Status Epilepticus Associated With Subtentorial Posterior Fossa Lesions

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Background: Nonconvulsive status epilepticus (SE) is a frequent complication in critically ill patients in the intensive care unit. While seizures have been reported in association with subtentorial posterior fossa lesions, the frequency of occurrence of SE among these patients is not known.

Objectives: To examine prevalence, clinical features, potential risk factors, and outcome of SE among patients presenting with subtentorial posterior fossa lesions.

Design: Retrospective review of our hospital database was conducted to identify patients with posterior fossa lesions complicated by SE over 1 year between April 1, 2007, and May 1, 2008.

Setting: Tertiary care setting.

Patients: Patients with subtentorial posterior fossa lesions admitted to the hospital for neurological or neurosurgical care.

Methods: A retrospective review of the inpatient database at St Joseph’s Hospital and Medical Center, Phoenix, Arizona, was conducted to identify patients with subtentorial posterior fossa lesions who were admitted to our tertiary referral hospital from April 1, 2007, to May 1, 2008. We also accessed information from operating room records to identify the number of patients who underwent neurosurgical intervention of these lesions. We then cross-referenced the EEG database to identify those patients within this group who had SE. All patients admitted to the hospital for neurological or neurosurgical care.

Results: Over 1 year, 13 of 501 patients (2.6%) admitted to the hospital with posterior fossa lesions had SE. Some patients had risk factors for SE such as sepsis, use of particular drugs, or intracranial bleeding, while others had no other clear identifiable cause.

Conclusions: Status epilepticus can be a potential complication in patients with posterior fossa cranial lesions and can be seen in up to 2.6% of such patients. Most have unfavorable outcome.

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Nonconvulsive status epilepticus (NCSE) has been increasingly recognized as a complication in critically ill, often comatose patients. Risk factors associated with this complication include advanced age, multisystem organ failure, sepsis, and acute toxic encephalopathy. Specific neurological pathologic findings associated with increased risk of NCSE include spontaneous subarachnoid hemorrhage. Other central nervous system associations include acute stroke, brain neoplasm, and meningitis. Early recognition and treatment of status epilepticus (SE) are indicated because failure to treat may result in further neurological damage.

In the literature, there have been reports of seizures associated with posterior fossa lesions. In these reports, causes of postoperative seizures included intraoperative ventriculoperitoneal shunt or ventriculostomy placement, hemorrhage remote from the site of surgery, and metabolic causes. However, to our knowledge there are no reports in the literature highlighting the frequency and cause of SE (convulsive or nonconvulsive) in patients with subtentorial posterior fossa lesions. We encountered several cases of SE on emergent electroencephalographic (EEG) recordings and continuous EEG monitoring among those who underwent posterior fossa surgery. Following this, we conducted a systematic retrospective database review to further explore the association between patients with posterior fossa lesions and SE.
tients who were thought to have SE also had continuous EEG monitoring, and interpretations were based on visual review of the recordings by neurologists who are board-certified clinical neurophysiologists. A review of the demographics, imaging studies, and electrophysiological data was then performed. Cause of the posterior fossa lesions, type of surgical intervention, postoperative complications or comorbidities, information regarding treatment interventions, and clinical course were also investigated.

### RESULTS

A total of 501 patients were admitted with subtentorial posterior fossa lesions during the study period. Of these patients, 76 had posterior fossa tumors, 105 had vascular malformations within the posterior fossa, 216 had cerebellar infarcts or nontraumatic cerebellar hemorrhage, 42 had traumatic cerebellar hemorrhage, and the remainder had miscellaneous lesions including demyelinating lesions and arachnoid cysts. Of the 501 patients, 191 underwent a neurosurgical intervention for the lesions, either emergent or elective. For those who underwent surgery, the surgical techniques included suboccipital, retrosigmoid, posterior fossa, modified orbitozygomatic, and supracerebellar approaches.

Thirteen of the 501 patients were found to have NCSE identified on EEG. Thus, the prevalence rate of NCSE with subtentorial posterior fossa lesions in this studied population was approximately 2.6% per year. The group consisted primarily of women as they constituted 12 of the 13 patients. Ages ranged from 19 to 83 years, with a median age of 73 years and a mean age of 64 years (Table). All 13 patients presented with acute mental status changes, and 3 of the 13 had clinical seizures prior to onset of the mental status change. Mental status changes consisted of a decline in consciousness for most cases or failure to return to consciousness postoperatively or unexplained agitation for some cases. All cases had emergent EEG followed by continuous EEG monitoring, which identified NCSE. Of the patients who were identified as having NCSE, most demonstrated generalized epileptiform activity, with 7 showing generalized periodic epileptiform discharges (Figure 1) and 3 having bilateral independent periodic epileptiform discharges. Only 2 of the 13 had focal periodic discharges or focal seizures (Figure 2).

The latency to status onset from the time of surgery varied from 1 to several days, to monitor treatment response. Most patients were responsive to treatment with multiple antiepileptic drugs including benzodiazepines, fosphenytoin sodium, levetiracetam, phenobarbital, propofol, and pentobarbital. Many patients were treatment responsive, although some showed EEG patterns consistent with persistent NCSE despite the use of myriad medications. All patients underwent continuous EEG monitoring to follow their treatment response. One patient remained in refractory SE at the time of his transfer to hospice despite aggressive management including barbiturate coma.

In general, outcome for this group of patients with posterior fossa lesions who went on to develop NCSE was poor. Six of 13 patients had care withdrawn and died in the hospital or were transferred to hospice. Four of 13 were sent in poor neurological condition to subacute rehabilitation or skilled nursing facilities. Of note, the 2 patients with EEG findings showing focal SE were among the group with a fair outcome, i.e., they were transferred to subacute rehabilitation facilities. Only 3 of 13 patients were transferred to acute rehabilitation facilities with favorable prognoses.

### COMMENT

Our study shows that NCSE, although infrequent, can be a potential complication in up to 2.6% of patients with subtentorial posterior fossa lesions. In most cases, NCSE followed a neurosurgical intervention. Those with focal periodic discharges had better neurological outcome compared with those who had generalized or bilateral periodic discharges. To our knowledge there are no studies in the literature that reported SE and its association with posterior fossa lesions.

The subtle presentation of NCSE underscores the need to identify patients who may be at increased risk for development of this complication. This is particularly true...
given the associated high mortality rate in intensive care units in those patients with multisystem organ failure. Many patients in our study also had acute medical complications such as renal insufficiency, sepsis, and ventilation-dependent respiratory failure. Litt et al studied 24 patients with NCSE and found that illness severity at the time of NCSE onset was the major determinant of poor prognosis in this population. They also found that a generalized pattern was highly correlated with death. Similarly, most of our studied patients with NCSE had a generalized pattern and poor prognoses; the 2 patients with focal NCSE had a more favorable outcome.

Several retrospective analyses have investigated the association between posterior fossa lesions and seizures.

### Table. Patients With Posterior Fossa Lesions and Status Epilepticus

<table>
<thead>
<tr>
<th>Patient No./Age, y</th>
<th>Lesion</th>
<th>Surgical Procedure</th>
<th>Latency to Status Epilepticus, d</th>
<th>Type of Periodic Discharges on EEG</th>
<th>Risk Factors</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/64</td>
<td>Right cerebellar IPH</td>
<td>Posterior fossa craniotomy</td>
<td>8</td>
<td>GPEDs</td>
<td>Sepsis; cephaline use</td>
<td>Lorazepam; fosphenytoin sodium; levetiracetam</td>
<td>Poor: withdrawal of care</td>
</tr>
<tr>
<td>2/81</td>
<td>Left cerebellar IPH</td>
<td>Posterior fossa craniotomy</td>
<td>1</td>
<td>BIPEDs</td>
<td>UTI; cefuroxime use</td>
<td>Midazolam; fosphenytoin sodium; levetiracetam</td>
<td>Poor: hospice placement</td>
</tr>
<tr>
<td>3/79</td>
<td>Right superior cerebellar artery aneurysm</td>
<td>Aneurysm coiling</td>
<td>30</td>
<td>PLEDs</td>
<td>Ventriculoperitoneal shunt placement; UTI; levofloxacin use; cephaline use</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: SNF placement</td>
</tr>
<tr>
<td>4/75</td>
<td>Left PICA aneurysm; fourth ventricular IVH</td>
<td>Suboccipital craniectomy for evacuation of IVH; left PICA aneurysm clipping</td>
<td>1</td>
<td>GPEDs</td>
<td>Pneumonia; respiratory failure; cephaline use</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: withdrawal of care</td>
</tr>
<tr>
<td>5/73</td>
<td>Foramen magnum meningioma</td>
<td>Suboccipital craniectomy for microsurgical resection</td>
<td>1</td>
<td>GPEDs</td>
<td>External ventricular drain; trace IVH</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: withdrawal of care</td>
</tr>
<tr>
<td>6/73</td>
<td>Right cerebellar IPH; left lateral IVH</td>
<td>Posterior fossa craniotomy × 2</td>
<td>1</td>
<td>GPEDs</td>
<td>Pneumonia; levofloxacin use; cephaline use</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: multisystem organ failure; death</td>
</tr>
<tr>
<td>7/68</td>
<td>Cavernous malformations in left thalamus, tectum, and cerebellum</td>
<td>Posterior fossa craniotomy (supracerebellar approach) for tectal cavernous malformation resection</td>
<td>1</td>
<td>GPEDs</td>
<td>Intraoperative bleeding; postoperative cerebellar infarct; hyponatremia</td>
<td>Lorazepam; fosphenytoin sodium</td>
<td>Favorable: acute rehabilitation</td>
</tr>
<tr>
<td>8/60</td>
<td>Pontine cavernous malformation</td>
<td>Retrosigmoid craniotomy</td>
<td>6</td>
<td>BIPEDs</td>
<td>External ventricular drain placement</td>
<td>Fosphenytoin; levetiracetam</td>
<td>Poor: hospice placement</td>
</tr>
<tr>
<td>9/56</td>
<td>Basilar tip aneurysm</td>
<td>Right OZ craniotomy for aneurysm clipping</td>
<td>1</td>
<td>PLEDs</td>
<td>Bupropion hydrochloride use</td>
<td>Lorazepam; fosphenytoin sodium</td>
<td>Favorable: acute rehabilitation</td>
</tr>
<tr>
<td>10/54</td>
<td>Vasogenic edema in cerebellum and occipital lobes due to posterior reversible encephalopathy</td>
<td>None</td>
<td>1</td>
<td>BIPEDs</td>
<td>Sepsis</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: hospice placement</td>
</tr>
<tr>
<td>11/27</td>
<td>Pineal cavernous malformation</td>
<td>Suboccipital craniotomy for resection of cavernous malformation</td>
<td>6</td>
<td>GPEDs</td>
<td>None</td>
<td>Fosphenytoin sodium</td>
<td>Favorable: acute rehabilitation</td>
</tr>
<tr>
<td>12/19</td>
<td>Ganglioglioma in right cerebellum</td>
<td>Retrosigmoid craniotomy</td>
<td>8</td>
<td>PLEDs</td>
<td>Sepsis</td>
<td>Lorazepam; fosphenytoin sodium; phenobarbital; levetiracetam</td>
<td>Poor: SNF placement</td>
</tr>
<tr>
<td>13/83</td>
<td>Bilateral cerebellar infarcts; basilar tip aneurysm</td>
<td>Modified OZ approach for aneurysm clipping</td>
<td>4</td>
<td>PLEDs</td>
<td>Acute postoperative infarct; brainstem infarct; cephaline use; levofloxacin use</td>
<td>Fosphenytoin sodium; levetiracetam</td>
<td>Poor: SNF placement</td>
</tr>
</tbody>
</table>

Abbreviations: BIPEDs, bilateral independent periodic epileptiform discharges; EEG, electroencephalography; GPEDs, generalized periodic epileptiform discharges; IPH, intraparenchymal hemorrhage; IVH, intraventricular hemorrhage; OZ, orbitozygomatic; PICA, posterior inferior cerebellar artery; PLEDs, periodic lateralized epileptiform discharges; SNF, skilled nursing facility; UTI, urinary tract infection.
although most association was with tumors. Suri et al reviewed 511 patients with posterior fossa lesions, of whom 30 went on to develop postoperative seizures following posterior fossa surgery. Of the 250 patients who underwent posterior fossa surgery via the suboccipital approach (in a sitting position), 24 developed postoperative seizures. The sitting position was implicated as significant in the cause of seizures within this population when compared with patients undergoing posterior fossa surgery in a prone or lateral position. In addition, a statistically significant increased risk of seizures was found in patients with pneumocephalus, postoperative hematoma, and hydrocephalus. A higher incidence of seizures was also observed in patients with preoperative ventriculoperitoneal shunt or intraoperative ventriculostomy placement. Etiological associations of postoperative seizures included vestibular schwannomas, medulloblastomas, astrocytomas, epidermoid cysts, meningiomas, and hemangioblastomas. Sixty-six percent of the patients had the seizure within 3 hours of surgery,
and generalized tonic-clonic was the most common seizure type (80%). No reports of subclinical seizures or SE were reported. Fukamachi et al also described 3 patients with tumors of the posterior fossa who developed seizures within 48 hours postoperatively. In our sample, SE was not limited to those with tumors.

Little et al studied the association of NCSE in patients with spontaneous subarachnoid hemorrhage and found that advanced age, being female, need for ventriculostomy, and structural lesions were more common in this population. In addition, the most common outcome in this group was the decision to withdraw care. Similarly, we also found that most of the patients were female, although it remains unclear why this apparent sex predilection exists. Our results were also consistent with the finding of increased incidence in the elderly population. This may in part reflect the increased incidence of comorbidities at the time of ictus. The fact that there has been an association with ventriculostomy placement and onset of SE is perhaps something that should be considered when determining the timing of shunt placement, although this may also reflect the cumulative effect of additional brain injury lowering the threshold to develop NCSE.

Copeland et al found that 4.3% of patients undergoing ventricular shunting developed postoperative seizures. We found 1 case of NCSE that temporally followed ventriculoperitoneal shunt placement rather than the initial craniotomy for posterior fossa lesion treatment. In this situation, seizure activity may be related to new cortical injury resulting from placement of the shunt. While 1 patient had an intraoperative hemorrhage, the remainder of the patients went on to develop postoperative NCSE in the absence of any intraoperative complications. Posterior fossa lesions may serve as epileptogenic foci, although they do not necessarily predict seizure localization, ie, most patients had generalized ictal patterns.

Advanced age appeared to correlate with increased incidence of NCSE as well as poor prognosis thereafter. Notably, almost half of these 13 patients with NCSE and posterior fossa lesions were also being treated with cephalosporins. Literature reports have shown an association between cephalosporin use and neurological toxic effects including seizures and NCSE. Thus, clinicians should perhaps avoid administering drugs that lower seizure threshold in this population. Moreover, the threshold for ordering an EEG and continuous EEG monitoring should be low in patients with a posterior fossa lesion who develop altered mental status, particularly in the first few days following craniotomy.

Our study may also suggest the possible use of prophylactic anticonvulsant treatment in some patients with posterior fossa lesions, especially in the first week after surgery. Prevention of NCSE as a complication of posterior fossa surgery could result in an improved prognosis for such patients. In addition, such a prophylactic measure may also be cost-effective given the increased morbidity and mortality in those patients who do develop NCSE. Because of the low reported incidence of NCSE in this population, the prophylactic use of antiepileptic drugs is not necessarily warranted; however, identifying those patients within this population who have additional risk factors for developing NCSE might lead to consideration of this strategy. Further studies are needed to investigate whether prophylactic anticonvulsant use could prevent SE in high-risk neurosurgical populations.

Nonconvulsive SE can be seen in approximately 2.6% of patients with subtentorial posterior fossa lesions and correlates frequently with a poor prognosis. While comorbidities, patient demographics, and specific causes appear to be associated with increased risk of NCSE, further research is required to explore the potential causes of this complication.

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Author Contributions: Dr Maganti had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Treiman and Maganti. Acquisition of data: Grill and Maganti. Analysis and interpretation of data: Grill, Treiman, and Maganti. Drafting of the manuscript: Grill and Maganti. Critical revision of the manuscript for important intellectual content: Treiman and Maganti. Administrative, technical, and material support: Treiman and Maganti. Study supervision: Treiman and Maganti.

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REFERENCES