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New Daily Persistent Headache Treated with Botulinum Toxin Type A: Case Report

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Abstract

New Daily Persistent Headache (NDPH) is a primary headache disorder, characterized by chronic and unremitting daily headache with abrupt onset and more than three months in duration. It lacks typical clinical features. It may be self-limiting within months or years without therapy, or be refractory to most treatments.

Our study describes a typical case of New Daily Persistent Headache, refractory to different therapies that was partially responsive to repeated cycles of botulinum toxin type A. A 19-year-old woman, without prior headache history, suffered since eight months from a daily and unremitting headache, with features of tension-type headache. She was submitted to various examinations and finally diagnosed as NDPH. Her pain was unresponsive to multiple pharmacological and non-pharmacologic treatments. After three cycles of botulinum toxin type a she experienced a satisfactory relief of pain and good improvement of her quality of life. We propose botulinum toxin type A as an effective treatment for refractory cases of NDPH.

Keywords: Headache; Chronic headache; Headache therapy; New daily persistent headache; Botulinum toxin type A

Abbreviations

NDPH: New Daily Persistent Headache; EBV: Epstein-Barr Virus; HSV: Herpes Simplex Virus; CMV: Cito Megalo Virus; CSF: Cerebro Spinal Fluid; TNF∝: Tumor Necrosis Factor Alfa; CNS: Central Nervous System; VAS: Visual Analogue Scale; EEG: Electro Encephalo Gram; MRI: Magnetic Resonance Imaging; DWI: Diffusion Weighted Image; EBNA: Epstein-Barr Nuclear Antigen; VZV: Varicella-Zoster Virus; NSAIDs: Non-Steroideal Anti-Inflammatory Drugs; PREEMPT: Phase III Research Evaluating Migraine Prophylaxis Therapy; QoL: Quality of Life.

Case Presentation

New Daily Persistent Headache (NDPH) is a primary headache disorder, characterized by chronic and unremitting daily headache with abrupt onset and more than three months in duration, first described by Vanast [1] in 1986 and later clinically better characterized [2-3]. It lacks typical clinical features, the pain being suggestive of chronic migraine without aura or tension-type headache. A percentage of NDPH sufferers may report some trigger events such as a febrile illness, surgical interventions or stressful events. It has two subtypes: it may be self-limiting within months or years without therapy, or be refractory to most treatments, frequently representing a major therapeutic challenge. The pathogenesis of NDPH is unknown, but in some cases association with viral infections (EBV) [4], (HSV-CMV) [5], and elevation of CSF Tumor Necrosis Factor ∝ (TNF∝) levels, a pro-inflammatory cytokine involved in brain immune and inflammatory processes [6], were reported. A pathogenetic hypothesis is a CNS inflammation triggered by a viral infection. One paper described widespread joint hypermobility, specifically in the cervical spine, as a predisposing factor for the development of NDPH [7]. It appears in the International Classification of Headache Disorders, 3rd Edition, in the fourth chapter (Other primary headache disorders) at the point 4.10 [8] (Table 1).

M. L., Female, a 19 year-old university student, first seen in August 2013, with left renal hypoplasia and Raynaud's phenomenon, without prior headache history, referred since December 24, 2012 (this date was specifically remembered) the onset of a daily, continuous and unremitting headache localized bilaterally in the forehead and occipital region, with pressing/tightening features, painful tension in both shoulder muscles and lack of general and local autonomic symptoms. The intensity of pain was variable, generally moderate, but with paroxysms of disabling intensity (VAS 8/10). No history of familial headache, nor surgical interventions. No psychiatric features were diagnosed. The patient did not remember head or cervical traumas, nor a febrile illness prior to the onset of headache. The quality of life of the patient was deeply affected by the continuous pain, that compromised her course of studies.

Neurological examination was unremarkable, apart slight muscle hypotonia with generalized joint hypermobility. EEG and angio-MRI with DWI, as well as routine blood tests, physical-chemical CSF examination and CSF pressure were normal. Radiogram of the cervical spine showed rectification of the physiological lordosis. Serum viral antibodies anti-HSV IgG-IgM 1-2, anti-CMV IgG-IgM, EBNA IgG, anti-measles IgM, anti-parotitisIgM, anti-Echovirus IgG-IgM, anti-Coxsackie A-B IgG-IgM were negative, while anti-measles IgG, anti-parotitisIgG, anti-VZV IgG were positive and anti-VZV IgM were slightly positive. CSF viral antibodies anti-HSV 1-2, anti-VZV, anti-CMV, anti-EBV and anti-adeno- and entero-virus were negative.

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Table 1: New Daily Persistent Headache (NDPH): ICHD-3 Diagnostic Criteria.

A. Persistent headache fulfilling criteria B and C
B. Distinct and clearly remembered onset, with pain becoming continuous and unremitting within 24 hours
C. Present for > 3 months
D. Not better accounted for by another ICHD-3 diagnosis.
E. ICHD-3: International Classification of Headache Disorders, 3rd Edition

The pain was refractory to various symptomatic and prophylactic drugs, including NSAIDs, acetaminophen, dipyrone, rizatriptan, and riboflavin, amitryptiline, propranolol, flunarizine, pizotifen, pregabalin, duloxetin. "She was also not responsive non-pharmacologic therapy as acupuncture and positioning of bite-plane. A cycle of i. v. acyclovir was performed without success".

After informed consent, she was treated with botulinum toxin type A (Botox) 195 U s. c. since January 2014, with cycles every three months, following PREEMPT sites of injection and dose paradigm for chronic migraine plus follow-the-pain pattern [9]. The pain partly relieved after first cycle and subsided almost completely after third cycle, becoming tolerable although the patient never became headache free (VAS 2/10). She is still regularly in treatment (after more than four years of strictly monitored follow-up), and consistently experienced marked improvement of headache immediately after each cycle, with subsequent worsening of pain, and she did not complain of remarkable side effects. In spite of the incomplete relief of pain, the patient reported a substantial improvement of her Quality of Life (QoL), being able to begin studying again, and recently she graduated.

Discussion

In our case, the clinical features of headache, suggestive of tension-type headache, but with clearly remembered onset and subsequent continuous and unremitting pattern, the substantial normality of clinical and instrumental examinations and the refractoriness to most therapies were in accordance with NDPH, of refractory subtype. It was not possible to single out a specific trigger factor for the onset of the headache, such as a viral infection or traumatic events, and serum and CSF viral antibodies were not clinically significant. Angio-MRI did not detect abnormalities such as arterial vasospasm.

We postulated possible efficacy of botulinum toxin type A on the basis of the reported partial responsiveness of this headache entity in a single case, at the dose of 100 units for three cycles of therapy [10]. More recent papers also anecdotally recommended various patterns of this treatment, in particular at PREEMPT dose of 155 U [11-12], but we used a higher dose of Botox (195 U). This therapy is still not approved in Italy for NDPH, due to the lack of controlled studies. In our case we can reasonably exclude a spontaneous remission of the headache because of the persistence of less severe pain, clearly relieved after each cycle of the therapy. Botulinum toxin type A was the only effective treatment in this case, and strongly contributed to the improvement of QoL of the patient, without side effects.

We propose botulinum toxin type A as an effective treatment for refractory cases of NDPH, and we believe this case report could represent a stimulus to perform more observations on the efficacy of this therapy in chronic refractory primary headaches, including **New Daily Persistent Headache (NDPH)**, in view of the inclusion in national and international therapeutic guidelines.

Consent

The patient expressed informed consent in writing to the therapy and to the publications of data concerning her illness and treatment.

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