Letters to the Editor

Bilateral adrenal lymphoma presenting as Addison's disease

Sir,

In their article, 'Bilateral adrenal lymphoma presenting as Addison's disease',¹ Dr Pagliuca and associates state that: 'presentation of lymphoma with the clinical and biochemical features of Addison's disease . . . has only been reported once.'

The fact is that at least 8 such cases have been reported in the English language medical literature, including one reported by us, in the article: 'Lymphoma presenting with adrenal insufficiency: adrenal enlargement on computed tomographic scanning as a clue to diagnosis', published in 1988.²

The case reported by Dr Pagliuca *et al.* may be added to the list of reports in which enlarged adrenal glands seen on computed tomographic scanning during investigation of adrenal insufficiency could serve as a clue to the diagnosis of adrenal lymphoma.

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Loperamide related toxic megacolon in *Clostridium difficile* colitis

Sir,

Antidiarrhoeal drugs are used excessively to treat diarrhoea when adequate hydration or, if occurring after antibiotic use, metronidazole would be more appropriate. We report a case where loperamide, used inadvertently to treat *Clostridium difficile* colitis, may have precipitated toxic megacolon.

A 68 year old woman was given courses of amoxycillin, clindamycin and flucloxacillin for a dental abscess. She developed frequent watery bowel motions for which she was prescribed loperamide 2 mg eight hourly. The diarrhoea eased but after 2 weeks' treatment, she started to vomit repeatedly and became dehydrated and confused, requiring hospital admission. She was pyrexial, and had a soft, distended abdomen. X-ray showed dilatation (> 10 cm) of the transverse and descending colon. A toxic megacolon was diagnosed. Sigmoidoscopy showed inflamed rectal mucosa but no pseudomembrane. A cytopathogenic toxin, neutralized by *Cl. sordelli* antitoxin,

was found in the faeces, which also grew *Cl. difficile*. She was treated with intravenous fluids and metronidazole, and later with vancomycin by nasogastric tube and sigmoidoscopic decompression of the colon. Despite 3 days' intensive medical therapy, the abdomen became more distended and signs of peritoneal irritation developed. A laparotomy was performed, but no colonic perforation was found, and the colon was decompressed by a transverse colostomy. After this, she improved steadily and made a full recovery. The colostomy was later reversed.

Toxic megacolon may complicate inflammatory bowel disease, and *Cl. difficile* has sometimes been implicated.¹ Toxic megacolon is a rare complication of *Cl. difficile* colitis. In only one previous case has a clostridial cytotoxin been found.² The use of opiates or diphenoxylate may have precipitated some cases.^{2,3} There is one report of loperamide associated toxic megacolon in a patient with ulcerative colitis,⁴ but none in *Cl. difficile* colitis. The data sheets for diphenoxylate and loperamide recommend that they should not be used in inflammatory bowel disease, nor in antibiotic induced colitis. Antidiarrhoeal drugs may prolong the toxic manifestations of bacterial bowel infections although improving the diarrhoea. The delayed transit may encourage bacterial epithelial penetration and local microbial proliferation. Diarrhoea in such patients appears to be protective, and antidiarrhoeal drugs should be used with great caution if at all.⁵

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Silent nocardia cerebral abscesses in treated dermatomyositis

Sir,

The difficulties presented by opportunistic infections in immunosuppressed patients are well known. We report a

patient with dermatomyositis receiving prednisolone and azathioprine who developed multiple cerebral abscesses from which *Nocardia asteroides* was cultured. These were clinically silent and proved to be fatal.

A 51 year old female presented in October 1987 when, she developed proximal muscle weakness, myalgia and an erythematous rash over the proximal interphalangeal and metacarpophalangeal joints. The creatine kinase was elevated at 7420 IU/l and polymyositis was confirmed by a needle muscle biopsy. She was commenced on high dose oral prednisolone. Azathioprine was added to the regime but reduced after 3 months because of leucocytopenia. In July 1988, she developed severe oral candidiasis which was treated with oral fluconazole.

Muscle power gradually improved over the next 12 months, but in February 1989, she was re-admitted complaining of lassitude and increasing weakness over the preceding month. At that time she was receiving prednisolone 30 mg on alternate days and azathioprine 50 mg daily. She was mildly cushingoid and drowsy but afebrile. There was a small 0.5 cm diameter abscess on the anterior abdominal wall below the umbilicus. Her moderate proximal muscle weakness and generalized wasting were unchanged from when she was reviewed 2 months earlier. There was no evidence of pyramidal or cerebellar dysfunction. The total white cell count was $8.7 \times 10^9/l$. Grey-green pus was aspirated from the abdominal abscess. This and a set of blood culture bottles were sent for microbiological examination but no organisms were identified or cultured. The patient was commenced on intravenous metronidazole and flucloxacillin on admission and the azathioprine stopped.

Her clinical condition remained unchanged over the next 4 days and no new neurological signs developed. She then suffered 2 generalized tonic/clonic seizures which were terminated with intravenous diazepam. Several hours later, she had a fatal cardiopulmonary arrest. Necropsy revealed that the abdominal abscess extended down to the peritoneum. There were numerous metastatic abscesses beneath the parietal pleura over the upper 4 ribs on the right side, each measuring approximately 2 cm in diameter. Multiple cerebral abscesses were also found. The largest were situated in the right occipital lobe, left frontal lobe and the right cerebellar hemisphere. The liver showed marked steatosis but no active inflammatory process and low-grade polymyositis was noted in several muscle samples. No evidence of malignancy was uncovered. Subsequent microbiological studies demonstrated *Nocardia asteroides* in abscesses from each site.

This case illustrates the need for constant vigilance for infection in immunocompromised patients. There was no evidence for malignancy and we therefore assume that the treatment of dermatomyositis with steroids and azathioprine predisposed to nocardiosis. Detailed microbiological studies should be undertaken in any similar patient who presents with a non-specific illness, particularly when there is evidence of infection such as the cutaneous abscess in this case. It has been suggested that more invasive investigations are warranted when nocardiosis is suspected, such as bronchoscopy with bronchial brush biopsy or even percutaneous or surgical lung biopsy.^{1,2} Interestingly, in spite of neurological examination on several occasions, no signs of the cerebral abscesses were found throughout her admission up to 12 hours prior to death. The possibility of cerebral involvement should

always be considered in patients known to have nocardia infection and detailed neuroradiological investigation undertaken, preferably with cranial computed tomography.

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Discharge from osteomyelitis sinus with heparin therapy

Sir,

Heparin has been in use for around 40 years for the treatment and prevention of thrombosis. Despite its widespread use, there has been a surprisingly small range of adverse effects. We describe a previously unreported reaction to the use of subcutaneous heparin and discuss a possible aetiology.

A 62 year old man was admitted to the coronary care unit with chest pain suggestive of myocardial infarction. Cardiac enzymes did not rise and he was discharged after 5 days with a diagnosis of angina. Whilst in the coronary care unit he was given heparin 5000 units subcutaneously twice daily as prophylaxis against deep venous thrombosis.

At the age of 30 he had suffered from severe osteomyelitis affecting both femora and both humeri. He had been left with discharging sinuses which had necessitated numerous operative explorations and he was on long term flucloxacillin which was necessary to prevent discharge.

Six hours after the first dose of heparin he noticed a serous discharge from his right femoral sinus. This persisted whilst he was on heparin and he stated that a similar phenomenon had occurred previously with heparin. He continued on flucloxacillin, but the discharge continued until 24 hours after he had stopped the heparin.

He was readmitted 10 days later with a further episode of chest pain which was subsequently confirmed to be a myocardial infarction. He was again given heparin whilst in the coronary care unit and again developed a discharge from his sinus. He refused further heparin; the sinus became dry within 24 hours and remained so for the duration of his 10-day stay in hospital.

Although heparin does not possess intrinsic fibrinolytic activity, it does, in combination with anti-thrombin III, inhibit the formation of thrombin, and also inhibit the activation of fibrin stabilization factor.¹

In our patient, it is possible that chronic infection in the osteomyelitis sinuses led to a dynamic balance of fibrin