Discussion

Successful bone-marrow transplantation from an unrelated donor has been reported for treatment of acute myeloid leukemia in remission.\(^1\) It has not been reported before in the treatment of severe aplastic anemia with evidence of sustained engraftment, though unsuccessful attempts have been made.\(^*\)

Both the patients reported on here received multiple blood transfusions. Multiple blood transfusions are associated with an increased risk of graft rejection in aplastic anemia,\(^1\) though possibly the use of cyclosporin A permitted engraftment in our patients despite this problem.\(^1\) Graft-versus-host disease occurred in both patients but in each case the acute episodes responded to treatment. The man had chronic graft-versus-host disease of the skin, which seemed to respond to prednisone and azathioprine. Both patients had stormy courses after grafting. Some of the infectious complications in the woman may have been related to the delay in bone-marrow transplantation since she had proved septicaemia before starting. Herpes zoster infections are common after grafting.\(^1\) The hepatic and renal failure in the man was probably related to drug treatment, including intravenous cyclosporin A and antibiotics.\(^1,2\) These patients show, however, that unrelated volunteers may donate marrow successfully for the treatment of severe aplastic anemia.

There are many logistical problems in this procedure that cause delay in identifying suitable donors, and the ethical questions raised in giving an anaesthetic to a healthy volunteer need wider discussion. The use of mismatched family donors has not yet been explored in aplastic anemia, mainly because the increased problems encountered using these donors in leukemic patients\(^1\) may prove difficult to overcome in patients with aplastic anemia, who are generally more ill. Despite the problems encountered in the management of these two patients, bone-marrow transplantation from unrelated, histocompatible donors does offer a chance of cure in severe aplastic anemia.

References


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Pyoderma gangrenosum associated with primary thrombocythaemia

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Abstract

Pyoderma gangrenosum is most commonly associated with inflammatory bowel disease and rheumatoid arthritis, but it has been associated with various haematological malignancies. A 54-year-old man with no history of bowel disease or arthritis presented with a leg ulcer, which healed after treatment. Results of bone marrow aspiration were compatible with primary thrombocythaemia. Seven weeks later there was pronounced recurrence of the ulceration and pyoderma gangrenosum was diagnosed.

The appearance of pyoderma gangrenosum associated with blood disorders may differ from that associated with bowel and joint disease.

Introduction

Pyoderma gangrenosum has been rarely associated with various haematological malignancies. We report an association with primary thrombocythaemia.

Case report

A 54-year-old Caucasian man presented with a four-week history of increasing ulceration on the outer aspect of the left lower leg. There was no history of bowel disease, varicose veins, or arthritis, and peripheral pulses in the legs were strong. Results of investigations at this time were: haemoglobin 15.1 g/dl, red cell count 6.6 x 10\(^6\)/l, packed cell volume 0.464, white cell count 16.4 x 10\(^3\)/l, and platelets 1210 x 10\(^3\)/l; leucocyte alkaline phosphatase activity was normal. The
results of bone marrow aspiration were compatible with primary thrombocythaemia. The ulcer healed successfully after treatment with oral flucloxacillin and local application of aureomycin cream. He started on a course of busulphan for his blood disorder.

Seven weeks later there was a pronounced recurrence of the ulceration, now covering the entire outer aspect of the left lower leg. On examination the ulcer had a ragged undermined margin with a bluish tinge, and the edge resembled a collapsed bulla. The appearance was suggestive of pyoderma gangrenosum and biopsy confirmed this diagnosis. Rheumatoid factor was absent, serum protein concentrations and immunoglobulin electrophoresis were normal, and sigmoidoscopy (up to 18 cm) showed no abnormality. He was given prednisolone 40 mg daily, which produced a rapid improvement in the lesion in two weeks and complete healing in five. He now remains in good health without any medication.

Discussion
Pyoderma gangrenosum is most commonly associated with inflammatory bowel disease and rheumatoid arthritis, though it has been reported in association with various forms of leukaemia,1,2 myelofibrosis,3 and polycythaemia rubra vera.1,4

References
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Chlorpropamide-alcohol flushing, aldehyde dehydrogenase activity, and diabetic complications

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Abstract
Many diabetics who take chlorpropamide (a sulphonylurea compound) experience facial flushing after drinking even small amounts of alcohol. These flushers have a noticeably lower prevalence of late complications of diabetes (microangiopathy, macroangiopathy, and neuropathy) than non-flushers. This flush reaction is accompanied by increased blood acetaldehyde concentrations, suggesting an inhibition of aldehyde dehydrogenase activity. In the present study the activity of this enzyme in erythrocytes was assessed in the absence of chlorpropamide. Erythrocyte homogenates obtained from flushers and non-flushers were incubated with acetaldehyde and the rate of metabolism studied. Flushers eliminated acetaldehyde more slowly at a low range of concentrations (0-30 µmol/l), suggesting a difference in aldehyde dehydrogenase activity. Further studies are needed to clarify the role of this enzyme in the pathogenesis of diabetic complications.

Introduction
For 25 years facial flushing after intake of small amounts of alcohol has been a well-known side effect of chlorpropamide medication,1 a sulphonylurea derivative used in the treatment of type II diabetes (non-insulin-dependent or maturity-onset diabetes). The implications of the flush were not known until 1978, however, when Leslie and Pyke2 reported that chlorpropamide-alcohol flushing was inherited as an autosomally dominant trait in type II diabetes. This was followed by reports of a lower prevalence of diabetic retinopathy,3 large-vessel disease,4 peripheral neuropathy,5 and diabetic nephropathy6 in the flushers than in the non-flushers. The prevalence of chlorpropamide-alcohol flushing in type II diabetes has varied considerably at around 30%.

Since the flush reaction seemed to be related to the pathogenesis of angiospasm, studies of its biochemical basis were warranted. We found that flushers had higher blood concentrations of acetaldehyde, the first metabolite of ethanol, than non-flushers during a chlorpropamide-alcohol challenge test.7 We also found higher concentrations of chlorpropamide in flushers than in non-flushers,8 which accords with the fact that chlorpropamide-induced inhibition of aldehyde dehydrogenase leads to a rise in blood acetaldehyde concentrations.8 Barnet et al.9 did not detect this difference in chlorpropamide concentrations between flushers and non-flushers, although they confirmed our finding that acetaldehyde concentrations were increased during the flush. This discrepancy can be explained by the different size of the populations studied (105 subjects in our study and 21 in theirs9). Furthermore, we found a considerable overlap in serum chlorpropamide concentrations, whereas the difference in blood acetaldehyde concentrations was highly significant with a minimal overlap. Obviously other factors might be of importance. This prompted us to study the role of aldehyde dehydrogenase in diabetes.

Acetaldehyde is converted to acetate by aldehyde dehydrogenase, which is distributed in various organs, the highest activity being found in the liver.10 Two major isoenzymes have been isolated from mammalian livers; one is mitochondrial with a low Km for aldehydes, the other is cytosolic with a high Km.