Nummular headache in children: A case series and systematic literature review

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Abstract
Background: Nummular headache is a rare primary headache disorder potentially disabling and refractory to treatment. Of over 300 reported cases, only 9 are children.

Design/Methods: We searched our institutional database and PubMed for “nummular headache” and synonyms and evaluated select articles from reference lists of substantial reviews.

Results: Seven children were identified from our institution and nine from 107 unique publications. Mean age at onset was 9.7 and 11.9 years in our cohort and the literature, respectively, with a female:male ratio of 2:1. Location and quality varied, and allodynia was reported in five. Frequency ranged from every other week to continuous. Imaging was normal except in four cases. Migraine was often comorbid. Published cases were frequently refractory to treatment whereas four of our cohort improved with therapy for comorbid migraine.

Conclusions: Nummular headache is rarely reported in children. We describe characteristics of seven new and nine previously published pediatric cases.

Keywords
adolescent, literature review, nummular headache, pediatric

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Background
Nummular Headache (NH) was first coined by Pareja and colleagues in 2002 while describing 13 cases.1 Characteristics of NH include continuous or intermittent pain localized to a fixed round or elliptical, sharply-contoured area of the scalp, 1–6 cm in diameter.2 The incidence of NH in one large series was 6.4/100,000/year.3 The pathophysiology of NH remains unclear, with both peripheral and central mechanisms proposed.4 With no clinical trials, treatment recommendations for NH are largely derived from small series at best.

To date, over 300 primary and secondary cases have been described.4–6 However, no reports include more than one pediatric case, and no formal review has established the characteristics in the pediatric population. We report seven new cases of NH in children and a systematic review of pediatric cases from the existing literature.

Methods
We performed a retrospective analysis of a prospective cohort at our tertiary care pediatric headache center followed by a systematic review of the literature. We searched the database of the Cincinnati Children’s Headache Center for patients under 18 years old diagnosed with NH by a headache specialist. A consent form was signed by all patients.

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included patients’ guardians for entry of data from their visit into a password secured research database. Use of this database for research purposes was approved by the Institutional Review Board of the Cincinnati Children’s Hospital Medical Center.

We conducted a PubMed search from January 1, 2002 through September 25, 2021 for the following terms: “nummular headache” OR “coin shaped headache” OR “coin shaped cephalalgia” similar to those used in a recent review. In addition, articles were screened from the reference lists of relevant reviews. All English-language articles and abstracts describing children with NH were included. All cases of primary and secondary NH in patients under 18 years old in both cohorts were reviewed. The following details were extracted: age at NH onset, sex, size and location(s), quality, severity and timing of pain, local trophic changes, comorbid headache disorders, imaging obtained, management and clinical course. Descriptive statistics were analyzed with Excel (Microsoft Office Excel, Redmond, Washington, USA) and are reported as ratios and percentages.

Results

A total of 8916 children and adolescents under the age of 18 were seen at our Headache Center between 2016 and 2021, 7 of whom were diagnosed with NH by a Headache Medicine certified neurologist by International Classification of Headache Disorders (ICHD) criteria (Table 1). Mean age at onset was 9.7 (range 5–13) years with four females and three males. Reported pain diameter in our three documented cases ranged from 2.5 to 4 cm and locations were described as “right of midline at the vertex,” “left parieto-occipital,” “right parieto-temporal,” “top” in two and not clearly documented in two others. Alldynia was reported in three. Pain was most commonly described as pressure or sharp with average intensity of 5 ± 1 on a 10-point scale. Frequency varied from every other week to continuous with severe exacerbations. Migraine or its subtypes was present in six of our seven cases, though details were not always well-documented making it difficult to distinguish between NH and migraine attacks in some cases. Other coexisting headache disorders included tension-type headache, medication overuse headache, and a preliminary diagnosis of primary stabbing headache. Imaging was normal except for Case 1 with a 5 mm pineal cyst and Case 2 with mega-cisterna magna; both were considered incidental findings.

Of our cohort, Case 1 improved with repletion of coenzyme Q10 and vitamin D, and returned with only migraine 1 year later which again responded to conservative management. Case 2 underwent washout for medication overuse headache with an increase in topiramate dose and vitamin D supplementation, but did not return for follow up. Case 3 improved halfway into topiramate titration to 50 mg (0.68 mg/kg) twice daily with washout for medication overuse headache. Case 4 presented with new daily persistent headache (NDPH) with NH phenotype, refractory to cyproheptadine, valproate, amitriptyline, topiramate, vitamin D, coenzyme Q10, and occipital nerve blocks but naproxen helped alleviate exacerbations. Onabotulinum toxin A (BoNT-A) 30–40 units injected at the periphery of painful area in addition to 155 units for typical chronic migraine treatment reduced duration and severity of attacks. Severity was further reduced when transitioned to levetiracetam 1500 mg twice daily. NH in Case 5 resolved with valproate titration to 500 mg (5.6 mg/kg) twice daily, vitamin D and folate, but chronic migraine persisted. Case 6 was recently diagnosed and was not on preventive therapy at the time of this publication. Attacks are usually no longer than 20 seconds but ibuprofen was recommended for clustered attacks. Case 7 was also recently diagnosed; ibuprofen was recommended for acute therapy and topiramate titration was initiated for prevention with vitamin D and coenzyme Q10.

An additional nine pediatric cases from 107 unique publications were identified (Figure 1 and Table 1). Mean age at onset was 11.9 (range 4–17) years with five females, two males and two with unreported sex. Diameter was 1–5 cm with alldynia reported in two. Locations can be found in Table 1. Pain was most commonly described as pressure with a mean average intensity of 4.4 ± 0.8 on a 10-point scale. Only a single literature case was associated with trophic changes. Attack frequency was most commonly continuous. Migraine or its subtypes were comorbid in two. Three additional reports did not include individual case descriptions or clinical course, but were the youngest age of onset in a reported series. Imaging revealed Langerhans cell histiocytosis in one literature case and a cholesterol cyst in another. The majority of literature cases were refractory to treatment with the exception of lesionectomy of Langerhans cell histiocytosis and spontaneous remission without removal of cholesterol cyst.

Discussion

Nummular headache is rarely reported in children. True incidence and prevalence are unknown even in adults but one study showed NH represented 1.25% of patients presenting to a general neurology outpatient office for headache. In our tertiary pediatric headache center, a database search since 1997 identified only seven cases, all during or after 2016. This equates to 0.08% of patients seen since 2016 suggesting NH is less common and/or extremely underrecognized in the pediatric population. A recent series showed a female predominance in 64.4%, with a similar predominance in 64.2% of cases reported here, though two additional literature cases did not report sex.

The variety of pain characteristics in this series and literature cases supports the ICHD-3 criteria which does not include a specific quality. Mean intensity of our cohort is similar to that reported in the general population (5.2 ±
| Author, year | Case | Age at onset, Sex | Location | Diameter | Quality | Intensity (1–10 scale) | Pattern | Local abnormalities | Comorbidities | Imaging | Treatment |
|--------------|------|------------------|----------|----------|---------|------------------------|---------|-------------------|--------------|---------|-----------|
| Pareja, 2004 | 13 F | 13 F (may be age at publication) | Vertex | 2.5 cm | Pressure | 5 | Continuous mild with severe exacerbations 1–7 days | None | | CT normal | Metamisol improved acutely. Refractory to indomethacin and nerve blocks |
| Cohen, 2005 | 16 F | | | | | | | | | | |
| Dach, 2006 | 6 F | Vertex | 2.5 cm | Pressure | 5 | Continuous mild with severe exacerbations 1–7 days | None | | CT normal | Metamisol improved acutely. Refractory to indomethacin and nerve blocks |
| Dabscheck, 2010 | 4 M | Right Parietal | 1–2 cm | Episodic (15–20 sec), up to 4/day | Blond patch w/ reduced sensation | MRI normal | Refractory to acetaminophen Lesionectomy |
| Guerrero, 2012 | 12 F | B/l parietal and occipital | 4 cm | Oppressive | 5 | Continuous | None | MRI normal | Refractory to acetaminophen Lesionectomy |
| Rodriguez, 2015 | 11 F | Left Lateral Frontal | 4 cm | Oppressive | 5 | Continuous | None | MRI normal | Refractory to acetaminophen Lesionectomy |
| Silva Rosas, 2018 | 12 M | Left Lateral Frontal | 4 cm | Oppressive | 5 | Continuous | None | MRI normal | Refractory to acetaminophen Lesionectomy |
| Thomas, 2020 | 16 F | Left parietal, occasionally on opposite side | 3–4 cm | Dull | 4 | Continuous dull with exacerbations of pressure-like, sharp and oppressive | Alodynia, dysesthesia | MRI normal | Rest and sleep alleviated. NSAIDs had minimal effect |
| Garcia-Iglesias, 2021 | 17 F | Right Occipital | 5 cm | Pressing | 5 | Intermittent (1 min, up to 4/day) | None | MRI: cholesterol cyst 5 mm pineal cyst | Spontaneous remission |
| Case 1 | 13 F | ND | ND | Constant and sharp | 6 (6–9) | No | MWOA TTH | Vitamin D, coenzyme Q10, sumatriptan, ibuprofen |
| Case 2 | 13 F | Unilateral, middle, top | ND | Constant, crushing, pressure, squeezing | 7 (6–9) | Daily, 4–8 hours | Alodynia | Mega-cisterna magna | Washout, vitamin D, increased topiramate |

(continued)
| Author, year Case | Age at onset, Sex | Location | Diameter | Quality | Intensity (1–10 scale) | Pattern | Local abnormalities | Comorbidities | Imaging | Treatment |
|-------------------|------------------|----------|----------|---------|------------------------|---------|---------------------|--------------|---------|-----------|
| Case 3            | 10 F             | ND       | ND       | Multiple qualities described<sup>a</sup> | 5 (3–7) | ND<sup>a</sup>       | Allodynia  | MOH, Hypothyroid   | Normal MRI   | Washout, topiramate |
| Case 4            | 13 F             | Right of midline at vertex | 3.5–4 cm | Aching | 4                     | Daily (NDPH), constant | Allodynia  | MOA, CM | Normal MRI/MRA | Increased topiramate, vitamin D, coenzyme Q10, BoNT-A, levetiracetam |
| Case 5            | 5 M              | Top      | ND<sup>a</sup> | Stabbing | 5 (2–9) | Daily, 1–14 hours then 0.5–3 hours | No | MOA, MWA, CM, MOH | Normal MRI | Vitamin D, folate, increased valproic acid |
| Case 6            | 7 M              | Left parieto-occipital | 2.5 cm | Pressure, sharp | 5 (3–7) | Every other week to 5/day, <1 minute | No | Possibly primary stabbing headache | Normal MRI | Ibuprofen |
| Case 7            | 7 M              | Right parieto-temporal | 4 cm | Throbbing, pressure | 4 (2–9) | 2–3/week, 1–24 hours | No | MOA | Pending MRI | Ibuprofen, vitamin D, coenzyme Q10, topiramate |

BoNT-A: onabotulinum toxin-A; CM: chronic migraine; CT: computed tomography; MOH: medication overuse headache; MRI: magnetic resonance imaging; MWOA: migraine without aura; MWA: migraine with aura; ND: not well documented; NSAID: non-steroidal anti-inflammatory medication; TTH: tension-type headache.

<sup>a</sup>Some children had difficulty distinguishing features and timing between nummular headache and other headache types.
1.6 on a 10-point scale). Similar to the general population, children experience a pattern described as continuous, intermittent, or continuous with intermittent exacerbations. Allodynia is reported in up to 48.6% of the general population and in two previously reported pediatric cases. An additional three cases from our cohort experienced allodynia, though it is unclear if this was exclusively in the region of NH pain or generalized related to comorbid migraine. No trophic changes were present in our cohort.

Average age at onset and pain characteristics are relatively similar between our cohort and literature cases. Frequency of attacks in the literature was mostly continuous whereas our cohort’s pattern was more varied. The most notable difference is the frequency of migraine in six of our cohort but only two of the literature. Similarly, many of our cases responded to migraine therapies. Some of our cases may have had attacks which met criteria for both migraine and NH and were therefore diagnosed with both, whereas three of the literature cases were only reported as part of a series without any details. When a single headache type fulfills criteria for more than one primary headache disorder, the ICHD-3 manual recommends using all available data to establish the most likely diagnosis. It is possible that our cohort contains a disproportionate number of patients who may have been reclassified as exclusively migraine had they not been lost to follow up. While this is a limitation of the current study, it also supports ICHD-3 recommendations to establish the appropriate diagnosis over time.

The pathophysiology of NH remains unclear. The well-demarcated pain suggests a peripheral process. However, this is problematic given lack of therapeutic response to local nerve blocks in the majority of cases and painful areas crossing the midline demonstrated in two of our cohort. The high rates of other coexisting primary disorders brings into question whether NH is truly a distinct pathogenetic entity. 100% of our cohort had another primary headache diagnosed either concurrently or subsequently, compared to 46.7% described in the general population. The only case in our cohort without migraine was only recently diagnosed and seems to be developing a distinctly unrelated type of headache on the contralateral side most consistent with primary stabbing headache. The subsequent development of migraine after a diagnosis of NH was described in one of the literature cases as well. These cases may support a common underlying pathogenic etiology. Secondary causes of NH have been reported in children and adults, so imaging should always be obtained.

Treatment of NH remains difficult. Gabapentin has been shown to be most frequently used and can be effective in up to two-thirds of patients with NH. Many of our cases reported resolution or improvement after treatment for comorbid migraine and medication overuse headache with other anticonvulsants along with lifestyle modifications.

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**Figure 1.** Nummular headache literature review.
and vitamin repletion when necessary. Of note, we supplement vitamins based on documented deficiencies and not exclusively as primary prevention therapy. BoNT-A has been shown to be effective in NH. BoNT-A improved but did not resolve pain in our case with NH-type NDPH. Once pain stabilized, further improvement in severity was achieved with levetiracetam.

This report is limited by its retrospective nature and small sample size, although the latter may also reflect the natural rarity of the disorder in this population. A number of literature cases had no case descriptions and some of our cases had unclear details. As an underrecognized disorder, even neurologists are at risk of underdiagnosing NH. Further reports in children would improve our understanding of this rare disorder and its true prevalence in children.

Conclusions
This is the first systematic review of NH in children with an additional seven cases from our cohort. Though potentially rarer in children, characteristics of NH are overall similar to those described in adults. Other coexisting or subsequently diagnosed primary headache disorders appears more common in children, however. Additionally, our data show that treatment for comorbid migraine when present may be an effective strategy for NH in children, especially with anticonvulsants when preventive therapy is warranted. Further studies are necessary to establish the mechanism and optimal management of NH in both adults and children.

Clinical implications
- Characteristic of nummular headache in children are similar to those in adults.
- Migraine may be comorbid in children with nummular headache.
- Treatment for comorbid migraine may be effective for nummular headache in children.

Abbreviations
NH, nummular headache; NDPH, new daily persistent headache; BoNT-A, Onabotulinum toxin A

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