SHORT REPORTS

Plasma exchange v peritoneal dialysis for removing Bence Jones protein

A major cause of renal failure in multiple myeloma is damage by light chains or Bence Jones protein (BJP). Serum BJP concentrations may rise in renal failure[1-3] to levels comparable to or above those in the urine. It is therefore rational to attempt their removal to prevent further damage, but the value of doing so in practice remains uncertain.[1] Because BJP molecules are relatively small it seemed possible that appreciable quantities could be removed by peritoneal dialysis. We have recently treated a patient with both plasma exchange and peritoneal dialysis and have been able to compare the amounts of BJP removed by the two methods.

Case report

A 64-year-old man was admitted to hospital on 4 October 1977 with a short history of increasing confusion and oliguria. On examination he was dehydrated with scattered petechiae. He was apyrexial, pulse rate was 100 beats/min, and blood pressure was 95/60 mm Hg. There was no clinical evidence of cardiac failure but a chest radiograph suggested bronchopneumonia. The abdomen was soft and the spleen palpable 2 cm below the costal margin. He was confused but there were no localising neurological signs. Laboratory results were as follows: erythrocyte sedimentation rate 140 mm in 1 hour, haemoglobin 7·9 g/dl, white cell count $2·4 \times 10^9$/l, platelets 18×10^9/l, calcium 3·4 mmol/l (13·6 mg/100 ml), phosphate 2·4 mmol/l (7·4 mg/100 ml), urate 0·7 mmol/l (11·8 mg/100 ml), sodium 129 mmol(mEq)/l, potassium 4·0 mmol(mEq)/l, chloride 90 mmol(mEq)/l, bicarbonate 21 mmol(mEq)/l, urea 30·1 mmol/l (181 mg/100 ml), total protein 114 g/l, albumin 22 g/l, creatinine 1130 μmol/l (12·8 mg/100 ml). An IgA paraprotein accounted for 48% of the total protein, and IgG and IgM concentrations were subnormal. Bone marrow findings were consistent with multiple myeloma.

He was rehydrated overnight and antibiotics were given. Next morning (5 October; see table) haemoglobin was 6·5 g/dl, total protein 90 g/l, calcium 2·86 mmol/l (11·4 mg/100 ml), and urea 34·7 mmol/l (209 mg/100 ml). The jugular venous pressure was raised 2 cm and there was clinical and radiological pulmonary oedema. He remained anuric with no response to frusemide, ethacrynic acid, and bumetanide. A Haemonetics Model 30 cell separator was used to remove 1·25 l of plasma without replacement, and the signs of congestion improved. The next day 5·33 l plasma was exchanged for blood and plasma. Despite some improvement in pulmonary oedema and urine output the blood urea continued to rise, so peritoneal dialysis was started on 7 October. His clinical condition deteriorated despite improvement of uraemia and he died on 10 October with massive haemorrhage from the upper respiratory tract.

BJP concentrations were measured by immunodiffusion[4] on samples of dialysate, urine, and serum. The table shows the amounts removed in these fluids. Serum concentrations of BJP were about a hundredfold higher than those in the dialysate and double the urine values.

Comment

One would expect to find BJP in peritoneal dialysate; indeed appreciable quantities of complete immunoglobulin molecules may also be present.[5] In our patient, however, the concentrations of BJP were such that about ten times as much could be removed by a 5 l plasma exchange as by peritoneal dialysis using 50 l of fluid. Because of oliguria quantities excreted in the urine were relatively small. It therefore seems that plasma exchange remains the most rational way of removing BJP in these circumstances if a satisfactory diuresis cannot be obtained.

We thank Dr A T Otaki for referring this patient.

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Insulinoma (apud cell carcinoma) in a diabetic

Insulinomas are uncommon and in diabetics they are exceedingly rare. Only five well-documented cases of this association exist.[1] We describe a case of insulinoma (apud (amine precursor uptake decarboxylation) cell carcinoma; apudoma) in a diabetic with evidence of proinsulin, gastrin, and pancreatic polypeptide hypersecretion.

Case report

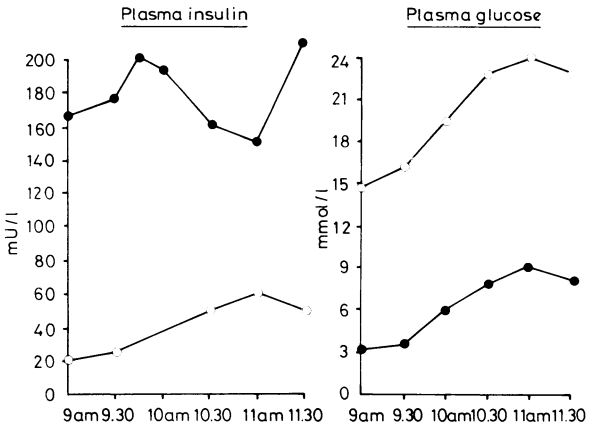
A 43-year-old man developed diabetes mellitus in 1970 (plasma glucose 14·8 mmol/l (266 mg/100 ml)). Over the next three years he was treated with glibenclamide and phenformin at the Roe Valley Hospital, Limavady (Dr J E Gibbon). Insulin treatment was begun in June 1973 but was discontinued in February 1976 because of recurrent hypoglycaemia. In March 1976 he lost weight and began to vomit frequently. A pancreatic tumour was found at laparotomy. On admission to our care in June 1976 his plasma glucose was 1·2 mmol/l (24 mg/100 ml) with plasma insulin by radioimmunoassay (RIA) 116 mU/l (usual range 1-15 mU/l). Insulin antibodies were absent and no insulin had been given for three months. Plasma fractionation showed that the 6000 molecular weight immunoreactive insulin fraction represented only 14% of the total. A 50-g oral glucose tolerance test (0, 30, 60, and 120 min) showed plasma glucose concentrations of 3·1, 6·0, 7·9, and 8·2 mmol/l (56, 110, 124, and 130 mg/100 ml) with corresponding plasma insulins of 165, 195, 160, and 120 μU/ml (figure). Plasma gastrin (RIA) was 290-500 ng/l (usual range 0-150 ng/l). There was considerable acid hypersecretion (residual acid 38·3 mmol (mEq)/l, one-hour basal level 32·4 mmol (mEq)/l, and one-hour pentagastrin-stimulated acid 42·2 mmol (mEq)/l). Plasma glucagon, secretin, and vasoactive intestinal peptide (RIA) were within normal limits.

Quantities of BJP removed in plasma, dialysate, and urine

Date (October)	Serum BJP (g/l)	Blood urea (mmol/l)	Plasma		Dialysate		Urine	
			Volume removed (l)	BJP removed (g)	Total volume (l)	BJP removed (g)	Volume (l)	BJP excreted (g)
5	4·0	34·7	1·25	5·0			0	0
6	4·0	46·4	5·33	17·5			0·53	ND
7	3·8	48·2			28·5	1·0	0·37	ND
8	4·0	41·2			48·9	2·0	0·20	0·37
9	4·8	37·0			52·1	1·8	0·02	0·04
10	4·0	27·1			31·0	1·4	0	0

ND = Estimation not done.
Conversion: SI to traditional units—Urea: 1 mmol/l ≈ 6 mg/100 ml.

At further laparotomy an inoperable pancreatic carcinoma with extensive hepatic secondaries was found. Biopsy of a liver nodule showed scattered cells containing insulin and pancreatic polypeptide (identified by specific immunohistochemistry). Histologically the tumour was a malignant apudoma of the type C pattern with trabecular formation and rosettes. The concentrations of insulin and pancreatic polypeptide in the liver tumour were 0·032 IU/g and 25·9 ng/g wet tissue respectively. Streptozotocin treatment was started. After a total of 8 g intravenously the glucose tolerance test was again diabetic with plasma glucose concentrations of 14·9, 16·2, 19·5, and 24·0 mmol/l (266, 292, 351, and 432 mg/100 ml). Corresponding insulin values had fallen to 20, 25, 40, and 60 mU/l (figure). Plasma gastrin had fallen to 150 ng/l. The residual acid was 4·6 mmol (mEq)/l, basal acid 6·9 mmol (mEq)/l, and one-hour pentagastrin-stimulated value 17·2 mmol (mEq)/l. The patient improved, gained energy and weight, and again required insulin. He enjoyed good health for 12 months and received intermittent courses of streptozotocin, Eventually hypoglycaemia recurred, he became resistant to streptozotocin and died 18 months after his first chemotherapy. Necropsy confirmed the finding of malignant apudoma.



Responses of plasma insulin and glucose to 50-g oral glucose tolerance test before (●—●) and after (○—○) 8 g streptozotocin.

Conversion: SI to Traditional Units—Glucose: 1 mmol/l ≈ 18 mg/100 ml.

Comment

The main differential diagnosis of insulinoma in a diabetic is factitious insulin administration,[2] ruled out in this case both by the pattern of plasma fractionation of insulin and by the specific insulin staining in a liver metastasis. There was a short remission with streptozotocin, as described by others.[3 4] The pancreatic tumour secreted gastrin, proinsulin, and insulin. A liver secondary stained positively for pancreatic polypeptide. Patterns of multiple hormone secretion in insulinomas have previously been described.[3 5] The concentrations of pancreatic polypeptide and insulin extracted from the liver secondary were low. That might reflect either lower levels than those in the primary tumour or decreased storage capacity for the hormones. Insulinomas may be rare in diabetics because the original insult to the pancreas either protects against tumour formation or simply leaves a decreased number of islet cells available for mitotic change. In the present case some normal islet cells remained, so the apudoma may have developed from these.

We are grateful to the United States National Cancer Institute, National Institutes of Health, for supplies of streptozotocin.

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Cytomegalovirus retinitis misdiagnosed as Hodgkin's lymphoma deposits

Cytomegalovirus (CMV) retinitis is rare and only one instance has been recorded in Hodgkin's disease.[1] In that case the patient was visually symptom-free, the diagnosis being an incidental necropsy finding. This report may alert physicians to the fact that the gross fundal changes of CMV retinitis may so closely resemble malignant lymphoma deposits that they may be misdiagnosed.

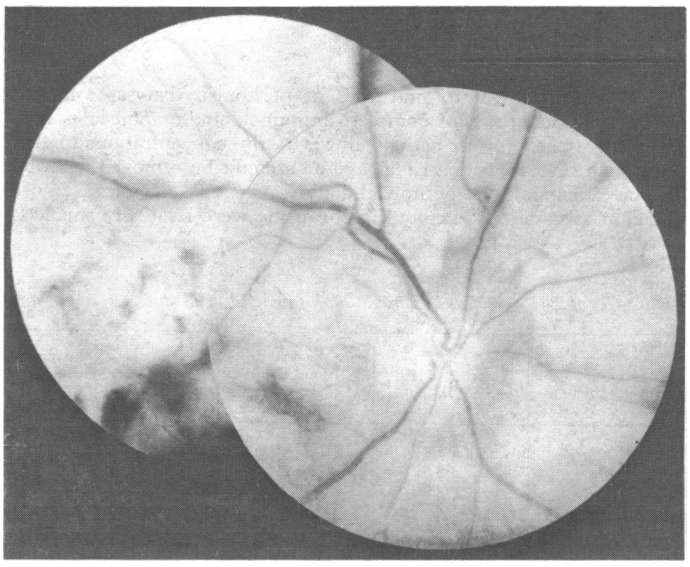
Case report

A 25-year-old man had mixed cellularity Hodgkin's disease diagnosed in 1969. Two complete remissions were obtained with radiotherapy and courses of chemotherapy. In 1975 he relapsed with bone disease and was given Chl VPP (chlorambucil, vinblastine, procarbazine, and prednisolone).[2] In 1976 chemotherapy was stopped because of a hypocellular bone marrow and stored packed red cells were transfused. Two weeks later he developed "shadows" in the right eye, which obliterated vision except for a narrow central horizontal strip. Over the next two weeks vision progressively deteriorated and on admission the eye was blind. He had no complaint about the left eye. The right optic disc was pale with attenuated arterioles showing early sheathing. There were scattered whitish areas in the fundus with associated haemorrhages and a lower-half exudative detachment (figure). Hodgkin's tumour was diagnosed with a central retinal artery occlusion. The left eye was normal except for one doubtful small retinal deposit. Nevertheless, one week later extensive disease had developed in this eye. The appearance of the fundus resembled that in the right eye and again suggested malignancy. Other than for mild headache, his general condition was good.

Investigations showed haemoglobin 11·7 g/dl, white cell count $7{\cdot}5 \times 10^9$/l (7500/mm^3), lymphocytes 4%, and platelets 158×10^9/l (158 000/mm^3). A CAT scan of the orbits showed abnormal patchy increase in density in the fat content of both muscle cones, worse on the right, thought possibly to be due to Hodgkin's deposits. Four separate cerebrospinal fluid (CSF) samples were taken. Cytocentrifuge smears in two samples showed reactive lymphocytes and atypical cells considered to be malignant. A CMV serum titre was not measured. On admission he was given dexamethasone, mustine, intrathecal methotrexate, and, later, radiotherapy to both orbits. Two weeks after admission sight deteriorated rapidly in the left eye. This was mainly attributed to a central retinal artery thrombosis, and conventional doses of streptokinase were started. Shortly afterwards the patient collapsed and died. Necropsy showed that the cause of death was cerebral haemorrhage. There were scattered foci of treated Hodgkin's disease but no active disease was found. Both retinae showed cellular changes very suggestive of CMV infection, and electron microscopy revealed particles typical of cytomegalovirus.

Comment

While physicians know that systemic CMV infection may occur in Hodgkin's disease, CMV retinitis alone, or predominantly, is perhaps



Fundus of right eye, posterior pole, showing intraretinal deposits.