

Brief Communications

New Daily Persistent Headache Following Dengue Fever: Report of Three Cases and an Epidemiological Study

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Introduction.—Dengue fever is currently a significant public health problem as an emerging pandemic-prone viral disease in many parts of the world. Up to 100 million individuals, distributed in over 100 countries, are estimated to be infected annually, putting nearly half of the world's population at risk. The headache associated with dengue fever is considered to be very intense, bilateral, throbbing, frontal, and retro-orbital. New daily persistent headache (NDPH) is a relatively rare headache entity. It has already been reported that systemic infectious disease may precede the onset of NDPH. We report the data of an epidemiologic study analyzing the cases of NDPH among 450 subjects who had dengue fever.

Method.—The study was performed in a medium-size town in southeastern Brazil (Franca, population 370,000). During the year 2015, 600 cases of dengue fever were reported to the Franca Health Authority. All these patients were contacted by telephone, and 450 of the patients were located and interviewed.

Results.—Of these 450 interviews, three possible cases of NDPH were identified.

Conclusion.—The observed prevalence of NDPH attributed to dengue fever was 1:150 cases of dengue fever (0.67%).

Key words: Dengue fever, NDPH, epidemiology

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INTRODUCTION

Dengue fever is currently a significant public health problem as an emerging pandemic-prone viral disease in many parts of the world (WHO report 2018).¹ Up to 100 million infections are estimated to occur annually in over 100 endemic countries, putting nearly half of the world's population at risk.¹

Dengue fever flourishes in poor urban areas, suburbs, and the countryside as well, but affects more

affluent neighborhoods preferentially in tropical and subtropical countries. Dengue fever is a mosquito-borne viral infection causing severe flu-like illness and, sometimes, causing a potentially lethal complication known as severe dengue.

The diagnosis is often challenged because of the vast variability of common infectious diseases that may cause fever or similar symptomatology. Many dengue cases are underreported and several may be misdiagnosed.

The individual should suspect dengue fever when a high fever (40°C/104°F) is accompanied by two of the following signs or symptoms: severe headache, pain behind the eyes, nausea, vomiting, swollen glands, muscle, and joint pains or rash.¹

The headache associated with dengue fever is considered to be very intense, bilateral, throbbing, frontal,

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and retro-orbital. Most patients have associated symptoms such as nausea and vomiting, photo- and phonophobia. In this regard, nausea or vomiting, photo- and phonophobia are not necessarily related to the headache, since the infection could itself cause these symptoms without any pain.²

Headache in dengue fever is prolonged, lasting about 8 days.³ Although more prolonged headache associated with dengue is possibly more common than it seems, reports of persistent headaches following dengue fever are rare in peer-reviewed literature.

Recently we have published⁴ two cases of persistent headache following dengue fever that fulfilled ICHD3⁵ criteria for New daily persistent headache (NDPH). These reported patients attended a private clinic.⁴

NDPH is a relatively rare headache entity and appears as criterion 4.10 (other primary headaches) in the ICHD3.⁵

According to ICHD-3⁵, NDPH “is unique in that headache is daily from onset, and very soon unremitting, typically occurring in individuals without a prior headache history. Patients with this disorder invariably recall and can accurately describe such an onset.”⁵ NDPH may have features suggestive of either migraine or tension-type headache.

It has already been reported^{6,7} that systemic infectious disease may precede the onset of NDPH. The presumptive agents so far linked to the above-mentioned headache entity are as follows: salmonella, adenovirus, toxoplasmosis, herpes zoster, EBV, and *E. coli* urinary tract infections.⁶ Flu-like illness, rhinitis, gastroenteritis have also been associated as a triggering factor, once again suggesting an infectious etiology as a precipitating factor.⁷

In this article we evaluated the prevalence of NDPH among the subjects who had dengue fever in a city of Brazil.

METHODS

The study was performed in a medium-size town in southeastern Brazil (Franca, population 370,000). During the year 2015, 600 cases of dengue fever were reported to the Franca Health Authority. All 600 patients studied in this report were positive in serological tests regarding dengue fever. These patients

were contacted by telephone, and 450 of the patients were located and interviewed. Of these 450 interviews, three possible cases of NDPH were identified, which were seen by a headache specialist (CAB), who confirmed the diagnosis. This study was approved by the UNIFACEF Ethical Committee protocol number (CAAE 92010717.7.0000.5384).

RESULTS

Three women with NDPH were identified among the 450 patients with dengue fever.

Case Reports.—*Female, 49 Years Old, Housewife.*—Prior to contracting dengue fever 16 months ago, she had episodic migraine, with attacks less than once a week, with a duration of 6-12 hours, with very low impact on her everyday life. Since contracting dengue, on the third symptomatic day, a headache started and has been continually present every day since. Such pain was across the whole head, particularly focused in the temples and was pulsatile on most days. About 4 or 5 days a week, the pain was intense, albeit without interrupting her activities. Associated with the pain, were a moderate photophobia, intense phonophobia and, on occasions, nausea and pallor were also present. She did not know of any first-degree relatives with chronic headache. She had no history of hypertension, no alcoholism, smoking, or diabetes mellitus. Physical and neurological examinations were unremarkable. There was pain on pressure on both the major occipital and supraorbital nerves on the right side, but according to her, such pain was different from the continuous spontaneous pain.

The patient believes that post-dengue headache is distinct from her previous primary headache as well, especially with regards to its intensity. She claims that the pain has interfered with her social and marital life. She received neurological treatment for some months using propranolol and/or amitriptyline with no improvement, leading her to suspend the therapy. An investigation involving neuroimaging and cerebrospinal fluid was unremarkable.

Female, 31 Years Old, Shoes maker.—Previous to contracting dengue fever nine months prior to presentation, this patient denied having suffered any previous headache. On the second day of dengue

infection, she developed an intense, pulsatile, bilateral and nuchal headache, associated with nausea, and vomiting. Even though the acute viral illness ceased within 5 days, the headache did not remit; in fact, since then it has continued daily, being present practically all the time. Its intensity waxes and wanes, and is ranged usually between mild or moderate. Two to three times a month the headache became intense, often compelling the patient to lie down. When moderate, the pain was usually nonpulsatile. During exacerbations, it was bilateral, pulsatile with photophobia, phonophobia, and worsening with effort. Vomiting occurred rarely. As she worked from home, her professional burden was intermittent, as she performed her activities only when the pain was less intense. Physical and neurological examinations were without abnormalities, except for allodynia on the entire scalp. The neuroimaging investigation and cerebrospinal fluid study were considered normal. She started neurological treatment with migraine medications (propranolol and amitriptyline) though that was considered unsuccessful. Currently, she prefers to alleviate the attacks of severe pain with a combination of analgesics or ibuprofen. The patient reported taking about six tablets per month of acetaminophen plus acetylsalicylic acid and caffeine, as well as 2 or 3 tablets of ibuprofen per month. She reported that the condition remains stable and finds it acceptable to live this way.

Female, 29 Years Old, Office Assistant.—She contracted dengue fever about 14 months prior to presentation. She had no previous history of headache. She reported that from the first day of the infection, a headache started and has not remitted. Pain was usually bitemporal, sometimes nuchal, without side predilection. It had been present every day since then. Its intensity was variable; about 10 days a month it was quite mild, on other days it was moderate and exacerbations were lasting a whole day about twice a month when it acquired migrainous features. Physical and neurological exams were unremarkable, except for hypertonia and tenderness on palpation of nuchal muscles and lateral flexion of the neck. She sought a neurologist, who prescribed anti-inflammatory drugs for exacerbations and stretching exercises. The patient preferred not to use medications for mild pain. She believed that the condition was waning, but the pain had persisted every single day until her last consultation.

DISCUSSION

The observed prevalence of NDPH attributed to dengue fever was 1:150 cases of dengue fever (0.67%). This figure should be accepted with reservations since it represents the findings from a single community in only one of more than 5,500 municipalities in Brazil.

There are four distinct serotypes of the virus, namely DEN-1, DEN-2, DEN-3, and DEN-4, which are closely related and may cause different kinds of damage to the organism. We were unable to correlate any of the serotypes with the NDPH attributed to dengue fever.

To the best of our knowledge, this is the first epidemiological study of NDPH probably attributed to dengue fever.

The three patients were females, but no conclusion should be drawn from this fact, due to the small number of cases. All of them displayed migrainous features, although the third case had both migrainous and tension-type features.

In ICHD-2⁸ the diagnostic criteria required tension-type features for the pain in NDPH. In the present study, all cases displayed migrainous features and such a finding is in agreement with Robbins and colleagues⁹, who called for a change in ICHD-2 diagnostic criteria. Consequently, our findings are in agreement with the current and already modified criteria (ICHD-3)⁵ for NDPH, which do not require the headache in NDPH to have tension-type features.

In all three cases, patients could remember the very day headaches started, always in close relationship to an acute episode of dengue fever, which led us to consider the NDPH as being in fact associated with dengue fever. The mechanisms through which the infection triggers the onset of a NDPH are still unknown. They may be of central or peripheral origin.

The prevalence of NDPH is estimated to be 0.03-0.1% in the general population.¹⁰ In the present study, it is at least six times higher. This strongly suggests that the cases of NDPH observed in Franca are not overlapping cases, aleatory associated with dengue fever. Instead, the dengue fever was the trigger factor of an NDPH.

Due to the overlapping of epidemic zones, Zika virus and chikungunya virus may be co-infections with dengue fever. These types of infections were not routinely evaluated in our patients.

STATEMENT OF AUTHORSHIP

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