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Opinion

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Jury Duty Headache: Sentencing New Daily Persistent Headache to the Secondary Headache Section of the Proposed 4th Edition of the International Classification of Headache Disorders

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Abstract

New daily persistent headache is a syndrome marked by a daily headache from onset typically occurring in individuals without a prior headache history. It can go on unabated for years without improvement. It is recognized as one of the most treatment refractory headache conditions. Since the second edition of the International Classification of Headache Disorders, new daily persistent headache has been recognized and classified as a primary headache disorder. There has been no justification for this classification. Vanast in his original description suggested the condition was secondary to a viral infection while our group and others noted triggering events suggesting secondary etiologies in almost 50% of sufferers. Thus, labeling new daily persistent headache as a primary headache disorder does the syndrome and its sufferers a disservice as it almost solidifies the notion that if typical secondary evaluations are normal the work-up can end there. That then leads to trying various non-specific treatments that typically fail to make any improvement in the patient's headaches. Individuals with new daily persistent headache are frustrated. Thus, it is imperative we keep trying to find secondary etiologies as eventually something may turn up which can then be treated. Based on our prior research. New Daily Persistent Headache should be classified as a secondary headache disorder and newly proposed criteria are suggested for the upcoming 4th iteration of the International Classification of Headache Disorders.

Keywords: New daily persistent headache; Secondary headache; Primary headache; International classification of headache disorders; Chronic daily headache

Abbreviations

NDPH: new daily persistent headache; CSF: cerebrospinal fluid

Opinion

I began studying New Daily Persistent Headache (NDPH) in 1997 and myself and Dr Li were the first to define the chronic refractory form of the disorder as well as noting specific triggering events

outside of infection which Vanast had documented in his original manuscript on the remitting form of NDPH 16 years earlier [1, 2]. In the beginning, we thought everyone with NDPH had the same con-



dition with the same underlying etiology (which was unknown at that time) and because neuroimaging and laboratory studies were typically negative in this patient group, we had no other therapy options outside of treating as chronic migraine or tension-type-headache, and in most instances the treatments failed miserably. This was likely because these were truly secondary headaches, and we were not treating the underlying cause. From very early on after its recognition NDPH became known as one of the more treatment refractory conditions and that notion even remains today amongst headache specialists and patients [3]. Since the second edition of the International Classification of Headache Disorders (ICHD-2) NDPH has been recognized and classified as a primary headache disorder [4]. In reality, there has been no justification for this classification. Vanast in his original description suggested the condition was secondary to a viral infection (Epstein-Barr virus) while our group and others noted triggering events suggesting secondary etiologies in almost 50% of sufferers and in those who initially denied a triggering event a possible trigger could be teased out in many instances after a second or third return visit and a re-hashing of the history [5-7].

Thus, I truly believe labeling NDPH as a primary headache disorder does the syndrome and its sufferers a disservice as it almost solidifies the notion that if typical secondary evaluations including brain and vessel imaging and general laboratory studies are normal the work-up can end there. That then leads to trying various non-specific treatments that typically fail to make any improvement in the patient's headaches. As someone who has spent most of his career studying this disorder and eventually finding various subtypes with secondary underlying causes and with successful distinct treatments, it is really essential to state that in those individuals with 'true NDPH' thus no prior headache history and one day out of the blue a headache develops that never goes away that something indeed happened to that patient on that day or during the prior week that makes the headache initiate. It does not occur by happenstance or without cause.

Thus, it is imperative we keep trying to find secondary etiologies as eventually something may turn up which can then be treated. These patients are frustrated, and they lose hope, and that's not what we want as headache specialists to have happen. This brings me to my first ever case of NDPH. It occurred in a 30 something year old woman who was late for jury duty. She was in the car, and she could not find the location of the courthouse as the directions she had written down were incorrect. She became frantic. Thus, she called her husband on her cell phone and screamed into the receiver, asking for him to find her the correct directions. She immediately developed a pressure-like headache after the screaming event (non-thunderclap) that never went away. She had no prior headache history and when I met her, it was two years into her syndrome. At that point in time, I had no idea why the headache was occurring as she had normal neuroimaging and medications including tricyclics, beta blockers, calcium channel antagonists had done nothing. I can remember the patient vividly. She was thin, lanky and most likely hypermobile thus fitting the typical body habitus picture that we would not recognize and publish about in NDPH

patients for another 9 years [8]. In retrospect, this now seems like a classic case of Valsalva induced NDPH which we published on in 2019 and is most likely caused by an abnormal reset of cerebrospinal fluid (CSF) pressure to an elevated state for that individual [9]. I truly believe, if I would have prescribed her a CSF volume lowering medication like acetazolamide, indomethacin or spironolactone, she would have readily improved and probably become pain-free. In addition, if I would have utilized the 3Ts model for NDPH (triggering event, thunderclap onset and Trendelenburg position) and investigated further, her MRI, even though read as a negative study, probably would have at least shown a crowded posterior fossa or a mega cisterna magna or a cavum septum pellucidum/vergae which are "normal" neuroanatomic features typically not documented by neuroradiology but which can predispose the patient for NDPH development after a Valsalva event because they raise CSF pressure/volume at baseline for that individual and then the head pain threshold point is more easily reached and overcome with the Valsalva maneuver [10].

If I had put her in the Trendelenburg position, her headache would have most likely immediately worsened solidifying the hypothesis that this was from CSF pressure elevation above her head pain threshold point. Finally, it's feasible she would also have had underlying nutcracker physiology which would have led to spinal cord epidural venous congestion and pushed her CSF pressure/volume toward her head pain threshold point at baseline and which would have then been overcome by the rise in CSF pressure with the screaming event and could not be reset because of the ongoing venous congestion issues [11].

I can say all this now because I've had a handful of other patient cases mimicking this scenario and then getting headache alleviation either with CSF volume/pressure lowering medication or with lumbar vein coil embolization to correct the anatomic/venous congestion issues. Certainly, this could've been low CSF volume from a microscopic leak, but the Trendelenburg position would have helped to decipher this in addition. I'm not sure if this patient's headache ever resolved as I had moved from the area but from the hundreds of NDPH patients that I've seen over the years it is feasible that she could still have continued with unabated head pain for decades as the underlying secondary cause of her headache was never treated. What's important to state is that at the time this would have been considered a primary headache disorder under ICHD criteria, but after years of additional knowledge about the NDPH condition, it was almost definitely secondary.

Proposed Changes for ICHD-4

NDPH should be removed from the Primary headache section, and the following should be added to the Secondary headache section.

New Daily Persistent Headache

Description

New daily persistent headache (NDPH) is defined as a daily persistent headache from onset in individuals without a prior headache

history. Typically, patients can name the date their headache began as it is so foreign to them to have head pain. The headache may or may not have migrainous associated symptoms. NDPH should be regarded more as a symptom complex and not a specific individual headache disorder as a multitude of secondary etiologies can lead to a daily headache from onset [12]. All individuals require neuroimaging of the brain and intracranial/cervical artery and veins as well as basic laboratory testing.

Secondary causes for NDPH have been attributed to viral infection, alterations in CSF pressure/ volume more high than low and not meeting criteria for idiopathic intracranial hypertension, high cervical spine irritation in individuals with underlying hypermobility issues but without a defined traumatic event, after a single very stressful life event (e.g. unexpected death of a child or spouse), post-surgical/procedural, after exposure to medications, supplements, vaccines and industrial solvents and after a single thunder-clap headache (probably a subtype of reversible cerebral vasoconstriction syndrome but not meeting ICHD criteria for that disorder). Continued ongoing evaluation for secondary etiologies is suggested based on evolving published literature.

Diagnostic criteria:

- A. Persistent headache fulfilling criteria B-E
- B. No or minimal prior headache history
- C. Distinct and clearly-remembered onset, with pain becoming continuous and unremitting within 24 hours
- D. Present for >3 months
- E. Headache may or may not have migraine associated features
- F. Secondary etiologies should be ruled in and there should be ongoing evaluation for secondary underlying causes based on published literature

Comments

Two recognized forms of NDPH:

Remitting form: headache ceases with or without treatment by two years from onset

Refractory form: headache continues daily persistent after 2 years from onset although may be altered in intensity with or without treatment

NDPH Secondary Subtypes:

1. NDPH Attributed to Infection (Typically Viral)

Comment: acute serum viral titers can be normal but very elevated chronic IgG titers can be noted. Past documented viral associations include parvovirus, cytomegalovirus, Epstein-Barr virus, and herpes simplex 1 but further research is needed.

2. NDPH Attributed to an Abnormal Reset of CSF Pressure to an Elevated State

Comment: typically defined by patients as a holocranial pressure like headache which is worse first thing in the morning, worse

with physical exertion and barometric pressure changes and head pressure immediately worsens in the Trendelenburg position. Other secondary causes of elevated CSF pressure like Chiari malformation, posterior fossa tumor, cerebral vein thrombosis need to be ruled out. Patients will have no disc edema and if lumbar puncture is completed CSF opening pressures will be within normal documented ranges, but CSF volume removal will improve headache intensity.

a. Post Valsalva

Comment: Single Valsalva events including cough, sneeze, screaming, emesis, coitus, lifting a heavy object have been noted to trigger daily persistent head pain.

b. With Nutcracker Physiology

Comment: Specific imaging techniques can demonstrate left renal vein compression with secondary retrograde flow through the left second lumbar spinal vein resulting in congestion of the spinal epidural venous plexus. Specific treatment with either renal auto transplant or lumbar vein coil embolization has been noted to improve daily persistent headache in this scenario.

C. Post Travel to Higher Altitude or After Airplane Travel

d. From Presumed Specific Neuroanatomic Issues on Imaging including: a crowded posterior fossa, large mega cisterna magna, large cavum septum pellucidum/vergae, large developmental venous anomaly

3. NDPH With Cervical Spine Hypermobility and Pain Attributed to Upper Cervical Spine Irritation

Comment: Secondary to cervical spine hypermobility issues, this patient population can develop upper cervical spine/facet irritation sometimes from a very early age. This can eventually lead to headache when the trigemino-cervical complex is sufficiently activated. In many instances no triggering event is noted in this population. However, seemingly innocuous situations such as going on a long car trip, sleeping in a hotel room or after being on an amusement park ride which can put further burden on an already irritated cervical spine can trigger a daily persistent headache from onset. Examination for cervical and systemic hypermobility as well as cervical spine pain trigger zones is necessary.

4. Post Surgical or Post Procedural with Presumed Hyperextension of the Neck

Comment: Because of hypermobility issues or with age these patients have developed presumed cervical facet irritation at baseline but not yet reaching a headache pain threshold point. Post a procedure typically with prolonged hyperextension of the cervical spine (intubation, extended otolaryngic or dental manipulation) the patient develops a daily persistent headache typically starting at the occipitocervical region and radiating to the cranium. This can occur immediately after the post procedure or within several days post procedure. Examination for cervical and systemic hypermobility as well as cervical spine pain trigger zones is necessary. These patients can do very well with pain anesthesiologic procedures directed at the cervical spine pain generator.

5. NDPH With a Single Thunderclap Headache at Onset

Comment: This is a presumed subtype of reversible cerebral vasoconstriction syndrome without neuroimaging evidence of vasospasm as there is typically a delay from onset of headache to imaging. Should resolve with calcium channel antagonists.

6. NDPH Attributed to a Single Stressful Life Event

Comment: Mechanism of this headache is unknown but may relate to cytokine activation

7. NDPH From Cranial Suture Irritation

Comment: Headache should start spontaneously without head trauma although very remote trauma sometimes decades in the past can be noted on history. Exam should demonstrate pain localized to cranial suture line(s) and this should mimic the patient's headache.

8. NDPH From Exposure to Medication, Supplements, Vaccines and Industrial Solvents (Refrigerants, Insecticides)

Comment: Headache can start daily during or just after exposure or after stopping an offending agent (typically medications such as serotonin reuptake inhibitors)

9. NDPH Attributed to a Presumed Secondary Condition Which Has Yet to Be Defined

Conclusion

NDPH is not one distinct headache disorder but a unique clinical headache symptom complex that can be caused by an ever-expanding list of secondary conditions which can extend beyond the central nervous system. The key is to keep looking for that secondary cause that can be successfully treated. Keeping NDPH in the "Primary" headache section of the ICHD criteria is incorrect and should be changed with the upcoming 4th iteration.

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Conflict of Interest

No conflict of interest.

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