arteries could be obscured by normal or increased production in the microcirculation. Our findings, if applicable to man, suggest that diminished PGI₂ production may have a role in the increased propensity of diabetics to atherosclerosis but is less likely to be important in the pathogenesis of microangiopathy.

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Chronic osteomyelitis due to *Clostridium difficile*

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Abstract

Osteomyelitis caused by anaerobic bacteria is rarely reported, and a case of chronic osteomyelitis of the femur may be the first in which *Clostridium difficile* was the causative agent. The organism was isolated over several months and, although initially sensitive to penicillin, it developed resistance during this time. The organism's repeated isolation may have been due to the presence of resistant spores. Although the patient had no gastrointestinal symptoms the source of the organism was probably the patient's own gastrointestinal tract. Infection from the environment cannot, however, be excluded. Treatment was finally successful with metronidazole.

Introduction

With the exception of antibiotic-associated diarrhoea and pseudomembranous colitis *Clostridium difficile* is rarely a cause of infection. We describe a patient with chronic osteomyelitis of the femur due to this organism.

Case report

A 21-year-old man, who was injured in a motor accident while in Britain, sustained a fracture of the midshaft of the left femur which was treated with an open Kirschner nail. Eight months later, after his return to Australia, swelling developed over the injured site. He was admitted to hospital, where a large abscess surrounding the femoral shaft was drained. Microscopy of the pus showed numerous leucocytes but no organisms. Aerobic and anaerobic cultures were sterile. Treatment was started with cloxacillin 1 g intravenously and probenecid 500 mg orally every six hours. He developed a discharging sinus and after eight weeks the wound was explored again. On exposure of the femoral shaft thick pus was seen; the wound was debrided, the infected area lavaged, and the Kirschner nail removed. Microscopy of the pus on this occasion showed numerous leucocytes and a few Gram-positive bacilli. Culture produced a moderately heavy growth of a *Clostridium* species, initially thought to be *C. sporogenes* but later identified as *C. difficile* by the criteria of Holdeman et al.¹ The organism was shown to produce a toxin which was neutralised by *C. sordellii* antitoxin using a monolayer of VERO cells. The patient was treated with intravenous benzylpenicillin, 6 g daily, which was later increased to 8 g daily. Subsequently, a sinus appeared again, and a sinogram showed a large irregular cavity around the femoral shaft at the site of the fracture. Radiological investigations suggested osteomyelitis, and at a further operation a quantity of tissue and sequestrum was removed. Culture of bone and tissue again grew *C. difficile*. Over the next two months swabs from a discharging sinus consistently yielded *C. difficile* on either direct or enriched culture. Radiological changes over this period were consistent with chronic osteomyelitis and the patient was maintained on high doses of phenoxymethyl penicillin.

Up to this time the broth-disc dilution technique of Wilkins and Thiel² had indicated that the organism was sensitive to 1.2 mg/l penicillin, and its repeated isolation was disconcerting. Since resistant spores were possibly being formed in vivo smears of discharging pus were stained by the Ziehl-Neelsen method. Bacterial spores were present, even though vegetative organisms could not be detected. On the next occasion that *C. difficile* was isolated, however, it had developed resistance to phenoxymethyl penicillin; the minimum inhibitory

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concentration was 12.5 mg/l. Treatment was changed to metronidazole 400 mg three times daily and cultures rapidly ceased to grow *C difficile*. The organism was not isolated over the succeeding 18 months and radiological changes suggested a resolving infection. The patient had no gastrointestinal symptoms at any time during the illness.

Discussion

Osteomyelitis caused by anaerobic bacteria is rare, and we are not aware of any previous reports of *C difficile* causing this disease. *C difficile* was first isolated by Hall and O'Toole,³ who found it to be part of the normal gastrointestinal flora of infants. Smith and King⁴ reported the isolation of *C difficile* from several extraintestinal sites, and more recently it has been implicated as the causative agent of pseudomembranous colitis.⁵

The interesting features of this case are the unusual site of infection for this organism, the length of time over which the organism was isolated despite apparently appropriate treatment, and the development of penicillin resistance during treatment.

The source of the organism was probably the patient's own gastrointestinal tract, but the possibility of environmental infection cannot be excluded. Possibly the infection did not occur until after the initial drainage. The first abscess may have been sterile, as suggested by the first culture results, and merely a response to the foreign body present. It is unclear why the organism persisted for so long. On some occasions only very few

organisms were present and thus enrichment media were required for isolation. The production of spores in vivo could explain the organism's persistence. The development of resistance to antibiotics during treatment is certainly not uncommon, and its occurrence in the present case added interest to an already interesting case. It is worth noting that transferable drug resistance in *C difficile* has recently been reported.⁶

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Twin pregnancy with complete hydatidiform mole (46,XX) and fetus (46,XY): genetic origin proved by analysis of chromosome polymorphisms

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Abstract

In a case of complete hydatidiform mole with fetus the genetic origins were defined by the use of chromosomal polymorphisms. The fetus had a normal 46,XY karyotype with evidence of the presence of both maternal and paternal chromosomes. The mole was 46,XX and of androgenetic origin. There was no evidence of a maternal contribution, and duplication of paternal chromosomes was shown.

In such atypical molar pregnancies examining genetic polymorphisms yields much more information than do sex chromosome studies and karyotyping, particularly in confirming the diagnosis and defining the origin and aetiology of the condition.

Introduction

Hydatidiform mole may be separated into two entities on the basis of histopathology,^{1,2} cytogenetics,³⁻⁸ and biochemical

markers.^{5,7} Complete moles lack the presence of a fetus, are almost always female, and are androgenetic in origin.^{3-5,7} In contrast, partial moles have a range of villi from normal to hydatidiform, focal rather than conspicuous hyperplasia, and evidence for the presence of a fetus.² When karyotype analysis of the placenta and fetus has been carried out partial moles have generally been found to be triploid.^{1,6-10} Cases of mole with co-existent fetus must now be assessed in the light of these findings.

Patient and methods

The patient was a 27-year-old woman who had given birth to a normal girl in 1972 and a normal boy in 1976. She presented in her third pregnancy at eight and a half weeks of gestation with a uterus size of 14 weeks. Ultrasound examination showed the presence of a fetus. When she was seen again three weeks later with painless vaginal bleeding and an enlarged uterus no fetus was detected on scanning. The pregnancy was terminated by suction evacuation at 15½ weeks because of a suspected mole.

Macroscopic examination of the specimen showed a large mass of molar tissue comprising clusters of translucent thin-walled cysts ranging from 2 to 20 mm in size, encased in clotted blood. A small portion of apparently normal placenta associated with some membranous material was seen and appeared to be separate from the main bulk of the vesicular mass. Also present was a partially macerated male fetus with a crown-rump length of 4.5 cm and a foot length of 6 mm, and therefore estimated to be between 8 and 10 weeks of gestational age. Further examination showed no external abnormalities, all limbs being present and with the normal number of digits. On dissection no abnormalities were detected in the internal organs.

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