Postoperative Central Nervous System Infection: Incidence and Associated Factors in 2111 Neurosurgical Procedures

Shearwood McClelland III and Walter A. Hall

Department of Neurosurgery, University of Minnesota Medical School, Minneapolis

Background. Postoperative central nervous system infection (PCNSI) in patients undergoing neurosurgical procedures represents a serious problem that requires immediate attention. PCNSI most commonly manifests as meningitis, subdural empyema, and/or brain abscess. Recent studies (which have included a minimum of 1000 operations) have reported that the incidence of PCNSI after neurosurgical procedures is 5%–7%, and many physicians believe that the true incidence is even higher. To address this issue, we examined the incidence of PCNSI in a sizeable patient population.

Methods. The medical records and postoperative courses for patients involved in 2111 neurosurgical procedures at our institution during 1991–2005 were reviewed retrospectively to determine the incidence of PCNSI, the identity of offending organisms, and the factors associated with infection.

Results. The median age of patients at the time of surgery was 45 years. Of the 1587 cranial operations, 14 (0.8%) were complicated by PCNSI, whereas none of the 32 peripheral nerve operations resulted in PCNSI. The remaining 492 operative cases involved spinal surgery, of which 2 (0.4%) were complicated by PCNSI. The overall incidence of PCNSI was 0.8% (occurring after 16 of 2111 operations); the incidence of bacterial meningitis was 0.3% (occurring after 4 of 1587 operations), and the incidence of brain abscess was 0.2% (occurring after 3 of 1587 operations). The most common offending organism was *Staphylococcus aureus* (8 cases; 50% of infections), followed by *Propionibacterium acnes* (4 cases; 25% of infections). Cerebrospinal fluid leakage, diabetes mellitus, and male sex were not associated with PCNSI ($P > .05$).

Conclusions. In one of the largest neurosurgical studies to have investigated PCNSI, the incidence of infection after neurosurgical procedures was <1%—more than 6 times lower than that reported in recent series of comparable numerical size. Cerebrospinal fluid leak, diabetes mellitus, and male sex were not associated with an increased incidence of PCNSI. The results from this study indicate that the true incidence of PCNSI after neurosurgical procedures may be greatly overestimated in the literature and that, in surgical procedures associated with a high risk of infection, prophylaxis for *S. aureus* and/or *P. acnes* infection should be of primary concern.

Multiple factors have contributed to the increasing number of diagnosed CNS infections, including prolonged lifespan, increased incidence of solid-organ transplantation, and improved diagnostic imaging modalities [1]. The development of postoperative CNS infection (PCNSI) after neurosurgical procedures represents a significant threat and requires immediate medical and/or surgical intervention. The first site of inflammation after a CNS infection is the choroid plexus, in which ∼100,000 bacterial organisms per g of tissue are necessary to produce a PCNSI [2].

After neurosurgical procedures, PCNSI most commonly presents as meningitis, epidural abscess, subdural empyema, and/or brain abscess [1, 3–5]. A recent study involving >6200 craniotomies identified CSF leakage and male sex as independent risk factors for PCNSI development [8]. Multiple studies have examined the role of antibiotic prophylaxis in relation to PCNSI after neurosurgical procedures, with recent studies demonstrating that antibiotic prophylaxis decreases the incidence of PCNSI [6, 8].

Previous studies involving a minimum of 1000 intracranial neurosurgical procedures have reported the

Received 5 February 2007; accepted 13 March 2007; electronically published 21 May 2007.

Reprints or correspondence: Dr. Walter A. Hall, Dept. of Neurosurgery, State University of New York–Syracuse, 6th Flr. Jacobsen Hall, Upstate Medical University, 750 E. Adams St., Syracuse, NY 13210 (hallw@upstate.edu).

Clinical Infectious Diseases 2007; 45:55–9

1058-4838/2007/4501-0011$15.00
DOI: 10.1086/518580

incidence of PCNSI after neurosurgical procedures to be 5%–7%, with an incidence as high as 10% when antibiotic prophylaxis was not administered [6–9]. To more definitively establish the incidence of PCNSI in the population of patients undergoing neurosurgical procedures and the potential risk factors, this retrospective study was performed using a sizable patient population in which every patient received antibiotic prophylaxis.

MATERIALS AND METHODS

The operative records and postoperative course of 2111 cases involving neurosurgical procedures occurring in patients seen at the University of Minnesota (Minneapolis) from February 1991 through December 2005 were retrospectively reviewed for the incidence of PCNSI, the identity of offending organisms, and the factors associated with infection. In addition to cases of meningitis, epidural abscess, subdural empyema, and/or brain abscess, both bone-flap infections and wound infections were categorized as PCNSIs. All operations were elective and performed by a single surgeon (W.A.H.), and every operation was preceded by a prophylactic antibiotic protocol consisting of a perioperative 1-g dose of cefazolin (or a 1-g dose of vancomycin if the patient was allergic to penicillin) administered intravenously at the time of anesthesia.

Surgical scrub. Before every operation, Betadine Surgical Scrub (Purdue Pharma) and alcohol were applied to the operative site, followed by application of DuraPrep Surgical Solution (3M) to the same site. Once the site was dry, the patient was draped in a sterile manner. During each intracranial procedure, the head was shaved at the operative site prior to the Betadine and alcohol scrub.

Data collection and statistical analysis. The patient age at operation and sex, development of PCNSI, and offending organism(s) were recorded for each operation. Neurosurgical cases were categorized to have an origin of cranial, spinal, or peripheral nerve. Statistical analysis was performed using GraphPad Software. *P* values <.05 were considered to be statistically significant.

RESULTS

Demographic characteristics. The mean age at operation was 44.9 years (median age, 45 years; 1119 men and 992 women). Sixteen of the 2111 neurosurgical procedures were complicated by PCNSI, yielding a total incidence of 0.8%. Of the 1587 cranial operations, 448 were craniotomies for a tumor, mass, and/or lesion; 407 were brain biopsies; 312 were shunt and/or ventricular operations; 184 were transnasal and/or transphenoidal operations, 114 were nontumor craniotomies; 69 were Ommaya reservoir implantations; 46 were burr hole, aspiration, and/or drainage procedures; and 7 operations were categorized as miscellaneous (table 1).

Of the 492 spinal operations, 38 involved resection or biopsy of a tumor and/or mass, 9 involved cyst resection, 9 involved Chiari type I decompressions, and 4 involved myelomenigocele repair, with the remaining 432 spinal operations involving laminectomies, discectomies, foraminotomies, and lumbar drain placement and/or instrumentation (table 1). The remaining 32 operations involved the peripheral nervous system, of which 5 were for tumor resection, 2 involved neuroma resection, and the remaining 25 included 4 operations for lysis and/or graft repair and 21 operations for nerve release, transposition, exploration, and/or resection (table 1).

Cranial operations. Of the 1587 cranial operations, 14 (0.8%) were complicated by PCNSI, most commonly caused by *Staphylococcus aureus* (6 cases; 42.9% of cranial infections), followed by *Propionibacterium acnes* (4 cases; 28.6% of cranial infections) and multiple-organism infection (2 cases). Of the remaining post–cranial operation infections, 1 was caused by *Pseudomonas aeruginosa,* and 1 infection was culture negative (table 2). None of the *S. aureus* infections were due to methicillin-resistant strains. More-specific information relating PCNSI isolates with corresponding neurosurgical procedures is listed in table 2. Infection of an indwelling device comprised 5 cases of PCNSI (35.7% of cranial infections), and 4 cases of PCNSI manifested as meningitis (28.6% of cranial infections). The remaining incidences of PCNSI manifested as brain abscess (3 cases), superficial wound infection (1 case), and subdural empyema (1 case). The neurosurgical procedures after which PCNSI occurred involved ventriculoperitoneal shunt placement (5 cases), first-time craniotomy for a tumor, mass, and/or lesion (5 cases), brain biopsy (2 cases), Ommaya reservoir placement (1 case, which occurred prior to subsequent chemotherapy access), and transnasal hypophysectomy (1 case). The neurosurgical procedures associated with the highest rate of PCNSI were CSF shunting (1.6%), followed by Ommaya reservoir placement (1.4%) and craniotomy for a mass, tumor, and/or lesion (1.1%) (table 1).

Spinal and peripheral nerve operations. Of the 492 spinal operations, 2 (0.4%) were complicated by PCNSI. Each infection following a spinal operation was caused by methicillin-susceptible *S. aureus,* with the neurosurgical procedures involving 1 thoracic tumor resection and 1 cystic sacral mass drainage and resection, neither of which involved an indwelling foreign body (table 1). None of the remaining 32 peripheral nerve operations were complicated by PCNSI (table 1).

Identity of offending organisms and demographic characteristics of infections. Among the 2111 neurosurgical procedures, the most common offending organism causing PCNSI was *S. aureus* (8 cases; 50% of infections), followed by *P. acnes* (4 cases; 25% of infections) (table 2). The mean age of the 16 patients who developed PCNSI was 37.4 years, and the mean age of the patients who did not develop infection was 44.8

Table 1. Distribution of neurosurgical case load.

Surgery description	No. of operations	No. of PCNSI cases	Infection rate, %
Cranial procedures			
Craniotomy for tumor, mass, and/or lesion	448	5	1.1
Brain biopsy	407	2	0.5
CSF shunting	312	5	1.6
Transphenoidal and/or transnasal	184	1	0.5
Nontumor or nonmass craniotomy	114	0	0
Ommaya reservoir placement	69	1	1.4
Burr hole, aspiration, and/or drainage	46	0	0
Miscellaneous	7	0	0
Subtotal	1587	14	0.8
Spinal procedures			
Laminectomy, discectomy, foraminotomy, instrumentation, and/or lumbar drain placement	432	0	0
Biopsy of tumor and/or mass	38	2	5.3
Cyst resection	9	0	0
Chiari I decompression	9	0	0
Myelomeningocele repair	4	0	0
Subtotal	492	2	0.4
Peripheral nerve procedures			
Nerve release, transposition, lysis, exploration, and/or graft repair	25	0	0
Tumor resection	5	0	0
Neuroma resection	2	0	0
Subtotal	32	0	0

NOTE. PCNSI, postoperative CNS infection.

years. Statistical analysis, using unpaired 2-tailed t tests, did not reveal this difference to be significant ($P = .122$).

Four hundred eighty-two (23%) of the 2111 operations were performed in patients who had undergone previous neurosurgical intervention. Of these operations, only 4 (0.8%) were complicated by postoperative PCNSI (3 craniotomies and 1 spinal surgery). A χ^2 analysis revealed no significant difference ($P > .05$) between this infection incidence and that associated with the 1629 cases in patients who had not undergone a previous neurosurgical procedure (12 [0.7%] of which were complicated by infection), and no significant difference ($P = .10$) in PCNSI incidence was revealed between male and female patients. The factor most strongly associated with PCNSI was foreign body implantation, which occurred in 7 of the 16 cases complicated by PCNSI. Neither CSF leak, nor preoperative diagnosis of diabetes, was strongly associated with PCNSI, each occurring in only 2 of 16 cases of PCNSI.

DISCUSSION

Since the origination of neurosurgery, PCNSI has posed a formidable challenge to the field. The advent of germ theory by Louis Pasteur and its subsequent application to surgical sterilization by Joseph Lister in the late 19th century allowed for a marked reduction in the rates of postoperative sepsis, resulting in an expansion of the depth and breadth of operative neurosurgical procedures that could be performed safely [10–13]. The safety of neurosurgical procedures was further enhanced by the clinical application of Alexander Fleming's original penicillin mold extract in the 1940s in the operating room through the work of Howard Florey and Ernst Chain, allowing for nonemergent lesions to be treated neurosurgically with a previously unattainable level of postoperative safety, thereby opening the door for elective neurosurgery [14].

Since the advent of elective craniotomy operations, the reported rates of PCNSI (defined as meningitis, epidural abscess, subdural empyema, brain abscess, bone-flap infection, and/or wound infection) following intracranial neurosurgical procedures have been relatively variable, ranging from <1% to >8% in published series [6–9, 15–28]. Only 5 of these series have involved >1000 intracranial operations [6–9, 18]. Of these series, 2 involved a North American population, with 1 series systematically excluding CSF shunting procedures because of their "unique liability for infection" [6–9, 18]. To address this dearth of large case series, we examined the incidence of PCNSI in the first single-center North American report to involve >1500 intracranial operations, without systemic exclusion of

Table 2. Classification of infectious organisms involved in cases of postoperative CNS infection.

Pathogen	No. of cases	Type(s) of surgery after which infection developed (no. of cases)	Percentage of total infections (percentage of cranial infections)
Staphylococcus aureus	8 (6 cranial, 2 spinal)	Craniotomy for tumor (3), craniotomy for open brain biopsy (1), stereotactic brain biopsy with no craniotomy (1), VP shunt placement (1), sacral mass resection (1), thoracic tumor resection (1)	50.0 (42.9)[a]
Propionibacterium acnes	4	VP shunt placement (2), Ommaya reservoir placement (1), VP shunt removal (1)	25.0 (28.6)
Multiorganism	2	VP shunt placement (1), craniotomy for tumor (1)	12.5 (14.3)
Pseudomonas aeruginosa	1	Craniotomy for tumor	6.3 (7.1)
Culture-negative	1	Transnasal hypophysectomy	6.3 (7.1)
Total	16 (14 cranial and 2 spinal)		

NOTE. VP, ventriculoperitoneal.

[a] *S. aureus* was involved in 100% of spinal infections.

CSF shunting procedures (table 1). In addition, we decided to compare our PCNSI findings after spinal operations, because only a limited number of series in the literature focus exclusively on PCNSI after spinal operations, with an infection rate varying from 1% to 21% [29–32].

In our series, the rate of PCNSI after 1587 intracranial operations was 0.8%, which is >6 times lower than that in other comprehensive series involving at least 1000 intracranial operations [6–8]. The incidence of PCNSI after spinal neurosurgical procedures (492 operations) in our series was 0.4%, which is lower than any rate previously reported [29–32]. The overall incidence of PCNSI in our series of 2111 operations (including 32 cases occurring after peripheral nerve procedures) was 0.8%.

The 0.3% incidence of bacterial meningitis after intracranial neurosurgical procedures (4 cases that developed after 1587 operations) reported in our series compares favorably with series of comparable patient size, being ∼5 times lower than the 1.4%–1.9% incidence of postneurosurgical bacterial meningitis reported in the literature [7–8, 33]. The 0.2% incidence of brain abscess (3 cases that developed after 1587 operations) likewise compares favorably with the 0.6% rate previously reported [7]. Of note, having undergone previous neurosurgical procedures did not correlate with an increased risk of PCNSI, because the 0.8% infection incidence in this population was not statistically different from the 0.7% incidence in patients undergoing neurosurgical procedures for the first time.

The most common offending organism in our series was *S. aureus* (accounting for 50% of infections), which is in concert with previous reports [7–8, 24, 27, 30]. *P. acnes* played a significant role in our series (accounting for 25% of infections), which is also in accordance with previous reports [8, 27]. Also substantiated in the literature was the increase in infection risk because of foreign body placement, which was associated with nearly one-half of the infections in our series. An interesting finding in this series was that *Enterobacter, Acinetobacter, Proteus,* or *Candida* species were not causes of PCNSI, differing from the findings of previous reports [8, 9, 20, 24]. Although the patients who developed PCNSI were younger than those who did not develop infection, this trend was not strong enough to be statistically significant.

Previous studies examining PCNSI in >1000 patients have evaluated CSF leakage, male sex, operating surgeon, previous neurosurgical operation, and absence of antibiotic prophylaxis as risk factors for PCNSI following craniotomy [8, 34]. Because all patients in our study received antibiotic prophylaxis and received care from the same neurosurgeon, 2 of these risk factors were eliminated as potential confounders. The findings of our study revealed neither male sex nor previous neurosurgery to be risk factors for PCNSI. Although the low number of PCNSI cases relative to the large number of overall neurosurgical cases in this series somewhat limits the ability of our study to detect statistical significance, further analysis of the 16 cases of PCNSI revealed the involvement of CSF leak in only 2 cases and diabetes in only 2 cases, making neither a statistically significant risk factor for PCNSI.

In one of the first series in the United States to examine PCNSI after >2000 neurosurgical procedures, the incidence of infection after neurosurgical procedures was 0.8% after cranial operations, 0.4% after spinal operations, and 0% after peripheral nerve operations. The incidence of infection after cranial operations in our series was >6 times lower than that recently reported in series with comparable patient size (>1000 patients). Nearly one-half of PCNSI cases were associated with implantation of a foreign body, and neither CSF leak, diabetes, nor male sex were risk factors for PCNSI. The results from our series indicate that the true incidence of PCNSI after neurosurgical procedures may be greatly overestimated in the literature and that, in operations associated with high risk of infection, prophylaxis against *S. aureus* and/or *P. acnes* infection should be of primary concern.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

References

1. Hall WA. Cerebral infectious processes. In: Loftus CM, ed. Neurosurgical emergencies, vol. 1. Park Ridge, IL: American Association of Neurological Surgeons Publications, **1994**:165–182.
2. Borges LF. Infections in neurologic surgery: host defenses. Neurosurg Clin N Am **1992**; 3:275–8.
3. Marion DW. Complications of head injury and their therapy. Neurosurg Clin N Am **1991**; 2:411–24.
4. Nathoo N, Nadvi SS, van Dellen JR. Cranial extradural empyema in the era of computed tomography: a review of 92 cases. Neurosurgery **1999**; 44:748–53.
5. Nathoo N, Nadvi SS, van Dellen JR, Gouws E. Intracranial subdural empyemas in the era of computed tomography: a review of 699 cases. Neurosurgery **1999**; 44:529–35.
6. Raggueneau JL, Cophignon J, Kind A, et al. Analysis of infectious sequelae of 1000 neurosurgical operations: effects of prophylactic antibiotherapy [in French]. Neurochirurgie **1983**; 29:229–33.
7. Korinek AM. Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. The French Study Group of Neurosurgical Infections, the SEHP, and the C-CLIN Paris-Nord Service Epidemiologie Hygiene et Prevention. Neurosurgery **1997**; 41:1073–81.
8. Korinek AM, Baugnon T, Golmard JL, van Effenterre R, Coriat P, Puybasset L. Risk factors for adult nosocomial meningitis after craniotomy: role of antibiotic prophylaxis. Neurosurgery **2006**; 59:126–33.
9. Mollman HD, Haines SJ. Risk factors for postoperative neurosurgical wound infection: a case-control study. J Neurosurg **1986**; 64:902–6.
10. Miller JT, Rahimi SY, Lee M. History of infection control and its contributions to the development and success of brain tumor operations. Neurosurg Focus **2005**; 18:e4.
11. Alexander JW. The contributions of infection control to a century of surgical progress. Ann Surg **1995**; 201:423–8.
12. Goodrich JT. Landmarks in the history of neurosurgery. In: Rengachery SS, Wilkins RH, eds. Principles of neurosurgery. Baltimore: Mosby-Wolfe, **1994**:1.2–1.25.
13. Meade RH. An introduction to the history of general surgery. Philadelphia: WB Saunders, **1968**.
14. Barker FG 2nd. Efficacy of prophylactic antibiotics for craniotomy: a meta-analysis. Neurosurgery **1994**; 35:484–92.
15. Cabantog AM, Bernstein M. Complications of first craniotomy for intra-axial brain tumor. Can J Neurol Sci **1994**; 21:213–8.
16. Cushing H. Concerning the results of operations for brain tumor. JAMA **1915**; 64:189–95.
17. Fadul C, Wood J, Thaler H, Galicich J, Patterson RH Jr, Posner JB. Morbidity and mortality of craniotomy for excision of supratentorial gliomas. Neurology **1988**; 38:1374–9.
18. National Noscomial Infection Surveillance (NNIS) System. National Noscomial Infection Surveillance (NNIS) System report, data summary from January 1992 through June 2003, issued August 2003. Am J Infect Control **2003**; 31:481–98.
19. Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. Neurosurgery **1998**; 42:1044–56.
20. Haines SJ, Goodman ML. Antibiotic prophylaxis of postoperative neurosurgical wound infection. J Neurosurg **1982**; 56:103–5.
21. Chang SM, Parney IF, McDermott M, et al.; Glioma Outcomes Investigators. Perioperative complications and neurological outcomes of first and second craniotomies among patients enrolled in the Glioma Outcome Project. J Neurosurg **2003**; 98:1175–81.
22. Holloway KL, Smith KW, Wilberger JE Jr, Jemsek JG, Giguere GC, Collins JJ. Antibiotic prophylaxis during clean neurosurgery: a large, multicenter study using cefuroxime. Clin Ther **1996**; 18:84–94.
23. Vernet E, Adell C, Trilla A, et al. Usefulness of risk indexes for the prediction of surgical site infection in patients undergoing neurosurgical procedures [in Spanish]. Med Clin (Barc) **2004**; 122:92–5.
24. Erman T, Demirhindi H, Gocer AI, Tuna M, Ildan F, Boyar B. Risk factors for surgical site infections in neurosurgery patients with antibiotic prophylaxis. Surg Neurol **2005**; 63:107–13.
25. Zhao JZ, Wang S, Li JS, et al. The perioperative use of ceftriaxone as infection prophylaxis in neurosurgery. Clin Neurol Neurosurg **1995**; 97:285–9.
26. Zentner J, Gilsbach J, Daschner F. Incidence of wound infection in patients undergoing craniotomy: influence of type of shaving. Acta Neurochir (Wien) **1987**; 86:79–82.
27. van Ek B, Bakker FP, van Dulken H, Dijkmans BA. Infections after craniotomy: a retrospective study. J Infect **1986**; 12:105–9.
28. Quadery LA, Medlery AV, Miles J. Factors affecting the incidence of wound infection in Neurosurgery. Acta Neurochir (Wien) **1977**; 39: 133–41.
29. Horwitz NH, Curtin JA. Prophylactic antibiotics and wound infections following laminectomy for lumber disc herniation. J Neurosurg **1975**; 43:727–31.
30. Apisarnthanarak A, Jones M, Waterman BM, Carroll CM, Bernardi R, Fraser VJ. Risk factors for spinal surgical-site infections in a community hospital: a case-control study. Infect Control Hosp Epidemiol **2003**; 24:31–6.
31. Schnoring M, Brock M. Prophylactic antibiotics in lumbar disc surgery: analysis of 1,030 procedures. Zentralbl Neurochir **2003**; 64:24–9.
32. Mastronardi L, Tatta C. Intraoperative antibiotic prophylaxis in clean spinal surgery: a retrospective analysis in a consecutive series of 973 cases. Surg Neurol **2004**; 61:129–35.
33. Federico G, Tumbarello M, Spanu T, et al. Risk factors and prognostic indicators of bacterial meningitis in a cohort of 3580 postneurosurgical patients. Scand J Infect Dis **2001**; 33:533–7.
34. Korinek AM, Golmard JL, Elcheick A, et al. Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. Br J Neurosurg **2005**; 19:155–62.