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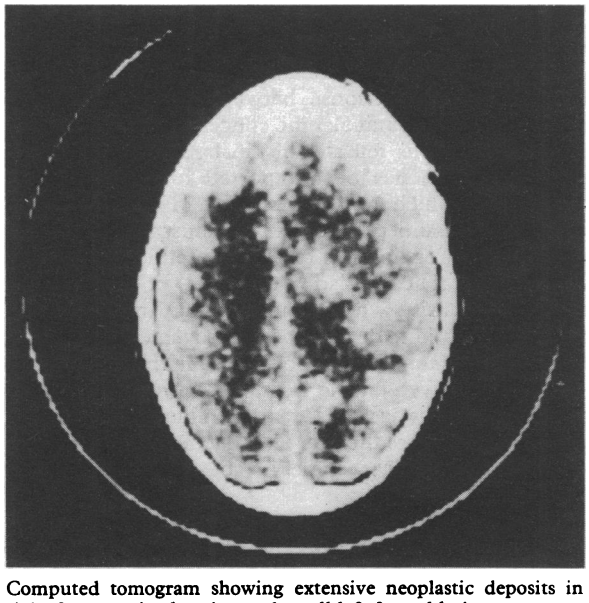
SHORT REPORTS

Cerebral glioma after cranial prophylaxis for acute lymphoblastic leukaemia

Intracranial sarcomas, meningiomas, and, more rarely, gliomas have been reported after cranial irradiation for unrelated conditions, with latent periods of many years.[1] We report on a child who developed a diffuse glioma nine years after successful treatment for acute lymphoblastic leukaemia.



Computed tomogram showing extensive neoplastic deposits in right frontoparietal region and small left frontal lesion.

Case report

A 3 year old girl presented in September 1974 with pallor, limb pain, cervical adenopathy, and hepatosplenomegaly. Initial haemoglobin concentration was 5·3 g/dl, white cell count $2{\cdot}4\times10^9$/l with 11% blast cells, and platelet count 26×10^9/l. Examination of marrow aspirate confirmed a diagnosis of acute lymphoblastic anaemia. She was treated according to the Medical Research Council UKALL III protocol, and remission was achieved by week 4. Prophylactic treatment of the central nervous system consisted of five weekly intrathecal injections of methotrexate 10 mg/m^2 body surface area and cranial irradiation using a 4 MeV linear accelerator with two opposed fields of 12×19 cm. The total dose was 24 Gy (2400 rad) delivered over 19 days in 12 fractions. Maintenance chemotherapy with mercaptopurine daily, methotrexate weekly, and vincristine and prednisolone every four weeks was continued until October 1977.

She remained well until December 1983, when she complained of frontal headaches and nausea for one month. There were no clinical or haematological abnormalities. On review 12 days later the headaches were worse and she had developed weakness of the left arm.

Examination showed a short attention span, bilateral papilloedema, left facial weakness, monoparesis of the left arm, cortical sensory loss, dyspraxia, dysmetria, mild dysdiadochokinesia, and a left Babinski's sign. She was treated with dexamethasone. A computed tomogram (figure) showed extensive neoplastic deposits in the right frontoparietal region and a small left frontal lesion. Marrow aspirate showed no sign of recurrence of leukaemia. Right frontal craniotomy and a frozen section of the mass showed a malignant glioma. Right anterior lobectomy with incomplete removal of the tumour was performed. Twelve hours after operation her condition deteriorated and she rapidly lost consciousness. A repeat scan showed right cerebral oedema. Intensive resuscitation failed, and she died three hours later. At necropsy there was pronounced cerebral oedema with early uncal herniation, and an astrocytoma was confirmed by histological examination.

Comment

Certain criteria must be met to sustain a diagnosis of neoplasia induced by radiation. The tumour must occur within the irradiated field and after a latent period sufficient to exclude its having been present at the time of radiotherapy. The tumour should differ histologically from the original lesion, and neurocutaneous syndromes predisposing to malignancy must be excluded. Primary conditions treated with radiation that have subsequently been associated with neoplasia have ranged from tinea capitis to pituitary adenomas[2] and medulloblastomas,[3] and the radiation dosage has ranged from 1·4 to 60 Gy (140 to 6000 rad). The latent period has usually exceeded five years.

Cure rates for acute lymphoblastic leukaemia in childhood have dramatically improved since the introduction of effective prophylactic treatment of the central nervous system with intrathecal methotrexate and cranial irradiation. The relative contributions of each to the subsequent development of a cerebral tumour cannot be assessed, but current trends have led to the reduction of radiation dosage from 24 to 18 Gy (2400 to 1800 rad) for all risk categories.

Two other cases of glioma after treatment of acute lymphoblastic leukaemia have been reported.[4,5] With the long latency of cerebral tumours related to treatment new cases may come to light, and continued close surveillance of patients after treatment is mandatory. It is essential to report new cases so that the incidence of this delayed complication can be assessed and possible risk features identified. Further modification of prophylactic treatment of the central nervous system may be possible, especially in patients at low risk, without affecting long term survival.

We thank Mr A J W Steers, consultant neurosurgeon, for his help in managing this patient.

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Proliferative glomerulonephritis associated with Crohn's disease

Extraintestinal manifestations of inflammatory bowel disease are well described and can affect many systems. The suggestion has arisen that circulating immune complexes may be connected with some of these complications, and hence it might be expected that renal complications would be a recognised extraintestinal feature.

Case report

A 49 year old woman presented with a three month history of lower abdominal pain, frequency of micturition, and nocturia. Abdominal examination showed a mass in the right iliac fossa. Blood pressure was 120/80 mm Hg. Her urine contained albumin +++ and blood +. Haemoglobin concentration was 13·3 g/dl, urea 7·8 mmol/l (46·8 mg/100 ml), and creatinine 0·12 mmol/l (1·4 mg/100 ml), and normal results were obtained on intravenous urography and cystoscopy and on barium enema, at which contrast refluxed into the terminal ileum. She had a coliform urinary tract infection, and treatment with antibiotics produced symptomatic improvement.

Nine months after her initial presentation her blood pressure was 200/115 mm Hg. During this period she had been tired and anorectic, lost 8 kg in weight, and had occasional pains in the right iliac fossa. Further investigations showed haemoglobin concentration 11·9 g/dl; erythrocyte sedimentation rate 38 mm in the first hour; urea 13·3 mmol/l (79·9 mg/100 ml); creatinine 0·20 mmol/l (2·3 mg/100 ml); calcium and phosphate concentrations and alkaline phosphatase activity normal; serum albumin 28 g/l (normal 33-48 g/l); creatinine clearance 28 ml/min; 24 hour urinary protein excretion 3·43 g (unselective); serum IgG 4·2 g/l (normal 8-16 g/l), IgA 0·2 g/l (normal 1·2-4·0 g/l), and IgM 0·3 g/l (normal 0·5-1·6 g/l); and normal serum complement concentrations. Tests for antinuclear factor and latex and sheep cell agglutination tests yielded negative results.

Her hypertension was treated and renal biopsy performed. Histological examination showed several glomeruli with extensive sclerosis; others were enlarged with hypercellularity associated with expansion of the mesangial areas and sclerosis (figure). Immunofluorescence showed focal peripheral deposition of IgG, IgM, and fibrinogen. IgA, C3, and Clq were absent. The glomeruli examined by electron microscopy were largely sclerotic and essentially unhelpful. Interpretation of the renal biopsy was difficult, but the most likely diagnosis was mesangial proliferative glomerulonephritis with sclerosis. After renal biopsy she developed abdominal pain, vomiting, and abdominal distension. Laparotomy showed gross Crohn's disease affecting only the terminal ileum, and this was confirmed by histological examination. A right hemicolectomy with ileal resection was performed.

Over the 12 months after operation she felt well and gained over 5 kg in weight. Her serum albumin concentration was normal; creatinine 0·17-0·19 mmol/l (1·9-2·1 mg/100 ml); creatinine clearance 26-32 ml/min; and 24 hour urinary protein excretion 2·2-4·9 g. Circulating immune complexes were measured before and after the operation. Although $C3_c$ and Clq complexes were raised, there was no significant difference in the values before and after resection.

Comment

The association between Crohn's disease and glomerulonephritis seems rare. We have found only one reported case.[1] Four cases of glomerulonephritis associated with ulcerative colitis have been reported.[2-4]

Although it has been suggested that the glomerular lesions seen in the above cases were secondary to deposition of immune complexes, no immune complexes were shown in the serum. In our case immune complexes were found but the concentrations were not strikingly high and remained unchanged after operation. Interestingly, experimental evidence suggests that inoculation of lymph node or intestinal tissue from patients with Crohn's disease can induce glomerular immune complexes in mice deficient in T cells.[5]

In our case symptoms and signs of Crohn's disease had been present for at least nine months before renal biopsy and laparotomy. During this period there was persistent proteinuria and haematuria, the patient developed hypertension, and renal function deteriorated considerably. After resection renal function did not deteriorate further. There seems to be some circumstantial evidence that the glomerulonephritis was directly associated with the Crohn's disease. Our case possibly represents one end of a range of glomerular changes occurring in patients with inflammatory bowel disease, which are usually not clinically evident.

We thank Dr J C Leonard, Dr P J Whorwell, and Dr A M Lessells for their help in producing this paper.

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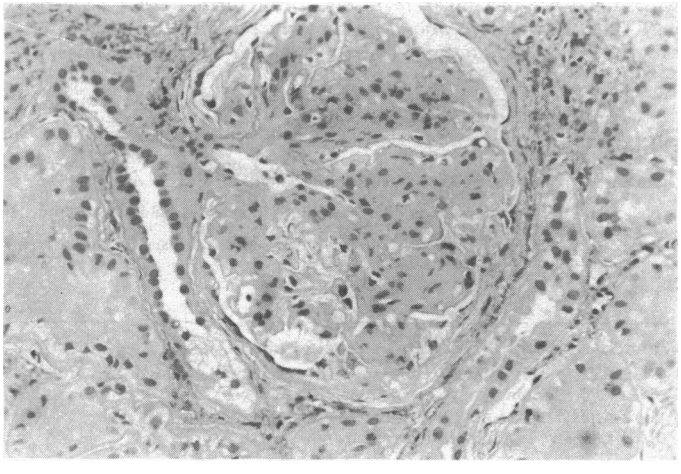

Glomerulus showing mesangial hypercellularity with sclerosis. ×258.

Algorithm for modified alkaline diuresis in salicylate poisoning

The use of forced alkaline diuresis in patients poisoned with salicylate is well established. Even in fit young patients, however, such treatment may cause fluid overload[1] or death.[2] Prescott *et al* showed that alkali alone removed salicylate at least as effectively as conventional forced alkaline diuresis, but the optimum treatment regimen had still to be determined.[3] In the light of this we devised an algorithm for modified alkaline diuresis that has proved effective and simple to administer and has much less risk of producing an overload of fluid (figure). We report its use in six patients.

Patients, methods, and results

The regimen was used in six patients (aged 19-69) with no history of cardiovascular or renal disease or clinical evidence of heart failure. The fluids used contained 1·26% sodium bicarbonate and 5% dextrose. Sodium