

## *Helicobacter pylori* infection presenting as childhood recurrent headache: A case report

Madhura Shivalingaiah<sup>1</sup>, Mallesh Kariyappa<sup>2</sup>, Anil Kumar Hanumanna<sup>3</sup>, Kalpana Ramesh Yelsangikar<sup>1</sup>

From <sup>1</sup>Senior Resident, <sup>2</sup>Professor, <sup>3</sup>Assistant Professor, Departments of Pediatrics, Bengaluru Medical College and Research Institute, Bengaluru, Karnataka, India

**Correspondence to:** Dr. Mallesh Kariyappa, 210/A-3, Sharavathi Block, National Games Village, Koramangala, Bengaluru - 560 047, Karnataka, India. E-mail: drmalleshk2@gmail.com

Received - 12 April 2019

Initial Review - 09 May 2019

Accepted - 03 June 2019

### ABSTRACT

Headache in children and adolescents is common and there is a steady increase in the incidences in recent years. Migraine has been attributed as the most common cause of recurrent headache under the age of 6 years. Migraine is reported in 3.9% of children aged 7–15 years which increases from 1.7% in 7 years old to 5.3% in 15 years old. Many studies have focussed on the association between headache and *Helicobacter pylori* infection which is acquired early in the childhood beyond the age of 10 years through fecal-oral route transmission. Here, we report a case of *H. pylori* infection in a 13-year-old female child who presented with a history of recurrent headache refractory to standard treatment. Later, the child was diagnosed to have *H. pylori* gastritis. Headache responded to 4 weeks course of *H. pylori* eradication therapy.

**Key words:** Antral polyp, *Helicobacter pylori*, Migraine, Recurrent headache

A steady increase in the number of incidences regarding headache in children and adolescents has been observed in recent years. Migraine is the most frequent type of recurrent headache under the age of 6 years [1]. Migraine is reported in 3.9% of children aged 7–15 years, which increase from 1.7% in 7 years old to 5.3% in 15 years old [2]. Migraine is characterised by episodic attack that may be moderate to severe in intensity, focal in nature, have a throbbing quality and may be associated with nausea, vomiting, light sensitivity and sound sensitivity. Compared to adults, pediatric migraine is shorter in duration and often has bilateral, bifrontal in the point of location. Migraine is classified into four types: Migraine with aura (classic migraine), migraine without aura, and other types of migraine and cluster headache. Migraine without aura is the most common type. The duration of headache is usually 4–72 h in adults and 1–72 h in children. The migraine that persists beyond 72 h is classified as status migrainosus [3]. In recent years, researchers have explored the potential role of *Helicobacter pylori* infection in the pathogenesis of migraine.

*H. pylori* is a Gram-negative spiral bacteria found in association with gastric epithelium and is acquired early in childhood beyond the age of 10 years, with the major route of transmission being fecal-oral route. Infection through *H. pylori* results in persistent activation of the immune system, resulting in triggering of local and systemic release of a wide variety of vasoactive substances which has been attributed in the pathology of headache [4,5]. The most commonly implicated vasoactive substance are calcitonin gene-related peptide (CGRP) and serotonin. Stimulation of

serotonergic cells causes increased cerebral blood flow which is considered as a cause of pain in migraine. Only a limited literature is available focusing on the incidences of *H. pylori* infections causing recurrent headache in children, especially from South India. The present case focused on elaborating the pathological association of *H. pylori* infection in children causing recurrent headaches.

### CASE REPORT

A 13-year-old female child second born to the second degree consanguineously married couple presented with a history of headache on and off for 6 months. There was a history of vomiting and photophobia and sometimes non-characteristic abdominal pain during headache. There was no history of headache in the family. The child was developmentally normal for the age and was immunized up to date.

On physical examination, her height was 143 cm (3<sup>rd</sup> and 10<sup>th</sup> centile), weight was 34 kg (10<sup>th</sup> and 25<sup>th</sup> centile), and body mass index was 16.6 (10<sup>th</sup> and 25<sup>th</sup> centile). His pulse rate was 84/min, respiratory rate was 18/min, and blood pressure was 110/70 mmHg. Systemic examination was unremarkable. Laboratory investigation revealed hemoglobin of 12.6 g/dl and other parameters were within normal limits. The child was evaluated for headache. Ocular, sinus, and auditory evaluations revealed no abnormalities. C-reactive protein and erythrocyte sedimentation rate were done to rule out vascular causes of headache which came normal. Neuroimaging (computed

tomography brain) was done which was also normal. Psychiatrist consultation suggested no psychiatric intervention. Migraine with cyclical vomiting syndrome (CVS) was diagnosed after consultation with neurologist.

For prophylaxis, flunarizine tablet was used along with naproxen sodium during the period of headache; however, the frequency and severity of headache remained constant. In view of the refractory headache, often associated abdomen pain, upper gastrointestinal (GI) endoscopy was performed which revealed the presence of antral polyp. The specimen obtained from the antral biopsy was tested with rapid urease test which gave positive results suggesting the presence of *H. pylori* infection. *H. pylori* eradication treatment was initiated with clarithromycin 250 mg BD, tinidazole 500 mg BD, and lansoprazole 30 mg BD for 14 days followed by lansoprazole for another 2 weeks. The child showed symptomatic improvement in 4 days and symptom free at the end of 4 weeks and the latest follow-up.

## DISCUSSION

Headache is a common complaint in children and adolescents. Headache can be a primary problem or secondary problem. Migraine is the most common form of primary headache and most common cause of recurrent headache under the age of 6 years [1]. Headache can be mild to severe and may have one or all symptoms such as nausea, vomiting, photophobia and phonophobia. Aura associated with migraine is a neurologic warning that migraine is going to occur. Aura may be visual, sensory or dysphasic [2].

CVS is a functional disorder that is considered to be a manifestation of migraine diathesis. It is characterized by stereotypical episodes of severe nausea and vomiting lasting several hours or days with a return to baseline health in between episodes. Diagnostic criteria for the diagnosis of CVS, recommended by North American society for pediatric gastroenterology, hepatology, and nutrition, are as follows [6]: All of the criteria must be met to meet this consensus definition of CVS.

- At least five attack in any interval or a minimum of three attacks during a 6-month period
- Episodic attacks of intense nausea and vomiting lasting from 1 h to 10 days and occurring at least 1 week apart
- Stereotypical pattern and symptoms in the individual patient
- Vomiting, during attacks, occurs at least 4 times in an hour for at least 1 h
- Return to baseline health between episodes
- Not attributed to another disorder.

Many factors such as genetics, food and medication, sleep disorder, stress, different smell, menstruation, trauma, and alcohol have been recognized as triggering factors for migraine [7]. Pain in migraine occurs as a result of activation of the trigeminal vascular system. Neuropeptides such as CGRP, substance P, and vasoactive intestinal peptide are released when trigeminal fibers or trigeminal ganglion is activated. This release of neuropeptides has been proposed as a cause of pain mechanism in migraine.

CGRP is a powerful vasodilator which produces dilatation of dural vessels and an increase in blood flow [8]. Furthermore, studies have shown that serotonin plays a significant role in the causation of headache [9].

In recent years, the role of infectious agents, immune responses on migraine have gained more attention. Many studies have shown the association between headache and *H. pylori* infection. Tunca *et al.* in their study found a significant association between migraine and *H. pylori* infection and concluded that *H. pylori* should be examined in migrainous patients and eradication of infection may be helpful for the treatment of the disease [10]. Another study by Su and Zhou suggested a frequent association of *H. pylori* infection with migraine [11].

The research explained that GI neuroendocrine cells such as enterochromaffin cells can secrete serotonin and some other factors that stimulate the synthesis of serotonin can cause central nervous system perturbation through brain–gut axis which can demonstrate that the most migrainous patients are associated with the GI disorder. It has been suggested that the pathogenic role of *H. pylori* infection in migraine is based on the relationship between the host immune response against the bacterium and the chronic release of vasoactive substances [12]. During infection, bacteria releases toxins in infected tissue, thus promoting the special cascade of events related to host immune response resulting in alterations of vascular permeability. Thus, prolonged oxidative injury caused by persistent infection and release of vasoactive substances might be involved in local cerebral blood circulation changes during migraine attacks [12].

Hence, prompt identification of *H. pylori* infection should be done in all cases of migraine. In the present case, the child had received standard treatment for migraine without relief. Hence, she was evaluated for *H. pylori* infection. Various tests are available for diagnosis of *H. pylori* infection. Endoscopic antral biopsy for rapid urease test, histology, and culture is the gold standards in the diagnosis. Other tests include serology, breath urea test, and polymerase chain reaction. The urea breath test has sensitivity and specificity of 100% and 98%, respectively. Rapid urease test on biopsy specimen has a sensitivity of 90–95% and specificity of 98% [13]. In the present case, the child was subjected to upper GI endoscopy which showed antral polyp. The antral biopsy specimen was positive for *H. pylori* infection. Thus, the diagnosis of *H. pylori* infection was confirmed and *H. pylori* eradication therapy was initiated. Various drugs used for the treatment of *H. pylori* infection include amoxicillin 50 mg/kg/day, metronidazole 20 mg/kg/day, tinidazole 20 mg/kg/day, clarithromycin 15 mg/kg/day, omeprazole 20 mg OD (<10 years) and 20 mg BD (>10 years), colloidal bismuth subcitrate 480 mg/1.73m<sup>2</sup>/day, and furazolidone 6–8 mg/kg/day [13].

## CONCLUSION

Any child presenting with recurrent chronic headache should be evaluated for *H. pylori* infection, especially older children and adolescents. Early initiation of *H. pylori* eradication

therapy helps in resolution of symptoms of headache, decreases morbidity, school absenteeism, fecal-oral spread, complications of peptic ulcer disease, and possibly long-term complications like adenocarcinoma.

## ACKNOWLEDGMENT

We acknowledge Dr. Sarala Sabapathy, HOD, Department of Pediatrics, Dr. Anusha and Dr. Deepthy Alice Varghese, Junior Residents, Bangalore Medical College and Research Institute, Bengaluru, and the patient herself and her parents for permitting us to report this case.

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*Funding: None; Conflict of Interest: None Stated.*

**How to cite this article:** Shivalingaiah M, Kariyappa M, Hanumanna AK, Yelsangikar KR. *Helicobacter pylori* infection presenting as childhood recurrent headache: A case report. *Indian J Child Health*. 2019; 6(7):397-399.

Doi: 10.32677/IJCH.2019.v06.i07.017