistance to streptomycin (57·6%), tetracyclines (36%), chloramphenicol (12·5%), and ampicillin (12%). The proportion of strains resistant to these five drugs increased during 1974-8, as shown in table II. Resistance to cephaloridine, trimethoprim, gentamicin, and nalidixic acid was rare (< 1%). All strains were sensitive to polymixin B.

The most common resistance patterns were SSu (25% of all strains), SSuT (17%), and Su (16%).