agglutinating antibodies could be detected against the isolated strain, but by the time the enteritis was over the titre had risen to 1/1280. When we saw the patient in our outpatient clinic the titre had declined to 1/160. After the arthritis had disappeared no antibodies could be detected. Radiological examination of the sacroiliac and ankle joints showed no abnormalities. Tissue typing showed HLA-A 2,28; B 12,27. Eight weeks after the onset of the arthritis all signs and symptoms had disappeared.

Comment

The findings in this case suggest that the oligoarthritis was reactive to the *C jejuni* enteritis. The arthritis started two weeks after the onset of the enteritis, and the antibody titre against the isolated campylobacter significantly increased. Other known causes for acute arthritis could be excluded. Moreover, reactive arthritis after certain infections occurs especially in HLA-B 27-positive patients.[1] This antigen was present in our patient. We do not know of other reports of reactive arthritis associated with *C jejuni* infections. One report[2] attributes exacerbations of a Reiter syndrome to *Campylobacter fetus* infections. This species, however, is distinct from *C jejuni*. *C jejuni* is now identified more often as a cause of enteritis.[3] Possibly, therefore, reactive arthritis after *C jejuni* infection is not rare and will be diagnosed more often in the future.

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Renal carcinoma with thrombocytopenia, clubbing, and hypertrophic osteoarthropathy

Renal carcinoma has not been reported in association with thrombocytopenia, while clubbing and hypertrophic osteoarthropathy in the absence of pulmonary metastases has also not been described.

Case report

A 71-year-old man was admitted in December 1974 with aching in his left loin, weight loss of 18 kg in two months, and clubbing of fingers and toes. His erythrocyte sedimentation rate (ESR) was 120 mm in the first hour (Westergren). Skeletal *x*-ray survey and bone scan showed hypertrophic osteoarthropathy of the tibiae, fibulae, and femora. Investigations with normal results included the following: urine microscopy, intravenous urography, blood and platelet counts, chest radiograph, sputum cytology, bronchoscopy with washings for cytology, barium enema, barium meal, liver biopsy, faecal fat excretion, urinary and serum protein electrophoresis, and bone marrow aspiration. His left loin pain and his raised ESR persisted until his death.

In April 1976 a radiograph of the renal areas was normal, as was his platelet count and findings on urine microscopy. In July 1977 he was found to have developed asymptomatic thrombocytopenia (platelet count below 40 10^9/l). At that time he was receiving regular paracetamol and dextropropoxyphene (Distalgesic) tablets for his loin pain, but the thrombocytopenia was unaffected by the withdrawal of the drug.

He received no other medication during the illness. The cause of the thrombocytopenia was not identified, the results of the following being normal: bone marrow aspiration and trephine, diffuse intravascular coagulation screen, serum and urinary protein electrophoresis, estimation of immunoglobulins and antinuclear factor, liver function tests, urine microscopy, platelet surface IgG estimation, and tests for platelet antibodies with and without paracetamol and dextropropoxyphene. In December 1977 the spleen was just palpable. In February 1978 the patient was found to have haematuria. Urine microscopy had been normal on six previous occasions. An abdominal radiograph showed calcification within the upper pole of the left kidney; intravenous urography and renal arteriography showed that the calcification was within a renal carcinoma. The previous *x*-ray films were reviewed and again passed as normal. An inoperable locally invasive renal carcinoma was found at laparotomy. The patient recovered sufficiently to go home for a month, but was subsequently readmitted with a terminal bilateral bronchopneumonia. He had never had macroscopic haematuria.

Necropsy—A large, poorly differentiated renal cell carcinoma with pseudosarcomatous change in some areas was found. Tiny foci with the more typical pattern of renal papillary carcinoma still remained and a thin rim of normal kidney surrounded parts of the tumour. The tail of the pancreas, the left adrenal, and the spleen were affected by a mass of necrotic tissue, and multiple, small, wedge-shaped infarcts with associated thrombosed vessels were seen in the spleen. No definite invasion of the spleen by malignant cells was seen, and no viable tumour was identified in the necrotic material. There were no secondary deposits in any other organ and the left renal vein was not invaded. His terminal bronchopneumonia was confirmed.

Comment

The variable clinical presentation and course of renal carcinomas are well known.[1 2] This patient presented with loin pain three years before he had other symptoms or radiological evidence of renal carcinoma. Hypertrophic osteoarthropathy and clubbing have been described only in association with pulmonary metastases and have disappeared after resection of the metastases.[3] In this case only the legs were affected by the hypertrophic osteoarthropathy, although the fingers were clubbed, and no metastases were seen. Haematuria occurred only when the thrombocytopenia was well established. The thrombocytopenia had no clear cause and contrasts with the more usual thrombocythaemia seen with carcinomas. The thrombocytopenia may be related to splenic infarction.

We thank Dr R W E Watts for permission to report this case.

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Acute renal failure after TAB and cholera vaccination

Reactions to TAB and cholera vaccination ranging from local erythema to constitutional disturbance are commonplace.[1] We record here an episode of acute renal failure and hepatitis after vaccination, which apparently has never been reported.

Case report

A fit 21-year-old man who several years earlier had undergone vaccination with TAB and cholera was revaccinated with typhoid A and B and cholera 0·5 ml subcutaneously. Within one hour he vomited and complained of headache and abdominal pain. He vomited several times during the following night and one episode of diarrhoea occurred; fluids were encouraged throughout this period. He developed myalgia. The next day he had neck stiffness and his temperature rose to 37·4°C. On the third day of the illness he was admitted to hospital because he had been anuric since the injection.

Examination showed jaundice, but he was not clinically dehydrated. There was obvious tenderness of the neck, limb, and abdominal wall muscles. The blood pressure was 90/70 mm Hg and the pulse rate was 80 beats/min, regular and of good volume. The heart sounds were normal and the chest clear. The results of examination was otherwise normal.

Investigations showed: haemoglobin 15·2 g/dl, white cell count 23·6 × 10^9/l; blood concentrations of urea 23·0 mmol/l (138 mg/100 ml), potassium 3·8 mmol(mEq)/l, sodium 129 mmol(mEq)/l, total CO_2 20 mmol(mEq)/l, and creatinine 0·38 mmol/l (4·4 mg/100 ml). Bilirubin concentration was raised at 75 μmol/l (4·5 mg/100 ml), alanine transaminase at 160 IU/l, and aspartate transaminase at 85 IU/l; alkaline phosphatase concentration was normal.

There was no history of exposure to nephrotoxins, contact with infectious disease, or excessive exercise. The following blood tests all gave normal or negative results: blood culture, viral studies, Paul-Bunnell test, Leptospira complement fixation test, immunoglobulin and complement estimations,

autoantibody profile, platelet count, clotting screen, tests for Australia antigen, antistreptolysin O titre, *Cryptococcus neoformans* titre, serum fibrin degradation products, haptoglobins, and creatine phosphokinase. Widal tests confirmed a good immune response to the vaccine with titres of 1/1280 for *Salmonella typhi* H and O antigens and 1/640 for *Salmonella paratyphi* A and B H antigens.

He was given an infusion of isotonic saline and 250 mg of intravenous frusemide. Urine flow started two hours later. The urine was normal in colour and microscopy showed granular casts in only one of six samples examined. No white cells or red cells were found in any of the specimens, though a trace of protein was found in two. The patient's condition steadily improved and he became asymptomatic over the next few days. Within two weeks his renal and hepatic function tests gave normal results.

Comment

A careful search was made to find a cause for acute renal failure other than the vaccine. But all relevant tests gave negative results, and the possibility of contamination of the vaccine was excluded by the uncomplicated vaccination of two other subjects from the same phial of vaccine.

An immune complex glomerulonephritis in a patient previously exposed to the antigen could have occurred, but the rapid onset of the illness and the laboratory results make this unlikely. Dehydration was not a prominent feature of the illness and seems an improbable mechanism for the renal failure. Neither would dehydration explain the hepatitis. Myoglobinuria as a cause of renal failure is characterised by dark urine and raised serum creatine phosphokinase concentrations, both of which were absent in this case.[2] The hepatorenal syndrome is unlikely in that liver function was not severely impaired and the condition usually has a poor prognosis.[3]

In many cases of acute renal failure the actual mechanism remains obscure,[4] but this patient's acute intrinsic renal failure seems most logically explained by an episode of acute renovascular shutdown of indeterminate cause but related to a reaction to the vaccine.

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Bottle feeding, early gastroenteritis, and inflammatory bowel disease

Breast milk contains several factors,[1] including immunoglobulins, that may protect particularly against gastrointestinal infection. In addition there has been interest in the role of IgA in antigen exclusion[2] early in life. Some patients with ulcerative colitis are sensitive to milk,[3] and Acheson and Truelove[4] reported a significant deficiency of breast-feeding in patients with ulcerative colitis compared with controls. In the light of reports of infectious agents, possibly acquired early in life, being associated with Crohn's disease[5] we have examined the pattern of breast-feeding in these patients as well as in patients with ulcerative colitis and in controls.

Patients, methods, and results

We questioned 57 patients with Crohn's disease and 51 with ulcerative colitis. Patients with proctitis and those whose mothers were dead or unavailable were excluded. For each patient two age- and sex-matched healthy controls were selected. A questionnaire giving details of place of birth (town, country, home, hospital), occupation of father at time of birth, breast-feeding or bottle feeding, length of time of breast-feeding, order in family, history of gastroenteritis in first six months of life, and a history of atopy was completed. Breast-feeding was considered to have ceased when any other food was started.

The results (table) showed that 29·9% of patients with ulcerative colitis compared with 11·8% of controls had never been breast-fed ($P = 0.005$). The difference in the two groups was lost in patients who were breast-fed for two weeks or more. No such differences appeared in the Crohn's disease group. Nevertheless, there was a significant difference in a history of early gastroenteritis in patients with Crohn's disease—10·5% as compared with controls 0·9% ($P = 0.005$). No significant relationship was found with place of birth, social class, or order in the family. The incidence of atopy did not differ in the bottle-fed and breast-fed patients.

Results of inquiry into history of breast-feeding or bottle feeding in patients with ulcerative colitis or Crohn's disease

	No of patients (%)	No of hospital controls (%)	No of normal controls (%)	Total controls (%)	Significance*
Ulcerative colitis ..	51	51	51	102	
Mean age ..	36·7	36·5	36·7	36·6	
Male	17 (33·3)	17 (33·3)	17 (33·3)	34 (33·3)	
Female	34 (66·6)	34 (66·6)	34 (66·6)	68 (66·6)	
Bottle fed ..	15 (29·4)	6 (11·8)	6 (11·8)	12 (11·8)	P = 0·005
Gastroenteritis ..	4 (7·8)	0 (0)	1 (2·0)	1 (1)	NS
Crohn's disease ..	57	57	57	114	
Mean age ..	33·3	32·9	32·8	32·9	
Male	22 (38·6)	22 (38·6)	22 (38·6)	44 (38·6)	
Female	35 (61·4)	35 (61·4)	35 (61·4)	70 (61·4)	
Bottle fed ..	11 (19·3)	11 (19·3)	11 (19·3)	22 (19·3)	NS
Gastroenteritis ..	6 (10·5)	1 (1·7)	0 (0)	1 (0·9)	P = 0·005

*Fisher's exact test, patients *vs* hospital + normal controls.

Comment

The results for ulcerative colitis are in agreement with those of Acheson and Truelove.[4] No such effect was seen in Crohn's disease. The observation that only a short period of breast-feeding was necessary to eliminate the effect in ulcerative colitis suggests that whatever factor is responsible was operative only shortly after birth. Thus either bottle feeding is harmful or breast-feeding protective. The harmful effect of bottle feeding might result from sensitisation to cows' milk early in infancy, possibly as a result of increased permeability to macromolecules. Bottle feeding might also alter bacterial flora at a time when sensitisation to bacterial antigens may occur. This may be relevant to the possibility that ulcerative colitis results from an abnormal immune response to enterobacteriaceae.

Patients with Crohn's disease had a significantly increased incidence of gastroenteritis within the first six months independent of bottle feeding. A possible explanation for this finding in Crohn's disease is that a pathogenic infection occurs which persists, becoming manifest as Crohn's disease only later in life. Subacute sclerosing panencephalitis and chronic hepatitis B are two examples of an abnormal response to a viral infection with a prolonged latent period. Rotavirus infection is a well-recognised cause of infantile gastroenteritis, and there is some evidence for its possible association with Crohn's disease,[5] but a persistent carrier state for this virus has not been shown.

Our findings suggest that an event associated with bottle feeding occurs within the first two weeks of life which predisposes to the development of ulcerative colitis later in life in some individuals. Similarly, an event related to gastroenteritis but independent of breast-feeding or bottle feeding may predispose to the later development of Crohn's disease.

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