Postoperative fever workup in pediatric neurosurgery patients

Nataly Raviv, MD, Nicholas Field, MD, and Matthew A. Adamo, MD

Department of Neurosurgery, Albany Medical Center, Albany, New York

OBJECTIVE Fevers are common in the postoperative period, and adult data indicate that workup for an isolated fever is not warranted in the first 4 postoperative days (PODs). Pediatric literature on the subject similarly questions the value of further investigation during the first 2 PODs. The purpose of this study was to determine the incidence of acute fever in the postoperative pediatric neurosurgical population, as well as to assess the utility of performing further workup on these patients.

METHODS A single-institution retrospective study was performed to assess pediatric neurosurgery patients following surgical intervention for the diagnoses of craniosynostosis, Chiari malformation, and brain tumors from 2009 to 2018. Fevers were identified during the first 4 PODs and were defined as a temperature $\geq 38.0^{\circ}\text{C}$. The patient charts were queried for urinalysis and urine culture (UA/Ucx), chest radiographs, blood cultures, CSF culture, respiratory viral panel, white blood cell (WBC) count, transfusion history, development of wound infection, and placement of external ventricular drains (EVDs) or lumbar drains. Thirty-day postoperative microbiology results and readmissions were reviewed. Descriptive statistics were performed using logistic regression analysis.

RESULTS Two hundred thirty-five patients were evaluated, and 61% had developed fevers within the first 4 PODs. Thirty-eight (26.6%) of the 143 febrile patients underwent further workup, and those with high fevers ($> 39.0^{\circ}\text{C}$) were more likely to undergo further evaluation, which most commonly included UA/Ucx (21.7%). Approximately 1% (2/235) of the patients were found to have an infection during the first 4 days, and 8 additional patients developed a complication following the initial 4 days and within the first 30 PODs. The development of infectious complications within the first 4 PODs did not correlate with acute postoperative fevers ($p = 0.997$), nor did the development of complications within the 30 days following surgery ($p = 0.776$); however, multiple days of acute postoperative fevers ($p = 0.034$) and the presence of an EVD ($p = 0.001$) were associated with the development of infectious complications within 30 days. Acute postoperative fevers were associated with EVD placement ($p = 0.038$), as well as blood product transfusions and an increased WBC count ($p < 0.001$).

CONCLUSIONS Isolated fevers manifesting within the first 4 PODs are rarely associated with an infectious etiology. Additional factors should be taken into consideration when deciding to pursue further investigation.

<https://thejns.org/doi/abs/10.3171/2020.5.PEDS2019>

KEYWORDS pediatric; neurosurgery; postoperative; fever; infection

POSTOPERATIVE fevers in the days following surgery are common in both the adult and pediatric populations.^{1,2} Most are the result of the inflammatory and pyrogenic cytokine response to surgery and resolve spontaneously; however, a workup is often performed, as a postoperative fever can be a sign of a significant underlying clinical process.³ Therefore, patients frequently undergo an often invasive and costly workup to rule out infectious etiologies.

The differential for postoperative fever includes both infectious and noninfectious causes, such as the natural inflammatory response, perioperative medications, transfused blood products, pneumonia, urinary tract infection (UTI), deep vein thrombosis, surgical site infection, and bacteremia.⁴ Fevers due to the trauma of surgery are thought to resolve within the first 2–3 days, and the course is dependent on the type and invasiveness of the surgery. Head trauma is believed to be associated with a longer fe-

ABBREVIATIONS CBC = complete blood count; CXR = chest radiograph; EVD = external ventricular drain; LD = lumbar drain; POD = postoperative day; UA/Ucx = urinalysis and urine culture; UTI = urinary tract infection; WBC = white blood cell.

SUBMITTED January 6, 2020. **ACCEPTED** May 27, 2020.

INCLUDE WHEN CITING Published online September 18, 2020; DOI: 10.3171/2020.5.PEDS2019.

ver course, particularly operations and processes involving the hypothalamus. Fevers occurring within the 1st week of surgery can be caused by community-acquired infections that predate surgery or can be attributable to nosocomial infections. Respiratory and urinary infections are most common, though surgical site and intravascular catheter infections can cause fever in the acute postoperative period.³ The most common morbidities associated with the 30-day postoperative period in neurosurgery patients include surgical site infection, intracranial abscess, UTI, sepsis, meningitis, osteomyelitis, and ventriculitis.⁵ Complications are 2.6 times more likely to arise following cranial cases than spine surgeries.⁶

Fever workups can involve invasive and comprehensive testing such as a complete blood count (CBC), blood cultures, chest radiographs, and urinalysis and urine culture (UA/Ucx), which expose patients to venipuncture, radiation, and catheterization. Neurosurgical patients may also have CSF sent for analysis and culture if an external ventricular drain (EVD) or lumbar drain (LD) is placed.

In this study, we examined the first 4 postoperative days (PODs) in neurosurgical pediatric patients in order to establish the incidence of postoperative fevers in this time period and evaluate our institution's diagnostic approach to these findings, as well as the association of fever development with existing and impending infections and wound complications.

Methods

We performed a retrospective study to assess pediatric neurosurgery patients 18 years of age and younger, who had undergone surgery for intracranial tumor resection, craniosynostosis repair, or Chiari decompression at our institution between 2009 and 2018. We selected these pathologies as representative of the pediatric neurosurgery population, as cranial procedures have been shown to have higher rates of complications than spine surgeries,⁶ thus necessitating increased vigilance and a lower threshold for workup. Additionally, these patients commonly develop fevers and remain as inpatients for the first few PODs, as opposed to other populations such as those with shunts, who are generally discharged the following day, precluding data collection. If a patient had undergone multiple procedures, only one was included in our analysis. For tumor patients, we examined only the initial resection and excluded biopsies that had been followed by resections. The day of surgery was considered operative day 0, and data were collected from day 0 to POD 4. Patients with identified preoperative infections were excluded from the study.

Fevers were identified during the first 4 PODs and were defined as a temperature $\geq 38.0^{\circ}\text{C}$ (100.8°F). The patient charts were queried for UA/Ucx, chest radiographs (CXRs), blood culture, CSF culture, respiratory viral panel, white blood cell (WBC) count, perioperative transfusion history, placement of EVDs and LDs, and the development of wound complications. The 30-day postoperative microbiology results as well as readmissions for complications and infections were also reviewed.

At our institution, a positive UA automatically triggers

the performance of a Ucx, so all patients with a positive UA also had Ucx testing. Chest radiographs and radiology reports were reviewed, and findings were considered positive when infiltrates suspicious for an infectious process were identified. Cerebrospinal fluid cultures were only performed in patients with EVDs or LDs. Note, all EVDs placed at our institution utilized antibiotic-impregnated catheters.

Study approval was granted by the Albany Medical Center Institutional Review Board. Descriptive statistics were performed using a two-tailed logistic regression analysis with IBM SPSS Statistics for Mac, version 25 (IBM Corp.). Statistical significance was defined as $p < 0.05$.

Results

Two hundred thirty-five patients were evaluated in this study, and 61% (143/235) had developed fevers within the first 4 PODs. Fevers were most common in the craniosynostosis population (89%), followed by tumor resection (65%) and Chiari decompression patients (25%). Thirty-three of the 143 febrile patients had high fevers ($\geq 39.0^{\circ}\text{C}$), 105 experienced more than one recorded fever (multiple fevers), and 83 experienced at least one fever per day over multiple days (multiple days of fever). Thirty-eight (26.5%) of the febrile patients underwent further workup, and those with high fevers ($\geq 39.0^{\circ}\text{C}$) were more likely to undergo further evaluation, which most commonly included a UA/Ucx (31/143 [21.7%]). In the first 4 PODs, UA was performed on 31 patients. Blood cultures were drawn on 21 patients, CSF cultures on 9, and CXRs were obtained in 14 patients. Sixty-nine patients received blood transfusions, and 58 of these patients developed fevers. CBCs were collected on the majority of patients (210/235), as our Pediatric Intensive Care Unit generally obtains postoperative labs.

Just over 1% (2/143) of the patients with fevers were found to have an infection during the first 4 days (1 UTI and 1 CSF infection), and 8 additional patients (6 of whom had experienced acute postoperative fevers) developed a complication after the initial 4 days and within the first 30 PODs (1 wound dehiscence requiring return to the operating room for closure with negative cultures, 1 CSF leak requiring repair, 3 CSF infections, and 3 UTIs). Table 1 includes a summary of the results. Two of these patients were afebrile during the acute postoperative period. Six patients experienced fevers only within the first 2 PODs, and 3 patients experienced fevers during both the POD 1–2 and POD 3–4 time frames.

The development of postoperative fevers did not correlate with acute infection ($p = 0.997$). However, multiple days of acute postoperative fevers were found to be associated with the development of an infectious complication within 30 days ($p = 0.034$). The presence of an EVD was found to be associated with both postoperative infections and complications within the first 30 PODs ($p = 0.001$ and 0.000 , respectively). Acute postoperative fevers were found to correlate with EVD placement ($p = 0.038$), blood product transfusions ($p < 0.001$) and an increased WBC count ($p < 0.001$). Results of our analysis are listed in Table 2.

TABLE 1. Summary of results

Variable	No. of Patients/Total (%)
Total no. of patients	235 (100)
Craniosynostosis repair	65/235 (27.7)
Endoscopic/open	13/52
Chiari decompression	63/235 (26.8)
Duraplasty	37/63 (58.7)
Tumor biopsy/resection	107/235 (45.5)
Postop fever	143/235 (60.9)
Craniosynostosis	58/65 (89.2)
Chiari	16/63 (25.4)
Tumor	69/107 (64.5)
High fever ($\geq 39^{\circ}\text{C}$)	33/235 (14)
Multiple fevers	105/235 (44.7)
Multiple days of fever	83/235 (35.3)
EVD or LD placement	39/235 (16.6)
Fever workup	38/143 (26.6)
UA w/ or w/o Ucx	31/235 (13.2)
CXR	14/235 (6.0)
Bcx	21/235 (8.9)
CSFcx	9/235 (3.8)
Infections w/in first 4 PODs	2 (0.9)*
Infections w/in 30 days (including first 4 PODs)	8/235 (3.4)†
Complications w/in 30 days (including first 4 PODs)	10/235 (4.3)‡

Bcx = blood culture; CSFcx = cerebrospinal fluid culture.

* One UTI and 1 CSF infection.

† Three UTIs and 3 CSF infections.

‡ One wound dehiscence and 1 CSF leak.

Discussion

The postoperative neurosurgical infection rate within the first 30 days has been reported at 5.3% in a large analysis of 132,000 patients; infections included surgical site infections (1.8%), as well as other infectious complications such as UTIs or pneumonia (3.9%).⁷ Such complications can be dangerous and can significantly affect a patient's postoperative course and overall outcome. Postoperatively, patients are monitored closely as inpatients, and at discharge, patients and their guardians are counseled regarding concerning signs or symptoms that may indicate a developing complication requiring medical attention.

One such indicator is fever, yet the literature broadly agrees that fevers in the first 48 hours following surgery are generally noninfectious.⁸ Some adult studies have extended that period to the first 4 days, stating that fevers persisting beyond or developing on or after POD 5 are more concerning for an infectious process.⁸ Other studies have suggested that fevers $\leq 38.9^{\circ}\text{C}$ (102°F) are usually associated with noninfectious causes, while higher fevers should raise suspicion for an infectious etiology.⁸

Vermeulen et al. performed a prospective triple-blind study involving 308 postoperative adult patients who demonstrated the limited value of measuring postoperative

TABLE 2. Results of the statistical analysis

Independent Variable	Dependent Variable	p Value
Fever	Acute infection*	0.997
	Complications†	0.776
Multiple fevers	Acute infection*	0.996
	Complications†	0.792
Multiple days of fevers	Acute infection*	0.674
	Complications†	0.222
High fevers	Acute infection*	0.200
	Complications†	0.282
Transfusion	Fever*	0.00
EVD placement	Fever*	0.038
EVD placement	Acute infection*	0.257
EVD placement	Complications†	0.000
EVD placement	Infectious complications†	0.001
Decadron use	Fever*	0.234
Multiple days of fevers	Infectious complications†	0.034
WBC count	Fever*	0.00

Boldface type indicates statistical significance.

* Within the first 4 PODs.

† Within 30 PODs.

temperatures for detecting infectious complications.⁴ Of the 61 patients (19.8%) who developed a postoperative fever $\geq 38^{\circ}$, only 7 (11%) were found to have an infection. Of the 19 patients (6%) found to have an infection, only 7 (37%) were febrile, whereas 63% of infected patients remained afebrile. Therefore, fevers were shown to be a nonspecific and insensitive indicator of infection. A study examining postoperative fever in the elective pediatric surgical population queried 6943 patients, 30.6% of whom had developed postoperative fevers within the first 48 hours following surgery.⁹ The authors found that early postoperative fever in the first 2 PODs is common in this population and is rarely associated with an infectious etiology.

In our study of neurosurgical pediatric patients, 8 of the 10 postoperative complications occurred in tumor patients, with 1 complication occurring in each of the other examined populations—craniosynostosis repair and Chiari decompression. The 2 cases of acute infection within the first 4 PODs included a UTI in a patient with a complicated course following a cranial vault reconstruction and a CSF infection in a 5-year-old following EVD placement and resection of a fourth ventricular tumor. The cranial vault reconstruction had been performed for sagittal craniosynostosis in a 6-month-old child, and the patient's postoperative course was complicated by an episode of apnea and bradycardia with subsequent intubation. The patient developed fevers the following day, and a workup revealed a positive UA. Urine cultures grew *Pseudomonas aeruginosa*. The patient lacked risk factors that would increase his susceptibility to such complications; thus, his Foley catheter was removed on POD 1. The second patient had undergone placement of an EVD for hydrocephalus, followed by resection of a fourth ventricular tumor 5 days

later. Fever workup on POD 3, which was 8 days after EVD placement, revealed CSF cultures positive for *Staphylococcus epidermidis* and *S. auricularis*. These cases do not alter our recommendations, as the child with the UTI demonstrated concerning signs and symptoms that warranted further workup, and the infected CSF was identified more than 4 days after placement of the EVD, which falls within the time frame concerning for the development of CSF infection.

Regarding the 8 other cases with complications occurring outside the first 4 PODs, one involved the noninfectious dehiscence of a surgical incision, another the development of a CSF leak requiring repair, and the remaining 6 involved infectious processes, 3 with the development of UTIs and 3 with CSF infections. The first noninfectious complication involved wound dehiscence in an 8-year-old following resection of a temporal lobe tumor. The patient was taken for wound washout and closure, and the breakdown was noted to be superficial with negative cultures. The other noninfectious complication occurred in a 2-year-old with a Chiari malformation and both cervical and thoracic syringes, who had undergone decompression with dural augmentation. Postoperatively, the patient was afebrile and did well. Unfortunately, she developed a CSF leak on POD 10, which required reexploration and CSF fistula repair.

A patient with a history of Crohn's disease and chronic UTIs had undergone resection of a right thalamic astrocytoma and was found to have a UTI with cultures positive for *Escherichia coli* on POD 6. For the procedure, the patient had a Foley catheter placed, which was removed on POD 2. She did not experience fevers, and it remains unclear what prompted the UA and Ucx apart from her history of chronic infections. Another patient had undergone resection of a left frontoparietal tumor and had a Foley catheter placed for 2 days. She was afebrile during the acute postoperative period until POD 8, and workup at this time revealed a *P. aeruginosa* UTI. Another patient, who had undergone resection of a fourth ventricular medulloblastoma with Foley catheter removal on POD 1, experienced fevers on the 1st and 4th PODs. Acute workup was negative. Fevers and urinary symptoms on POD 11 prompted UA/UCx to be sent, which revealed a *P. aeruginosa* infection.

A patient with a history of tuberous sclerosis had undergone resection of a subependymal giant cell astrocytoma with placement of an intraoperative EVD. The patient experienced transient fevers during the first 2 PODs. The fevers restarted on POD 5, prompting a workup, and CSF cultures were positive for *Acinetobacter baumannii*. Another patient had undergone a suboccipital craniotomy for resection of a left cerebellar vermian mass, with placement of an EVD on the same day but prior to surgery. The patient experienced fevers on the first 2 PODs. CSF was sent for culture and analysis on PODs 1 and 7 with negative findings. The EVD remained in place for 11 days and was removed prior to discharge. The patient returned with wound breakdown and fevers and was found to have CSF cultures positive for *S. epidermidis*. The final patient had undergone resection of a fourth ventricular medulloblastoma with intraoperative placement of an EVD. The

patient experienced fevers on PODs 1–3. The EVD was removed after 11 days, and CSF drawn immediately prior to removal of the system was sent for gram stain and culture, which were negative. The patient began to leak CSF from the EVD site on POD 15. He was afebrile and had no signs of infection at that time; however, CSF sent during the subsequent ventriculoperitoneal shunt placement was positive for *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*), *S. epidermidis*, and *S. hominis*, which prompted removal of the system.

Postoperative fevers are common, and our results are consistent with studies in the adult literature that have reported that fevers in the first 4 PODs are rarely associated with infectious processes. Additionally, febrile workups can be invasive and costly (see Table 3 for costs at our institution). Therefore, pediatric neurosurgical patients who develop isolated fevers in the acute period (PODs 0–4) without other concerning signs or symptoms do not require a workup. Furthermore, we agree with the adult literature suggesting that fevers developing outside of this period, from POD 5 and beyond, are more concerning for infection, and thus the decision to pursue further workup is reasonable. Neither high fevers nor multiple fevers in the first 4 PODs were found to be associated with infectious processes in our study and, therefore, do not necessitate workup if the patient is otherwise doing well. The correlation between multiple days of fevers and the development of delayed infections was interesting though not clinically significant, and the identification of multiple days of fevers in the first 4 PODs should not prompt additional action and does not alter our recommendation for workup of fevers manifesting beyond the first 4 PODs.

Thirty-nine of our patients had an EVD or LD placed, one of which was placed for a CSF leak following a Chiari decompression; 38 were placed in association with brain tumors. EVD-related infection is a known major complication related to neurosurgery, and this was confirmed by our results. A study by Jamjoom et al.¹⁰ examining CSF infections related to pediatric EVD placement reported an EVD-related infection rate of 8.1%.¹⁰ Our study yielded an EVD-related infection rate of 10.3% (4/39). Jamjoom and colleagues further demonstrated that the risk of infection is increased with a drain that remains in place for 8 days or longer and with an increased frequency of sampling CSF

TABLE 3. Fever workup costs

Variable	Cost in US\$
Test	
CBC w/ differential	153
UA	21
Ucx	206
CXR	647
Bcx	371
CSFcx	206
CSF cell count & differential	225
Acid-fast bacilli smear & culture	220
Total cost	2,049

from the drain.¹⁰ Given these findings, we believe that an acute fever workup within the first 4 PODs without signs or symptoms particularly concerning for ventriculitis or meningitis initially precludes CSF analysis and cultures until other etiologies are worked up, as sampling increases the risk of developing infections and the median time to infection is reported to be 9 days.¹⁰ Given the literature and our findings, we have begun to limit the time frame during which we keep EVDs in place by challenging patients earlier and inserting a shunt when appropriate in order to minimize the risk of CSF infection. Future analysis of our outcomes will tell whether these measures decrease our infection rates.

Our study is limited by its design as a single-institution retrospective review. The number of subjects was restricted by our decision to evaluate certain postoperative populations; however, we believe these patients are representative of the overall pediatric neurosurgical population. Not all febrile patients had a workup, and those who did undergo further evaluation often did not undergo a full workup. It is uncertain what prompted these specific workups, and this ambiguity is a limitation in our analysis. However, our results and recommendations are consistent with the literature on postoperative fevers, and we believe that they are applicable to the broader pediatric neurosurgical population.

Conclusions

Isolated fevers manifesting within the first 4 PODs are rarely associated with an infectious etiology in pediatric neurosurgical patients. Other clinical factors should be considered when deciding to pursue further investigation and expose these patients to additional costly and invasive testing.

References

1. Galicier C, Richet H. A prospective study of postoperative fever in a general surgery department. *Infect Control*. 1985; 6(12):487–490.
2. Garibaldi RA, Brodine S, Matsumiya S, Coleman M. Evidence for the non-infectious etiology of early postoperative fever. *Infect Control*. 1985;6(7):273–277.
3. Weed HG, Baddour LM, Ho VP. Fever in the surgical patient. *UpToDate*. November 25, 2019. Accessed July 10, 2020. <https://www.uptodate.com/contents/fever-in-the-surgical-patient>

4. Vermeulen H, Storm-Versloot MN, Goossens A, et al. Diagnostic accuracy of routine postoperative body temperature measurements. *Clin Infect Dis*. 2005;40(10):1404–1410.
5. Sherrod BA, Rocque BG. Morbidity associated with 30-day surgical site infection following nonshunt pediatric neurosurgery. *J Neurosurg Pediatr*. 2017;19(4):421–427.
6. Rolston JD, Han SJ, Lau CY, et al. Frequency and predictors of complications in neurological surgery: national trends from 2006 to 2011. *J Neurosurg*. 2014;120(3):736–745.
7. Karhade AV, Cote DJ, Larsen AM, Smith TR. Neurosurgical infection rates and risk factors: a National Surgical Quality Improvement Program analysis of 132,000 patients, 2006–2014. *World Neurosurg*. 2017;97:205–212.
8. Narayan M, Medinilla SP. Fever in the postoperative patient. *Emerg Med Clin North Am*. 2013;31(4):1045–1058.
9. Corkum KS, Hunter CJ, Grabowski JE, Lautz TB. Early postoperative fever workup in children: utilization and utility. *J Pediatr Surg*. 2018;53(7):1295–1300.
10. Jamjoom AAB, Joannides AJ, Poon MT, et al. Prospective, multicentre study of external ventricular drainage-related infections in the UK and Ireland. *J Neurol Neurosurg Psychiatry*. 2018;89(2):120–126.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: all authors. Acquisition of data: Raviv, Field. Analysis and interpretation of data: Raviv. Drafting the article: Raviv. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Raviv. Study supervision: Adamo.

Correspondence

Matthew A. Adamo: Albany Medical Center, Albany, NY. adamom@amc.edu.