Headache with Focal Neurologic Signs in Children at the Emergency Department

Davide Massano, MD, Sebastien Julliand, MD, Lakshmi Kanagarajah, MD, Maxime Gautier, MD, Audrey Vizeneux, MD, Monique Elmaleh, MD, Marianne Allison, MD, Emilie Lejay, MD, Silvia Romanelli, MD, Laurence Teisseyre, MD, Catherine Delanoe, MD, and Luigi Titomanlio, MD, PhD

Objective To identify predictors of secondary headache in children consulting at the pediatric emergency department (ED) for headache with a focal neurologic deficit.

Study design In this prospective cohort study, we enrolled children aged 6-18 years presenting to the ED of a tertiary care hospital with moderate to severe headache and focal neurologic deficit. Enrollment took place between March 2009 and February 2012. Children with a history of trauma, fever, or neurosurgical intervention were excluded from the study. The final diagnosis was made after 1 year of follow-up. Our primary aim was to identify any differences in the frequency of clinical signs between children with a final diagnosis of primary headache and those with a final diagnosis of secondary headache.

Results Of the 101 patients included in the study, 66% received a final diagnosis of primary headache (94% migraine with aura), and 34% received a final diagnosis of secondary headache (76.5% focal epilepsy). On multivariate analysis, children with bilateral localization of pain had a higher likelihood (aOR, 8.6; 95% CI, 3.2-23.2; P < .001) of having secondary headache.

Conclusion Among children presenting to the ED with focal neurologic deficits, a bilateral headache location was associated with higher odds of having a secondary cause of headache. Additional longitudinal studies are needed to investigate whether our data can aid management in the ED setting. (J Pediatr 2014;165:376-82).

The prevalence of any type of headache in children ranges from 37% to 51% and increases gradually during adolescence. 

Headache is one of the most common reasons for consultation in the pediatric emergency department (ED). Triage systems have been developed and adapted to the pediatric population to differentiate urgent from nonurgent patients, allowing appropriate and efficient management. In children with certain brain disorders, headache can be associated with focal neurologic signs or symptoms; these children represent a true diagnostic challenge to physicians, owing to the possibility of severe underlying disease.

The differential diagnosis in children with headache and focal neurologic signs includes primary etiologies, such as migraine with aura, and secondary etiologies, such as trauma, infection, and vascular, neoplastic, and epileptic disorders. Diagnostic criteria for migraine have been established by the International Classification of Headache Disorders—II revision (ICHD-II). Achieving a diagnosis in children can be challenging at times; important reasons for this include poor description of pain by children and several childhood periodic syndromes that can be common precursors of migraine. As in adults, migraines in children can be classified into 2 major subtypes: migraines without aura, which are headaches with specific features and associated symptoms, and migraines with aura, which are characterized primarily by focal neurologic deficits that usually precede or sometimes accompany the headache. Unlike in adults, however, migraine in children may persist for less than 4 hours, and may have a bilateral distribution in young children.

The aim of the present study was to investigate the etiology of headache with focal neurologic deficits in children, and to identify those clinical features associated with a diagnosis of secondary headache in this population.

Methods

This was a monocentric prospective cohort study of children presenting to the ED of a pediatric tertiary care hospital in Paris, France with headache associated

CT  Computed tomography
ED  Emergency department
EEG  Electroencephalography
ICHD-II  International Classification of Headache Disorders—II revision
IEH  Ictal epileptic headache
MRI  Magnetic resonance imaging

From the 1Pediatric Emergency Department and 2Pediatric Migraine and Neurovascular Diseases Clinic, Robert Debré Hospital–Assistance Publique Hôpitaux de Paris, Paris Diderot University, Paris, France; 3Department of Radiology, Basildon University Hospital, Essex, United Kingdom; and 4Pediatric Radiology Department and 5Neurophysiology Unit, Robert Debré Hospital–Assistance Publique Hôpitaux de Paris, Paris Diderot University, Paris, France

*Contribution equally.

The authors declare no conflicts of interest.
with 1 or more focal neurologic deficits. Focal deficits result from the impairments of nerve, spinal cord, or brain function and affect a specific region of the body. These were defined according to the ICHD-II guidelines as symptoms related to focal brain (usual cerebral) disturbance. Patients were enrolled between March 2009 and February 2012. The hospital’s Institutional Review Board approved the study protocol. Written informed consent was obtained from parents, and assent was obtained from the children.

All consecutive patients aged 6-18 years presenting to the ED with headache and a focal neurologic deficit were eligible for this study. Age 6 years was chosen as a cutoff because children are usually able to describe their symptoms at this age. No patients were missed, because at least 1 physician who was familiar with the study procedures was constantly present in the ED.

Pain was assessed using the Faces Pain Scale–Revised or the Visual Analog Pain Scale, and the pain level “moderate or severe” was defined as a value ≥4. Only children with a history of moderate or severe headache were included in the study. Children with a history of fever in the preceding 24 hours, head trauma in the preceding 7 days, or a history of neurosurgical intervention were excluded from the study.

ED physicians, together with the parents and child, completed a structured questionnaire containing questions relating to demographic information, coexisting medical conditions, previous episodes of headache, symptoms of the current headache attack (ie, duration, localization of pain, quality of pain, nausea, vomiting, phonophobia, photophobia, aggravation by physical activities, trigger factors), and characteristics of associated neurologic signs (further classified into visual, motor, sensory, or a combination) for statistical analysis.

After the child was discharged from the ED, the family received a headache booklet in which to record any further headache attacks, their characteristics, associated signs, triggers, and response to prescribed treatments. Children were followed up over 1 year at the Neurologic Clinic of the same hospital following the current standards of care for their diagnosis.

Neuroimaging (head computed tomography [CT] scan or brain magnetic resonance imaging [MRI]) or electroencephalography (EEG) was performed if clinically indicated. An awake and asleep EEG was performed during the ED consultation to support or exclude a diagnosis of epilepsy if the child was in an altered state of consciousness without a reasonable explanation based on iatrogenic (eg, benzodiazepine administration), clinical, radiologic, or metabolic factors. An awake and asleep EEG was performed during follow-up in children with either a history of signs suggestive of seizures (eg, blinking, ocular jerks, limb twitches, tongue and lip movements, tachycardia, altered respiratory patterns) or episodes of altered consciousness of uncertain etiology.

At the end of the 1-year follow-up period, a final diagnosis of the acute episode was made by a pediatric neurologist who had access to all data and was blinded to the aim of the study. The diagnosis of primary headache was defined according to ICHD-II criteria (Table I).

**Table I. International Headache Society diagnostic criteria for migraine without aura and migraine with aura**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine without aura</td>
<td>A. At least 5 attacks fulfilling criteria B-D</td>
</tr>
<tr>
<td></td>
<td>B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated). In children, attacks may last 1-72 hours.</td>
</tr>
<tr>
<td></td>
<td>C. Headache with at least 2 of the following characteristics:</td>
</tr>
<tr>
<td></td>
<td>● Unilateral location (commonly bilateral in young children)</td>
</tr>
<tr>
<td></td>
<td>● Pulsating quality</td>
</tr>
<tr>
<td></td>
<td>● Moderate or severe pain intensity</td>
</tr>
<tr>
<td></td>
<td>● Aggravation by or causing avoidance of routine physical activity</td>
</tr>
<tr>
<td></td>
<td>D. During headache, at least 1 of the following:</td>
</tr>
<tr>
<td></td>
<td>● Nausea and/or vomiting</td>
</tr>
<tr>
<td></td>
<td>● Photophobia and phonophobia</td>
</tr>
<tr>
<td></td>
<td>E. Not attributed to another disorder</td>
</tr>
<tr>
<td>Migraine with typical aura</td>
<td>A. At least 2 attacks fulfilling criteria B-D</td>
</tr>
<tr>
<td></td>
<td>B. Aura consisting of at least 1 of the following, but no motor weakness:</td>
</tr>
<tr>
<td></td>
<td>● Fully reversible visual symptoms including positive features (eg, flickering lights, spots, lines) and/or negative features (eg, loss of vision)</td>
</tr>
<tr>
<td></td>
<td>● Fully reversible sensory symptoms including positive features (eg, pins and needles) and/or negative features (eg, numbness)</td>
</tr>
<tr>
<td></td>
<td>● Fully reversible dysphasic speech disturbance</td>
</tr>
<tr>
<td></td>
<td>C. At least 2 of the following:</td>
</tr>
<tr>
<td></td>
<td>● Homonymous visual symptoms and/or unilateral sensory symptoms</td>
</tr>
<tr>
<td></td>
<td>● At least 1 aura symptom developing gradually over ≥5 min and/or different aura symptoms occurring in succession over ≥5 min</td>
</tr>
<tr>
<td></td>
<td>● Each symptom lasting ≥5 and ≤60 min</td>
</tr>
<tr>
<td></td>
<td>D. Headache fulfilling criteria B-D for migraine without aura begins during the aura or follows aura within 60 min</td>
</tr>
<tr>
<td></td>
<td>E. Not attributed to another disorder</td>
</tr>
</tbody>
</table>

**Statistical Analyses**

All data are reported as median (IQR) unless otherwise specified. Categorical variables are described as frequency and percentage. Means of quantitative variables were compared using the t test, and categorical variables were compared using the χ² test. The level of significance was P < .05 (2-sided tests). Multivariate logistic regression analysis included variables associated with the outcome with a P value <.20 in the univariate analysis and then selected with an Akaike information criterion stepwise procedure. aORs and their 95% CIs were calculated. All statistical analyses were performed using R (R Institute for Statistical Computing, Vienna, Austria).

**Results**

During the study period, a total of 79,433 patients aged 6-18 years presented to our ED. Of these patients, 2086 (2.63%) suffered from moderate to severe nonfebrile, nontraumatic headache, and 102 (0.13%) presented with at least 1 associated focal neurologic deficit. One family refused to provide consent (Figure). A total of 101 patients (55 females and 46 males) were enrolled. The median age at presentation to the ED was 11.2 years (IQR, 9.3-13.3 years), with no statistical difference between the sexes. For 77 patients (76.2%), this was the first episode of headache with neurologic deficit; 34 patients (33.6%) had a previous diagnosis of migraine.
Clinical Features of the Presenting Episode and Management

Clinical features of the acute attacks are presented in Table II. The median duration of the headache attack was 4.0 hours (IQR, 3.0-7.0 hours). The painful episode lasted more than 24 hours in 22 patients (21.8%), including 2 days in 3 patients, 3 days in 3 patients, and 9 days in 2 patients. Isolated visual deficits were scored in 37 (37.9%) of patients, isolated motor deficits in 12 (11.7%), isolated sensory deficits in 7 (6.8%), and an association of more than one deficit in 47 (45.6%) of patients. Neurologic deficit was no longer evident by 1 hour after initial onset in 72 patients (71.3%). Thirty-one patients (30.6%) underwent neuroradiologic imaging during the ED consultation (27 head CT scans and 4 brain MRIs with magnetic resonance angiography). Brain MRI was performed within 4 hours of onset of the episode to rule out a diagnosis of stroke, and was normal in 1 of the 4 children. The remaining 3 children were diagnosed with ischemic arterial stroke (n = 2) or cerebral venous sinus thrombosis (n = 1).

An awake and asleep EEG was performed within 1 week in another 47 patients (46.5%) to support or exclude a diagnosis of epilepsy. Patients with abnormal EEG findings underwent supplemental EEG in accordance with current standards of care.

At the end of the study period, 67 patients (66.3%) were diagnosed with primary headache, and 34 (33.7%) were diagnosed with secondary headache (Figure). In the primary headache group, 63 patients were diagnosed with migraine with aura attack. Aura was visual in 19 children (30.2%), motor in 9 (14.3%), sensory in 5 (7.9%), and a combination in 30 (47.6%). Three children considered to have probable migraine with aura, but did not meet the IHCD-II criteria. One child experienced an episode of sporadic hemiplegic migraine.

In the secondary headache group, 26 children were considered to have experienced a seizure: 14 were diagnosed with benign childhood occipital epilepsy (Panayiotopoulos syndrome), 5 with temporal lobe epilepsy (in 2, with seizures secondary to a dysembryoplastic neuroepithelial tumor), 4 with epilepsy with centrotemporal spikes, and 3 with other focal epilepsies (2 occipital lobe, 1 parietal lobe). Two children were diagnosed with arterial ischemic stroke, 2 with cerebral venous sinus thrombosis, 2 with arteriovenous malformation, and 2 with intracranial neoplasm (1 astrocytoma, 1 medulloblastoma). Children with a painful episode lasting more than 24 hours were found in both the primary (n = 15) and secondary (n = 8) headache groups.

Follow-Up and Final Diagnosis

During the 1-year follow-up period, another 74 brain MRIs were performed, either at the initial admission or within 1 month after the acute episode on an outpatient basis. Thirteen children underwent brain MRI after undergoing a head CT scan at the ED. In these children, the brain MRI was either normal (n = 7) or helped characterize pathological anomalies revealed by the initial CT scan (n = 6). Overall, MRI disclosed brain disorders considered the cause of an acute episode in 10 of 78 children (12.8%), including 2 with a dysembryoplastic neuroepithelial tumor, 2 with a unilateral Sylvian artery ischemic stroke, 2 with cerebral venous sinus thrombosis, 2 with a cerebral arteriovenous malformation, and 2 with an intracranial neoplasm (1 astrocytoma and 1 medulloblastoma). Small (<5 mm) white matter lesions were found in 2 children from the primary headache group. Eight children did not undergo neuroradiological investigation because they had already undergone imaging for a previous similar episode.

An awake and asleep EEG was performed within 1 week in another 47 patients (46.5%) to support or exclude a diagnosis of epilepsy. Patients with abnormal EEG findings underwent supplemental EEG in accordance with current standards of care.

At the end of the study period, 67 patients (66.3%) were diagnosed with primary headache, and 34 (33.7%) were diagnosed with secondary headache (Figure). In the primary headache group, 63 patients were diagnosed with migraine with aura attack. Aura was visual in 19 children (30.2%), motor in 9 (14.3%), sensory in 5 (7.9%), and a combination in 30 (47.6%). Three children considered to have probable migraine with aura, but did not meet the IHCD-II criteria. One child experienced an episode of sporadic hemiplegic migraine.

In the secondary headache group, 26 children were considered to have experienced a seizure: 14 were diagnosed with benign childhood occipital epilepsy (Panayiotopoulos syndrome), 5 with temporal lobe epilepsy (in 2, with seizures secondary to a dysembryoplastic neuroepithelial tumor), 4 with epilepsy with centrotemporal spikes, and 3 with other focal epilepsies (2 occipital lobe, 1 parietal lobe). Two children were diagnosed with arterial ischemic stroke, 2 with cerebral venous sinus thrombosis, 2 with arteriovenous malformation, and 2 with intracranial neoplasm (1 astrocytoma, 1 medulloblastoma). Children with a painful episode lasting more than 24 hours were found in both the primary (n = 15) and secondary (n = 8) headache groups.

Statistical Analyses

Univariate logistic analysis, considering a diagnosis of primary vs secondary headache, found that primary headaches were associated with older age at the initial ED visit (11.7 years vs 10.5 years; P = .05), previous diagnosis of migraine (38.8% vs 23.5%; P = .12), and parental history of primary headache (50.8% vs 30%; P = .04). Inverse correlations were found between primary headache and first
episode of headache with neurologic deficit (70.1% vs 88.2%; \(P = .04\)), bilateral localization of pain (32.8% vs 85.3%; \(P < .0001\)), and pulsating quality of pain (61.8% vs 74.6%; \(P = .18\)). There was no statistical correlation between age and bilateral location of pain.

On multivariate analysis, bilateral localization of headache pain was the sole clinical feature associated with a diagnosis of secondary headache. Children with bilateral headache and a focal neurologic deficit had an aOR of 8.6 (95% CI, 3.2-23.2; \(P < .001\)) of having secondary headache compared with children with unilateral pain. Specifically, 22 of 67 children (32.8%) in the secondary headache group experienced bilateral pain during the ED episode. These children received a final diagnosis of migraine with aura \((n = 21)\) or sporadic hemiplegic migraine \((n = 1)\). In contrast, 29 of 34 children (85.3%) in the secondary headache group experienced bilateral pain. The remaining 5 children with a unilateral location of pain (14.7%) were diagnosed with benign childhood occipital epilepsy.

When analyzing children consulting for a first episode only \((n = 77)\), bilateral localization of pain was the sole variable significantly associated with secondary headache \((aOR, 13.4; 95\% CI, 3.9-45.8; P < .001)\). A subgroup analysis was performed to determine whether children with bilateral occipital pain \((n = 28)\) had increased odds of having secondary headache compared with children with bifrontal or bitemporal pain \((n = 25)\), which is usually considered more typical of migraine. No statistical difference between these 2 subgroups was detected \((P = .61)\).

### Discussion

We aimed to investigate the clinical features of children attending the ED for nonfebrile, nontraumatic headache with focal neurologic deficits, to identify the factors that could allow differentiation of primary and secondary headaches. We have shown that bilateral localization of headache is a reliable clinical feature that significantly increases the odds of secondary headache in children.

Headaches with focal neurologic deficits present a diagnostic challenge to the ED. To our knowledge, there are no clear diagnostic guidelines to assist emergency physicians in differentiating primary headache, essentially migraine with aura,\(^9,18\) from a potentially life-threatening secondary headache in children. Despite the fact that migraine with aura has a relatively high prevalence in the pediatric population,\(^1,2\) published expert opinions are scarce and pertain mainly to the adult population.

A recent population-based study in the US found that there remains significant variability in the evaluation of pediatric headache in the ED.\(^19\) More than 20% of children discharged with a final diagnosis of migraine underwent a head CT scan, which is of unclear diagnostic utility in children with nontraumatic headache and normal neurologic exam findings.\(^20,21\) Quality and location of pain, factors that influence medical decision making in children with headache, were not evaluated owing to the retrospective nature of the dataset. Cranial autonomic symptoms, such as nasal congestion, conjunctivitis, and a sense of aural fullness, are present in the majority of children with migraine.\(^22\) Is it likely that some of these patients were misdiagnosed with sinus-related headache when in reality they were experiencing acute attacks of migraine, either with or without aura.

It is known that seizures can either occur during or within 1 hour of a typical migraine with aura attack (migraine-triggered seizure; ICHD-II classification 1.5.5) or can be followed by postictal headache (headache attributed to seizure; ICHD-II classification 7.6.2). Rarely, migraine headache may represent an isolated ictal phenomenon (ictal epileptic headache [IEH]).\(^23-25\) Criteria for diagnosing IEH include confirmation by EEG obtained during the acute episode with simultaneous intravenous antiepileptic drug administration.\(^26,27\) Thus, the diagnosis of migraine-triggered seizures, postictal headache, and IEH could be underestimated if EEG is not available in the emergency setting, and also if clinicians are unaware of these potential differential diagnoses.

In the present study, we diagnosed migraine with aura in approximately two-thirds of our patients. Three patients
were diagnosed with probable migraine with aura because the required IHCD-II criteria were not met. One child was diagnosed with hemiplegic migraine, a familial or sporadic condition due to a mutation in the genes for specific voltage-gated channels or Na+/K+ pumps, causing cerebral vasospasm. The unique aura in this form of migraine does not follow the classical biphasic progression of a typical aura and can last from less than 1 hour to several days.

We scored white matter lesions on brain MRI in 2 children diagnosed with migraine with aura. These white matter lesions are quite common in adults with migraine, especially in those with a patent foramen ovale. White matter lesions also have been reported in children with migraine, but their clinical significance remains unclear.

The main cause of secondary headache in our population was focal seizures. The most frequent diagnosis was benign occipital epilepsy or Panayiotopoulos syndrome (13.9%). This syndrome has an estimated prevalence of 6% in nonefibrate seizures of childhood and is largely underdiagnosed. Usually only a single attack occurs, which explains why the syndrome is often misdiagnosed as vasovagal syncope, gastrointestinal pathology, or migraine with aura attack. This high prevalence can explain why we observed such a high number of children with a final diagnosis of seizures in our series. The clinical hallmarks are headache, vomiting, pallor, and cardiorespiratory and thermoregulatory disturbances. Panayiotopoulos syndrome is a frequent cause of autonomic status epilepticus in children and can lead to ictal cardiorespiratory arrest.

Vascular brain disorders are other differential diagnoses that should be taken into account, given that prompt identification can improve prognosis. Arterial ischemic stroke, cerebral venous sinus thrombosis, and cerebral arteriovenous malformations are rare in the pediatric population, but were detected in 5.9% of our cohort of children with moderate to severe headache and focal neurologic deficit. Pediatric stroke represents a true diagnostic challenge in the ED. Headache in stroke is usually localized to the side of the occluded artery, but it can be occipital and bilateral in the case of basilar or vertebral artery occlusion. In cerebral venous sinus thrombosis, a migraine-like episode is sometimes the initial symptom, with subsequent progressive neurologic deficit. If a cavernous sinus is involved, unilateral ocular pain, proptosis, and oculomotor palsies are often encountered. In patients with cerebral arteriovenous malformations, headache can be the initial clinical presentation, with migraine-like characteristics. Brain tumors were diagnosed in 2% of our cohort and can present with progressive headache with focal neurologic deficits owing to increased intracranial pressure. Presentations with acute headache due to intratumoral hemorrhage can be observed as well.

Assigning a diagnosis of migraine with aura requires at least 2 episodes fulfilling definite criteria (Table 1), to allow differentiation of these cases from migraine-like episodes. In our cohort, the majority of children consulted for a first episode of headache with neurologic deficits (76.2%). Assessing the nature of onset and progression of neurologic deficits could aid physicians in diagnosing migraine with aura.

The onset of neurologic deficits in focal epilepsy is abrupt and generally lasts 1 to 2 minutes. In stroke, the onset of neurological deficits is also abrupt, tending to be maximal at onset and can last 1 hour, as in transient ischemic attack, or longer as in stroke. In contrast, neurologic signs in migraine with aura are progressive and are typically characterized by biphasic progression of symptoms (positive symptoms followed a few minutes later by negative symptoms), with resolution within 20-60 minutes. During the course of a focal epileptic seizure, neurologic signs also may show biphasic progression, but likely at a faster rate than seen in migraine with aura. This difference is related to the rapid neuronal recruitment and activation in epilepsy as opposed to the slow, spreading cortical depression of migraine with aura. Accurately defining the duration and progression of neurologic symptoms is often difficult in children, especially very young children, however.

Our study found bilateral headache to be significantly associated with a diagnosis of secondary headache (aOR, 8.6; 95% CI, 3.2-23.2; P < .001), which also applies to first episodes (aOR, 13.4; 95% CI, 3.9-45.8; P < .001). Our results suggest that children with bilateral headache should be promptly investigated to identify potential causes of the headache. We also found that the 5 children with secondary headache with unilateral pain received a diagnosis of benign epilepsy. In contrast, a radiologic and electrophysiologic workup can be deferred in children presenting with unilateral pain, particularly those with neurologic deficits exhibiting the typical progression of an aura and lasting less than 1 hour. Our results are particularly striking if we consider that migraine in children can manifest with bilateral pain, usually of frontal or temporal location.

This study has several limitations. First, the design is monocentric; however, we began with a very large number of patients, which ultimately allowed the inclusion of 101 patients. Second, a final diagnosis of the presenting episode was made at the 1-year follow-up; however, we considered that the bias would have been greater had the diagnoses been made in the ED setting. Assessing the patterns of similar episodes, the results of additional brain imaging or electrophysiologic studies, as well as the clinical course over a 1-year period seemed more appropriate for reaching a definitive diagnosis. Furthermore, all children were followed up at our hospital, and the final diagnoses were made by a pediatric neurologist who had access to all data and was blinded to the aim of the study. Finally, the children presented with acute headache to a tertiary-level ED with an in-hospital pediatric migraine clinic, which is not a true general representation of all children presenting to the ED with headache and focal neurologic deficits.

In conclusion, we report a high frequency of migraine with aura in children who attended our hospital’s ED for moderate to severe headache and focal neurologic deficit. Bilateral
headache in children with focal neurologic signs orients the diagnosis toward secondary headache, necessitating an urgent workup.

We would like to thank all the families and physicians who accepted to participate in our study.

Submitted for publication Dec 19, 2013; last revision received Mar 18, 2014; accepted Apr 29, 2014.

Reprint requests: Luigi Tottoniano, MD, PhD, Pediatric Emergency Department, Pediatric Migraine and Neurovascular Diseases Clinic, Robert Debré Hospital–Assistance Publique Hôpitaux de Paris, Paris Diderot University, Sorbonne Paris Cité, 48 Bid Séjourier, 75019 Paris, France. E-mail: luigi.tottoniano@rodb.aphp.fr

References