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BRIEF REPORT

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Non-hypothalamic cluster headache: the role of the greater occipital nerve in cluster headache pathogenesis

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Abstract Cluster headache is marked by its circadian rhythmicity and the hypothalamus appears to have a significant influence over cluster pathogenesis. However, as not all cluster patients present in the same manner and not all respond to the same combination of medications, there is likely a non-hypothalamic form of cluster headache. A patient is presented who began to develop cluster headaches after receiving bilateral greater occipital nerve (GON) blockade. His headaches fit the IHS criteria for cluster headache but had some irregularities including frequent side shifting of pain, irregular duration and time of onset and the ability of the patient to sit completely still during a headache without any sense of agitation. This article will suggest that some forms of cluster headache are not primarily hypothalamic influenced and that the GON may play a significant role in cluster pathogenesis in some individuals.

Key words Cluster headache • Hypothalamus • Greater occipital nerve • Nerve blockade

Introduction

Cluster headache is marked by its circadian rhythmicity. Episodic cluster periods start at the same time each year, individual cluster headaches occur at the same time each day and the duration of each cluster headache is almost the same for every attack. These clinical features along with the hormonal alterations documented in cluster patients suggest a role for the hypothalamus in cluster genesis. PET studies by May et al. [1] showing hypothalamic activation during cluster headache attacks solidified the notion of a hypothalamic influence in cluster headache. The concept of the hypothalamus acting as a cluster headache generator has also been entertained. However, not all cluster patients present in the same manner and not all respond to the same medications, suggesting that there must be atypical and even non-hypothalamic forms of cluster headache. A patient is presented who had no prior history of cluster headache but who began to develop cluster attacks after receiving bilateral greater occipital nerve (GON) blockade for chronic daily migraine. The post-procedure headaches fit the IHS criteria for cluster but had some irregularities including frequent side shifting of pain, irregular duration and time of onset of attacks and the ability of the patient to sit completely still during a headache without any sense of agitation. This article will suggest that some forms of cluster headache are not primarily hypothalamic driven and that the GON may play a significant role in cluster pathogenesis in some individuals.

Case report

A 54-year-old man with a long history of refractory chronic migraine underwent bilateral GON blockade for persistent

pain in his occipito-nuchal area. The GON block was completed after written consent utilising 9 cc of 1% lidocaine and 1 cc of 40 mg triamcinolone (5 cc applied to each side). He tolerated the procedure without complications and for the first four days had a decrease in his head and neck pain. On day 5 he began to develop a new type of headache. Whereas his typical daily pain was constant and bifrontal/bioccipito-nuchal in location, the new headaches were only one-sided in and around his eye, of severe intensity, lasting 30–90 min and associated with eyelid ptosis, lacrimation and nasal rhinorrhoea. He denied any nausea, vomiting, photophobia or phonophobia. The headaches occurred 2–4 times per day. During a headache he remained completely still without any sense of agitation. The headaches were always one-sided but readily switched sides with every attack or every other attack without a set pattern. For example, one day the headaches would occur consecutively on the right side, right side and left side and the next day only on the left side. The headaches would also start at any time during the day with great irregularity. One day they would take place at 9:30 am, 3:00 pm and 8:00 pm and the next day at 10:45 am and 3:45 pm. Headache duration was also not constant although most headaches lasted from 30 to 75 min. The patient presented to the office during a typical attack. He had unilateral eyelid ptosis, lacrimation and rhinorrhoea but was able to sit completely still without any sense of agitation even though the pain level was severe. In regard to treatment the headaches readily and consistently responded to oxygen therapy, normally alleviating the pain within 10–15 min. Sumatriptan was never tried as the patient had a history of cardiac ischaemia. A prednisone taper provided some relief but did not stop the cycle. Bilateral GON blockade was completed three weeks into the cycle of headaches to try to stop them. It decreased the number of attacks by one per day but did not completely shut off the cycle. After one month on topiramate (dose 200 mg/day) the frequency of headaches decreased and the patient started to have some headache-free days. After three months the cycle stopped and he has had no recurrence of this type of headache with a one-year follow-up. The patient had a history of cigarette smoking and ETOH abuse but had taken neither for many years. There was no family history of cluster headache. Prior to his transformation into chronic migraine he suffered from episodic migraine headaches, which were not at all similar to this new type of headache. Brain MRI and MRA of the intracranial and extracranial carotid circulation, completed after the onset of the cluster-like headaches, were normal.

Discussion

The presented patient developed cluster headaches after GON blockade. The lack of rhythmicity of the headaches, the frequent side shifting of attacks and the ability to sit still during a headache are all qualities uncharacteristic of “hypothalamic influenced cluster”. The hypothalamus oversees an individual’s internal circadian clock thus a hypothalamic governed disorder will present with fixed periodicity and rhythmicity as is seen in primary cluster headache. The hypothalamus also plays a role in locomotion in animals [2]. Hypothalamic stimulation causes animals to become active and move around, suggesting it is hypothalamic activation that leads to the agitation and inability to sit still which is a hallmark of cluster headache. The fixed location of headache in cluster with little if any side-shifting during or between cluster periods reflects that only one side of the hypothalamus is activated during a cluster attack and cluster period as represented by the ipsilateral only findings on PET [1]. The presented patient did indeed have cluster headache, but with irregular features. If this was not hypothalamic-influenced cluster, what could be triggering his cluster attacks?

In this patient the cluster headaches occurred after GON blockade, thus questioning if the GON could be a potential generator of cluster attacks. Anatomical and clinical research data suggest that the GON can produce pain in the typical location of cluster and the autonomic symptoms noted in cluster headache. Sensory neurons in the trigeminocervical complex receive ipsilateral and contralateral input from the GON [3]. Electrophysiological studies suggest that there is a convergence of dural and cervical afferents in the GON and then onto the trigeminocervical complex in humans [4]. GON stimulation has been shown to cause frontal head pain in humans [5]. In addition, Piovesan et al. [5] documented a patient who after GON stimulation developed not only pain in the head area innervated by the ophthalmic division of the trigeminal nerve but also ipsilateral conjunctival injection and lacrimation. Thus it appears that short-lasting GON stimulation is able to produce a cluster-like headache. The method by which the GON was stimulated or activated in this patient after a blockade procedure can only be hypothesised. It is well recognised that some patients who undergo nerve blockade for pain control develop a worsening of their pain when the blockade wears off. This suggests that once the nerve is unblocked it becomes hyperexcited or stimulated. The block procedure itself (needle insertion) could also have activated the GON. Recently the author completed a GON block on a cluster patient who began to develop a cluster headache during an office visit. Almost immediately after needle insertion the cluster headache worsened for several minutes then it completely alleviated suggesting possible GON activation by the block procedure then suppression once the anaesthetic started to take effect.

However, one must question how, after a single GON block, an individual could develop a full-blown cluster period lasting months as happened in this patient. One may consider that in this individual the GON was the primary generator or trigger of the cluster headaches but the hypothalamus then became secondarily activated leading to a long-lasting cluster period. A connection exists between the GON and the hypothalamus via the trigemino-hypothalamic pathway (trigeminocervical-hypothalamic connection). Theoretically after the GON was stimulated in this individual the hypothalamus was then secondarily activated via this anatomic connection. In this scenario as the hypothalamus was being activated secondarily this could lead to an irregular pattern of hypothalamic firing and thus an atypical cluster presentation. The frequent side-shifting of attacks suggests that the hypothalamus was activated bilaterally (unilaterally at irregular intervals) instead of the persistent same side activation noted in typical primary cluster. The patient did undergo bilateral GON blockade.

The clinical presentation of this case patient suggests that there can be a non-hypothalamic form of cluster headache and that the GON may play a significant role in cluster pathogenesis in some patients. Secondary hypothalamic activation may have been needed to sustain the syndrome. It is possible that the patient developed spontaneous new onset cluster headache at age 53, but the close temporal profile to the GON procedure and the fact that only women appear to have a second peak of cluster onset in their fifties and sixties suggest against this scenario [6].

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