Original Article

Cranial Autonomic Symptoms, Neck Pain: Challenges in Pediatric Migraine

Zeliha Haytoglu, Mihriban Ozlem Herguner[1]

Department of Pediatrics, Faculty of Medicine, Cukurova University, [1]Department of Pediatrics, Division of Pediatric Neurology, Faculty of Medicine, Cukurova University, Adana, Turkey

Abstract

Objectives: More than just a headache, migraine attack is a severe, prolonged head pain preceded and/or followed by a constellation of symptoms. Getting a proper diagnosis will be the most challenging step of migraine care. When cranial autonomic symptoms (CASs), and/or neck pain are observed, children are often exposed to advanced tests for additional diseases. The aim of this study was to investigate the frequency of these symptoms in migraine and to compare the clinical characteristics of patients with and without these symptoms. Frequency of the patients that exposed to the additional investigations was searched. **Materials and Methods:** In this prospective study between February 2016 and March 2017, 170 pediatric patients who were referred to our tertiary teaching hospital with migraine were enrolled. **Results:** A total of 170 children, 61 male (35.9%) and 109 female (64.1%) were included in the study. CASs were present in 68 patients (40%), single symptom in 31 (45.6%), and multiple symptoms in 37 (54.4%) patients. Of 68 patients with CAS, 24 (35%) patients were referred to allergists and all were tested for inhaler specific IgE and skin tests. Seventy (32.9%) patients had neck pain/stiffness in which 28 (40%) were exposed to radiation. CAS and neck pain were more frequent in patients with frequent attacks ($P = 0.04$ and $P = 0.032$, respectively). Neck pain was more frequent in patients with CAS ($P = 0.029$). **Conclusions:** It is important for pediatricians and primary care physicians to be aware of the common nature of CASs and neck pain/stiffness in children with migraine to prevent unnecessary procedures. High frequency of migrain attacks was associated with high frequency of CAS and neck pain.

Keywords: Cranial autonomic symptoms, migraine, neck pain, pediatrics

Introduction

Migraine headaches are common in children and adolescents, with a wide spectrum of clinical forms. Migraine patients often see multiple physicians for multiple symptoms. Cranial autonomic symptoms (CASs) include conjuctival injection, lacrimation, nasal congestion, rhinorrhea, eyelid edema and forehead/facial sweating, and aural fullness.[1] These findings are often characteristic of trigeminal autonomic headaches, although studies in patients with migraine have shown that cranial autonomic manifestations may be accompanied by headache episodes.[2-4] In the presence of accompanying nasal and ocular symptoms in children with headache, these findings were generally interpreted as an allergic symptom. Failure to be aware of CASs associated with migraine may cause physicians to misdiagnose. Newly, in the reports of 3rd edition of the International Classification of Headache Disorders (ICHD-3), a comment that migraine attacks can be associated with CASs was added.[1]

In addition to the headache phase of the migraine, migraine attack may also consist of prodromal, aura, and postdromal symptoms.[5] Division of prodromal symptoms includes general complaints, symptoms related to the head, abnormalities of eyes or sight, sensory intolerance, mood and behavior variations, abdominal symptoms, and neck pain.[6-8] Parents and primary care providers usually do not make the connection between these symptoms and migraine. Migraine training is often inadequate. Physicians have limited time to spend with patients. Diagnosis is based on history; with limited time, history is cursory and important details are missed. In addition, physicians have limited confidence beyond their specialty such as gastroenterologists deal with stomach and intestine symptoms, allergists, and otorhinolaryngologists deal with ear, nose, and sinus symptoms.[8] The aim of this study was to evaluate the clinical features, accompanying CAS and neck pain in pediatric patients with migraine who were referred to our tertiary teaching hospital. It is aimed to draw attention to the importance of failure to recognize these symptoms as a part of on-going migraine clinics which may lead to unnecessary investigations.

Materials and Methods

In this prospective study, 170 children and adolescents who were referred by their primary physician for neurological assessment

Address for correspondence: Dr. Zeliha Haytoglu, Department of Pediatrics, Faculty of Medicine, Cukurova University, Adana, Turkey.
E-mail: zelihahayt@yahoo.com

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due to headaches to the outpatient pediatric neurology clinic of our tertiary teaching hospital from February 2016 to March 2017 and meeting the diagnostic criteria for migraine according to the ICHD-3 were enrolled. A semi-structured questionnaire including demographics, the patient's and family's medical history, and headache history age at onset, location, quality, frequency, duration of episodes, aura, and associated CASs was carried out. Visual analog scale was used to identify the severity of headache (0 = no pain, 1–3 = mild pain, 4–6 = moderate pain, 7–8 = severe pain, and 9–10 = unbearable pain). Frequency of headache was assessed using the questions "On how many days in the last 3 months have you experienced headache?" The average days per month were calculated.

Prodromal symptoms with an onset of 2 or more hours before the headache were recorded. The presence of neck pain/neck stiffness was assessed by the self-administered questionnaire. Referral to the different departments for the neck pain/stiffness and CAS were questioned. The study was conducted according to the ethics principles of the Declaration of Helsinki. Written informed consent was obtained from the parents and/or patients.

Statistical analysis

All analyses were performed with SPSS Statistics version 22 for Windows (IBM, Chicago, IL, USA). $P < 0.05$ was considered the level of significance. Bivariate comparisons were made using Chi-square test, Fisher's exact test, Student's *t*-test, and Mann–Whitney U test as appropriate.

Results

One hundred and seventy patients diagnosed with migraine according to the ICHD III criteria[1] were enrolled. Of 170 patients, 109 (64.1%) were female and 61 (35.9%) were male. Mean age of the patients was 13.1 ± 3.4 years. Episodic migraine was diagnosed in 97 patients (57%) and chronic migraine was diagnosed in 73 patients (43%). Aura was reported in 55 patients (32.3%). Thirty patients (20%) had a visual aura and 22 (12.9%) had sensory aura. Headache location was unilateral in 51 patients (30%) and bilateral in 119 patients (70%). Family history of migraine was present in 109 patients (64.3%). Vertigo was reported in 114 patients (67%). The median frequency of headache attacks was 15 days per month (interquartile range [IQR]: 10–30). Median length of disease history was 12 months (IQR: 3–12). The median scale of headache severity was 6 points (IQR: 5–8). Of 170 pediatric migraineurs, 68 patients (40%) had at least one CAS. Of 68 patients with CAS, 31 patients (45.6%) had one and 37 patients (54.4%) had more than one CAS. CASs were bilateral in 46 patients (67.6%). Types of CASs were demonstrated on Table 1. Mean age of the patients with and without CAS was 14.4 ± 2.7 years and 12.1 ± 3.1 years, respectively. Patients with CAS were older than the patients without CAS ($P = 0.006$). Frequency of headache attacks was higher in patients with CAS than the patients without CAS ($P = 0.04$). The premonitory symptom of neck pain/stiffness was reported in 70 (41.5%) patients. Of 68 patients with CAS, 40 (60.3%) patients had neck pain/stiffness. Of 102 patients without CAS, 30 (29.4%) patients had neck pain/stiffness. Comparing the patients with and without CAS, more patients with CAS were found to have the symptom of neck pain/stiffness ($P = 0.032$). Twenty-nine of 70 patients (41.4%) with neck pain/stiffness were referred to different departments including orthopedic, neurosurgery, physical therapy, and rehabilitation. Self-stretching exercises, pragmatic advice such as the use of cold or hot packs, and taping suitable activities were advised. All of the patients were exposed to radiation. Plain films of cervical spine, computed tomography of the C-spine, and cervical-spine magnetic resonance were performed totally in 28 patients with neck pain. Nonsteroidal anti-inflammatory drugs were prescribed in (63/70) 90% of patients. Of 68 patients with CAS, 24 patients had a history of referral to a specialist pediatric allergist for the diagnosis of allergic disease. Five patients with lacrimation, five patients with rhinorrhea and lacrimation,ten patients with lacrimation and conjunctival injection and three patients with eyelid edema, conjunctival injection and facial flushing. One patient with conjunctival injection, aural fullness, and facial flushing was referred. All were tested both with inhaler specific IgE and skin prick test. All tests were negative. Table 2 demonstrates the comparison of patients with and without CAS and neck pain.

Discussion

Migraine is a syndrome of episodic brain dysfunction with systemic manifestations. Headache is the tip of migraine iceberg. Migraine patients often see multiple physicians for multiple symptoms. In our study, we found that 40% of the patients with migraine had CAS, of which 35% were exposed to skin test for allergic disorders. Recognition of CAS as a common component of migraine is important. Conjunctival injection,

Table 1: Type of cranial autonomic symptoms in migraine

CAS (one symptom), *n*=31	*n* (%)	CAS (more than one symptom), *n*=37	*n* (%)
Lacrimation	16 (9.4)	Lacrimation/conjunctival injection	10 (5.9)
Conjunctival injection	5 (2.9)	Conjontival injection/rhinorrhea	7 (4.3)
Eyelid edema	5 (2.9)	Lacrimation/aural fullness	7 (4.3)
Rhinorrhea		Lacrimation/rhinorrhea	7 (4.3)
Nasal congestion		Facial flushing/eyelid edema/conjunctival injection	3 (1.8)
Aural fullness	5 (2.9)	Facial flushing/aural fullness/conjontival injection	3 (1.8)

CAS=Cranial autonomic symptoms

lacrimation (or both), nasal congestion, rhinorrhea, eyelid edema, forehead and facial sweating, forehead/facial flushing, and/or miosis and ptosis were included in the ICHD-II.[9] In ICHD-III, aural fullness was added as a CAS.[1] The incidence of CAS in migraine reported in different studies ranges from 27% to 73%.[2-4,10-14] A population-based study demonstrated a prevalence of 26.9% of at least one unilateral autonomic feature associated with migraine.[2] Previously, in an Italian study involving patients with migraine from a tertiary referral headache center, unilateral autonomic features were reported in 45.8% of the patients.[10] In a study from Tawain of the studied migraineurs, 56% had at least one autonomic symptom. In this study, CAS in migraine was reported more likely to be bilateral and less intense.[11] Regarding the CAS in pediatric age group, it was reported that 62% of the pediatric migraineurs had CAS.[13] In contrast to adult series in our pediatric patients, the majority of CAS were observed bilaterally (68%) and with more than one symptoms (53.6%). In accordance with the results of our study in a large study including pediatric migraneurs, CASs were reported in 55% of the patients and also it was reported bilaterally in 70% of the patients.[14] Conjunctival injection and together with conjunctival injection and lacrimation were the most frequent symptoms in our patients with migraine and CAS. In our study, these symptoms were generally misdiagnosed as a component of allergic diseases, and testing for allergy was performed in 35% of the patients with CAS.

Misdiagnosis of migraine as a sinus headache is common.[15-17] A large study, entitled American Migraine Study II, showed that many people who were diagnosed with migraine thought they had "sinus" headache. In this study, only about 50% who were diagnosed with migraine knew they had migraine before the study. CAS during headaches was present in 75% of these subjects suffering from migraine. Nearly 59% had been seen in consultation by an otolaryngologist and 25% by an allergist. Otolaryngologists diagnosed sinus headache most frequently (54%); sinus headache was also the most common diagnosis by allergists (38%), allergy was diagnosed in nearly 25% of the patients by allergists.[16]

An other important finding in our study was the high frequency of neck stiffness/pain (41.5%). A 2010 study of 113 patients found that neck pain occurred with the migraine attacks more often than nausea, even though nausea is closely associated with migraines.[18] In a large population study from Spain, individuals with self-reported migraine were approximately 2 and 3 times more likely to have neck pain lasting at least 6 months compared to individuals without headache.[19] In another large population study from the United States, 38% of individuals with severe headache or migraine assessed by self-report had neck pain in the past 3 months versus 11% of individuals without severe headache or migraine.[20]

We showed that CAS was significantly more frequent in individuals with neck pain/stiffness compared to individuals without neck pain/stiffness, indicating a possible shared pathophysiological mechanism with migraine and CAS. Kelman *et al*. also reported that CAS was associated with more frequent headache episodes.[21] It can be suggested that asking specifically about CASs and neck stiffness is of value in trying to understand the mechanisms behind these and the association with pain generation within the trigeminovascular system.

Neck pain can arise from many local structures including muscles, ligaments, facet joints, and visceral structures of the

Table 2: Comparison of patients with and without cranial autonomic symptoms and neck pain/stiffness

Variable	Migraine with CAS (*n*=68)	Migraine without CAS (*n*=102)	*P*
Age (years)	14.4±2.7	12.1±3.1	0.006
Sex, *n* (%)			
Female (*n*=109)	48 (70.6)	61 (59.8)	0.64
Male (*n*=61)	20 (29.4)	41 (40.2)	
Severity of headache (visible analog scale), median	7 (IQR 5.7-9)	6 (IQR 4-8)	0.1
Lenght of headache history, median	12 months (IQR 3-19.5)	12 months (IQR 2-24)	0.95
Frequency of headache attack, median	23 days/months (IQR 12-30)	12 days/month (IQR 4-30)	0.04
Aura (*n*=56), *n* (%)	31 (45.5)	25 (24.5)	0.06
Neck pain/stiffness (*n*=70), *n* (%)	40 (58.8)	30 (29.4)	0.029
Variable	**Migraine with neck pain/stiffness (*n*=70)**	**Migraine without neck pain/stiffness (*n*=100)**	***P***
Age (years)	14.6±2.9	12.4±3.4	0.008
Sex, *n* (%)			
Female (*n*=109)	41 (58.6)	68 (68)	0.3
Male (*n*=61)	29 (41.4)	32 (32)	
Severity of headache (visible analog scale), median	7 (IQR 5.2-8)	6 (IQR 5-8)	0.3
Lenght of headache history (months), median	12 (IQR 4-24)	12 (IQR 3-24)	0.6
Frequency of headache, median	30 days/month (IQR 12-30)	15 days/month (IQR 6-30)	0.04
Aura (*n*=55), *n* (%)	29 (41.4)	26 (26)	0.16

IQR=Interquartile range, CAS=Cranial autonomic symptoms

neck.[22] Careful history and physical examination are essential in the diagnostic evaluation of patients with neck pain. The differential diagnosis of neck pain is extensive, and although most neck pain is benign and self-limiting, the real challenge to the clinician is to distinguish serious spinal pathology or nerve-root pain from nonspecific neck pain. Our report revealed that radiologic evaluation was performed unnecesseraly in 41% of the patients with neck pain; also pragmatic therapies and exercise were advised instead of migraine therapy.

The strength of the present study is that CASs were also observed by the same investigator and not by the report of the patients alone. The limitation of our study is small sample size from a single center; however, our center is a referral center for neurologic diseases in pediatric age group.

Conclusions

To avoid unnecessary investigations and to improve the diagnosis of migraine, appropriate measures must be held. The first step can be rising the awareness of the migraine symptoms by both health-care providers and the caregivers of the pediatric patients. In pediatric age group, CAS and neck pain/stiffness can be observed during the migraine clinic. We found that pediatric patients with frequent migraine attacks can also have high frequency of CAS and neck pain. Frequent CAS and neck pain have a negative impact on the patients' quality of life, and by ignoring these symptoms as a clinical part of migraine and making unnecessary investigations produces an economic burden.

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Conflicts of interest

There are no conflicts of interest.

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