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New Methods of Control Against Postoperative Methicillin-Resistant *Staphylococcus aureus* Infection

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Abstract: The incidence of postoperative infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in Japan has been increasing dramatically. In March 1990, we assigned special doctors in infection control (infection control doctor, ICD), and defined comprehensive controls against MRSA infection. A total of 3536 cases of digestive tract surgery performed at our department were studied during the period between September 1987 and August 1997. We changed the use of antibiotics to prevent postoperative infection. Cefazolin (CEZ) was employed for surgery of the upper digestive tract, including esophagus, stomach, duodenum, and gallbladder. Cefotiam (CTM) was employed for surgery of the lower digestive tract, liver, and pancreas. In esophageal resection, the tracheal tube was extracted during the early postoperative period, and for cervical esophagogastroanastomosis, the autosuture was changed to layer-to-layer anastomosis. We have achieved successful control of postoperative MRSA infection, the incidence having decreased to 0.3% (9/2703). In conclusion, our methods of control against postoperative MRSA infection implies that comprehensive measures of prevention, including the reviewed specification and usage of antibiotics and operation management, have been well implemented. This value is the lowest and the first of any domestic hospital or institute in Japan, suggesting a continued and significant decrease.

Key Words: MRSA infection, digestive tract surgery, postoperative infection, infection control doctor

Introduction

Since the late 1980s in Japan, the number of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) has increased remarkably in many medical fields.[1–3] From its initial manifestation, a hospital-acquired infection was suspected as the etiology and measures to prevent this infection were taken in most domestic hospitals and institutes; however, there have been few reports of continued and significant decreases in the incidence of MRSA infections during this decade.

In September 1987, a case of postoperative MRSA enteritis occurred in our hospital on which occasion, we initiated management to prevent cross-infection of this hospital-acquired infection. Nevertheless, this failed to stop a significant increase in the number of cases of MRSA infections. In March 1990, we assigned specialist doctors in infection control, known as infection control doctors (ICD), who revised operative management strategies and improved the usage of antibiotics. In the 7 years since, we have achieved successful control of postoperative MRSA infection, reaching a decrease in the incidence of this infection to 0.3% (9/2703) of all cases of digestive tract surgery. This value is the lowest of any domestic hospital or institute in Japan, suggesting a continued and significant decrease. This report describes the decreasing trend of postoperative MRSA infections, our successful control strategies, the current nosocomial etiology of MRSA infection in Japan, and the problems associated with the control of postoperative MRSA infection.

Patients and Methods

We reviewed 3536 cases of digestive tract surgery performed at our department during the period between September 1987 and August 1997. The cases were divided into semiannual-period groups, and the following items were studied: the overall incidence of postoperative infections, the sites of infections, the incidence of postoperative MRSA infection, and the organisms isolated from the infection sites.

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Table 1. Changes in methods of control to prevent hospital infection

	Former period	Latter period
Thorough washing of hands	———	———
Isolating MRSA patients		
• only infected patients	———	
• isolating asymptomatic infected patients	———	
• isolating only patients with MRSA detected in the respiratory organs or open wounds		———
Periodic fumigation of the recovery room	———	
Checking for MRSA carriers among staff members	——— Only outbreak	
Checking for MRSA carriers within the hospital environment	——— Only outbreak	
Checking for MRSA carriers among patients	——— Only patient transferees from other wards or hospitals	
Enforcing stringent requirements of patients' eligibility to be admitted into the recovery room		———
Designating appropriate postoperative antibacterial drugs		———
Revising postoperative management and operative methods		———

MRSA, methicillin-resistant *Staphylococcus aureus*

MRSA was determined by standard methodology established by the Japanese Society of Chemotherapy for the microdilution antimicrobial susceptibility testing of bacteria.[4]

Our measures to prevent postoperative MRSA infection, as shown in Table 1, began with the strict requirements that all medical staff scrub with an antiseptic solution and that the usage of third-generation cefem family antibiotics was limited. Since March 1988, recovery rooms in the surgical ward have been periodically sterilized and patients with MRSA have been isolated. Between March and August 1990, the entrance to the recovery rooms in the surgical ward was strictly standardized, methods to control postoperative MRSA infection that focused on cross-infection were discussed again, and the antibiotics used in operative management were specified according to each organ treated by surgical procedures. Furthermore, strategies of operative management to reduce the high incidence of postoperative MRSA infection were improved.

To reduce the risk of MRSA contaminating the recovery rooms of the surgical ward, patients with advanced-stage disease or little expectation of recovery, those with a tracheotomy and/or on respiratory support, those suspected of being infected with any bacteria, those diagnosed with mental disorders, and patients not allocated a bed due to all beds being occupied by other patients, were banned from entering the recovery rooms of the surgery department (Table 2). The isolation of patients with MRSA was classified into either a complete or a relative group (Table 3). The complete group included patients with MRSA isolates derived from sputum or the respiratory tract, regardless of their infectious symptoms, patients with acute MRSA enteritis, and patients defined as being a source of MRSA hospital-acquired infection but who would not cooperate with our control procedures. The relative group included patients with MRSA isolates derived from a wound or drained fluid. Drainage was defined

Table 2. Standards for patients admitted to the recovery room

- Patients eligible for admission to the recovery room
  (1) Those who have undergone surgery under general anesthesia
  (2) Those transferred from the ICU following surgery
  (3) Transferred patients requiring constant observation following surgery
- Patients not allowed to be admitted to the recovery room
  (1) Terminally ill patients with no hope of recovery
  (2) Those with a tracheotomy or respiratory support
  (3) Those suffering from contagious diseases
  (4) Those suffering from mental illness
  (5) Those requested temporary admission into the recovery room due to full bed occupancy in the ward

Table 3. Definition of the adoptability of isolating patients detected with MRSA

A: Complete adoptability
— Patients in whom MRSA was detected in sputum or respiratory tract secretion cultures, regardless of whether infection symptoms were present
— Patients suffering from acute stage MRSA enterocolitis
— Patients who contracted hospital infection due to a lack of understanding and/or cooperation

B: Relative adoptability
— Patients in whom MRSA was detected in wound or drain cultures, but in whom closed drainage was possible
— Patients with minimal secretions

Table 4. Designation of prophylactic or therapeutic antibacterial drugs

Operation	Prophylactic drugs	Therapeutic drugs
Upper G.I. gallbladder	First-gen. cefems such as CEZ	Second-gen. cefems such as CTM, CZOP, FMOX ↓ Carbapenems such as IPM/CS, PAPM/BP
Lower G.I. liver, pancreas	Second-gen. cefems such as CTM	Third-gen. cefems such as CPR, CZOP, FMOX ↓ Carbapenems such as IPM/CS, PAPM/BP
Peritonitis		Third-gen. cefems such as CPR, CZOP, FMOX ↓ Carbapenems such as IPM/CS, PAPM/BP

gen., generation; CEZ, cefazolin; CTM, cefotiam; CPR, cefpirome; CZOP, cefozopran; FMOX, flomoxef; IPM/CS, imipenem/cilastatin; PAPM/BP, panipenem/betamipron

as closed drainage with a small volume of drained fluid.

The antibiotics used in the perioperative phase were specified according to each organ treated by a surgical procedure. The ICDs monitored the specification and usage of the antibiotics (Table 4). To prevent postoperative MRSA infection, cefem antibiotics were administered during surgical treatment. Cefazolin (CEZ), which is a first-generation antibiotic of the cefem family, was employed for surgery of the upper digestive tract, including esophagus, stomach, duodenum, and gallbladder, while cefotiam (CTM), a second-generation antibiotic of the cefem family, was employed for surgery of the lower digestive tract, liver, and pancreas.

For colon and rectum cancer, the traditional antibacterial colon preparation, comprising kanamycin (200 mg) and metronidazole (50 mg) administered for 4 days prior to surgery, was discontinued.[5] Instead, a mechanical colon preparation was employed to wash out the bowel with the abluent.

Patients undergoing surgery for esophageal cancer had the highest incidence of postoperative MRSA infection. Fresh frozen plasma (FFP) was administered continuously during the early stage of these surgical procedures. Moreover, the tracheal tube was extracted during the early postoperative period, and the course of spontaneous respiration was controlled. For cervical esophagogastroanastomosis, the autosuture was changed to layer-to-layer anastomosis, according to procedures by Akiyama.[6]

All results were statistically analyzed by the *t*-method and a value of $P < 0.01$ was considered to be significant.

Results

The incidence of postoperative infections peaked at 16.8% during the period from March 1988 to August 1988 (Fig. 1), following which it decreased to between 9.6% and 12.6%, suggesting no significant difference. The incidence of postoperative MRSA infection also peaked at 6.6% during the period from March 1998 to August 1988, decreasing to within 3% up until February 1990, following which it decreased significantly and has since remained low at 0%–1.8%. The degree of MRSA organisms isolated from postoperative site of infection was compared between the period from September 1987 to February 1990, being the former period, and the period from March 1990, to the present, being the latter period. The degrees were 34.2% and 1.3%, respectively, this difference being significant. The degree of *Pseudomonas aeruginosa* isolated increased from 33.7% to 45.1%, suggesting no significant difference.

Regarding the site of postoperative MRSA infection, during the former period there were 11 cases of MRSA enteritis, 6 cases of respiratory tract infection, 6 cases of intra-abdominal abscess, 3 cases of wound infection, 2 cases of catheter sepsis, and 1 case of urinary tract infection, whereas during the latter period there were 3 cases of intra-abdominal abscess, 2 cases of MRSA enteritis, and 2 cases of respiratory tract infection.

The time that elapsed until postoperative MRSA infection was diagnosed ranged from 2.4 days to 31.8 days, which was the average period after surgery. In the latter period, the time of 31.8 days implied only the existence of a late-stage infection in the abdominal cavity resulting from suture insufficiency.

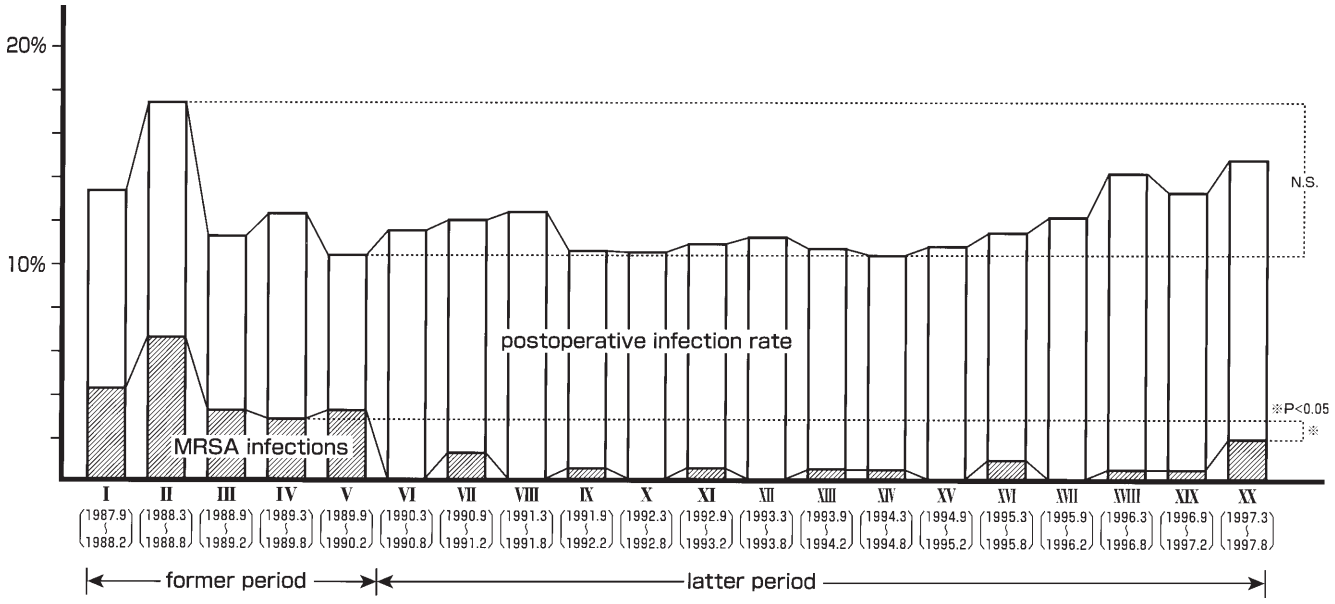

Fig. 1. Changes in the incidence of postoperative infections Sept. 1987–Aug. 1997

The antibiotics used to prevent MRSA infection in patients undergoing surgery for gastric cancer were reviewed. In the former period, patients were given the single administration of CTM or cefmetazole (CMZ), being second-generation cefem antibiotics, latamoxicef (LMOX) or cefmenoxim (CMX), being third-generation cefem antibiotics, and/or the combined administration of an aminogliycoside and the above-mentioned cefem antibiotics, for an average period of 11.2 days. Conversely, in the latter period, only CEZ, a first-generation cefem antibiotic, has been administered, and the average administration period has decreased to 3.1 days, suggesting a significant difference.

Discussion

Since the late 1980s in Japan, the incidence of infections caused by MRSA has been increasing in many medical fields, causing great concern.[1–3] Notably, many cases of MRSA enteritis have occurred following surgery of the upper digestive tract.[7–9] According to research conducted twice on a nationwide questionnaire, mortality rates were 23.1% and 11.8%, respectively, being significantly high.[10,11] Moreover, social problems associated with MRSA enteritis, such as litigation and/or attention from the mass media, have caused a sensation in Japan.

From the onset, a hospital-acquired infection was suspected as the etiology of MRSA, and measures to prevent this infection or to isolate patients with MRSA were discussed intensively. However, the most effective measures of control yet remain to be established, as various factors unique to Japan have combined to produce the results. In most domestic hospitals and institutes, attempts to reduce the incidence of MRSA hospital-acquired infections and to isolate patients with MRSA are taken very seriously and have been preceded by trial and error.

The introduction of measures to prevent MRSA infection has been inhibited by the medical service system in Japan which includes such problems as an insufficiency of single rooms, a high cost of instituting measures to prevent MRSA hospital-acquired infection, the system of national health insurance (NHI), and a lack of guidelines for the usage and specification of antibiotics.

A fundamental insufficiency of single rooms exists, with approximately one single room per 50 beds in a general ward. Therefore, it is physically impossible to assign a single room to all patients with MRSA. Moreover, it is a fact that patients on controlled respiration and/or compromised hosts are occasionally assigned to the general ward.

It is common knowledge that measures to prevent MRSA hospital-acquired infection are expensive with almost all costs charged to the hospital or institute. There is little subsidy from the government and/or the NHI.

Under the NHI law in Japan, most patients have medical insurance, and 70%–90% of health care costs are charged to this insurance. Under this system, patients cannot receive medical care services at their own expense. In other words, patients are not allowed to choose options regarding whether payment is based on the insurance, is made at their own expense, or is made

by a combined payment. If patients could pay the health care costs at their own expense, a considerable sum of money would be needed. According to the payment option based on insurance, it is impossible that the costs involved in instituting measures to prevent MRSA hospital-acquired infection would be charged to the hospital or institute.

Until recently in Japan, extraordinarily large doses of antibiotics were frequently repeated. In the surgical field, the third-generation cefem family of antibiotics or carbabenem antibiotics were administered prophylactically after operations over a long period,[12] while before surgery for colon and rectum cancer, unabsorbable oral antibiotics were routinely administered.[5] Since the Japanese guidelines for the usage and specifications of antibiotics have not yet been established, antibiotics with a wide antibacterial spectrum have a tendency to be prescribed for a long period. Moreover, expensive drugs in the standard of the NHI scheme have been specified to obtain profits for the hospital or institute.

For postoperative management, mechanical ventilation controls with a respirator, nutrition controls with intravenous hyperalimentation (IVH), and the administration of H2-blockers have been routinely employed.

Following surgery for esophagus cancer, it has been recommended that the IVH is administered during preoperative management, while mechanical-assisted ventilation control with a respirator and the administration of H2-blockers are carried out during postoperative management.[13] However, endotracheal intubation can easily be contaminated by the MRSA bacteria, resulting in an increased incidence of postoperative MRSA infection. Furthermore, the MRSA bacteria lodged in the respiratory tract are scattered in the air, spreading new MRSA hospital-acquired infections.[14,15] The excess administration of H2-blockers causes gastric acidity to decrease to a low level, changing the conditions of the bacterial florae in the digestive tract. This is one reason that the incidence of postoperative MRSA infection is highest after surgery for esophageal cancer.

We experienced our first case of postoperative MRSA enteritis in September 1987, at which time we introduced the strict requirement that all medical employees scrub in order to prevent an increase in the incidence of this disease. During the period from September 1987 to February 1998, the incidence of postoperative MRSA infection was 4.1%, but this increased to 6.6% during the period from March 1988 to August 1988, accounting for half of the incidence of all postoperative infections (13.4%). During the period from September 1988 to February 1990, since isolation of patients with MRSA and entrance to the recovery rooms of the surgical department was strictly standardized, the incidence of postoperative MRSA infection decreased to within 3%. This incidence accounted for 25% of the incidence of all postoperative infections, which was not significantly different from 6.6%. We could not isolate all patients with MRSA, since it took several days to prepare a single room, and it could not be used immediately. Therefore, these patients were accommodated in a general room with several other patients, making it impossible to eliminate postoperative MRSA hospital-acquired infection even though we united all our efforts in one department of surgery. We believe that this fact exposes the poor medical service system in Japan and the resulting abnormal incidence of postoperative MRSA hospital-acquired infection.

In March 1990, we assigned special doctors in infection control (infection control doctor, ICD), and defined comprehensive controls of MRSA infection. We also reviewed the protocols of antibiotics used in the perioperative phase. This does not imply that MRSA antibiotics, such as vancomycin (VCM), were used to prevent postoperative MRSA infection as the use of VCM was considered to carry a risk of producing MRSA bacteria obtaining resistance against VCM. The purpose of the comprehensive control against MRSA infection was to prevent postoperative cross-infection. In fact, a number of studies have focused on MRSA growth under cross-infection. Aoyagi[16] reported on the relationship between MRSA growth and its inhibition by antibiotics. In an experiment on rats with MRSA, the MRSA bacteria could not grow under conditions created by bacterial florae lodged in vivo; however, MRSA growth was identified when more than two types of bacteria in the bacterial florae were inhibited by antibiotics. Furthermore, he studied a mixed culture model in the GAM fluid media in vitro, containing *Escherichia coli*, *Enterococcus*, *Bacteroides fragilis*, and MRSA. Although MRSA growth was not found initially, rapid MRSA growth was identified when two types of bacteria among *E. coli*, *Enterococcus*, and *B. fragilis* were inhibited by antibiotics. These results suggest that changes in the bacterial florae lodged in vivo by the inhibition of antibiotics were related closely to MRSA growth. On the other hand, Kawai[17] reported observing MRSA growth in the duodenum in an experiment on rats that received gastrectomy and MRSA inoculation.

Since March 1990, when we defined comprehensive controls of MRSA infection and improved the usage of antibiotics in surgical procedures, the incidence of postoperative MRSA infection has decreased significantly and has remained low at 0.6%–0.7%. This fact suggests that the incidence of postoperative MRSA infection, or MRSA growth, is related closely to the specification of antibiotics.

In patients undergoing surgery for thoracic esophagus cancer in Japan, mechanical-assisted ventilation control with a respirator is widely employed to prevent

respiratory disturbance for some days after surgery. As a result, the incidence of postoperative MRSA infection in the respiratory tract has shown the highest rate. Nevertheless, we have successfully controlled postoperative respiratory disturbance by changing the fluid infusion given during these surgical procedures.[13]

In conclusion, our successful control of postoperative MRSA hospital-acquired infection implies that comprehensive measures of prevention, including the reviewed specification and usage of antibiotics by ICDs and operation management, have been well implemented.

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