SHORT REPORTS

Value of radiochromium investigation in autoimmune haemolytic anaemia

Radioisotopic (111Cr) labelling of red cells to measure erythrocyte survival and assess the importance of the liver and spleen in the destruction of red cells is now standard practice in haematology laboratories. There is still disagreement, however, on the reliability of surface counting in predicting the outcome of splenectomy in individual patients with haemolytic disease, particularly those with autoimmune haemolytic anaemia. One group found that 111Cr studies identified patients likely to benefit from splenectomy,1 but others have found these investigations less reliable.2 We report here the results of such measurements in 12 patients with autoimmune haemolytic anaemia.

Patients, methods, and results

All 12 patients had a direct antiglobulin titre greater than 1:40 and evidence of haemolysis on the basis of normal laboratory criteria. Standard haematological methods were used. The spleen/liver ratio was assessed by body surface measurements, the ratio of organ uptake of radioactivity being measured when the intravenously injected 111Cr had left the circulation (t1/2Cr). A value greater than 2.5 is generally regarded as predicting a beneficial result from splenectomy.1 The splenic sequestration index (SSI), which is the percentage increment in spleen:heart radioactivity between zero time and t1/2Cr, was calculated as follows: SSI = R50 - R0, where R50 = spleen:heart ratio at t1/2Cr and R0 = spleen:heart ratio at zero time. A value greater than 100 is believed to indicate moderate to severe red cell sequestration in the spleen.3

Six patients were able to discontinue corticosteroids within two months after splenectomy. Three were men. Their average age was 42 years and the haemoglobin level at presentation ranged from 4.0-9.8 (mean 7.9) g/dl. In five of the six the sensitisation of the red cell was characterised: in four it was IgG alone, in the other IgG and complement. Six patients needed corticosteroids after splenectomy. All were women. Their average age was 52 and presenting haemoglobin levels ranged from 4.1-11 (mean 7.7) g/dl. In only three of these patients was the sensitisation of the red cells characterised and in all it was due to complement alone. The correlation between the spleen uptake of radioactivity and the results of splenectomy was poor (see figure). Theoretically the chances of success after splenectomy should be greatest in quadrants C and D and least in the quadrants A and B. But only three of the five patients in quadrants C and D had complete remission after splenectomy. Furthermore, of the five patients lying in quadrant A—the least favourable for splenectomy—three had a complete remission after operation.

Although the exact pathogenic mechanisms of HBsAg-negative, LMA-positive liver diseases remain obscure, it is of practical clinical interest that LMA is an autoantibody exclusively associated with HBsAg-negative acute and chronic liver diseases. Like AMA, which is of diagnostic value in primary biliary cirrhosis, LMA can be used to identify a substantial population within the great heterogeneous group of patients with CALD.

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Liquorice toxicity and the renin-angiotensin-aldosterone axis in man

We studied the electrolyte status and renin-angiotensin-aldosterone axis after the withdrawal of liquorice in four ill women aged 38 to 55 years admitted with chronic liquorice intoxication. They had consumed 25-200 g liquorice daily for six months to five years.

Methods and results

Plasma renin activity (PRA), plasma aldosterone, plasma angiotensin II, and urinary aldosterone were measured, using standard radioimmunoassay techniques.1-4 in these four patients on four occasions: (a) when they were first admitted and receiving a normal hospital diet, (b) on the fifth day of metabolic balance (sodium 10 mmol/mEq/day; potassium 100 mmol/mEq/day), (c) on the last day of balance, and (d) at two to four months' follow-up, on a normal home diet.

On a normal hospital diet urinary potassium excretion exceeded 40 mmol/24 h in all patients in the face of plasma potassium values of 1.6-2 mmol/l. On the fixed 10 mmol/day low-salt diet sodium balance was negative. The total urinary deficit ranged from 419 mmol over six days in one patient to 613 mmol over 11 days in another. In contrast, potassium balance was positive (423 mmol to 441 mmol over 6 to 11 days), and by the sixth day of low-salt diet plasma potassium had returned to normal in each case. In these patients plasma potassium rose above normal (5.5, 5.4, and 5.7 mmol/l) on days 10, 11, and 12, respectively, and potassium supplements had to be stopped. Plasma electrolytes remained normal thereafter, both during hospital admission and at follow-up two to four months later. Intravenous salt loading did not lead to excessive potassium excretion in any patient.

Renin, angiotensin, and aldosterone values during metabolic balance are summarised in the table. On the normal hospital diet all four patients had subnormal urinary aldosterone levels and PRA. These subnormal levels continued despite the low salt challenge of up to 12 days. Plasma aldosterone and plasma angiotensin II levels, while relatively normal under basal conditions, were abnormally low during low salt challenge.

Comment

The clinical features in all cases were similar to those described in previous cases of severe liquorice intoxication. In the first two to three days after the withdrawal of liquorice inappropriately excessive amounts of potassium were excreted in the face of subnormal plasma potassium levels. This hallmark of mineralocorticoid excess was presumably due to the continued action of the glycyrrhizinic acid component of liquorice on renal tubular potassium secretion. After this came a phase of sodium loss and potassium retention. This inversion of the urinary sodium: potassium ratio during salt deprivation was in strong contrast to the sodium and potassium retention noted in children with Conn's syndrome. Indeed this inversion will distinguish liquorice intoxication from primary aldosteronism without PRA, aldosterone, or angiotensin II having to be measured. Presumably the natriuresis and potassium retention are related to the effects of extracellular volume expansion and paralysis of the renin-angiotensin-aldosterone system similar to that observed in patients with primary aldosteronism after removal of an aldosterone-secreting tumour. The electrolyte response to intravenous salt loading was normal, thereby excluding an endogenous source of mineralocorticoid other than aldosterone. The normal follow-up electrolyte and renin-angiotensin-aldosterone axis assessment also supported this conclusion in all cases.

Subnormal urinary and plasma aldosterone levels and PRA clearly indicated suppression of the renin-angiotensin-aldosterone axis in all patients. Furthermore, these hormone and plasma angiotensin II blunted response to five days of low-salt challenge. Subnormal angiotensin II levels were noted only after salt deprivation and were therefore less discriminatory than PRA under normal basal conditions. In one patient the renin-angiotensin-aldosterone axis remained suppressed for at least 14 days after the withdrawal of liquorice, despite 12 days of salt restriction. This paralysis of the axis led to mineralocorticoid deficiency, as shown by raised serum potassium levels after continued salt restriction in three of the four patients. All patients showed normal values two to four months later, however, indicating that long-term suppression of the renin-angiotensin-aldosterone axis is uncommon despite several years of liquorice ingestion. This finding is in contrast to the prolonged suppression observed after the removal of some aldosterone-secreting tumours.6

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