Off-Therapy Headaches in Pediatric Brain Tumor Patients: A Retrospective Review

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Abstract
To determine the incidence, timing, and characteristics of headaches in a population of off-therapy pediatric brain tumor patients, a retrospective chart review was conducted on 3 subpopulations of children followed in a multidisciplinary neuro-oncology clinic in the Southeastern United States. Data collected included tumor type and location, treatment, associated symptoms, and description and timing of headaches. In all, 81 charts were reviewed from which headaches in 3 subtypes of tumors were identified (29 medulloblastomas, 36 cerebellar juvenile pilocytic astrocytomas [JPAs], and 16 craniopharyngiomas). Off-therapy headaches were noted in 6 (21%) of medulloblastomas, 10 (28%) of JPAs, and 19 (56%) of craniopharyngiomas. Almost half of those patients with prediagnosis headaches had recurrent off-therapy headaches. Given the incidence of this symptom, headache must be highlighted in posttreatment and late effects monitoring. Whether provided by the oncology team or primary care provider, headache assessment, treatment, and prevention counseling can be improved through utilization of newly developed tools and written educational materials. Experienced nurses can play key roles in this aspect of posttreatment pediatric care of brain tumor patients.

Keywords
off-therapy (OT), recurrent, late effects, headache

Assessment and treatment of the pediatric brain tumor patient with posttreatment headaches is a process in which the nurse plays a unique role. Often the nurse is the “first responder” when a family member calls to report the symptom of headache. Frequently, the obvious concern from both the nurse and family is whether the headache signifies a serious complication or is merely a benign, “garden-variety” type headache. The intent of this article is to provide background information and data to help nurses and other health care providers make informed decisions about this aspect of care, thus improving the standard of care for this special patient population.

Relatively few studies have evaluated the prevalence and relationship of headaches with pediatric brain tumors. The landmark project conducted by the Childhood Brain Tumor Consortium (1991) reported that 62% of the children with brain tumors (n = 3,291 subjects) experienced chronic or frequent headaches prior to their first hospitalization. Honig and Charney (1982) found that of children who had headaches secondary to a brain tumor (n = 72), 94% had neurologic or ocular abnormalities at the time of diagnosis. A total of 85% of these developed the abnormalities within 2 months of headache onset. Nearly two-thirds of these headaches were characterized by awakening from sleep or were present on awakening.

Studies concerning the relationship of headaches and brain tumors in adults are available but scarce since the 1990s (Forsyth, 1993; Pfund, Szapary, Jaszberenyi, Nagy, & Czopf, 1999; Suwanwela, Phanthumchinda, & Kaoropthum, 1994). A recent review of the literature concerning pediatric brain tumor patients with headaches revealed studies focused on presenting signs and symptoms at diagnosis. Dobrovoljac, Hengartner, Bolthaus, and Grotzer (2002) assessed the prediagnostic period in 252 children with primary brain tumors, finding headache to be among the most common presenting symptoms in children older than 2 years of age. A meta-analysis by Wilne et al. (2007) also found headache to be among the most frequent signs and symptoms of childhood central nervous system (CNS) tumor presentation.

In contrast to the above findings related to tumor diagnosis, data from general pediatric neurology populations...
reveal a low incidence of brain tumors in patients presenting with headache alone. When 133 general pediatric neurology records were reviewed by Maytal, Bienkowski, Patel, and Eviatar (1995), no relevant imaging abnormalities were found in cases of vascular, tension, mixed, psychogenic, and posttraumatic headache. This result was similar to findings in Lewis and Dorbad’s (2000) retrospective study of 302 pediatric neurology clinic patients with headache and a normal neurologic exam. In addition, Deda, Caksen, and Ocal (2000) looked at etiology of 125 pediatric headache patients in Turkey and found migraine to be the most common cause. Gallelli et al. (2005) noted increased incidence of headache in city-dwelling secondary school students compared with other geographic demographics, with chronic headache prevalent in nonsteroidal anti-inflammatory drug users. These results are reassuring to providers and parents of children with headache not accompanied by other neurologic symptoms.

The available studies of headache in children are helpful for general neurology practitioners and patients. However, health care providers in the area of pediatric neuro-oncology know well that in this special population, headache diagnosis may be more complicated. Headaches seem to persist throughout treatment as well as off therapy. Off-therapy (OT) headaches in childhood brain tumor patients raise the concern of recurrence of tumors. Literature searches for studies on surveillance of OT headaches have revealed a paucity of research in this area. Packer et al.’s (2003) childhood cancer survivor study looked at long-term neurologic and neurosensory sequelae in childhood brain tumor survivors and found survivors were at an increased risk for hearing impairment, legal blindness, cataracts, double vision, and seizure disorder compared with a sibling cohort. There is no mention of the incidence of headache in Packer et al.’s report.

Diagnosis and treatment of OT headaches is challenging, both in the characterization of the headache as well as the treatment choices and education of the family. Lundqvist, Clench-Aas, Hofoss, and Bartonova (2006) compared responses on a parent questionnaire to daily diary registration of headache in 2,126 children. They found that parents underreported headaches compared with children, particularly children with frequent headaches. This finding brings to light the idea that proper assessment of headache in the pediatric neuro-oncology patient may require careful questioning of both the patient and parent. Improvement in treatment begins with improved understanding of headache characteristics for specific pediatric populations. This hypothesis was the impetus for the following study.

**Background**

Complaints of headache among brain tumor patients were common in the authors’ pediatric neuro-oncology clinic. Headache during treatment phase was felt to be easily attributed to fatigue, nutritional issues, or medication effects. More challenging, however, were complaints of headache from OT clients. Many of these complaints were elicited during periodic visits to the Comprehensive Brain Tumor Clinic, which functions as a follow-up/late effects program. Frequently, additional follow-up visits were required for problem-oriented assessment and treatment of the headaches. The prevalence of these headaches on review of systems compared with other symptoms warranted investigation.

**Purpose and Methodology**

The purpose of the study was to determine the incidence and characteristics of headaches in a population of pediatric brain tumor patients attending a multidisciplinary clinic in a large Southeastern cancer center. Retrospective chart review was used for the period of time beginning January 1, 2003, and ending October 31, 2005. Informed consent was not required by the institution because of the confidential nature of retrospective chart review with no more than minimal risk to subjects. Data collection was guided by an original tool (Figure 1), which included demographics, tumor type and location, extent of disease, incidence of progression, treatments, associated symptoms, and description of headaches at presentation and OT. Headaches occurring while on therapy were not analyzed. There were no exclusions regarding age, race, or ethnicity.

**Results**

For the purposes of this study, 3 subtypes of brain tumor patients were identified and 81 charts reviewed. The 3 groups were medulloblastomas (n = 29), cerebellar juvenile pilocytic astrocytomas (n = 36), and craniopharyngiomas (n = 16). Within these groups, 20 of the 29 medulloblastoma patients (69%), 21 of the 36 cerebellar JPA patients (58%), and 10 of the 16 craniopharyngioma patients (62%) had headaches on initial presentation. As seen in Figure 2, OT headaches were noted in 21% of medulloblastomas, 28% of cerebellar JPAs, and 56% of craniopharyngiomas.

Table 1 reflects the comparison of headaches at presentation versus OT as well as whether radiation therapy or chemotherapy was received. Of the medulloblastoma patients with OT headaches, 67% had radiation therapy and 83% had chemotherapy. In the cerebellar JPA OT group, 0% had radiation therapy and 0% had chemotherapy. Of the craniopharyngioma OT headache patients, 44% had radiation therapy and 0% had chemotherapy. As shown in Table 2, extent of surgical resection in each of the groups varied. In all, 90% of medulloblastoma patients, 100% of cerebellar JPA patients, and 60% of the...
craniopharyngioma patients with pretreatment headaches had surgical gross total resection of their brain tumors.

Increased intracranial pressure was also associated with headaches at diagnosis. Of 17 patients whose tumor was located in the cerebellum (those with either medulloblastoma or cerebellar JPA) and who had headaches off-treatment, 15 had hydrocephalus at diagnosis. No patients had shunt malfunction at the time of assessment. Hydrocephalus did not correlate with headaches in the suprasellar (craniopharyngioma) group.

Almost half of all patients with prediagnosis headaches had significant posttreatment headaches. The incidence of frequent (i.e., 1 or more per week, group A) and occasional (i.e., 1 to 2 per month, group B) OT headaches was greater in cerebellar JPA and craniopharyngioma patients than in medulloblastoma patients. Cerebellar JPA patients had 4 group A and 6 group B headaches out of a total of 10, medulloblastoma patients had 2 group A and 0 group B headaches out of a total of 6, and craniopharyngiomas patients had 6 group A and 2 group B headaches out of a total of 9 headaches (Figure 3).

Migrainous features were present in more than half of the cerebellar JPA (7 out of 10) and craniopharyngioma (7 out of 11) patients with OT headaches, but in none of the 6 medulloblastoma patients OT. Migraine features noted were sensitivity to light and noise, nausea and vomiting, and headache worsening with activity. Additional symptoms experienced during headaches included double vision, dizziness, extreme fatigue, irritability, slurred speech, visual blurring, and unsteady walking and standing.

Discussion

As previously mentioned, data on the phenomenon of posttreatment headaches in children with brain tumors are conspicuously absent from scientific literature. The studies by Childhood Brain Tumor Consortium (1991) and Honig and Charney (1982) provide a database of prediagnosis headaches. The incidence and characteristics of OT headaches remains a question. On further review of adult headache literature, an interesting finding concerning tumor necrosis factor-α in new daily headache patients was linked to the possibility of a persistent state of central nervous system inflammation (Rozen & Swidan, 2007). This finding exemplifies the notion that chronic headaches may be multifactorial.

The current study looks at characteristics of recurrent headaches in a small population of pediatric patients. Results suggest that there is a higher frequency of headaches and specifically those with associated migrainous features noted in cerebellar JPA versus medulloblastoma patients. It is unclear as to why JPA patients experienced more headaches. There was no correlation with progression of the disease, extent of surgery, or type of treatment.

### Brain Tumor Headache Review

**Data Collection**

**Date of Review:** _______________________

1. **Patient Number** ______________________
2. **Age** _______________________________
3. **Gender** M F
4. **Tumor Type**
   - Cerebellar LGA
   - PF Ependymoma
   - Medulloblastoma
   - Suprasellar Mass
   - Cranioopharyngioma
   - Tectal Plate Mass
5. **Time of Headache Presentation**
   - Pre-diagnosis
   - On Treatment
   - Off Treatment
6. **Frequency of Headaches**
   - < 1/month
   - 1-2/month
   - 1 or >/week
7. **Migraine Features**
   - photophobia
   - phonophobia
   - worse with activity
   - nausea
   - vomiting
   - visual aura
   - throbbing quality
   - improves with sleep
   - unilateral
   - bilateral
8. **Associated Symptoms**
   - Weakness
   - Numbness
   - Ataxia
   - Dysarthria
   - Change in behavior
9. **Surgery** ___________________________
10. **Date of Surgery** _____________________
11. **Hydrocephalus**
    - Yes
    - No
12. **Shunted**
    - Yes
    - No
13. **Third Ventriculostomy**
    - Yes
    - No
14. **History of chemotherapy treatment***
    - Yes
    - No
15. **History of radiation treatment***
    - Yes
    - No
16. **Incidence of recurrence/progression***
    - Yes
    - No

*Addendum variables

**Figure 1. Brain Tumor Headache Review**
Table 1. Comparison of Headaches at Presentation Versus Off-Therapy and Types of Treatment

<table>
<thead>
<tr>
<th>Tumor Types</th>
<th>Surgery(^a)</th>
<th>Radiation</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastomas N=20 with pretreatment headaches</td>
<td>95%(^\ast) (100% with biopsy)</td>
<td>95%</td>
<td>90%</td>
</tr>
<tr>
<td>No HAs Off-Tx N=15</td>
<td>100%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>Off-Tx HAs N=6</td>
<td>100%</td>
<td>67%</td>
<td>83%</td>
</tr>
<tr>
<td>Cerebellar JPAs N= 21 with pretreatment headaches</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>No HAs Off-Tx N=13</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Off-Tx HAs N= 10</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Craniopharyngiomas N= 10 with pretreatment headaches</td>
<td>100%</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>No HAs Off-Tx N=5</td>
<td>67%</td>
<td>80%</td>
<td>0%</td>
</tr>
<tr>
<td>Off-Tx HAs N= 9</td>
<td>88%</td>
<td>44%</td>
<td>0%</td>
</tr>
</tbody>
</table>

NOTE: HA = headache; Off-Tx = off-therapy; JPA = juvenile pilocytic astrocytoma.
\(^a\) Biopsy only not included in surgical group.
Table 2. Comparison of Headaches at Presentation Versus Off-Therapy and Extent of Resection/Progression

<table>
<thead>
<tr>
<th>Tumor Types</th>
<th>% of Pts. With Recurrence/Progression</th>
<th>Gross Total Resection</th>
<th>Subtotal Resection</th>
<th>Biopsy Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastomas N=20 with headaches Pre-Tx</td>
<td>15%</td>
<td>90%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>No HA s Off-Tx N=15</td>
<td>20%</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Off-Tx HA s N=6</td>
<td>0%</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
</tr>
<tr>
<td>Cerebellar JPA s N=21 with headaches Pre-Tx</td>
<td>5%</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>No HA s Off-Tx N=13</td>
<td>8%</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Off-Tx HA s N=10</td>
<td>0%</td>
<td>90%</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>Craniopharyngiomas N=10 with headaches Pre-Tx</td>
<td>60%</td>
<td>60%</td>
<td>30%</td>
<td>0%</td>
</tr>
<tr>
<td>No HA s Off-Tx N=5</td>
<td>100%</td>
<td>0%</td>
<td>67%</td>
<td>33%</td>
</tr>
<tr>
<td>Off-Tx HA s N=9</td>
<td>22%</td>
<td>66%</td>
<td>22%</td>
<td>11%</td>
</tr>
</tbody>
</table>

NOTE: HA = headache; Off-Tx = off-therapy; JPA = juvenile pilocytic astrocytoma.

Figure 3. Off-Therapy Headaches in Pediatric Brain Tumor Patients
received. In addition, the high percentage of frequent OT headaches incurred by the craniopharyngioma patients may relate to the suprasellar location, extent of resection, recurrence rate, as well as multiple endocrine abnormalities suffered by these patients. Surprisingly, within each tumor type, the patients with posttreatment headaches generally had a lower rate of gross total resections and adjuvant therapy than the patients who had no headaches off-treatment. Extent of surgery or treatment may not relate to the incidence of OT headaches.

**Limitations**

The limitations of this study are similar to those expected with retrospective research. Data availability varied with each patient encounter and patient care provider. Also, the limited time frame of patient visits used in data collection decreased the subject group size. In addition, other causes for headaches (stress, diet, sleep, family history, etc.) could not be fully assessed in this retrospective review. Finally, during the initial data collection phase, investigators identified common variables in the eligible medical records, which prompted an addendum to the data collection tool. These additional variables are noted in Figure 1.

**Recommendations for Future Study**

Causes for recurrent headaches in the pediatric brain tumor population warrant further study. Posttreatment phase patients returning for routine surveillance and late effects monitoring would benefit from more thorough investigation into headache symptomatology. As a result of the current study, a standard headache questionnaire was developed (Figure 4). The Lundqvist et al. (2006) study suggests that the pediatric patient should provide historical data personally. If this is a valid assumption, the standard headache questionnaire responses could be elicited from both caregiver and patient, and then compared.

The following questions remain, however: Are these children prone to headaches based on family history and lifestyle? How have their sleep habits impacted headache frequencies? Are the headache frequency rates different from siblings in the same home? Studies that compare sibling cohorts would be valuable in answering some of these questions. Other cohorts, such as the pediatric migraine population, might also provide insight into etiologies such as inflammatory process as looked at in the tumor necrosis factor study by Rozen and Swidan (2007).

Improved understanding of OT headaches will lead to improved treatment of specific types of headaches in children. Standards of care for pediatric migraine should be considered for posttreatment brain tumor patients, because many of these patients have migraine features. Close collaboration with neurology colleagues will be essential in modifying these standards of care. Treatment studies might also lend insight into effectiveness and safety of medications such as triptans in brain tumor patients.

Emphasis in oncology research is in part focused on late effects. Neglecting headache as a possible late effect, regardless of exact cause, is a disservice to pediatric neuro-oncology patients. Central to this care is counseling followed by “take-home” written educational materials, which may help reduce the incidence of headaches. This aspect of patient care is an area where nurses can be instrumental.

**Nursing Role**

Proper triage of symptomatology, causation, frequency, and severity of headache is invaluable. Often such confounding triggers such as rebound phenomena (from caffeine, analgesics, etc), sleep deprivation, stress, and nutrition can be determined and addressed. If no discernible trigger can be found, the advanced practice nurse should perform a thorough neurologic exam to look for new or significant physical findings.

Conditions such as hypertension, papilledema, and abnormal neurologic findings may reveal the cause of the headache. Proper use of diagnostic tests including laboratory or radiologic evaluation will also help with proper diagnosis. If no progression or recurrence of tumor is present, care can then be focused on identifying triggers and treating symptoms. Once the headache is relieved or controlled, the nurse and/or nurse practitioner should counsel the patient and family about lifestyle modifications. Certain modifications may prevent many of the headaches. These changes include improving sleep habits, meal schedules, fluid intake, and stress reduction and eliminating food and environmental triggers. Prophylactic medications may be warranted to reduce headache frequency or improve quality of life, and the daily use of these should be emphasized during patient counseling.

The nurse has a key role in obtaining the patient history, assisting with diagnosis and management, and providing counseling to prevent further headaches. Working with pediatric brain tumor patients who have posttreatment headaches can be challenging but ultimately rewarding. In this pediatric subspecialty area, the nurse has the unique ability to participate in an outpatient setting, which can offer management of both acute and chronic pain. In addition, late effects surveillance
programs are prime opportunities for continued nursing involvement. Nursing expertise can be used to develop improved collaborative care plans, which, when shared with the child, family, and primary care provider, will lead to successful continuity of long-term care.

<table>
<thead>
<tr>
<th>Date:</th>
<th>Time:</th>
<th>Diagnosis:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Form completed by: ☐ Patient ☐ Mother ☐ Father ☐ Other:

**PLEASE CHECK ALL THAT APPLY FOR EACH QUESTION**

1. **When do the headaches occur?** ☐ morning ☐ afternoon ☐ evening ☐ bedtime ☐ other ____________

2. **What things seem to bring on the headaches?**
   - ☐ puberty
   - ☐ drugs or alcohol
   - ☐ tiredness
   - ☐ menstrual cycle
   - ☐ foods
   - ☐ not drinking enough
   - ☐ birth control pills
   - ☐ exercise
   - ☐ hunger
   - ☐ illness
   - ☐ stress
   - ☐ weather changes
   - ☐ sleep
   - ☐ not sure
   - ☐ other (please describe): ____________

3. **What occurs before the headache?**
   - ☐ change in vision
   - ☐ change in hearing
   - ☐ change in sense of touch
   - ☐ strange odor
   - ☐ strange taste
   - ☐ nothing
   - ☐ other (please describe): ____________

4. **How often do the headaches occur?** ☐ daily ☐ once a week ☐ once a month ☐ other ____________

5. **How long do the headaches last?** ☐ less than 1 hour ☐ 2-3 hours ☐ 4-6 hours ☐ all day ☐ other ____________

6. **What part of the head hurts?**
   - ☐ right
   - ☐ left
   - ☐ both sides
   - ☐ top of head
   - ☐ side of head
   - ☐ back of head
   - ☐ behind the eyes
   - ☐ all over
   - ☐ moves from ____________ to ____________

7. **How bad do the headaches feel?** Rate the headache pain on a scale of 1-10 with 1 being the least and 10 being the worst ____________

8. **What does the pain feel like?**
   - ☐ throbbing (pulses)
   - ☐ dull
   - ☐ sharp
   - ☐ steady
   - ☐ other: ____________

9. **What makes the headache worse?**
   - ☐ light
   - ☐ noise or sounds
   - ☐ activity
   - ☐ other (please describe): ____________

10. **What else occurs with the headache?**
    - ☐ double vision
    - ☐ dizziness
    - ☐ very tired
    - ☐ nausea
    - ☐ vomiting
    - ☐ blurry vision
    - ☐ irritability
    - ☐ slurred speech
    - ☐ unsteady walking and standing
    - ☐ no other symptoms
    - ☐ other (please describe): ____________

11. **What helps the headache?**
    - ☐ quiet area
    - ☐ darkness
    - ☐ sleep
    - ☐ reducing stress
    - ☐ nothing
    - ☐ medicines (which type): ____________
    - ☐ other (please describe): ____________

12. **Please note any of the problems listed below and who has them in your family:**
    - ☐ migraine headaches
    - ☐ mother
    - ☐ father
    - ☐ grandparent
    - ☐ sibling
    - ☐ other
    - ☐ brain tumors
    - ☐ mother
    - ☐ father
    - ☐ grandparent
    - ☐ sibling
    - ☐ other
    - ☐ aneurysm
    - ☐ mother
    - ☐ father
    - ☐ grandparent
    - ☐ sibling
    - ☐ other
    - ☐ other nervous system problems
    - ☐ mother
    - ☐ father
    - ☐ grandparent
    - ☐ sibling
    - ☐ other

Reviewed by: ____________

Data/Time: ____________

Figure 4. Standard Headache Questionnaire

References


**Bios**

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