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Expert Opinions

New Daily Persistent Headache Caused by a Multinodular Goiter and Headaches Associated With Thyroid Disease

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A 33-year-old female is presented with the first case to our knowledge of new daily persistent headache (NDPH) with a large right benign non-toxic multinodular goiter causing carotid and vertebral compression with complete resolution of the headache immediately after thyroidectomy. Although this may be quite rare, hypothyroidism or hyperthyroidism causing NDPH, migraine, or an exacerbation of pre-existing migraine is not. Clinicians should consider routinely obtaining serum thyroid-stimulating hormone (TSH) and free T4 in patients with new onset frequent headaches or an exacerbation of prior primary headaches.

Key words: new daily persistent headache, migraine, goiter, headache attributed to hypothyroidism, hyperthyroidism

(*Headache* 2016;00:00-00)

Primary new daily persistent headache (NDPH) is among the most difficult to treat primary headaches. At times, a treatable secondary cause of NDPH is found such as thyroid disease. Chronic headache due to hypothyroidism has been reported for almost 70 years.[1]

CASE HISTORY

This 33-year-old female was seen on February 2, 2016 with a 2-month history of bilateral ear pain described as sharp shooting pain behind both ears left more than right with an intensity of 2-3/10 at first for seconds and increasing duration and intensity and 5-10/10 the last week present all the day.

For the prior 3 weeks, she had headaches daily since onset described as generalized tingling, sharp, and pressure pain with an intensity of 3-9/10 and decreased to 2-3/10 with medications associated with nausea, light and noise sensitivity. No fever. No antecedent viral syndrome, psychological stressor, or antecedent surgery. Headache was a little better supine.

She was on gabapentin 300 mg tid for 5 days which had decreased the headache some but not the ear pain and tramadol for 1 day without help.

No prior history of headaches or ear pain.

She went to urgent care on January 28, 2016, where a CT of the brain without contrast, complete blood count, and comprehensive metabolic panel were normal. She had an MRI of the brain without contrast on January 29, 2016, which was normal.

Past medical history of a cervical and lumbar fusion and tubal ligation.

Neurological examination was normal. There was no evidence of Horner's syndrome. There was bilateral greater and lesser occipital nerve tenderness.

Bilateral greater and lesser occipital nerve blocks were performed by injection of 3 cc each of

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Conflict of Interest: None.

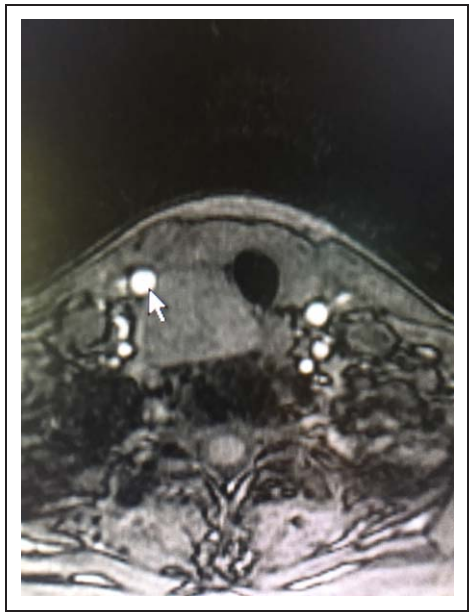

Fig. 1.—Axial MRI image of the neck shows anterior displacement of the right common carotid artery (arrow) by a right thyroid mass in contrast to the normal position of the left carotid artery.

1% lidocaine. Right after the injections, all of the head and ear pain was gone. She was placed on baclofen 10 mg ½-1 tid prn. An MRA of the neck was recommended to exclude dissection, which she declined. She was advised to take aspirin 81 mg daily for prevention of possible ischemic events if she had a cervical arterial dissection.

She was seen on February 9, 2016 and reported that the occipital blocks relieved the headaches for 2 days which then recurred daily and constant. She reported throbbing pain equally behind both ears, sides of the head, and bifrontal with an intensity of 3-10/10 with an average of 5-6/10 associated with nausea, light and noise sensitivity but no vomiting.

She had gone to an emergency room on February 7, 2016 and received an intravenous opiate, which temporarily decreased the intensity of the pain, and was placed on butalbital/acetaminophen/caffeine 50/325/40 mg and metoclopramide, which decreased the intensity of the pain. She was also taking gabapentin 300 mg tid and baclofen, which decreased the intensity of the pain. Neurological examination was normal. There was bilateral greater and lesser occipital nerve tenderness.

On February 9, 2016, thyroid functions were normal (thyroid stimulating hormone (TSH) 1.4, free T4 10.4).

MRA of the neck without contrast on February 26, 2016 (Fig. 1) showed anterior displacement of the innominate artery and the proximal right common carotid artery due to an enlarged right lobe of the thyroid gland. There was lateral displacement of the proximal right vertebral artery and mild mass effect on the right side of the trachea with left of midline and anterior displacement of the trachea. Curvilinear increased signal was present within the right lobe of the thyroid gland, which may represent flow within a vessel or could represent minimal subacute hemorrhage or calcification. A thyroid ultrasound on March 7, 2016 showed an enlarged diffusely nodule goiter of the right lobe of the thyroid gland.

She underwent a right thyroidectomy on March 25, 2016 with findings of a large right multinodular goiter with extension into the chest and under the common carotid artery tenting the great vessels forward and medial. The pathologist reported thyroid with nodular hyperplasia and focal dense lymphocytic infiltrates with germinal centers compatible with lymphocytic thyroiditis. When she awoke from surgery, the headaches were gone with no further headaches when seen for follow-up on August 31, 2016. TSH and free T4 were normal.

Questions.—Is thyroid disease associated with NDPH? What about other types of headaches? Did the goiter cause her headaches?

EXPERT COMMENTARY

Hypothyroidism.—Hypothyroidism can be a cause of headaches and an NDPH mimic.[2,3] The mechanism is not understood.

About 30% of patients with hypothyroidism have headaches. In a prospective study of 102 adults (83 females) of outpatients or inpatients in a headache and endocrinology clinic, 30% presented with headache 1-2 months after the first symptoms of hypothyroidism.[4] The headache was bilateral (80%), non-pulsatile (90%), continuous without paroxysmal attacks (95%), of mild intensity (89%), and usually responsive to salicylates. There was a history of migraine in 15.4% and no recent

Table 1.—Headache Attributed to Hypothyroidism

A. Headache fulfilling criterion C.
B. Hypothyroidism has been demonstrated.
C. Evidence of causation demonstrated by at least 2 of the following:
 1. Headache has developed in temporal relation to the onset of hypothyroidism or led to its discovery.
 2. Either or both of the following:
  a. Headache has significantly worsened in parallel with worsening of the hypothyroidism.
  b. Headache has significantly improved or resolved in parallel with improvement in or resolution of the hypothyroidism.
 3. Headache has at least 1 of the following 3 characteristics:
  a. Bilateral location
  b. Nonpulsatile quality
  c. Constant over time
D. Not better accounted for by another ICHD-3 diagnosis.

headaches in 69.7%. The headache decreased in intensity and duration after starting thyroid replacement near the 15th day in 58% and disappeared in 42% during a 12-month follow-up.

Lima Carvalho et al propose changing the International Classification of Headache Disorders (ICHD) criteria for headache attributed to hypothyroidism (Table 1)[5] as their cohort had much different headaches.[6] In a cross-sectional study of 213 mostly female adults recently diagnosed with hypothyroidism followed prospectively for 12 months, 34% reported headache (either a new headache starting or a previous primary headache with recent worsening in close relationship to other symptoms of hypothyroidism) with the following features: location (fronto-orbital, 49%; temporal, 37%, posterior part of the head, 15%; and unilateral, 47%); pulsatile, 63%; moderate to severe intensity, 72%; 4-72 hours duration, 78%; and nausea/vomiting, 60%. A history of migraine was more frequent in those with headache attributed to hypothyroidism (53%) than those without (38%). The frequency of headache was similar in those with hypothyroidism (TSH $\geq$ 5 mU/L) and those with subclinical hypothyroidism (high levels of TSH and normal range of free T4. After treatment with levothyroxine, 78% reported a decrease in headache frequency with similar benefit in those with both subclinical and hypothyroidism.

Bigal et al performed a case-control study of the prevalence of hypothyroidism in 65 patients with NDPH (48 females).[2] Hypothyroidism was much more common compared to the prevalence in 100 migraineurs (odds ratio [OR]=16) and 69 patients with chronic post-traumatic headaches (OR = 10.3).

Migraine may be co-morbid with hypothyroidism. In a study of 31,865 adult twins in Denmark using a questionnaire and self-reported co-morbidities, hypothyroidism was more common in female migraineurs (OR = 1.72) but not in male migraineurs (OR=.96).[7]

Interestingly, there is also contrary evidence that hypothyroidism may reduce the risk of headache. Hagen et al performed a population based study examining the possible association of thyroid dysfunction and headaches in 28,058 people in Norway.[8] The definition of headache used was any headache in the last year High TSH values were associated with a low prevalence of headache. In all age groups between 40 and 80 years, TSH was lower among those with headaches, especially migraine, than in those without headache. Among women with no history of thyroid dysfunction, headache was less probable (OR = 5) if TSH $\geq$10 mU/L than in those with normal TSH. The authors hypothesize that low beta-adrenergic activity could be a link between high TSH and low headache prevalence.

Conversely, headache disorders may be associated with an increased risk for development of new onset hypothyroidism. In a longitudinal retrospective cohort study of 8412 adults in the Fernald cohort who lived near Cincinnati, Ohio who received physical examinations and thyroid function testing every 3 years over 20 years, headache disorders were present in about 26% and new onset hypothyroidism developed in about 7% (hazard ratio = 1.21).[9] Those with possible migraine had an increased risk of 41%.

The authors suggest that inflammation due to migraine might predispose to thyroid autoimmunity. They also propose that production of anti-thyroid antibodies due to Hashimoto's thyroiditis could cause headache, which may be present long before the development of hypothyroidism.

MRI of the brain when obtained on patients with primary hypothyroidism can uncommonly show pituitary hyperplasia due to enlargement of thyrotroph cells due to lack of negative feedback which can be confused with a macroadenoma.[10]

Pseudotumor Cerebri (PTC) Associated With Thyroid Replacement.—There are 12 case reports (9 females) of thyroid replacement therapy associated with PTC with a duration of thyroid treatment prior to the diagnosis of PTC of 1-18 weeks.[11] There is a case report of PTC due to lateral sinus thrombosis associated with primary hypothyroidism.[12]

Hyperthyroidism.—Hyperthyroidism may be more common in female migraineurs. In the Norwegian study, hyperthyroidism was more common in female migraineurs (OR = 1.3) but not males.[8] In the Danish twin study, hyperthyroidism was more common among female and males migraineurs (OR = 1.80) more so in those with aura.[7]

New onset headache due to thyrotoxicosis caused by Grave's disease can present with a new daily persistent headache with migraine features and an increased frequency of pre-existing migraine.[13,14]

Enlargement of the Thyroid Gland (Goiter).—In the Danish twin study, enlargement of the thyroid gland (goiter) was more common in all migraineurs (OR = 2.08), more so in females and males with migraine with aura.[7]

There is a single case report of a 63-year-old female with a multi-nodular goiter (first diagnosed 13 years prior) displacing the left common carotid artery presenting with an ipsilateral Horner's syndrome and headaches mimicking paroxysmal hemicrania with resolution within 2 days of starting carbamazepine.[15] Goiter is a rare cause of Horner's syndrome usually due to benign pathology with an incidence of perhaps 0.14% due to compression of the cervical sympathetic chain[16] where the incidence of associated headaches is not known.

A Not So Incidental Goiter.—She presented with new daily persistent headaches with a duration of 3 weeks (subacute new daily persistent headache defined as a duration of 2 weeks to 3 months). The sharp shooting pain behind the ears lasting seconds suggested occipital neuralgia. The shooting pain progressed to lasting all day the week prior to presentation. She also had a 3-week history of constant daily since onset of headaches with migraine features. The MRA of the neck was obtained to exclude cervical arterial dissection as a possible cause and detected the enlarged right lobe of the thyroid, which was initially thought to be an incidental finding. The headache had been daily and fairly constant by the time of right thyroidectomy about 3 months after onset with findings of a large right multinodular goiter with extension into the chest and under the common carotid artery tenting the great vessels forward and medial and lymphocytic thyroiditis on pathology.

We are not aware of any previously reported cases such as the one presented here of goiter presenting with NDPH. The complete resolution of headaches immediately after surgery is consistent with a causal mechanism. The cause of the headache is not certain but may be similar to the mechanism of pain in arterial dissection with compression of periarterial sympathetic fibers travelling along the carotid artery.

CONCLUSION

Clinicians should consider routinely obtaining thyroid-stimulating hormone (TSH) and free T4 in patients with new onset frequent headaches or an exacerbation of prior primary headaches.

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