Review Article

New daily persistent headache

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Abstract

New daily persistent headache (NDPH) is a chronic headache developing in a person who does not have a past history of headaches. The headache begins acutely and reaches its peak within 3 days. It is important to exclude secondary causes, particularly headaches due to alterations in cerebrospinal fluid (CSF) pressure and volume. A significant proportion of NDPH sufferers may have intractable headaches that are refractory to treatment. The condition is best viewed as a syndrome rather than a diagnosis. The headache can mimic chronic migraine and chronic tension-type headache, and it is also important to exclude secondary causes, particularly headaches due to alterations in CSF pressure and volume. A large proportion of NDPH sufferers have migrainous features to their headache and should be managed with treatments used for treating migraine. A small group of NDPH sufferers may have intractable headaches that are refractory to treatment.

Key Words

Chronic daily headache, new daily persistent headache, intractable headache

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Introduction and Background

New persistent daily headache (NDPH) is a new-onset headache occurring in a person who does not have a past history of frequent headaches and which then persists on a daily basis for more than 3 months. The prominent feature of a NDPH is that the patient often remembers the date or the circumstance when the headache began. The headache is unremitting from the start or from within 3 days of its onset. It is one of the types of primary headache syndromes that present as a chronic daily headache, which is headache present for more than 15 days a month for more than 3 months. The common causes of chronic daily headaches are chronic migraine, chronic tension-type headache and hemicrania continua. NDPH was first described in 1986 by Vanast[1] as a benign headache syndrome that usually remits without treatment. In clinical practice, spontaneous resolution may occur; however, it is not infrequent for NDPH to be an intractable headache disorder that is unresponsive to standard headache therapies. New persistent daily headache is classified as a primary headache syndrome, but it must be remembered that a number of important conditions can present with a new-onset persisting headache, and these must be excluded prior to making a diagnosis of a primary headache disorder. It is perhaps more pragmatic to consider NDPH as a syndrome rather than a diagnosis as investigations to look for a secondary cause are imperative.

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Clinical Features

Only two population studies have been performed regarding NDPH. The first was performed in Spain and used the Silberstein–Lipton criteria, documenting a 1-year population prevalence of 0.1%.[2] A more recent study undertaken in Norway used the more restrictive ICHD-II criteria, documenting an NDPH prevalence of 0.03%.[3] This is a female-predominant disorder with female to male ratios being 1.4 to 2.6:1. The peak onset is in the 2nd to 3rd decades of life. It is also prevalent in the pediatric age group. No racial predilection has been reported.[4]

The striking feature of the condition is its abrupt (although not acute) onset. Patients often remember the date, circumstance and indeed, occasionally, the time of headache onset. In one study, 42% of patients recalled the exact day of onset, while an additional 41% recalled at least the month and the year of onset.[5] Headache onset occurred in relation to an infection or flu-like illness in 30%, extra cranial surgery in 12% and a stressful life event in 12%. More than one-third of the patients could not identify any precipitating event.[6] In another study, 46.5% patients recalled a specific trigger with a respiratory tract illness being the most common followed by a stressful

life event.[7] In children, almost half report headache onset during an infection.[8] Viruses that have been implicated include Ebstein Barr virus,[7] Herpes simplex virus and cytomegalovirus.[9] In a large study on NDPH, past history of headache was found in 38% of the patients (episodic migraine in 19%, episodic tension-type headache in 2%). None of the patients had a history of Chronic daily headache (CDH) or an increasing frequency of episodic headache just before the onset of NDPH.[10] In another large study, a past history of headache was obtained in 25.3% patients (episodic migraine in 7% and episodic tension type-headache in 18.3%).[5] Half the patients have a family history of frequent headaches.[5] The pain described by patients can be variable. Some describe a throbbing pain whereas others would note a dull aching pain. Most patients have a bilateral head pain. A unilateral headache should arouse the suspicion of hemicrania continua, although about 11.3% patients in a series complained of unilateral pain.[5] In some patients, the headaches would last a few hours, but occur on a daily or almost-daily basis. This may resemble migraine-like "attacks." In others, the pain would be continuous, occurring 24 h a day for 7 days a week. The headache may wax or wane. The pain severity is often moderate rather than severe and is often aggravated by physical activity. If ICHD criteria are not followed for the diagnosis of NDPH, then associated migrainous features are common, with nausea being the most frequent symptom (68%), followed by photophobia (66%) and phonophobia (61%).[6] Allodynia is noted by a quarter of the patients and autonomic symptoms have also been described.

Diagnostic Criteria

The criteria for the diagnosis of NDPH were proposed in 1994 (the Silberstein–Lipton criteria)[11] but not included in the International Classification of Headache Disorders until 2004 [Table 1]. The current ICHD criteria[12] exclude patients with migrainous features to their headaches, although the Silberstein–Lipton criteria and the original description by Vanast suggests that that should not be the case.

Indeed, several recent studies have not used the ICHD criteria for making a diagnosis of NDPH. In one study, in particular, the investigators studied 71 patients with NDPH to test whether they had migrainous features or not. Thirty-one (43.7%) met the current ICHD criteria for NDPH while 40 (50.3%) had migrainous features to their headaches and therefore could not be diagnosed as NDPH as per the ICHD classification. Both groups were similar in their pain levels, associated allodynia, medication overuse and response to treatment. The group with migrainous features was more likely to be women and have a history of anxiety or depression. The patients with NDPH fulfilling the ICHD criteria (i.e., having tension type-headache characteristics) were more likely to recall the exact day of onset.[5] In another study, NDPH patients were reviewed retrospectively. The patients were dichotomised into patients meeting ICHD-2 criteria (NDPH-S) and patients failing to meet ICHD-2 criteria due to prominent migrainous features (NDPH-M). A total of 92 NDPH patients were enrolled (59 [64.1%] NDPH-M, 33 [35.9%] NDPH-S). The patients with NDPH-M had higher headache intensity and MIDAS (migraine disability) scores. This study again suggested that migrainous features are common in NDPH patients but, unlike other studies, this suggests that those with a migrainous phenotype represented a more severe subgroup with a poorer outcome compared with NDPH without migrainous features.[13] It has been suggested that NDPH should be subclassified as migrainous or tension in type. This however is not universally accepted and, in practice, a majority of clinicians use a pragmatic approach, basing their diagnosis of NDPH around the defining feature of this condition (i.e., the abrupt onset of a daily headache with no background history of frequent or worsening headaches, and the unremitting nature of the headache from its onset or within 3 days of onset). It is hoped that a new definition of NDPH will lead to a better understanding of the condition and the factors that lead to its abrupt onset and unremitting nature.[14]

Table 1: International classification of headache disorders (2nd edition)[12]

Criteria for new daily persistent headache
Headache for more than 3 months fulfilling criteria B–D
Headache is daily and unremitting from onset or less than 3 days from onset
At least 2 of the following pain characteristics:
Bilateral location
Pressing/tightening (nonpulsating) quality
Mild or moderate intensity
Not aggravated by routine physical activity such as walking or climbing stairs
Both of the following:
No more than one of photophobia, phonophobia or mild nausea
Neither moderate or severe nausea or vomiting
Not attributed to another disorder

Pathophysiology

Cervical spine joint hypermobility is thought to be a predisposing factor leading to the development of NDPH. There is clear evidence of anatomical and functional convergence of the cervical and the trigeminal afferents in the trigeminal nucleus caudalis (TNC). Cervical spine joint hypermobility probably influences the afferent input into the TNC, which then results in the development of NDPH.[15] A proportion of patients with NDPH develop their headache disorder following an infection. It has therefore also been proposed that NDPH is a result of persistent inflammation in the nervous system. In a small study of 20 patients with NDPH, the levels of cerebrospinal fluid (CSF) tumor necrosis factor (TNF)-alfa were found to be elevated in 19 patients. It is unclear how elevated TNF-alfa levels result in the development of headache, but induction of calcitonin gene-related peptide (CGRP) may have a role to play.[16]

Differential Diagnosis

Secondary causes

The first question that needs to be asked when one sees a patient with a NDPH is whether the headache is due to a secondary cause [Table 2]. The main conditions that can present with a new and abrupt onset of headache include the headaches related to alterations in CSF pressure and volume, cerebral venous sinus thrombosis and chronic infections of the nervous system.

Table 2: Secondary causes of new daily persistent headaches

Spontaneous CSF leaks
Idiopathic intracranial hypertension
Cerebral venous sinus thrombosis
Chronic meningitis
Intracranial neoplasms
Chronic subdural hematomas
Posttraumatic headaches

Chronic subdural hematomas and posttraumatic headaches can also present in this manner.[17]

This is by no means an exhaustive list, but includes the main conditions that need to be considered in any patient who presents with a new-onset headache that reaches its peak severity within days and is present for longer than 3 months. Intracranial neoplasms and subdural hematomas almost always have other clinical features that would alert one to the possibility of a structural cause for the headache. A history of head trauma could make the diagnosis of a posttraumatic headache apparent, although it would be important to look at the headache features and examination findings. Alterations in CSF dynamics (pressure and volume) lead to headaches that can present abruptly. It is important to rule out an increase or a reduction in the CSF pressure or a reduction in CSF volume prior to making a diagnosis of a primary NDPH. Spontaneous CSF leaks typically present as an orthostatic headache, a generalised headache that comes on when the upright posture is attained and which resolves or improves significantly on lying down in the supine position.

The headache is not usually present in the morning, but comes on as the day goes on. The patient may give a history of an index event such as a lumbar puncture or epidural injection, a vigorous Valsalva manoeuvre such as with lifting, straining or coughing. It is however well recognised that the longer a patient suffers with a CSF leak-induced headache, the less pronounced the orthostatic component becomes. Thus, if seen months to years after the onset of a CSF leak, a patient may not give a history of orthostatic headaches because that trigger may not have been evident for a long period of time. In this situation, therefore, the headache may appear to be a primary NDPH. Cerebral venous sinus thrombosis most often presents with headaches that suggest a raised intracranial pressure with worsening of the headache on Valsalva manoeuvres. Patients may also have other neurological features such as seizures, altered consciousness levels and other focal neurological symptoms and signs. Rarely, however, a patient with cerebral venous sinus thrombosis may present solely with a headache with no features to suggest raised intracranial pressure. Idiopathic intracranial hypertension classically presents with a headache suggestive of raised intracranial pressure and with examination findings of papilledema. It is however well recognised that papilledema may be absent and the headache may not have any features, raising the suspicion of raised intracranial pressure. In these situations, a primary headache disorder may appear to be the most likely diagnosis. Caution must always be taken before reaching this conclusion, and it is entirely appropriate to perform further investigations before making a diagnosis of a primary NDPH.

Other Primary Headache Syndromes

When making a diagnosis of a NDPH, one often considers other primary headache syndromes, particularly chronic migraine and chronic tension-type headache. The feature that distinguishes NDPH from the other two entities is the abrupt onset of a headache that persists on a daily or nearly-daily basis. The unremitting character of the headache is present from its onset or within 3 days of onset. Occasionally, chronic migraine can have a rapid onset, but there is usually a history of frequent migraines prior to the development of the chronic form of the condition. Although a past history of headaches may be present in up to a quarter of the patients with NDPHs, a history of an increasing frequency of headaches prior to the abrupt onset of a new daily headache is not obtained. According to the ICHD classification, NDPH has all the characteristics of a tension-type headache. The distinguishing feature again is the abrupt onset and unremitting nature of the headache from onset.

Investigations

The evaluation of a patient with a NDPH should include neuroimaging, specifically brain magnetic resonance imaging (MRI) with gadolinium and MR or computed tomography (CT) venogram.[17] Gadolinium must be administered during an MRI scan so that signs of spontaneous CSF leaks such as pachymeningeal enhancement may be visible. Other changes that suggest spontaneous CSF leaks include sagging of the brain and cerebellar tonsillar descent, engorgement of venous sinuses and the pituitary gland and subdural collections. A venogram, CT or MR will help in the diagnosis of venous sinus thrombosis or, indeed, in ruling that out. If those studies produce negative results, then a lumbar puncture should be considered. The lumbar puncture would rule out a chronic meningitis and one can also measure the CSF opening pressures. If the CSF pressures are normal, it is useful to remove 20 mL of CSF and look for a change in the headache following the LP. An improvement may suggest a diagnosis of intracranial hypertension.

Apart from ruling out a secondary cause for the headaches, further investigations are often useful for patient reassurance.

Treatment and prognosis

The natural history of NDPH is unclear. In Vanast's initial description, 86% of men and 73% of women were headache-free within 2 years of headache onset.[1] Subsequent case series have shown the disorder to be more refractory to treatment and often with a poor prognosis.[5,6,18] In our experience, NDPH can continue for years to decades after onset and can be extremely disabling for the patient. Even with aggressive treatment, many patients with NDPH do not improve, and some headache experts think that primary NDPH is the most treatment refractory of all headache disorders. Three subforms of NDPH have been described based on prognosis: Persisting, remitting and relapsing–remitting.[5] Most patients in tertiary care have the persisting subform, and over half of these patients have

daily headache that persists for at least 2 years.[5] These patients are more likely to have comorbid anxiety or depression, and have NDPH onset at a younger age.[5] Most patients with NDPH that remit do so within 2 years of onset.[1,5] Patients who have the relapsing–remitting subform, where periods of continuous headache are interspersed with pain-free weeks or months, usually have their first remission within 2 years as well.[5] In reality, perhaps like episodic tension-type headaches and some patients with mild migraines, many patients with a self-limited remitting form of NDPH do come to medical attention at all as the condition alleviates without any therapy. Typically, patients with NDPH will begin to overuse medication because they have a daily chronic headache; however, getting patients with NDPH out of analgesic rebound typically does nothing to help relieve their pain; this is not the case for patients with migraine who suffer from analgesic overuse. Medication overuse also must be addressed because it may develop in up to half of all adult patients with NDPH.[4] Medication overuse is much less common in adolescents with NDPH.[19]

As the natural history of NDPH is so variable, the impact of prophylactic or other treatment is uncertain. Many patients with NDPH will fail every possible class of abortive and preventive medication without any sign of pain relief. In one series, 91% of the patients who remitted did so while on preventative medications, most frequently nortriptyline and topiramate.[5] Another series of five patient cases with refractory NDPH had successful treatment of NDPH with gabapentin or topiramate.[20]

Other prophylactic therapies that have been reported to be beneficial in either short case reports or small case series include clonazepam, botulinum toxin A and mexiletine.[5]

For acute treatments, symptomatic therapy with triptans seems reasonable. Unlike tension-type headache where triptans have no therapeutic gain, triptans seem to give at least some pain relief in up to one-third of the patients with NDPH, even if they lack migrainous features.[5] Intravenous methylprednisolone recently has been reported to cause partial or complete remission in a small series of patients with NDPH who reported an infectious trigger.[21] In a large series, over half of the patients treated with peripheral nerve blocks found it at least temporarily effective. The nerve blocks were performed with 0.5% bupivacaine in areas tailored to the location of the patient's pain, and included greater occipital, lesser occipital, auriculotemporal, supraorbital and supratrochlear nerve blockade.[5]

As there are no guidelines or randomized trials to guide the management of NDPH, perhaps it is best treated similarly to the closest manifesting headache phenotype, whether migrainous or tension in type.

Conclusion

The criteria used for diagnosing NDPH need to be re-evaluated so as to begin to understand this important and often intractable primary headache syndrome. Including the group of patients with migrainous symptoms may allow clinicians and researches to understand why the headaches have an abrupt onset and unremitting nature, which is the hallmark of the condition.

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