The clinical spectrum of Clostridium sordellii bacteraemia: two case reports and a review of the literature

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Abstract

clostridium sordellii is rarely associated with disease in humans. Since its first report in 1922 only a few cases of bacteraemia have been reported. This report describes two cases of C sordellii bacteraemia; the oldest and youngest patients reported to date. The first, is a previously well 81 year old woman presented with perianal infection, which was later complicated by thrombosis of the aorta, and the second is a 12 year old boy with epilepsy who presented with an ear infection. These cases are also highlighted to demonstrate the wide spectrum of presentation of sordellii bacteraemia.

Keywords: Clostridium sordellii; bacteraemia; aortic thrombosis; acute renal failure; renal cortical necrosis

Case 1

An 81 year old woman was admitted from a nursing home with profound lethargy and drowsiness. She had been unwell for two days and had lost her appetite. Until her current illness she had been self caring. There was an underlying history of hypothyroidism, smoker induced chronic airway disease, anxiety neurosis with occasional difficult behaviour (treated with long term thioridazine), and irritable bowel syndrome. She was obsessed with her bowels and on occasions was seen by the staff to be manually self evacuating.

On admission she was stuporous. Her pulse rate was 80/minute, blood pressure was 136/70 mm Hg, temperature was 36.7°C, and oxygen saturation was 90%. She was noted to have particularly long fingernails. System examination was unrevealing. On inspecting the back and buttocks, there was a widespread area of ill defined erythema and induration extending from the labia majora, involving the perineum and natal cleft, and extending up to the buttocks and sacrum. Within the erythema there were areas of haemorrhage and blisters with superficial erosions. Peri-anally frank tissue necrosis was seen, and extending from the anal margin, a 3 cm tear was evident. The anus itself was permanently dilated with faecal incontinence (figs 1 and 2).

Investigations showed a white blood cell count of 19 × 10^6/litre with 92% neutrophils, haemoglobin of 166 g/litre, and platelets at 117 000/cm². The erythrocyte sedimentation rate was greatly raised at 102 mm/1st hour. Activated partial thromboplastin time was 24.3 (control, 27) and fibrinogen was 11.2 mg/litre. C reactive protein was 390 (normal, < 12) mg/litre, urea 53 mmol/litre, and creatinine 502 µmol/litre. Serum amylase was normal (23 U/litre). Abdominal ultrasound showed a small sized right kidney at 7.1 cm and the left kidney measuring 9.4 cm with no evidence of urinary tract dilatation. The gall bladder contained stones. An infrarenal aortic aneurysm measuring 3 cm was identified but the mid and distal aorta were obscured.

A provisional diagnosis of sepsis was made and treatment was started with a combination of parenteral antibiotics in the form of cefuroxime,
metronidazole, and gentamicin. Blood culture was positive with large Gram positive bacilli in the anaerobic bottle after 24 hours incubation (Bactalert microbial detection system). Plates were incubated in a Don Whitley MK 3 anaero-
ic cabinet, and further identification of the iso-
late was performed using ATB 32A (Biomerieux
UK Ltd, Basingstoke, UK) and confirmed as C sordellii. Over the following 24 hours she be-
came hypotensive and less responsive. The lower
abdominal wall was cold to touch and pale.
Both femoral pulses were absent and she later
developed cyanosis of both legs. Her condition contin-
ued to deteriorate with shock and oligo-anuria and she died four days after admission.

Postmortem examination showed the lower
rectum to be oedematous, brown, and discoul-
sed, although the rest of the large bowel was
normal. The peritoneal cavity contained a small amount of clear fluid. The abdominal
aorta was thrombosed from the level of the
renal arteries downwards. The thrombus ex-
tended into the renal arteries and the kidneys
showed changes consistent with cortical necro-
sis.

Case 2
A 12 year old boy with tuberous sclerosis and
associated epilepsy was admitted with a one
week history of cough, fever, and lethargy.
He had been seen five days earlier with signs of an
ear infection in the right ear and started on
amoxicillin. However, his condition deterio-
rated and he was referred to hospital by his
general practitioner. On examination, he ap-
peared unwell but conscious with a pulse rate
of 124/minute, tachypnoea with respiratory
rate of 24/minute, and a temperature of
38.4°C. The right ear appeared red and auro-
scopy revealed evidence of otitis media. A systo-
litic flow murmur was audible over the precor-
dium. The chest was clear to auscultation and
abdominal examination was normal. Investiga-
tions showed a white blood cell count of
10.9 × 10^6/litre with 87% neutrophilia and a
left shift on blood film. C reactive protein was
75 (normal, ≤ 8) mg/litre. A chest radiograph
was normal. Blood cultures taken on admission
revealed a growth of Gram positive bacilli later
to be identified as C sordellii. Intravenous cefo-
taxime was started with gradual improvement;
the fever subsided after five days and he was
discharged home on oral antibiotics.

Discussion
Clostridium sordellii, a Gram positive spore
forming anaerobe, is one of the lesser known
members of the clostridia species. It is ubiqui-
tous in distribution, and is found in soil and as
part of the human intestinal flora. The organ-
ism was first described in 1922 by Sordelli who isolated the bacteria from a patient with postoperative gas gangrene. Since
then, occasional cases of myonecrosis and gas
gangrene have been described.
The pathogenicity of C sordellii was histori-
cally related to its ability to produce a lethal
factor previously known as β-toxin. This toxin
was found to be dermonecrotic and haemor-
rhagic when injected intradermally into rats
and guinea pigs. β-Toxin was subsequently
found to consist of two types of toxins, a lethal
(toxin (LT), a glucotransferase) and a haemor-
rhagic toxin (HT). LT causes local necrosis and
rapidly spreading oedema by increasing
vascular permeability. It is also leucocidal and
causes degranulation of mast cells. HT on the
other hand causes haemorrhagic fluid accumu-
lation in ligated rabbit ileal loop preparations
and is cytotoxic in cell cultures. Both LT and
HT bear antigenic as well as pathophysiological
resemblance to C difficile toxins B and A,
respectively, and antitoxin to C sordellii is used
to neutralise both C difficile toxin A and toxin B
by antigenic crossreactivity. As many as 43 dif-
f erent strains of C sordellii may exist, and not all
are toxicogenic. Considerable interstrain vari-
ation in the production of toxins occurs, possi-
ibly as a result of chromosomal and/or plasmid
mechanisms interacting with local conditions,
and this may account for the differences in
virulence and the clinically less severe cases.

Clostridium sordellii is a recognised animal
pathogen causing enteritis and enterotoxaemia
in sheep and cattle. Unlike humans, however,
fection in animals is thought to be caused by
igestion. Outbreaks among sheep flocks have
been reported recently in our area.

Human infection with C sordellii is rare in the
literature. Most of the cases reported over the
past two decades have been in healthy young
women, usually after delivery or in the
peurperium, often resulting from an infected
episiotomy site and lacerations of the birth
canal. A case of spontaneous endometritis in
a previously healthy 39 year old has also been
reported. Similarly Browdie et al described a
young previously well 23 year old man who
developed C sordellii infection after a deep lac-
eration of his thigh with a saw. Bacteraemia
was not detected in these patients and all these
cases had a terminal outcome. The clinical pic-
ture of the cases described conforms to a simi-
lar pattern, characterised by minimal or absent
pain, absence of fever and rash, a pronounced
neutrophilia and high haematocrit, and pro-
gressive hypotension that rapidly becomes
refractory to treatment. The presentation of
our first patient was similar. Our patient was
also found to have thrombosis of the aorta.
Involvement of a major artery has not been
reported before, although thrombosis of nearby
small vessels has been shown in the postmor-
tem reports of previous cases.

Empyema with associated pneumonia has
been reported previously in three patients, and
in one patient the clinical picture was also
complicated by infective endocarditis. How-
ever, unlike those presenting with myonecrosis
or gynaecological infections, where the out-
come has been universally fatal, respiratory
infections seem to carry a more favourable
prognosis. Our 12 year old patient is the first
adequately reported case of ear infection as a
result of C sordellii.

Clostridial bacteraemia is uncommon. Previ-
ously reported incidences range between 0% and 2.9%. More recently, a 10 year analysis
from a teaching hospital showed that clostridia

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were responsible for <1% of cases of bacteraemia.\textsuperscript{11} Similarly, in our district general hospital over a period of three and a half years (1996–99) we isolated 31 cases, accounting for 0.2% of all cases of bacteraemia. Among clostridia, bacteraemia caused by sordellii species is very rare and only a handful of documented cases have been reported (table 1).\textsuperscript{10,12–20} Bodey \textit{et al} reported their experience with clostridial bacteraemia over a 12 year period in patients with cancer and identified 136 episodes in 135 patients. Of these, only two cases of sordellii bacteraemia were identified.\textsuperscript{12} Our two cases of sordellii among 31 clostridial isolates over a 40 month period gives a high incidence of 6% of sordellii bacteraemia. Similarly, Alpern and Dowell reported a 5.7% incidence based on four isolates of \textit{C sordellii} from 86 patients with non-perfringens clostridial bacteraemia over a seven year period.\textsuperscript{21} However, both the details and outcome of these cases are not completely reported. This suggests that bacteraemia caused by \textit{C sordellii} is probably under-reported.

\textit{Clostridium sordellii} bacteraemia affects all ages and our two cases span the youngest and oldest patients reported. It can occur in previously healthy individuals, as described in a 29 year old postpartum patient and in our two patients.\textsuperscript{13} In our first patient, we suspect introduction of infection occurred by breaching the lower bowel mucosa through manual self evacuation and trauma to the anus. This portal of entry has been described previously with other clostridial infections but only recently for \textit{C sordellii}.\textsuperscript{22} Our second patient presented with an ear infection, and although the organism may have entered the bloodstream from other potential sites, no other site of infection was detected. More commonly, bacteraemia occurs in patients predisposed to infection because of underlying malignancy or immunosuppression.\textsuperscript{17} Of the cases reported in the literature, four had underlying malignancy and two were immunocompromised; one on immunosuppressants having recently undergone liver transplantation and the other with functional asplenia. Two other patients had severe alcoholism (table 1). In two patients,\textsuperscript{18,19} bacteraemia followed a diagnostic procedure, namely a transcutaneous liver biopsy\textsuperscript{16,17} and transrectal prostatic biopsy.\textsuperscript{17}

Pseudobacteraemia involving \textit{C sordellii} that occurred as a result of using contaminated tincture of thimerosal during subculturing in a clinical microbiology laboratory has been described,\textsuperscript{13} raising the important issue of implementing appropriate safeguards in the routine processing of culture material.

\textit{Clostridium sordellii} bacteraemia carries a high mortality. Among the 12 cases adequately reported in the literature, the mortality is 67%. Reviewing each of the reported cases in detail suggests that both the clinical course of illness and outcome is dependent on the site of infection. In the case reported by Cuninffe,\textsuperscript{17} the 55 year old patient had developed radiation colitis after radiotherapy and cystectomy for an advanced poorly differentiated bladder carcinoma. He presented with evidence of intra-abdominal infection by a gas producing organism and a perforated viscus, and necropsy showed a haemorrhagic and necrotic descending colon. Similarly, the first patient described briefly by Bodey \textit{et al} had colonic pathology.\textsuperscript{12} He was known to have metastatic melanoma to the colon and presented in septic shock and died within 24 hours. The 48 year old woman reported by Morey \textit{et al} developed shock and died 12 hours after a liver biopsy.\textsuperscript{17} The procedure was undertaken nine days after a liver transplant for primary biliary cirrhosis and the patient was on immunosuppressants. Necropsy revealed putrid exudates containing gas bubbles in the liver, pancreas, spleen, and myocardinum denoting widespread septicemia that probably antedated the procedure. Bitti \textit{et al} described a 29 year old woman who developed a retroperitoneal infection two days after a Caesarian section.\textsuperscript{19} More recently, Borer \textit{et al} reported a fatal case of a 73 year old man with metastatic cancer of the prostate who became acutely unwell with perirectal ischiorectal abscess formation 24 hours after a transrectal biopsy of the prostate.\textsuperscript{15} \textit{Clostridium sordellii} was isolated from both blood cultures and abscess fluid. These cases along with our 81 year old woman who had no malignancy or evidence of immunosuppression demonstrate that sordellii bacteraemia caused by visceral or internal

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Table 1  Reported cases of \textit{Clostridium sordellii} bacteraemia in the literature

<table>
<thead>
<tr>
<th>Ref</th>
<th>Age/Sex</th>
<th>Underlying condition</th>
<th>Presenting illness</th>
<th>Presumed portal of entry</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>18/M</td>
<td>Acute alcoholic intoxication</td>
<td>Cardiorespiratory arrest, myonecrosis, necrotic-haemorrhagic pancreatitis</td>
<td>GI/colon</td>
<td>Fatal</td>
</tr>
<tr>
<td>10</td>
<td>61/M</td>
<td>Rheumatic valvular disease</td>
<td>Pneumonitis, empyema</td>
<td>Oropharynx</td>
<td>Survived</td>
</tr>
<tr>
<td>12</td>
<td>54/M</td>
<td>Metastatic melanoma to colon</td>
<td>Septic shock</td>
<td>GI/colon</td>
<td>Fatal</td>
</tr>
<tr>
<td>12</td>
<td>40/F</td>
<td>Genitourinary malignancy</td>
<td>Postoperative wound infection</td>
<td>Unknown</td>
<td>Survived</td>
</tr>
<tr>
<td>15</td>
<td>37/M</td>
<td>IV drug abuse, sickle cell thalassaemia, inflammatory bowel disease, functional asplenia</td>
<td>Pneumonitis, back pain, bleeding from rectum</td>
<td>GI/Colon</td>
<td>Survived</td>
</tr>
<tr>
<td>16</td>
<td>48/F</td>
<td>Liver transplantation, immunosuppressive treatment</td>
<td>Septic shock</td>
<td>GI/colon</td>
<td>Fatal</td>
</tr>
<tr>
<td>17</td>
<td>55/M</td>
<td>Transitional cell carcinoma of the bladder, radiation colitis</td>
<td>Intra-abdominal sepsis, perforated viscus</td>
<td>GI/Colon</td>
<td>Fatal</td>
</tr>
<tr>
<td>13</td>
<td>29/F</td>
<td>Caesarian section</td>
<td>Septic shock, retroperitoneal sepsis</td>
<td>GI/Colon</td>
<td>Fatal</td>
</tr>
<tr>
<td>18</td>
<td>37/M</td>
<td>Chronic alcoholism/liver cirrhosis</td>
<td>Haematemesis, peritonitis, intravascular haemolysis</td>
<td>GI</td>
<td>Fatal</td>
</tr>
<tr>
<td>19</td>
<td>73/M</td>
<td>Metastatic prostate cancer</td>
<td>Perirectal and ischiorectal abscess</td>
<td>GI/Rectum</td>
<td>Fatal</td>
</tr>
<tr>
<td>Case 1</td>
<td>81/F</td>
<td>Traumatic self evacuation</td>
<td>Widespread cellulitis, perirectal necrosis</td>
<td>GI/Rectum</td>
<td>Fatal</td>
</tr>
<tr>
<td>Case 2</td>
<td>12/M</td>
<td>Epilepsy</td>
<td>Ear infection</td>
<td>Ear</td>
<td>Survived</td>
</tr>
</tbody>
</table>

Four other cases of \textit{C sordellii} bacteraemia have been reported but the description is incomplete and outcome not reported.\textsuperscript{15} Two further cases of endocarditis have been reported in one series but no details were provided.\textsuperscript{20} No further details given.
organ involvement is invariably fatal, regardless of underlying pathology and immune status. This might be caused, at least in part, by the paucity of initial signs of infection (concealed infection), which result in delayed presentation.

In contrast, superficial and cutaneous infections, even when accompanied by bacteraemia, have a favourable prognosis. This can be seen by the outcome of the 40 year old woman with postoperative wound infection and genitourinary malignancy reported by Bodey et al., the intravenous drug abuser reported by Spera et al., and our 12 year old patient. The successful outcome in these cases might be related to early identification and institution of appropriate antibiotic treatment.

The role of immunotherapy in sordellii infections is unknown. Whereas antitoxin treatment is recommended for *C botulinum* infection, and recommendations for specific immunoprophylaxis against *C tetani* depend on the patient’s previous immunisation history and the nature of the wound, *C sordellii* antitoxin has never been tested for potential efficacy by parenteral or enteral administration, and immunotherapy might have a plausible role in the overall management of these critically ill patients.

In conclusion, *C sordellii* is a rare infection, but one where a high index of suspicion is required to improve outcome. This should allow early identification of the infection and prompt the commencement of treatment.


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