patients undergoing dialysis were excluded and the remaining patients with uraemia compared with the controls a pronounced delay in gastric emptying was apparent (figure).

Comment

Delayed gastric emptying was shown in patients with symptomatic uraemia compared with asymptomatic controls. This abnormality may be confined to patients with uraemia not undergoing dialysis, and our observation of normal gastric emptying in three of four uraemic patients receiving dialysis confirms a previous report, which found no disturbance in gastric motility in 10 patients with renal failure undergoing haemodialysis.³

Possible explanations for the delay in gastric emptying include electrolyte disturbance, uraemic toxins, raised plasma concentrations of gastrointestinal hormones, and dysfunction of the autonomic nervous system. The influence of symptoms such as nausea on gastric function must also be considered as it is not clear whether delayed gastric emptying causes these symptoms or is a consequence of them.

Our finding may aid the interpretation of pharmacokinetic data in patients with uraemia and it provides a rationale for using drugs that promote gastric emptying in uraemic patients with nausea and vomiting.^{4,5}

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Renal Unit, Belfast City Hospital, Belfast

P T McNAMEE, MRCP, senior registrar
G W MOORE, FRCP, FFR, consultant radiologist
M G McGEOWN, MD, FRCP, consultant nephrologist
C C DOHERTY, MD, MRCP, consultant nephrologist

Department of Medicine, Queen's University of Belfast

B J COLLINS, MD, MRCP, senior tutor and senior registrar

Correspondence to: Dr B J Collins, Department of Medicine, Institute of Clinical Science, Royal Victoria Hospital, Belfast BT12 6BJ.

Primary lymphoma of the anal canal presenting as perianal suppuration

Primary lymphoma of the gastrointestinal tract is well documented, but to our knowledge lymphoma arising from the anal canal has not been reported. We report on a patient with anal lymphoma presenting as perianal suppuration.

Case report

An 89 year old woman presented with a two week history of throbbing perianal pain and discharge. There were no other symptoms attributable to gastrointestinal disease, although benign gastric ulceration had been diagnosed six months previously at endoscopy. Digital examination of the rectum then had not shown any abnormality but now showed a perianal abscess to the left of the anal margin that had discharged, leaving a large ulcerated area. Proctoscopy showed ulceration within the anal canal, but sigmoidoscopy to 17 cm did not show a lesion within the rectum. After debridement a biopsy specimen of pale, firm tissue at the base of the abscess cavity was obtained. General examination did not elicit palpable lymphadenopathy, hepatomegaly, or splenomegaly. Full blood count and differential white cell count were normal, as were results of liver function tests. A chest x ray film was normal.

Histological examination of the biopsy specimen showed a diffusely infiltrating undifferentiated tumour composed of large cells with vesicular nuclei containing several small nucleoli and with scanty surrounding cytoplasm. Staining of paraffin sections with monoclonal antibodies to leucocyte common antigen, cytokeratin, and epithelial membrane antigen was carried out using an indirect immunoperoxidase technique.¹ The cells of the tumour expressed leucocyte common antigen but not the epithelial

antigens cytokeratin or epithelial membrane antigen. The tumour was therefore diagnosed as a high grade malignant lymphoma and classified as a centroblastic lymphoma (Kiel classification) or diffuse histiocytic lymphoma (Rappaport classification).

Subsequent computed tomography of the abdomen and pelvis showed no enlargement of the lymph nodes, no masses, and a normal liver and spleen. Gastroscopy showed that the previous gastric ulcer had healed completely after treatment with cimetidine. After a course of radiotherapy, consisting of 4000 cGy (4000 rad) given in 20 fractions over four weeks, the lesion had resolved satisfactorily, and the patient was alive and well three months after treatment.

Comment

Lymphoma in the large bowel accounts for about 10% of all gastrointestinal lymphomas,^{2,3} but although the rectum is the commonest site within the large bowel, no series has described primary anal disease. The patient in this report appears to have had anal lymphoma as the case satisfied criteria for primary gastrointestinal lymphoma.⁴ Palpable lymphadenopathy and enlargement of lymph nodes were absent, total and differential white cell counts were normal, and although laparotomy was not performed, computed tomography did not detect further intra-abdominal disease.

The presentation of primary lymphoma as perianal suppuration is interesting in view of the recent description of lymphoma arising from lymphoid tissue associated with mucous membranes.⁵ Lymphoid tissue in the anal canal is aggregated around the anal glands in the intersphincteric plane, and infection of these glands is thought to be crucial in the pathogenesis of perianal abscess. Thus blockage of the glands by neoplastic infiltration probably contributed to the clinical picture.

Initial histological diagnosis was complicated by the undifferentiated nature of this tumour, and only after immunohistochemical staining with monoclonal antibodies could lymphoma be diagnosed definitely. This highlights the importance of such studies in poorly differentiated neoplasia, and some anal tumours reported as anaplastic carcinoma on purely histological grounds might, in fact, be lymphomas. Clearly, it is important to distinguish between carcinoma and lymphoma, and we would urge the use of immunohistochemical studies when the histogenesis of any anal tumour is in doubt.

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Departments of Clinical Surgery, Pathology, and Clinical Oncology, University of Edinburgh

R J C STEELE, FRCS, lecturer
O EREMIN, FRCS, senior lecturer
A S KRAJEWSKI, MRCPATH, senior lecturer
G L RITCHIE, FRCS, consultant radiotherapist

Correspondence to: Mr R J C Steele, University Department of Clinical Surgery, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW.

Fatal immune haemolysis associated with nomifensine

We report a fatal haemolytic reaction after treatment with nomifensine.

Case report

A 36 year old woman was admitted to Scunthorpe General Hospital as an emergency in February 1985, having collapsed within an hour of taking one tablet of nomifensine (Merital, 100 mg). She had taken the drug previously for one week but had stopped 10 days before presentation because of dizzy spells; there was no evidence of jaundice or red urine. On admission she was conscious but uncommunicative, pale, cyanosed with shallow

respiration, and shocked. Her pulse was thready (90 beats/minute) and her blood pressure 90/50 mm Hg. Initial laboratory investigation showed spontaneous red cell agglutination and free haemoglobin in the plasma. The haemoglobin concentration was 5.0 g/dl, bilirubin concentration 4 μ mol/l (0.23 mg/100 ml), and lactate dehydrogenase activity 1071 IU/l. There was severe acidosis. Acute intravascular haemolysis was diagnosed.

Her level of consciousness deteriorated, and she was transferred to the intensive care unit, where positive pressure ventilation was started. Within four hours after admission severe disseminated intravascular coagulation was evident with profuse bleeding from the rectum and all venepuncture sites; the platelet count, initially $226 \times 10^9/l$, had dropped to $67 \times 10^9/l$; the British corrected ratio was 2.5; activated partial thromboplastin time was 93 seconds; fibrinogen concentration was 0.7 g/l; and the concentration of fibrin degradation products was 320 mg/l. She was given a transfusion of blood, fresh plasma, cryoprecipitate, and platelets. Next morning her clinical condition appeared to have stabilised; however, urine output had dropped to 30 ml/h, and there was pronounced haemoglobinuria. Dialysis was considered, but lung compliance decreased rapidly and a shock lung syndrome became manifest. This failed to respond to methylprednisolone, and she died about 32 hours after admission.

Blood samples were sent for immunohaematological investigation¹ and for specific tests to assess the importance of nomifensine in precipitating the haemolysis.

The patient's blood group was 0 Rh positive (R_1r); the direct antiglobulin test gave positive results with antisera to IgG, IgM, and complement (C4, C3c, C3d); and the serum contained a strong mainly cold reacting autoantibody and panantibody. Tests for haemolysins, including the Donath Landsteiner antibody, gave negative results. Haptoglobin concentrations were low. The antibody caused agglutination of pooled O cells suspended in nomifensine solution (1 mg/ml in buffered saline pH 7.4) at 37°C but not of pooled O cells suspended in saline or that had been incubated in nomifensine solution and then washed; reactions with class specific antihuman globulins suggested that the antibody was mainly IgM but had an IgG component. Eluates from the patient's red cells agglutinated papainised pooled O cells only in the presence of nomifensine. Latex particles with bound nomifensine were agglutinated only with the patient's serum. Serum samples and eluates from control subjects (healthy subjects and patients suffering from autoimmune disease) gave negative results in all tests.

Comment

The serological findings strongly suggest that nomifensine precipitated the haemolysis by an immune mechanism. The drug and its antibody may have formed immune complexes that attached loosely to red cells and triggered complement activation, resulting in acute intravascular haemolysis²; this is an "innocent bystander" reaction. The relation between the haemolysis, the disseminated intravascular coagulation, and the shock lung syndrome is complex, but all may follow the initial massive activation of complement.

Immune haemolysis is a rare complication of treatment with nomifensine, and previous reports show many features similar to those in the present case.²⁻⁵ Since the introduction of nomifensine in 1977 over 3.5 million prescriptions have been issued in the United Kingdom. Only seven of the 20 cases of haemolysis associated with nomifensine seem to have resulted from the innocent bystander mechanism, but hitherto none has been fatal.

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Regional Blood Transfusion Centre, Sheffield S5 7JN

R J SOKOL, MD, MRCPATH, consultant haematologist and deputy director
S HEWITT, FIMLS, senior chief medical laboratory scientific officer
D J BOOKER, FIMLS, senior medical laboratory scientific officer
R STAMPS, FIMLS, medical laboratory scientific officer
MICHELLE TAYLOR, medical laboratory scientific officer

Scunthorpe General Hospital, Scunthorpe DN15 7BH

RHONA M STEWART, MRCP, MRCPATH, consultant haematologist

Correspondence to: Dr Sokol.

Toxic epidermal necrolysis associated with streptococcal septicaemia

We describe a case of toxic epidermal necrolysis in a patient with group A streptococcal septicaemia, an unreported association.

Case report

One week before admission a woman aged 76 developed a blister, presumably traumatic in origin, on a finger of her left hand. Three days later she developed constant upper epigastric pain with bilious vomiting and profuse watery diarrhoea. Over the next two days her left arm and axilla became painful, rendering the arm immobile by admission. Forty eight hours before admission she noticed an erythematous rash over the arm, which spread to the trunk, and blisters developed on the day of admission.

On admission she was alert but shocked, with peripheral cyanosis and impalpable pulses. Her blood pressure was 60/40 mm Hg and her heart rate 60 beats/minutes regular. A generalised erythematous rash was present, particularly over the abdomen and chest. Pustules of 1-2 mm were noted. Nikolsky's sign was elicited, the skin peeling off like wet tissue paper, especially over the breasts and abdomen. Tender lymph nodes were palpable in the left axilla and the groin.

Investigations on admission showed a haemoglobin concentration of 14.4 g/dl, white cell count $4.7 \times 10^9/l$ (98% neutrophils, 2% lymphocytes), erythrocyte sedimentation rate 10 mm in the first hour, urea concentration 19.1 mmol/l (115 mg/100 ml), bilirubin 20 μ mol/l (1.2 mg/100 ml), alanine transaminase 94 IU/l, total protein 49 g/l, albumin 20 g/l, prothrombin time 20 s (ratio 1.7), partial thromboplastin time 70 s (control 35 s), pH 7.11, carbon dioxide tension 4.4 kPa (33 mm Hg), oxygen tension 11.5 kPa (86.2 mm Hg), base excess -19.1 mmol(mEq)/l, and bicarbonate 10.6 mmol(mEq)/l.

Central venous catheterisation via the right subclavian route was performed. The initial pressure was +1 cm above the anterior axillary line. Four units of plasma were infused, and although this raised her central venous pressure to +5 cm, the blood pressure remained low. The clinical presentation suggested staphylococcal septicaemia with toxic epidermal necrolysis. Flucloxacillin (1 g every four hours), and fusidic acid (500 mg every eight hours) were given intravenously together with benzylpenicillin (2 megaunits every four hours) in case of coexisting streptococcal infection.

Despite receiving dopamine and dobutamine she remained hypotensive and anuric and developed atrial fibrillation, which was controlled by intravenous digoxin. Methylprednisolone 1 g was given intravenously for the metabolic acidosis. Her condition deteriorated rapidly, and she became comatose with an unrecordable blood pressure; she died eight hours after admission.

Results of bacteriological examination, which became available after death, showed group A β haemolytic streptococci in blood cultures, abdominal pus swabs, a finger swab, and a nasal swab all taken before death. A postmortem skin biopsy specimen showed spongiosis of the epidermis with foci of early necrosis in the upper epidermis. There was a moderately intense reactive infiltrate in the upper dermis, the features being compatible with toxic epidermal necrolysis of bacterial toxin (presumed staphylococcal) type.

Comment

Toxic epidermal necrolysis is well described and has many aetiological factors.¹ It is usually caused by drugs, and only septicaemia due to *Escherichia coli*² and staphylococcal skin infections have been reported as bacterial causes. The clinical features and histological findings in this case were those of toxic epidermal necrolysis due to staphylococcus and were so florid that initially staphylococcal septicaemia was diagnosed. However, *Streptococcus pyogenes* group A was subsequently isolated from all bacteriological specimens; there was no bacteriological evidence of staphylococcal infection, and in the absence of other aetiological factors there was little doubt that *Str pyogenes* group A infection had caused this complication.

Streptococcal infection is associated with various mucocutaneous manifestations including impetigo, erysipelas, cellulitis, and tonsillitis due to localised infections. More generalised conditions can exhibit the characteristic rash of scarlet fever, nodular blisters, milia, and abscesses. Exanthemas mimicking meningococcaemia as well as a generalised erythematous, non-purpuric papular rash have also been described.³⁻⁵

Whereas staphylococcal sepsis can occasionally mimic streptococcal sepsis, the converse rarely occurs, and toxic epidermal necrolysis appears to be a hitherto undescribed manifestation. Our report is a salutary reminder that fatal cases of streptococcal infection still occur,⁶ often as a result of minor trauma, and therefore in any acute bacterial infection the possibility of streptococcus should be considered.