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Case Report

Fusobacterium necrophorum infection associated with portal vein thrombosis

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This report describes a patient without obvious upper respiratory tract or gastrointestinal infection who developed portal vein thrombosis secondary to *Fusobacterium necrophorum* septicaemia. The patient responded well to systemic antibiotic therapy. The implications of *F. necrophorum* infection caudal to the head are discussed.

Introduction

Fusobacterium necrophorum is an anaerobic Gram-negative bacillus and a constituent of the normal oropharyngeal flora. It is also the agent of necrobacillosis, an infrequent but severe necrotizing infection. This infection occurs in both humans and animals, causing septicaemia with disseminated abscess formation.

Human necrobacillosis classically presents as Lemierre's syndrome. This is characterized by acute primary infection in the head, most commonly the oropharynx, of a previously healthy individual with secondary thrombophlebitis of the internal jugular vein and metastatic embolic abscesses at multiple sites.

Venous thrombosis of the internal jugular vein frequently occurs in association with an upper-respiratory-tract infection caused by *F. necrophorum* (Hagelskjaer Kristensen & Prag, 2000). We report a case of portal vein thrombosis in association with *F. necrophorum* septicaemia in a patient without the classical primary cephalic infective focus that characterizes Lemierre's syndrome.

Case report

A previously healthy 53-year-old man was admitted to hospital with a 14 day history of rigors, fever, vomiting and malaise. There had been a brief episode of generalized abdominal pain 12 days prior to admission but no history of sore throat or any other upper-respiratory-tract symptoms. He regularly consumed up to 40 units of alcohol per week. He was not taking any medication.

At the time of admission the man's temperature was 39·2 °C, his heart rate was 120 beats min^{-1} and blood pressure was 93/45 mmHg. Physical examination revealed hepatosplenomegaly without jaundice, ascites or stigmata of chronic liver disease. The rest of the patient's cardiovascular, respiratory and abdominal examination was normal.

Initial investigations revealed a neutrophil leukocytosis (white blood cell count, $19{\cdot}8\times10^9$ l^{-1}, with 93 % neutrophils), elevated erythrocyte sedimentation rate (118 mm h^{-1}) and elevated C-reactive protein (138 mg l^{-1}). Liver function tests were abnormal (serum albumin, 29 g l^{-1}; alkaline phosphatase, 194 U l^{-1}; total bilirubin, 23 μmol l^{-1}; conjugated bilirubin, 11 μmol l^{-1}; alanine aminotransferase, 38 U l^{-1}; γ-glutamyl transferase, 205 U l^{-1}; and aspartate aminotransferase, 75 U l^{-1}). Coagulation studies were within normal limits. Two sets of blood cultures were taken. Chest radiograph was normal. Treatment was initiated with intravenous cefuroxime 750 mg three times daily (t.d.s.). A non-Doppler ultrasound scan of the abdomen on day 2 revealed an 11 cm simple cyst within the spleen with no other abnormalities demonstrated.

After 48 h of treatment the patient remained pyrexial and the rigors persisted. The anaerobic bottle of one set of blood cultures taken on admission yielded a thin filamentous Gram-negative bacillus that initially grew only anaerobically on blood agar at 37 °C to produce small translucent/grey colonies. Intravenous metronidazole 500 mg t.d.s. was added to the treatment before a full identification became available. Some days later, the aerobic bottle from the same blood culture set grew the same organisms under the same conditions. No other organisms were isolated from the single blood culture set taken. No pathogens were isolated from urine cultures.

The organism isolated from blood cultures was identified as *F. necrophorum* using a conventional anaerobic biochemical profiling test kit (API rapid ID 32A, biomérieux). The species identification was confirmed along with sensitivities by the Anaerobic Reference Laboratory at the former Public Health Laboratory, Cardiff.

The patient improved clinically and after 5 days of combined antibiotic treatment became apyrexial. In the light of the identified organism, the history was revisited at this stage and it was confirmed that there was no recent history of sore throat or earache. Following the identification of *F. necro-*

phorum, antibiotics had been changed to intravenous benzylpenicillin 1·2 g four times daily (q.d.s.) and oral metronidazole 400 mg t.d.s. for 1 week, followed by oral clindamycin 300 mg q.d.s. for a further 5 weeks.

Although the patient's abdominal symptoms settled soon after admission and the ultrasound was normal, due to the persistent abnormality of the liver function tests, computed tomography of the abdomen was requested and this was undertaken on day 5 after admission. As shown in Fig. 1, this demonstrated portal vein thrombosis (arrow) and an enlarged spleen (13 cm). No other intra-abdominal abnormality was demonstrated and no potential source of infection. The patient was anticoagulated, initially with low-molecular-mass heparin and then with warfarin.

Doppler ultrasound of the portal vein on day 12 demonstrated that the portal vein was now patent. Imaging of the large bowel was normal. The patient made a complete recovery and was discharged home on day 19, at which time C-reactive protein was 5 mg l^{-1}. Antibiotic therapy was continued for a further 3 weeks and he was maintained on warfarin for a total of 3 months. At review 3 months post-discharge he remained asymptomatic, with no abnormal findings on clinical examination. Liver function tests were normal and warfarin was discontinued. The patient remains well 3 years from initial presentation.

Discussion

F. necrophorum infection is uncommon, more frequently seen in males than females and has a peak incidence in the winter months (Brazier *et al.*, 2002) (our patient was admitted to hospital in January). The association between *F. necrophorum* and septic venous thrombosis is well recognized. It most commonly occurs in the form of Lemierre's syndrome, in which thrombosis of the internal jugular vein is precipitated by an upper respiratory focus of infection. This is usually pharyngeal or tonsillar but foci in the face, ears, sinuses, mastoid and teeth have also been described (Hagelskjaer Kristensen & Prag, 2000). In addition there are reports of *F. necrophorum* meningitis complicated by thrombosis of the cerebral veins (Larsen *et al.*, 1997) or cavernous sinus (Jones *et al.*, 1990). Thrombosis is most probably due to the ability of *F. necrophorum* to cause platelet aggregation as has been demonstrated *in vitro* (Forrester *et al.*, 1985; Kanoe *et al.* 1989).

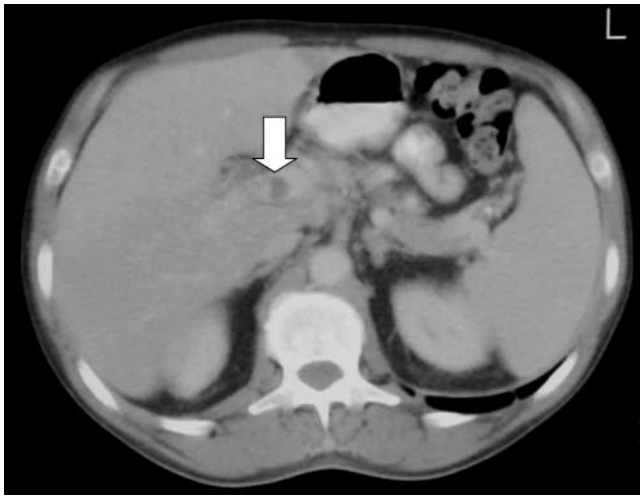

Fig. 1. Computed tomography of abdomen demonstrating thrombosis of the portal vein (arrow).

Primary foci of *F. necrophorum* infection in sites other than the head are uncommon but can occur in the urogenital or gastrointestinal tracts. Compared with Lemierre's syndrome, illness due to primary foci caudal to the head carries a higher mortality rate (up to 25 %); however, metastatic abscess formation does not generally occur (Hagelskjaer Kristensen & Prag, 2000). Short courses of antibiotic treatment (Hagelskjaer Kristensen & Prag, 2000) may be effective in these patients as compared to Lemierre's syndrome in which abscess formation necessitates longer courses of antibiotics, often for 6 weeks or more. It is important to exclude underlying malignancy in patients with non-head primary foci as up to 69 % of patients with gastrointestinal or urogenital primary infection with *F. necrophorum* have underlying malignancies of the affected system.

Portal vein thrombosis has been reported elsewhere in association with *F. necrophorum* infection (Soo *et al.*, 1999; Clarke *et al.*, 2003) and also in association with *Fusobacterium nucleatum* infection (Bultink *et al.*, 1999). Since the hepatic portal circulation exclusively drains the gastrointestinal tract, it is probable that the source of our patient's infection was the lower gastrointestinal tract, where *F. necrophorum* is known to be part of the commensal anaerobic flora in the caecum/vermiform appendix, colon and rectum. Subsequent investigation failed to identify any gross anatomical or functional abnormality of the gastrointestinal tract. Nevertheless, given the history of abdominal pain prior to admission and the absence of other systemic illness, we consider that the portal thrombosis was most probably due to a subclinical primary infection affecting the lower gastrointestinal tract, possibly a subclinical vermiform appendicitis. The patient remains well 3 years after this episode, hence underlying malignant disease is unlikely.

In summary, we report a patient with *F. necrophorum* septicaemia complicated by portal vein thrombosis who responded well to antibiotic treatment. Although it is rare, this diagnosis should be considered in a septicaemic patient with thrombosis in an unusual site, and underlying malignancy should be excluded in cases of confirmed *F. necrophorum* occurring at sites caudal to the head.

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