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Surgical Site Infection after Malignant Brain Tumor Resection: A Multicenter Study for Induction of a Basic Care Bundle

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Abstract

Patients with malignant brain tumors are possibly at increased risk for surgical site infections (SSIs) considering the various medical situations associated with the disease. However, the actual rate of SSI after malignant brain tumor resection has not been well established, despite the potential impact of SSI on patient outcome. To investigate the incidence of SSI following malignant brain tumor surgery, we performed a retrospective study in 3 neurosurgical units. Subsequently, aiming at the reduction of incidence of SSI, we performed a prospective study using a care bundle technique in the same units. The SSI incidence in the retrospective (n = 161) and prospective studies (n = 68) were 4.3% and 4.4%, respectively, similar to the previously reports on general craniotomies. A care bundle does not appear to enhance prevention of SSI. However, future, large studies with a new care bundle should be planned based on a zero tolerance policy.

Key words: surgical site infection, malignant brain tumor, care bundle, resection, surveillance

Introduction

Surgical site infection (SSI) is a relatively infrequent complication after cranial surgery; the reported SSI incidences range from 1.1% to 19.78%, with the average of 3.25%.[1)]

Patients with malignant brain tumors often harbor several potential risk factors for SSI such as advanced age, poor nutritional state owing to appetite loss, poor sanitary condition of the head skin due to low performance status, immunosuppression caused by steroid or chemotherapeutic agents, and surgical site skin problems caused by post-operative irradiation. Therefore, patients with malignant brain tumors theoretically are a high-risk group for SSI. Moreover, common preoperative measures intended to reduce the risk, such as smoking cessation, long-term glycemic control, and treatment of other infection sites, are often insufficient as patients with malignant brain tumors commonly require immediate treatment.

The incidence of SSIs after malignant brain tumor resection surgery has not yet been established. The incidence of SSIs in brain tumor surgery, including benign and malignant tumors, ranges from 2.04 to 5.3%.[2–5)] Chaichana et al. reported that the incidence of SSIs in glioblastoma resection surgery was 5%.[6)]

The consequences of SSI can be serious, and may also compromises essential adjuvant treatment for those patients such as irradiation and/or chemotherapy. To investigate the incidence of SSI associated with malignant brain tumor resection, a retrospective study was performed in 3 neurosurgical units. Furthermore, a care bundle technique, which is an aggregate of evidence-based practices expected to improve patient outcomes, has been introduced to reduce the incidence of SSI. A prospective surveillance study of SSIs that were

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treated with this technique was performed in the same neurosurgical units.

Materials and Methods

Retrospective study

Incidences of SSI in patients with malignant brain tumors were investigated in 3 neurosurgical units. The investigation covered patients treated from July 1, 2010 to June 30, 2012 in those institutions. The data were collected from the medical record review of patients who were ± 20 years and underwent malignant (metastatic or primary tumors with World Health Organization [WHO] grade[7] II-IV) brain tumor resection surgery. Emergency and recurrent cases were included in the study, while stereotactic biopsy and endoscopic biopsy cases were excluded.

The primary outcome measure was defined as the rate of SSI. The secondary outcome measures were as follows: age, sex, preoperative nutritional state (total protein, body mass index [BMI]), American Society of Anesthesiologists (ASA) physical status, diabetes mellitus, location of the tumor (supra- or infratentorial), previous surgery, length of operation, histology, steroid administration, artificial dural substitute, and postoperative chemotherapy and / or irradiation within 3 months after the surgery.

Wound infection, encephalitis, brain abscess, meningitis, and ventriculitis within 3 months after the surgery were identified based on the medical records. If an SSI event was encountered, we recorded the timing, infected locus, causal bacteria, and outcomes 6 months after the operation.

Prospective study

Surveillance was performed over 2 years in the same 3 neurosurgical units as in the retrospective study. The inclusion criteria were similar to the ones for the retrospective study. All cases with brain tumors presenting imaging studies indicating metastatic or primary brain tumors with WHO grade II-IV were included. Patients with <6 months of expected survival were excluded. The same primary and secondary outcome measures were used. The follow-up period was 3 months from the day of surgery.

The SSI was defined following the protocols by the National Healthcare Safety Network established by the Centers for Disease Control and Prevention (CDC):[8] operative wound infection were classified into superficial incisional, epidural/subdural infection were classified into deep, and brain abscess and meningitis were classified into organ/space SSIs. The definition based on the CDC was only applied for the prospective study. Therefore, the definitions of SSIs were different between the prospective and retrospective studies.

The care bundle consisted of 6 elements including pre-, intra-, and post-operative procedures were as follows (Table 1).

1. Preoperative shampoo

Preoperative shampoo must be performed in all patients either at night or in the morning immediately before surgery. Antiseptic solution was not required (CDC guideline, recommendation IB).[8]

2. Prohibition of hair shaving using a razor

Preoperative shaving using a razor was prohibited. This procedure has been reported to increase the SSI rate.[9] Instead, trimming the hair using hair clippers was recommended (CDC guideline, recommendation IA).[8]

3. Perioperative antimicrobial prophylaxis

The use of preoperative antibiotics within one hour prior to incision has been recommended in the guideline (Recommendation IA),[8] and was performed in this study: antibiotics must be administrated within one hour of induction, and be added every 3 hours. Any antibiotic drugs were permitted.

4. Sufficient drying time (>2 min) after disinfection with povidone-iodine

Povidone-iodine requires a drying time of more than 90–120 seconds, and may not be wiped off using gauzes, as recommended by standard guidelines for disinfectants. In this care bundle, >2 minutes were required from skin preparation with povidone-iodine to the incision. Any kind of additional disinfectant use was permitted after this procedure.

5. Sufficient surgical site irrigation before wound closure

Sufficient surgical site irrigation with warmed normal saline before wound closure was required. Surgical site irrigation, while safe and inexpensive, is considered to be a critical step to reduce the SSI although there has been very little evidence supporting the

Table 1 The care bundle introduced for preventing surgical site infections

- Preoperative shampoo
- Prohibition of hair shaving using a razor
- Perioperative antimicrobial prophylaxis
- Sufficient drying time (>2 min) after disinfection with povidone-iodine
- Sufficient surgical site irrigation before wound closure
- Hand hygiene at postoperative wound care

effectiveness of surgical site irrigation in reducing SSI occurrence.[10] We adopted this procedure as expecting it would play a crucial role in reducing contamination intraoperatively. In addition, we also expected this procedure would increase motivation among the medical staff to maintain a clean operative field.

6. Hand hygiene at postoperative wound care

Adequate hand hygiene had to be maintained at postoperative wound care. Any kind of disinfectant was permitted (Recommendation 1B).[8]

Almost all of these procedures were routinely performed in all 3 neurosurgical units, not as a care bundle in the retrospective study.

Both studies were approved by the respective institutional review boards.

The risk factors for SSIs were analyzed in the retrospective and prospective studies. The chi-square test, Fisher exact test, or Mann–Whitney U test was used to assess statistical significance. Statistical significance was defined as a P value less than 0.05. All analyses were performed using IBM SPSS statistics 23.0 (IBM, Armonk, NY, USA).

Results

Retrospective study

During the 2-year study period, 161 patients were registered (Table 2). All the patients underwent scheduled surgery with clean operative fields. Among those, 62 were women and 99 were men. The patient age ranged from 22 to 81 years (median, 63 years). The histological diagnosis was metastatic tumors in 95 cases, gliomas in 60 cases, malignant lymphomas in 3 cases, and other tumors in 3 cases.

SSI occurred in 7/161 (4.3%). The onset of SSI after surgery ranged from 14 to 78 days (median, 49 days). Three of the 7 patients were diagnosed with SSI more than 60 days after the surgery; 4 patients had deep infections, while 3 had superficial infections. The preoperative conditions of the 7 patients with SSI was poor: 4 cases were scored ASA 3, and 3 were scored ASA 2.

Microorganisms isolated from the wound swab cultures were Methicillin-resistant *Staphylococcus aureus* in 2 cases, Methicillin-sensitive *Staphylococcus aureus* (MSSA) in 1, *Serratia marcescens* in 1, and *Propionibacterium acnes* in 1. No microorganism was isolated from the swab culture in 1 case. Culture was not obtained in 1.

Prospective study

Sixty-eight patients were enrolled in the prospective study. Of those, 24 were women and 44 were men. The patient age ranged from 33 to 83 years (median, 65 years) (Table 2). The histological diagnosis was metastatic brain tumors in 40 cases, glioma in 24, malignant lymphoma in 2, and other in 3. Compliance with the care bundle protocol was 100%.

SSIs occurred in 3 cases (4.4%). One patient was highly emaciated (BMI, 14.6%) and seborrheic dermatitis was observed on his head before the surgery. MSSA was isolated (superficial infection) from the wound. The second patient developed meningitis (organ/space infection) 78 days after surgery. Increased count of multinuclear cells was observed in the cerebral spinal fluid, but no pathogen was isolated from the cerebral spinal fluid by culture. The patient received radio-chemotherapy followed by surgical resection. The patient's wound adaptation was poor and cerebral spinal fluid leakage was observed. The third case had been on steroids for more than three months before surgery to control peritumoral edema. *Enterobacter cloacae* was isolated from his operative wound (superficial infection).

No SSI vs SSI patients

In both studies, 219 (95.6%) patients had no SSI and 10 (4.4%) patients had complications of SSI (Table 3). There were no significant differences in any factors between the groups of patients (Table 3).

Discussion

The SSI incidence of 4.3% (7/161) in the retrospective study and 4.4% (3/68) in the prospective study are similar to the previous reports on craniotomy. However, caution should be taken in comparing SSI incidence across studies with different populations and diagnostic criteria.

In the present study, we could not discuss the risk factors for SSIs because of the limited number of the patients. Many risk factors for SSIs have been reported previously. Well-known risk factors are diabetic status, smoking history, long hospital stay, prior surgery, long duration of surgery, ventricular drainage, cerebrospinal fluid leakage, and implantations.[1–6,10–13] Schipmann et al. reported 20 independent risk factors for SSI after cranial neurosurgical procedures.[1] Some of those factors were present in our SSI cases. In our study, SSI occurred in 10 cases. Of those, ASA score was 3 in 4 cases and 2 in 4; no SSIs was observed in patients with ASA score of 1. Eight patients (80%) received steroid therapy, and 6 (60%) were second surgery cases. Schipmann et al. demostrated that the main independent risk factor for the development of SSIs was the duration of surgery.[1] However, surgical time did not show a significant association with SSI in our studies.

Table 2 Results of retrospective and prospective studies

	Retrospective study	Prospective study
Number of cases	161	68
Age	22–81 (median 63)	33–83 (median 65)
Man:Woman	99:62	44:24
Histological diagnosis		
metastatic tumor	95 (59.0%)	40 (58.8%)
glioma	60 (37.3%)	23 (33.8%)
malignant lymphoma	3 (1.9%)	2 (2.9%)
other tumors	3 (1.9%)	3 (4.4%)
ASA score		
1	28 (17.4%)	3 (4.4%)
2	72 (44.7%)	35 (51.5%)
3	29 (18.0%)	9 (13.2%)
no data	32 (19.9%)	21 (30.9%)
Body mass index	13.8–32.8 (median 21.1)	14.6–30.8 (median 21.0)
Diabetes mellitus	13 (8.1%)	4 (5.9%)
Total protein	4.6–8.4 (median 6.9)	5.5–8.3 (median 6.9)
Steroid use	112 (69.6%)	40 (58.8%)
Previous surgery	18 (11.2%)	7 (10.3%)
Tumor location		
supratentorial	127 (78.9%)	57 (83.8%)
infratentorial	34 (21.1%)	10 (14.7%)
supra- and infratentorial	0 (0%)	1 (1.5%)
Duration of surgery		
<3 hrs	53 (32.9%)	23 (33.8%)
3–6 hrs	86 (53.4%)	42 (61.8%)
>6 hrs	22 (13.7%)	3 (4.4%)
Artificial dura	13 (8.8%)	4 (5.9%)
Postoperative chemotherapy	85 (52.8%)	32 (47.1%)
Postoperative radiotherapy	101 (62.7%)	54 (79.4%)
SSI complication	7 (4.3%)	3 (4.4%)
Time for SSI occurrence (days)	14–78 (median 49)	9–78 (median 19)

The interval between the day of the surgery and the occurrence of SSI should be noted. Four of the 10 patients with SSI were diagnosed >2 months after surgery. Chaichana et al. also reported that SSIs occurred 28–286 days (median, 40 days) after glioblastoma resection surgery.[6] The CDC guideline recommend a 30-day follow-up for patients without surgical implants and a 90-day or 1-year follow-up for patients with surgical implants.[8] Postulated reasons for such delayed infection were 1) bone flaps as a kind of implant, and 2) steroid administration and chemo- or radiotherapy after surgery resulting in immunosuppression. Follow-up for the surveillance of SSIs after cranial neurosurgery should cover a sufficient time span after surgery.

The "zero-tolerance" policy, a policy targeting the elimination of SSIs, has become the mainstay of surgical management. Various procedures are performed in each neurosurgical unit, but there has been no established standard procedure to date.

Care bundle techniques have been reported to prevent SSIs in the neurosurgical field. Davies et al. reported a care bundle for cranial neurosurgery that included 3 elements: administration of antibiotics <60 min after induction, maintenance of intraoperative blood sugar <11 mmol, and maintenance

Table 3 Comparison of the presence or absence of SSI in the retrospective and prospective studies

	No SSI Group	SSI Group	*P* value
Number of cases	219	10	
Age	22–83 (median 64.0)	48–79 (median 60.0)	0.832
Man:Woman	138:81	5:5	0.508
Histological diagnosis			
metastatic tumor	128 (58.4%)	7 (70.0%)	0.488
glioma	81 (37.0%)	2 (20.0%)	
malignant lymphoma	5 (2.3%)	0 (0%)	
other tumors	5 (2.3%)	1 (10.0%)	
ASA score			
1–2	134 (61.2%)	4 (40.0%)	0.069
3	34 (15.5%)	4 (40.0%)	
no data	51 (23.3%)	2 (20.0%)	
Body mass index	13.8–32.8 (median 21.0)	14.5–31.2 (median 22.5)	0.505
Diabetes mellitus	15 (6.8%)	2 (20.0%)	0.164
Total protein	4.6–8.4 (median 6.9)	6.0–8.0 (median 7.4)	0.2
Steroid use	145 (66.2%)	8 (80.0%)	0.278
Previous surgery	24 (10.9%)	1 (10.0%)	0.1
Tumor location			
supratentorial	174 (79.5%)	10 (100%)	0.216
infratentorial	44 (20.1%)	0 (0%)	
supra- and infratentorial	1 (0.5%)	0 (0%)	
Duration of surgery			
<3 h	69 (31.5%)	6 (60.0%)	0.083
≥3 h	150 (68.5%)	4 (40.0%)	
Artificial dura	17 (7.8%)	0 (0%)	0.1
Postoperative chemotherapy	115 (52.5%)	2 (20.0%)	0.055
Postoperative radiotherapy	150 (68.5%)	5 (50.0%)	0.229

of body temperature at > 36°C.[4] The incidence of SSI was 5.3%, and application of the care bundle did not reduce the occurrence of SSIs. Le et al. reported the effectiveness of a perioperative care bundle for cranioplasty.[14] Their care bundle included perioperative vancomycin, a barrier dressing through post-operative day 3, and decolonization of the surgical incision using topical chlorhexidine from postoperative day 4–7.[14]

In the present study, we adopted simple procedures for the care bundle that can be executed easily in every neurosurgical unit (Table 1). The core idea of our care bundle was that all the medical staff involved in perioperative care must consciously perform the fundamental preventive procedures included in the bundle. We prepared a checklist of the care bundle, and went through the elements in the operating room or at the bedside with the neurosurgeons and nurses one by one. This method should raise awareness of SSI prevention among the medical staff, and we expected spiral-up effects. The effectiveness of care bundles for SSI prevention is expected to be observed in many aspects. Therefore, randomized clinical trials to test the efficacy of care bundles are difficult.

In our study, SSIs occurred in 3 patients, despite introducing the care bundle. Severe emaciation, problems with head skin, cerebrospinal fluid leakage, and a long duration of steroid use were considered as the main causes of SSIs in these patients. More attention should be paid if patients have strong risk factors, even under introduction of the care bundle.

Some important preventive methods for SSIs were not included in our care bundle that included control of intraoperative body temperature and blood sugar level, use of insides-drape, double glove technique, and post-operative wound dressing methods. These procedures should be considered for incorporation into future care bundles.

The present study had a number of limitations. First, the number of cases of SSIs was small. Second, the criteria for SSIs were different in the retrospective and the prospective study. Therefore, a direct comparison of the SSI rate and the risk factors obtained from the two studies was not straightforward. The incidence of SSI in the retrospective study might have been underestimated because of analysis of medical charts.

Although the care bundle did not appear to enhance prevention of SSI in malignant brain tumor surgery, this technique should continue to be performed because the included procedures were very fundamental, safe and cost-effective. Future, large studies with a new care bundle, which include promising procedures, should be planned based on a zero tolerance policy.

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Conflicts of Interest Disclosure

The authors declare that they have no competing interests.

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