MRSA enteritis causing a high stoma output in the early postoperative phase after bowel surgery

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ABSTRACT

INTRODUCTION Nosocomial MRSA infection has become an important healthcare issue. We present 6 cases of MRSA enteritis, acquired following bowel surgery and ileostomy formation.

PATIENTS AND METHODS The data set was obtained from the experience of one consultant surgeon over 6 years in one medical centre. The clinical features and course of six patients that developed MRSA enteritis postoperatively were obtained through review of case notes and laboratory data.

RESULTS Four male and two female patients (age range, 22–80 years) developed a clinical syndrome postoperatively requiring treatment within the high dependency unit. Three developed respiratory distress syndrome, and one died from multi-organ failure. Exploratory laparotomy carried out in three patients was negative. All patients were MRSA-negative on admission but had swabs positive for MRSA from ileostomy site postoperatively. All of the three patients who had ileostomy effluent cultured for MRSA had positive results.

DISCUSSION Fever, abdominal pain, distension and high stoma output in the early postoperative period following bowel surgery should alert the clinician to the possibility of MRSA enteritis. Patients require aggressive resuscitation and culture of ileostomy effluent for MRSA. Exploratory laparotomy has no obvious benefits. As MRSA enteritis has the potential to be a lethally effective disseminator of MRSA, such clinical features should prompt early instigation of appropriate infection control practices.

KEYWORDS

Enteritis/microbiology – Methicillin resistance – Staphylococcal infection – Ileostomies

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important nosocomial pathogen¹ that has become a significant healthcare issue.² As a result of selective antibiotic administration, there has been a world-wide exponential increase in the proportion of infections.³

Humans are a natural reservoir of *S. aureus* with colonisation occurring in intermittently in up to 30–50% of healthy adults.⁴ It can be an occasional normal inhabitant of the gastrointestinal tract (GIT) in up to 10% of healthy people⁵ and is rarely considered as a cause of enteritis because its growth and competitiveness is limited by the normal micro-organisms present in the intestinal flora.

We present our clinical experience of small bowel MRSA enteritis in the early postoperative phase in patients who have ileostomies. This is the first such case series to be presented in the literature.

Patients and Methods

Our data set was based upon the experience of one consultant surgeon over a period of 6 years in one medical centre. We

examined the clinical features of 6 patients who developed postoperative MRSA small bowel enteritis between 1998 and 2004 (Table 1) from respective case notes.

There were four male and two female patients with an age range from 22–80 years (mean age, 51 years). All patients had an American Society of Anesthesiologists (ASA) score of 2. No patients were on proton pump inhibitors or H₂-antagonists or had a history of MRSA prior to elective admission.

Nasogastric tubes were inserted during the peri-operative period and removed within 24 h. Cefuroxime 750 mg and metronidazole 500 mg were given at induction and continued in the postoperative period. The patients were placed on the open ward prior to development of symptoms.

All patients developed a rise in temperature postoperatively and a full septic screen was performed. This included bacterial swabs of the skin and stoma swabs, as well as blood, urine and throat cultures. These were repeated through out the diseased state.

Faecal effluent from the ileostomy was investigated for *Clostridia difficile*, *Salmonella* spp., *Shigella* spp.,

Table 1 The underlying pathological disease and operation performed

Patient	Year	Age (years)	Sex	Underlying pathology	Operation	Ileostomy
1	1998	60	M	UCCRC	Refashioning of ileostomy	Yes
2	2000	64	M	Rectal cancer	Low anterior resection and defunctioning stoma	Yes
3	2000	28	F	FAP	Defunctioning ileostomy formation (previous subtotal colectomy and IRA)	Yes
4	2001	63	M	Rectal cancer	Low anterior resection and defunctioning stoma	Yes
5	2004	22	F	Crohn's disease	Adhesionolysis and refashioning of stoma	Yes
6	2004	80	M	Ulcerative colitis	Restorative proctocolectomy with defunctioning stoma	Yes

UCCRC, ulcerative colitis colorectal cancer; FAP, familial adenomatous polyposis coli; IRA, ileo-rectal anastomosis.

Campylobacter spp., *Cryptosporidium* spp., *Escherichia coli* and for faecal viruses and parasites. This was the standard microbiology protocol in our institute for the identification of stool pathogens. This protocol was changed to include MRSA pathogens after the third case of small bowel enteritis in 2001. Specimens were cultured according to standard techniques.

Radiological studies included plain radiographs, ultrasonography, contrast computerised tomography (CT) and a gastrograffin enema. Three patients underwent explorative laparotomies.

Results

Clinical manifestation

The time to onset of disease after surgery was two (3/6 patients) and five (3/6 patients) days. All patients presented with a similar syndrome of symptoms including acute onset

of fever, abdominal cramps and distension and a high ileostomy output (Table 2). The time taken for the ileostomy output to decrease to less than 1 litre in 24 h was 7–40 days (median, 18.5 days).

The odourless effluent consisted of a watery brownish green frothy fluid with copious amounts of mucus (Fig. 1).

All patients required treatment within the high dependency unit for monitoring and replacement fluid therapy. Three patients developed respiratory distress syndrome requiring ventilatory support. Of these three patients, one progressed to multi-organ failure and one ultimately died at day 49. No patient developed any dermatological manifestations such as rashes. We measured length of hospital stay as an outcome measure (Table 3). Patients were discharged home at 11–44 days. There was a single mortality at 49 days.

Radiological investigations and exploratory laparotomy

Early investigations of all patients included plain radiographs of the chest and the abdomen, ultrasound,

Table 2 Clinical signs

Patient	Year	Postoperative day	Temperature maximum (°C)	Associated stoma output/day (ml/24-h)	Max stoma output during disease (ml/24-h)	Postoperative day stoma output is < 1 l
1	1998	5	38	1225	3200	Not applicable/mortality
2	2000	2	38.3	1525	5855	13
3	2000	5	38	1842	4980	No record
4	2001	5	38.8	2695	7940	18
5	2004	2	40.5	2030	3110	7
6	2004	2	38.5	1645	6150	40

Table 3 Length of hospital stay as an outcome measure

Patient	Year	MRSA found in ileostomy effluent	Exploratory laparotomy and result	Length of hospital stay (days)
1	1998	Not tested	Yes, negative	49 (mortality)
2	2000	Not tested	No	44
3	2000	Not tested	Yes, negative	150
4	2001	Yes	No	22
5	2004	Yes	No	11
6	2004	Yes	Yes, negative	90

contrast computerised tomography of the abdomen and pelvis, and, in one case, a gastrograffin enema. The common and only positive finding in all cases from these investigations was the presence of dilated small bowel. No cause for the underlying sepsis was noted in the three patients who had an exploratory laparotomy.

Bacteriological investigations

No patient was known to have MRSA infection prior to surgery. Results of MRSA screen at onset of disease showed all patients grew MRSA from the bacterial swab taken from their ileostomy. The results of MRSA culture from specimens taken from other sites was variable (Table 4). With the change in stool bacterial culture protocol, consecutive patients with suspected clinical manifestations of small bowel enteritis had ileostomy effluent examined for MRSA. These three consecutive patients had ileostomy effluent which exhibited distinctive Gram-stain appearance together with a heavy growth of MRSA in the absence of other bowel pathogens.

Figure 1 Specimen of ileostomy effluent from patient with MRSA enteritis (culture positive for MRSA).

Haematological and biochemical findings

Pre-operative blood results FBC, LFT, creatinine, urea and electrolytes for all patients were within normal limits. Results were extracted at the early onset of the disease state. At the onset of the disease (Table 5), the leukocyte count ranged from $2.7\text{--}17.5 \times 10^9/\text{l}$. Platelet count range was

Table 4 MRSA screen and results at onset of disease

Patient	Year	Routine effluent MRSA screen	Stoma	Stool	Blood	Cannula	Throat	Nose	Perineum
1	1998	N	Y	N	N	N	N	N	N
2	2000	N	Y	N	N	Y	Y	Y	Y
3	2000	N	Y	N	N	N	N	N	N
4	2001	Y	Y	Y	N	N	N	N	N
5	2004	Y	Y	Y	N	N	N	N	N
6	2004	Y	Y	Y	N	N	N	Y	Y

Y, yes; N, no.

Table 5 Haematological and biochemical markers during first few days following onset of disease

Patient	1	2	3	4	5	6
Haemoglobin (g/dl)	10.5–11.1	8.0–10.5	11.6–15.1	13.3–13.5	8.4–9.6	9.2–13.2
Leukocyte ($\times 10^9/l$)	13–15	11.96–14.86	7.64–11.08	11.5–17.52	3.0–7.84	2.7–9.72
Platelets ($\times 10^9/l$)	290–354	263–387	225–431	223–328	165–192	145–231
Na (mmol/l)	131–138	134–137	135–141	136–139	135–144	143–147
K (mmol/l)	4.3–4.5	4.0–5.2	3.8–5.9	3.2–3.5	4.3–4.5	3.6–3.9
Urea (mmol/l)	3.8–4.2	2.1–5.6	1.5–10.1	3.0–4.6	3.3–7.2	6.7–10.2
Creatinine ($\mu\text{mol/l}$)	80–101	72–88	59–118	72–81	74–104	68–83
Albumin (g/l)	26–34	25–29	27–36	28–29	16–32	26–30
Bilirubin ($\mu\text{mol/l}$)	7–29	10–27	9–28	5–9	10–24	24–41
ALP (U/l)	64–201	7–21	56–87	54–59	17–81	37–51
AST (U/l)	26–56	16–21	25–47	16–20	19–54	40–80
ALT (U/l)	23–92	2–41	23–98	11–14	6–37	40–67

ALP, alkaline phosphatase; AST, aspartate transferase;

ALT, alanine transferase.

from $145\text{--}387 \times 10^9/l$ and was within normal limits in all cases. The total bilirubin level was mildly elevated in five cases. One case had an elevated alkaline phosphatase level, whilst aspartate transaminase and alanine transaminase were not found to be deranged. Plasma albumin was below normal limits in all cases. The serum creatinine, urea and electrolytes were, surprisingly, within normal limits in the early stages of disease.

Discussion

The first reported case of MRSA enteritis was in the early 1980s.⁶ Since this time, the majority of case reports and series have arisen from Japan, where it appears that MRSA enteritis is associated with gastric surgery and antibiotic use, that allows for the colonisation and subsequent overgrowth of MRSA.^{7–9}

The biological mechanism by which MRSA enteritis is lethal is not completely understood. A murine model suggests that the production of endotoxin and the translocation of *E. coli* are important in the fatality of MRSA enteritic rats;¹⁰ in humans, it has been shown that MRSA can produce endo- and exotoxins which subsequently translocate across the GIT mucosa into the bloodstream thus inducing various biological responses,¹¹ such as production of interleukins 1 and 2 and tumour necrosis factor- α (TNF- α).

There are no previous reports of patients with ileostomies after bowel surgery developing small bowel MRSA enteritis. However, certain clinical settings such as

prolonged antibiotic treatment (more than 24 h after surgery) and the lack of peristalsis after a laparotomy may give the MRSA an opportunity to invade the intestinal tract more easily and cause enteritis.¹²

The two possible modes of MRSA transmission include the antegrade, through a nasogastric tube or retrograde migration through the ileostomy spout. The nasogastric tube may become contaminated as it passes through the nasal nares where *S. aureus* is a significant inhabitant in 15–44% of the general population.¹⁵ Within the stomach, mucosal trauma can occur leading to a breach in the gastrointestinal barrier, allowing *S. aureus* access to adjacent tissue or the bloodstream to cause sepsis.¹⁴

MRSA small bowel enteritis is characterised clinically by an acute onset in the early postoperative phase of fever, small bowel colic, abdominal distension and the production of a frothy, brownish-green, mucous watery effluent. The resulting systemic inflammatory response syndrome is associated with a high ileostomy output and associated sepsis that can lead to severe dehydration, shock and eventual multi-organ failure and, in some circumstances, death. This clinical scenario should alert the clinician to consider the possibility of MRSA small bowel enteritis at an early stage.

There has been considerable interest in recent years as to the specific phenotypes and genotypes of the organisms causing MRSA enteritis. Such information is of critical importance, not just for epidemiological surveillance purposes but also because identification of the particular strains involved may allow development of effective new

treatment modalities. In addition, accurate characterisation of isolates may assist in the identification of different sources of infection. Indeed, support for the theory that the organisms causing MRSA enteritis originate from the respiratory tract flora comes from the finding that phenotypic patterns were similar in isolates obtained simultaneously from the respiratory tract and faeces of affected patients.¹⁷

The main phenotypic markers used for identification of MRSA strains are staphylococcal enterotoxin (SE) typing (A–F) and measurement of toxic shock syndrome toxin-1 (TSST-1) titres.¹⁸ Genotypic characterisation has also been carried out using polymerase chain reaction (PCR) and pulsed field gel electrophoresis (PFGE).¹⁹ A recent study compared the genotypes and phenotypes of 12 MRSA enteritis-causing isolates with those of 186 non-enteritis isolates.²⁰ It was found that only 7 of the 186 non-enteritis isolates had characteristics indistinct from the enteritis isolates. Eight out of the 12 enteritis isolates showed increased production of the enterotoxin SE-A and TSST-1 when compared to the non-enteritis isolates. In addition, although the enteritis isolates all carried the *ent-C* gene which codes for SE-C, only three of them actually produced SE-C, whereas 157/187 of the non-enteritis isolates produced SE-C but not SE-A. The finding that MRSA enteritis isolates show increased production of SE-A and TSST-1 is supported by other studies.^{11,21} However, they also found that the majority of enteritis isolates were actually SE-A/SE-C co-producing strains. This may represent genetic variation in different centres. Since the majority of studies to date have been carried out on isolates obtained from Japanese hospitals, it would be interesting to see whether isolates from UK hospitals are similar in nature.

Genotypic and phenotypic typing of the isolates obtained from the patients in this study was not carried out at our centre. However, in view of the importance of accurate strain identification for epidemiological and treatment purposes, this is an important consideration for the future.

Therapy can be directed towards toxins and cytokines and has been the key in the management of postoperative MRSA enteritis.¹⁵ One drug used commonly to treat MRSA enteritis is vancomycin, which gives an immediate clinical response that is safe and effective.¹⁶ Administration of glucocorticoid hormone and γ -globulin was found to benefit patients with MRSA enteritis who developed ARDS.¹¹ γ -Globulins and fresh frozen plasma are also recommended to prevent and treat the toxic shock associated with MRSA enteritis because of the high titre of antibody to TSS-1.

Patients must be isolated and aggressive supportive treatment commenced to alleviate and/or prevent septic and hypovolaemic shock whilst isolating the pathogen. Radiological investigations should be performed to identify and exclude other causes of sepsis but we feel there should be a high threshold for exploratory laparotomies. None of

our patients gained benefit from exploratory laparotomies. In fact, all had significant morbidity, and one patient died. A septic screen must include the culture of the ileostomy effluent, but the results of this should not delay the instigation of treatment.

Conclusions

Reports on MRSA small bowel enteritis after gastrointestinal surgery are limited, possibly because of under-reporting secondary to failure of clinical diagnosis and of failure to send ileostomy effluent for MRSA culture routinely. It should be recognised that the presence of MRSA enteritis has the potential to be a lethally efficient disseminator of infection, in particular in the HDU and ITU setting.

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References

- Emori TG, Gaynes RP. An overview of nosocomial infections, including the role of the microbiology laboratory. *Clin Microbiol Rev* 1993; **6**: 428–42.
- Crowcroft NS, Catchpole M. Mortality from methicillin resistant *Staphylococcus aureus* in England and Wales: analysis of death certificates. *BMJ* 2002; **325**: 1390–1.
- Speller DC, Johnson AP, James D, Marples RR, Charlett A, George RC. Resistance to methicillin and other antibiotics in isolates of *Staphylococcus aureus* from blood and cerebrospinal fluid, England and Wales, 1989–95. *Lancet* 1997; **350**: 323–5.
- Casewell MW, Hill RL. The carrier state: methicillin-resistant *Staphylococcus aureus*. *J Antimicrob Chemother* 1986; **18** (Suppl A): 1–12.
- Christie CD, Lynch-Ballard E, Andiman WA. Staphylococcal enterocolitis revisited: cytotoxic properties of *Staphylococcus aureus* from a neonate with enterocolitis. *Pediatr Infect Dis J* 1988; **7**: 791–5.
- Scopetti F, Orefici G, Biondi F, Benini F. *Staphylococcus aureus* resistant to methicillin and gentamicin as a cause of outbreak of epidemic enteritis in a hospital. *Boll Ist Sieroter (Milan)* 1983; **62**: 406–11.
- Yoshida D, Fukunari H, Hojo I, Kitago K, Ito M, Nihei Z *et al.* Enterocolitis due to methicillin-resistant *Staphylococcus aureus* – report of two cases. *Bull Tokyo Med Dent Univ* 1992; **39**: 31–4.
- Milton-Thompson GJ, Lightfoot NF, Ahmet Z, Hunt RH, Barnard J, Bavin PM *et al.* Intragastric acidity, bacteria, nitrite, and *N*-nitroso compounds before, during, and after cimetidine treatment. *Lancet* 1982; **1**: 1091–5.
- Ruddell WS, Axon AT, Findlay JM, Bartholomew BA, Hill MJ. Effect of cimetidine on the gastric bacterial flora. *Lancet* 1980; **1**: 672–4.
- Nakamura Y, Aramaki Y, Kakiuchi T. A mouse model for postoperative fatal enteritis due to *Staphylococcus* infection. *J Surg Res* 2001; **96**: 35–43.
- Kodama T, Santo T, Yokoyama T, Takesue Y, Hiyama E, Imamura Y *et al.* Postoperative enteritis caused by methicillin-resistant *Staphylococcus aureus*. *Surg Today* 1997; **27**: 816–25.

12. Gray JD, Shiner M. Influence of gastric pH on gastric and jejunal flora. *Gut* 1967; **8**: 74–81.
13. Williams RE. Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. *Bacteriol Rev* 1963; **27**: 56–71.
14. Moss JP. Historical and current perspectives on surgical drainage. *Surg Gynecol Obstet* 1981; **152**: 517–27.
15. Garner JS. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1996; **17**: 53–80.
16. Takeuchi K, Tsuzuki Y, Ando T, Sekihara M, Hara T, Yoshikawa M *et al*. Clinical studies of enteritis caused by methicillin-resistant *Staphylococcus aureus*. *Eur J Surg* 2001; **167**: 293–6.
17. Watanabe H, Masaki H, Asuh N, Watanabe K, Oishi K, Kobayashi S *et al*. Enterocolitis caused by methicillin resistant *Staphylococcus aureus*: molecular characterisation of respiratory and digestive tract isolates. *Micobiol Immunol* 2001; **45**: 629–34.
18. Schmitz F-J, MacKensie CR, Geisel R, Wagner S, Idel H, Verhoef J *et al*. Enterotoxin and toxic shock syndrome toxin-1 production of methicillin resistant and methicillin sensitive *Staphylococcus aureus* strains. *Eur J Epidemiol* 1997; **13**: 699–708.
19. Saito K, Seki K, Ohara T, Shimauchi C, Honma Y, Hayashi M *et al*. Epidemiological typing of methicillin resistant *Staphylococcus aureus* in neonate intensive care units using pulsed-field gel electrophoresis. *Microbiol Immunol* 1998; **42**: 723–9.
20. Okii K, Hiyama E, Takesue Y, Kodaira M, Sueda T, Yokoyama T. Molecular epidemiology of enteritis-causing methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 2006; **62**: 37–43.
21. Takesue Y, Yokoyama T, Kodama T, Santou T, Nakamitsu A, Murakami Y *et al*. A study on post-operative enteritis caused by methicillin resistant *Staphylococcus aureus*. *Surg Today* 1993; **23**: 4–8.