

# NUMMULAR HEADACHE: UPDATE AND LITERATURE REVIEW

## Abstract

Nummular Headache is a primary headache (even if secondary cases were reported), included in the International Classification of Headache Disorders, 3<sup>rd</sup> Edition (ICHD-3 - 2018). The aim of this chapter is to review the epidemiological and clinical features, pathogenesis and treatment of nummular headache, following updated literature.

Although Nummular Headache is considered an uncommon headache, information regarding its true incidence and prevalence is lacking. In tertiary headache clinics, its observation is not so rare; until now, more than 540 cases have been described. Its clinical features include continuous or intermittent pain felt in a limited round or elliptic area of the scalp, with a diameter of 1-6 cm, mainly located in parietal, temporal or occipital regions, mostly unilateral but sometimes on the midline or bifocal. Its pathogenesis is unknown, but some clinical data suggest a peripheral origin of pain. The diagnosis is mainly clinical, and its assessment must rule out symptomatic cases due to an underlying lesion, with appropriate investigation. The most used and effective medical prophylactic treatments are gabapentin and botulinum toxin.

**Keywords:** Nummular Headache – Primary headache – Epicrania – Gabapentin - Onabotulinum toxin type A

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## I. INTRODUCTION

The vast majority of headaches coming to the attention of specialists and described by patients with plenty of details and sometimes imaginative expressions, generally share a severe or disabling intensity.

Nevertheless, there is a peculiar and unusual headache, with mild features both in intensity as in diffusion, called Nummular Headache (NH). This term, which is derived from the Latin term “*nummus*”, means “*coin-shaped headache*”. In fact, in NH, pain is circumscribed in a limited, well-defined, coin-shaped area of the scalp.

This headache was first described by Pareja et al. in 2002 (1) and later (2004) included in the Appendix of International Classification of Headache Disorders (ICHD-2) (2) at point A13.7.1; the article, curiously, contained an error in the title (“Numular” instead of “Nummular”, the last term later universally accepted). Following the publication of a large number of case reports and series, NH was recognized as a genuine clinical entity and included in the main body of ICHD-3 beta (2013) (3) and ICHD-3 (2018) (4), within “Other Primary Headaches”, at point 4.8 (Tab. 1).

## II. EPIDEMIOLOGY

At present, there are not population-based epidemiological studies concerning NH. There are in literature some large series, mainly from Spanish groups; two of these report a percentage of 4.1% NH cases on total patients seen in a headache clinic in ten years (5), or an annual incidence of 6.64 cases on 100.000 and 0.03% prevalence in general population (6). It is important to notice that these data come from headache specialists very fond in the diagnosis of NH, whilst many cases could be missed by other neurologists, or many NH patients do not consult a doctor because of mild pain, leading to an underestimation of this condition.

Following last published review of this clinical entity (7), more than 540 cases of NH were described. From the same review, F/M ratio shows a female preponderance, 1.6:1, previously estimated from 1.01 (6) to 1.8:1 (8). Mean age at onset is around 48 years, with a very wide range of 4-86 years and uniform distribution across different ages. So that, we can conclude that NH is an uncommon, but not exceptional headache, and it is not typical of a specific period of life. Nearly half of NH patients present a previous or concomitant diagnosis of another headache (migraine, tension-type headache, medication-overuse headache or primary stabbing headache) (9); more rarely trigeminal or occipital neuralgia (10). In 12.8% of cases a head trauma is found in clinical history (11).

## III. CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

In NH, pain is felt in a limited area of the scalp, round or rarely elliptical, with well-defined borders, with diameter ranging from 1 to 6 cm in the majority of cases. This area, mostly located in the parietal region, but also in occipital or temporal regions (rarely frontal), is generally unilateral, but some cases of a bifocal (5-12-13-14), multifocal (15) or over the midline (5-12-16-17) location were also described. It is not located in a territory innervated by a single cranial nerve. The area in which the pain is felt remains stable over time, even for

long periods. The pain is chronic in 75% of described cases, or with spontaneous temporary remissions (18), continuous or intermittent; its intensity is mostly mild to moderate, pressing or throbbing in character, but sometimes severe, stabbing or burning, and also with exacerbations and/or superimposed paroxysms (9-14). There is no information regarding a circadian pattern; there is an observation of one case of menstrual-related NH (19). In painful area, sensory symptoms as hypoesthesia, hyperesthesia, dysesthesia, tenderness and allodynia could be also experienced (18).

First articles on NH were dedicated to clinical and symptomatological characterization, including a second case series by Pareja et al. (16), to whom, soon after, other case reports were added, mainly dealing with first therapeutic attempts.

Other papers dealt with peculiar cases: patients with trophic changes of skin or hair in the affected area, such as skin atrophy or alopecia (20-21), or local changes in skin temperature (22). From other reports, symptoms different from those described in previous observations emerged, such as high intensity pain with exacerbations of lancinating quality (14), spontaneous or precipitated by local stimuli, head movements, physical efforts, Valsalva manoeuvre (23) or sexual activity (24), and with some migrainous features (25). Some cases were studied with pressure algometer, with the aim of studying pressure pain threshold in affected area and in other cranial regions; this threshold is locally lower and consequentially pain sensitivity is increased in painful area (26).

NH, as described in first observations, was classified between primary headaches. As such, for clarifying the diagnosis, it is mandatory in all cases to identify its clinical features (including the local presence of trophic changes) and to exclude systemic diseases or underlying structural lesions, by means of clinical history, physical examination, blood tests (including immunology screening), and neuroimaging. Differential diagnosis must exclude other forms labeled as epicranias, like epicrania fugax (7), supraorbital neuralgia or occipital neuralgia; if circumscribed, temporal arteritis could be differentiated from NH, by means of inflammatory markers. NH and primary stabbing headache could share some symptoms, especially exacerbations of stabbing pain, but the temporal pattern of NH is generally chronic and continuous.

#### **IV. SECONDARY CASES**

Since 2007 (27), many cases were described, in which typical pain was secondary to skin or subcutaneous tissue pathologies, bone or intracranial lesions. Following these case reports or case series, patients with NH-like symptoms were affected by superficial aneurysms (28), cranial or cutaneous malformations (29-30), calcific hematoma of the scalp (31), varicella-zoster shingles (32) and eosinophilic granuloma (33). Between intracranial lesions, there are arachnoid cysts (34), a pituitary adenoma (35) and a meningioma (27). A recent review (36) presented eight new cases (bone or cortical emangiomas, superficial inflammatory or cholesterol cysts, osteoma, cavernoma) and discusses previous observations of secondary NH. Another review dedicated to post-traumatic cases of NH, to date described, was published (5). These cases are not to be strictly labeled as secondary, because head injury is generally considered a precipitating event and not the cause of pain (9-36). Following these observations, patients with NH preceded by head injury present a higher mean age and are more frequently affected by cutaneous allodynia (5). In literature, some cases precipitated by

surgical manipulations (37-38-39) and by an insect bite (20) are also reported, and there are observations of NH associated with autoimmune disorders (rheumatoid arthritis, Sjögren syndrome, Sicca syndrome and antiphospholipid antibody syndrome) (40).

## V. PATHOPHYSIOLOGY

The pathophysiology of NH is not fully understood. Nevertheless, research pointed out some typical aspects of the pain suggesting pathogenetic mechanisms. A hypothesis supported by Pareja Spanish group, described it as an “epicrania”, attributed to a dysfunction of C-fibers of terminal branches of cutaneous nerves within epicranial tissues (41), as other painful entities (supra-orbital neuralgia, occipital neuralgia, trochleitis, epicrania fugax, primary stabbing headache), consistent with neuropathic pain (20-42). The observations supporting this hypothesis are that symptoms and signs are restricted to a sharply delimited area of the scalp, in the absence of diffuse hypersensitivity of pericranial structures (43), as in migraine and tension-type headache; furthermore, algometric measurements indicate that lowering of pain threshold is present only in the symptomatic area (26-44). In addition, the possible presence of trophic changes of skin and/or hair loss, in close temporal and spatial relationship with the pain, is in favour of the peripheral hypothesis, due to the importance of innervation for maintenance of normal skin structure (20). These data strongly suggest a peripheral mechanism, rather than central, as i. e. activation of trigemino-vascular system.

This hypothesis seemed not in accordance with the observation of some cases with painful area located in the midline (16-17-18) and the ineffectiveness, partial or temporary effectiveness of anesthetic infiltration of the affected area (17-37-45-46). But nerve fibers extending across cranial bones and crossing the midline were detected. Further, it has been observed (47) that some nerve branches responsible of pain extend in inner periosteum and in transdiploic or intradiploic layers, penetrating the skull and are inaccessible to the action of anesthetics.

Structural abnormalities detected in secondary forms could help elucidate even the pathogenesis of primary NH. In fact, the majority of symptomatic NH share lesions located within or adjacent to the scalp or skull bones, in close proximity with painful area. These lesions could damage peripheral fibers of cutaneous and/or pericranial and epicranial nerves. In primary forms, these lesions could be unremarkable to macroscopic observation.

There are also post-traumatic forms of NH, in which the trauma could precipitate the onset of pain because of the injury of epicranial tissues and nerve branches (5).

A dedicated article (48) showed no differences in mood state between NH patients and controls, nor any relationship between clinical parameters of nummular headache and levels of anxiety or depression.

## VI. TREATMENT

At present, there are not controlled clinical trials on the treatment of NH, and therapeutic attempts come from case reports or case series.

First cases of Pareja group were untreated or treated only with analgesics or NSAIDs because of mild intensity of pain (in many cases the patients did not require treatment),

frequently ineffective or scarcely effective. These drugs are still useful as acute treatment in case of exacerbations of pain. In one case with migraine features, triptans as acute therapy, and topiramate as prophylactic, were effective (25).

Many case report were published in which various prophylactic therapies were proposed: gabapentin (5-14-37-49-50-51-52-53), onabotulinum toxin Type A (9-45-54-55-56), tricyclic antidepressants (17-53-57-58), other antidepressants (9-14), pregabalin (9-59), indomethacin (12-23-60), with non-univocal results. Non-pharmacological treatments were tried in other cases: acupuncture (61) and transcutaneous electrical nerve stimulation (TENS) (46). More recently, other treatments were used: palmitoylethanolamide in monotherapy (62) and in association with topiramate (63), Neurotrophin, an extract of animal skin, used as analgesic in Japan (64-65), carbamazepine (9-52), metoprolol (59).

Some symptomatic cases positively responded to surgical excision of the underlying lesion (27-28-33). A series of 49 primary NH patients with associated Doppler signal within the area of pain was treated with minimally invasive arterectomy under local anesthesia with significant benefit (66). A systematic review of primary and secondary cases of NH who underwent various surgical treatments is also available (67). When the surgical resection of the underlying lesion is not possible, medical therapy is generally similar to primary cases.

Following the numerosity of presented cases and their clinical outcome, gabapentin at medium dosage (600-1200 mg) and onabotulinum toxin type A (a protocol for dosage and localization of injection was proposed by García-Azorín et al.: five injections of 5 UI of Botox within the painful area, one centrally and four periferally) (55) seem to-date the most used and effective treatments.

## **VII. PROGNOSIS**

The literature about the clinical outcome and prognosis of NH is relatively scarce. In the majority of cases it was described as a benign condition, and temporary or long-lasting spontaneous remissions (6-5-18) or after effective treatment (51-60) were reported. In some cases NH could not respond to treatments and may last for years. Secondary cases with an underlying treatable lesion may well respond to surgical treatment.

## **VIII. CONCLUSION**

NH can be defined an organic, primary headache syndrome, with a clearly definite symptomatology: the pain is circumscribed in a rounded or elliptical area of 1-6 cm in diameter and mostly unilateral localization (even if some bilateral and multifocal cases were described), generally fixed in time. The pain is usually of mild to moderate intensity, but severe pain and local exacerbations are described. In literature many cases secondary or associated to other pathologies are present. The typical topographic distribution and the associated features suggest a peripheral pathogenesis, like dysfunction of C-fibers of a terminal nerve, innervating the scalp or skull bones. Diagnosis is mainly clinical, but it is mandatory in all cases to rule out secondary forms by means of blood tests (including immunology screening) and neuroimaging. At present, treatment is based on limited evidence because the lack of controlled clinical trials: the most used and effective medical therapies for

NH are gabapentin and onabotulinum toxin type A, but surgical treatments for secondary cases and even for selected patients with primary NH have been successfully performed.

Tab. 1

<p><b>Diagnostic criteria of Classification ICHD-3</b></p> <p><b><u>4.8 Nummular Headache</u></b></p> <p><i>Description:</i> Pain of highly variable duration, but often chronic, in a small circumscribed area of the scalp and in the absence of any underlying structural lesion.</p> <p><i>Diagnostic criteria:</i> A. Continuous or intermittent head pain fulfilling criterion B B. Felt exclusively in an area of the scalp, with all of the following four characteristics:</p> <table border="1"><tr><td><ol style="list-style-type: none"><li>1. sharply contoured</li><li>2. fixed in side and shape</li><li>3. round or elliptical</li><li>4. 1-6 cm in diameter</li></ol></td></tr></table> <p>C. Not better accounted for by another ICHD-3 diagnosis.</p> <p>ICHD-3: International Classification of Headache Disorders, third Edition, 2018 (2)</p>	<ol style="list-style-type: none"><li>1. sharply contoured</li><li>2. fixed in side and shape</li><li>3. round or elliptical</li><li>4. 1-6 cm in diameter</li></ol>
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