A fatal case of pulmonary anthrax

Pulmonary anthrax is rare in Great Britain. This case illustrates some diagnostic problems and the possibility of infection from horticultural bone meal fertiliser.

Case report

A 53-year-old clerk in an engineering firm was seen initially with a three-day history of sore throat, pyrexia, chest pains, and slight abdominal tenderness. He was treated with amoxycillin and diazepam and referred to the casualty department, but discharged home when no other physical signs were detected. That night he developed worsening chest and abdominal pains, dyspnoea, and a cough. He was readmitted to hospital, where he died one hour later. On admission he was disorientated, pyrexial (38·5°C), severely dyspnoeic, and cyanosed. He had a tachycardia (120 per minute) constricted pupils, neck rigidity, and a tense abdomen. Blood examination showed haemoconcentration (haemoglobin 21·3 g/dl, packed cell volume 61·1%, and white blood count 19×10^9/l (19 000/mm^3)) and acidosis. Treatment with 8·4% sodium bicarbonate intraveneously, isoprenaline, hydrocortisone, and calcium gluconate was not beneficial.

A chest *x*-ray examination showed consolidation of the right mid-zone and lower zone and right pleural effusion and broadening of the superior mediastinal shadow (see figure). Blood cultures yielded *Bacillus anthracis* which showed resistance to pencillin (MIC>10 mg/l) but sensitivity to tetracycline, erythromycin, and gentamicin.

At necropsy there was a haemothorax and slightly collapsed and haemorrhagic right lung, with a 6-cm diameter mass in the right anterior mediastinum. There was a large blood-stained ascites and gelatinous oedema of the serosa. The small intestines showed areas of congestion and ulceration with general mucosal inflammation. No abdominal lymphadenopathy was present. The meninges were haemorrhagic over the superior surfaces of the cerebral hemispheres, and histologically showed early meningitic changes and numerous Gram-positive bacilli. Sections of the mediastinal mass and lymph nodes showed extensive necrotic and haemorrhagic changes with a proliferation of reactive primitive cells of lymphoid or histiocytic type, and microcolonies of organisms morphologically resembling *Bacillus anthracis*. Gram-positive bacilli resembling *Bacillus anthracis* were present in the ulcerated mucosal areas of the ileum. Apart from areas of congestion and the presence of few atypical lymphoid cells in the spleen, no other significant histological features were present in other organs.

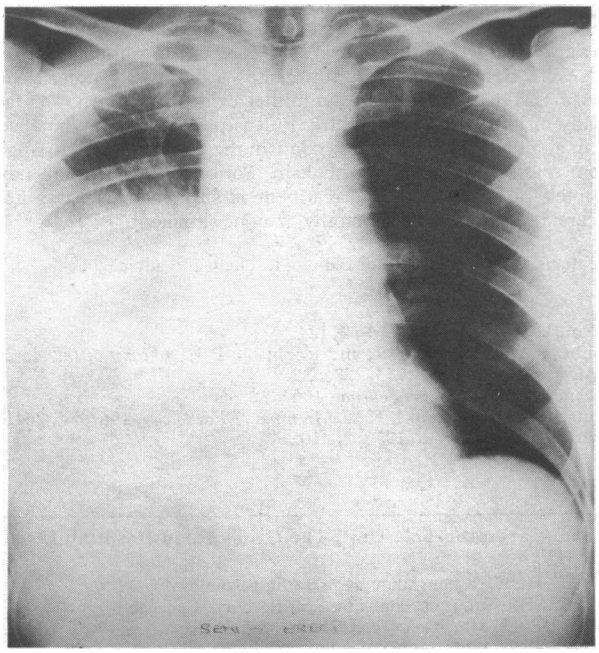
Epidemiological investigations revealed no potential sources of anthrax except bone meal, which the patient had used in large quantities in his garden, while continuing to smoke. Bacteriological examination of remnants, other retailer samples, and random garden soil samples proved negative.

Discussion

The rapid progression of the illness made clinical and radiological diagnosis impossible, and the necropsy appearances difficult, to interpret initially without the benefit of a clinical or bacteriological diagnosis. The radiological appearances are identical to those described by others[1] and these may arouse suspicion. The histopathology of the mediastinal mass simulated a lymphoid neoplastic tumour but the recognition of microcolonies within the nodes suggested a reactive process and indicated inhalation as the route of infection.

The laboratory recognition of *Bacillus anthracis* may not be easy but characteristic morphology, production of capsules on 0·7% bicarbonate medium, and susceptibility to specific gammabacteriophage are diagnostic. Pencillin resistance is rare, although one case has been noted,[2] and this must be considered when the response to pencillin treatment in anthrax is not prompt.

Probably in this case contaminated bone meal was the most likely source of the infecting organism.



Chest *x*-ray film showing consolidation of right middle and lower zones. There is a right pleural effusion and broadening of the superior mediastinal shadow.

I am grateful to Dr D. H G MacQuaide for permission to publish details of this case; to Dr R A Sladden for descriptions of the post-mortem and histological findings; to Dr J R Davies for carrying out specific gammabacteriophage tests on the strain isolated; and to H M Coroner for Northamptonshire for permission to report this case.

[1] Marc Laforce, F, *et al*, *Archives of Environmental Health*, 1969, **18**, 798.
[2] Christie, A B, *Infectious Diseases, Epidemiology and Clinical Practice*, 1st edn, p 771. Edinburgh, Livingstone, 1969.

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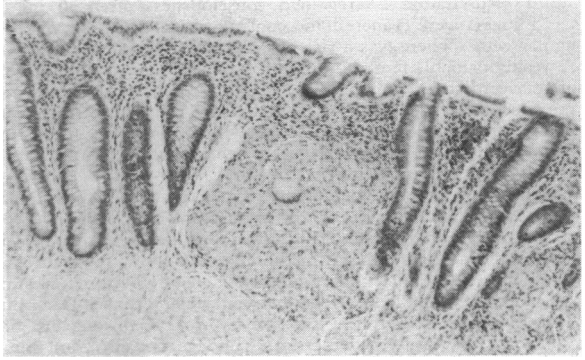
Crohn's disease of colon presenting as irritable bowel syndrome

Crohn's disease of the colon may be present when sigmoidoscopy and radiography of the whole alimentary tract show no abnormality. Three such cases were noted during a survey of patients with Crohn's colitis and they serve to emphasise the importance of routine rectal biopsy when investigating cases of "irritable bowel syndrome."

Case reports

A man aged 30 gave a 10-year history of intermittent abdominal pain and diarrhoea. His stools were semi-formed and did not contain blood. Three barium meals and one barium enema had been performed during the previous three years. None had shown any abnormality. On examination he was tense and introspective. Sigmoidoscopy showed no abnormality and a diagnosis of irritable bowel syndrome was made. A barium enema and barium meal and follow-through showed no abnormality. A colonic motility study elicited enhanced responses to both food and neostigmine, consistent with the irritable bowel syndrome. A rectal biopsy specimen taken routinely at sigmoidoscopy, however, showed the typical sarcoid-type granulomata of Crohn's colitis (see fig).



Photomicrograph of rectal biopsy in case 1 (×5).

The second case, a woman aged 26, presented with a six-month history of intermittent abdominal pain and diarrhoea, the stools being semi-formed and not containing blood. She was noted to be anxious but no other abnormality was found on examination, including sigmoidoscopy. The initial clinical diagnosis was that of the irritable bowel syndrome. A barium enema, barium meal and follow-through, and a colonic motility study showed no abnormality. A rectal biopsy specimen taken routinely at the initial sigmoidoscopy showed submucosal granulomata very similar to those of case 1.

The third case, a man aged 26, gave a six-month history of intermittent abdominal pain and diarrhoea with stools of ribbon-like appearance. Blood had been noted in the stool on two isolated occasions but had been attributed to haemorrhoids. Examination, including sigmoidoscopy, disclosed no abnormality, and a provisional diagnosis of the irritable bowel syndrome was made. A barium enema and barium meal and follow-through were normal but a rectal biopsy specimen showed typical sarcoid-type granulomata similar to those in the first case.

Discussion

The rectum is macroscopically affected in only about half the cases of Crohn's disease of the colon.[1] Biopsy of normal-looking rectal mucosa may be reluctantly performed when the history and examination findings are typical of the irritable bowel syndrome. This reluctance may be reinforced by a normal barium enema and barium meal and follow-through.

The cases presented here, however, illustrate the importance of biopsy under these circumstances. All three were young people with a tendency to anxiety or introspection, and their symptoms were entirely consistent with the irritable bowel syndrome. A striking histological feature of the rectal mucosa in these cases was the contrast between the pronounced submucosal granulomatous changes and the intact state of the surface mucosa. This characteristic distribution of the lesions presumably accounts for the normal macroscopic appearances on sigmoidoscopy and barium enema. A rectal biopsy should be carried out routinely in apparent cases of irritable bowel syndrome even when the rectal mucosa looks normal.

I thank Drs W Sircus and J N Webb for their advice and criticism, and Drs Sircus, M A Eastwood, and Anne Ferguson for permission to report the cases of patients under their care.

[1] Lennard-Jones, J E, Lockhart-Mummery, H E, and Morson, B C, *Gastroenterology*, 1968, **54**, 1162.

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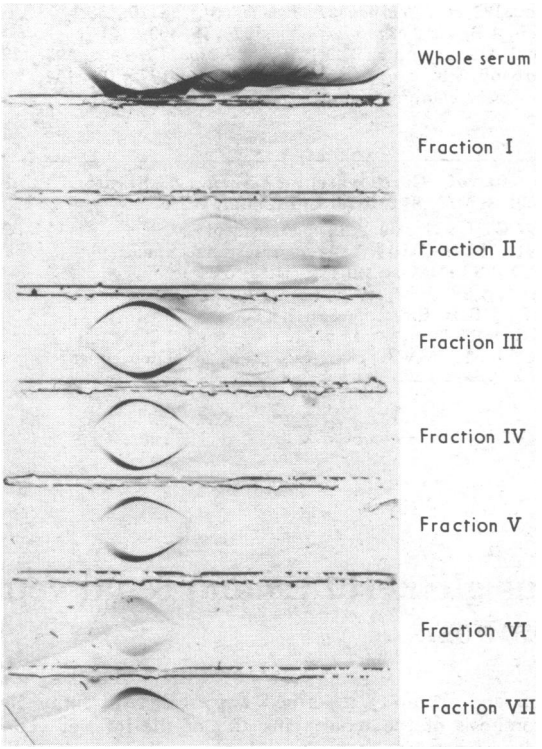
Immunodepressive serum treatment of acute heart transplant rejection

Immunodepressive factors in serum[1] appear to be naturally occurring proteins that depress lymphocyte activity in vitro. We have been studying them in heart transplant recipients for the past few years.[2] This report describes their use for the first time in acute cardiac allograft rejection.

Case report

A 15-year-old boy with fulminating cardiomyopathy received a heart transplant on 19 August 1974. Lymphocyte tissue culture studies showed a lack of immunodepressive factors in his serum[2] but a normal lymphocyte reactivity screen. Subsequently he began to reject severely, and despite steroids, azathioprine, and rabbit antihuman thymocyte globulin he continued to deteriorate with a drop in QRS voltage, biopsy on day 50 showing acute rejection. At the time, studies were being done on another heart recipient, who had the most powerful depressive factors encountered by our laboratory. We decided to transfuse two units of plasma from this patient into the first patient to try to reduce severity of rejection. The second patient underwent plasmapheresis, and two units of his plasma were absorbed with washed A and B cells. This was continued until the Coombs test result became negative. On 10 October the first patient was transfused with the depressive serum, tests showing that it depressed in-vitro lymphocyte responses. Clinically he improved and was successfully supported until retransplanted on 15 October. Subsequently he did well, returned to school, and was leading an active life.

Serum from the second patient was fractionated on Sephadex G-200; seven fractions were recovered, the highest molecular weight proteins being eluted in fraction I, and the lowest in fraction VII. Immunoelectrophoresis of each fraction (fig) after dialysis and concentration using a Diaflo 5UM2 ultrafiltration membrane showed that fractions I, III, and IV depressed the mixed lymphocyte responses, whereas the others did not.



Immunoelectrophoresis of serum fractions from second patient. Fraction I appeared to be α_2-macroglobulin. Fractions III and IV contained albumin and α-, β-, and γ-globulin; the latter was thought to be the effective component.

Discussion

There appear to be factors in normal human serum that inhibit or dampen lymphocyte activity, and these may be the equivalent of a normal hormonal regulatory mechanism. In some diseases they are increased, cellular immunity being impaired accordingly.[3] There appear to be three classes of depressive factors—α_2-macroglobulins, γ-globulin, and toxic factors related to uraemic states or toxic metabolic factors resulting from impaired hepatic or cardiac function. Possibly patients with chronic severe heart failure or after cardiopulmonary bypass have increased amounts of similar depressive factors, which after transplantation may dampen their cellular immunity by depressing lymphocyte activity.[2]

Occhino *et al*[1] have isolated an immunosuppressive peptide fraction from Cohn fraction IV of normal plasma that suppresses both the phytohaemagglutinin-induced lymphocyte proliferation in vitro and the in-vivo induction of splenic plaque-forming cells in mice. Most authorities agree that the factor must be added to the cultures early to have maximal effect. Cooperband *et al*[4] showed that the factor has its own receptor on the lymphocyte surface and that this differs from the receptor for mitogen activation. Other workers have suggested that inhibition may be mediated by the depressing substance neutralising the cellular mediators secreted by stimulated lymphocytes.

Several reports have emphasised the role of IgG as an immunodepressive; sera from dogs with kidney transplants contain an inhibitory factor that migrates with IgG, and human alloimmune plasma also has a direct inhibitory effect on responding lymphocytes in culture.[5]

Based on the Sephadex fractionation and immunoelectrophoretic studies the serum from the second patient appears to have contained two factors, one of high molecular weight—probably α_2-macroglobulin—and the other of lower molecular weight—probably