Cluster Headache Mimics

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This article discusses cluster headache and a variety of cluster mimics, with the intention of aiding the practitioner in differentiating between primary cluster headache and secondary forms of cluster. Secondary causes of cluster headache include infections, tumors, vascular abnormalities, and head trauma. In addition, other trigeminal autonomic cephalgias occasionally can be difficult to distinguish from primary cluster headache.

Introduction

Cluster headache is one of three primary headache disorders described in the International Headache Society's (IHS) [1] classification scheme. The existence of a variety of related cluster-like syndromes, the trigeminal autonomic cephalgias, and secondary forms of cluster headache combine to make the diagnosis of primary cluster headache challenging in some circumstances.

This article reviews the diagnostic features of cluster headache, the trigeminal autonomic cephalgias, and secondary forms of cluster headache with the intent of aiding the practitioner in differentiating between these disorders.

Primary Cluster Headache

Cluster headache is so named because in the most common episodic form of the disorder, headaches occur in cluster periods lasting 2 to 3 months, after which time they remit then typically recur after a variable period of time. Duration of an individual headache, as defined by IHS standards, ranges from 15 minutes to 3 hours, with an average of two attacks daily, although the range can be from one every other day to eight daily.

The head pain typically localizes to the ipsilateral orbit, forehead, temple, and even the occipitonuchal region. Pain spreads to the jaw or neck less frequently. Patients describe the pain, which comes on abruptly, as boring, burning, and tearing, with common descriptions including phrases such as "a hot poker in my eye" or "like my eye is being poked out." During an attack, patients characteristically are restless and will pace, rock, and even bang their heads against walls. Cluster headache also is termed the "suicide headache" in recognition of the desperation that patients exhibit, sometimes taking violent action to avoid another attack.

Associated headache symptoms can include ipsilateral lacrimation, rhinorrhea, nasal stuffiness, miosis, lid edema, forehead/facial sweating, ptosis, and scleral injection. Other less common symptoms may include abnormalities of cardiac rhythm such as atrial fibrillation, frequent premature ventricular contractions, first degree heart block, or sinoatrial block [2]. Some of these may reflect the increased vagal tone produced by severe pain. Attack-related changes in blood pressure and increased gastric acid secretion also have been reported. Although at least one autonomic symptom is required to make a diagnosis using the IHS classification, one report suggests that up to 3% of patients have typical headaches without accompanying autonomic symptoms [3]. In the episodic form of the disorder, attacks typically occur for 6 to 12 weeks then enter a remission period that lasts for approximately 12 months. Kudrow and Kudrow [4,5] have suggested that the onset of a cluster episode may correlate with changes in the number of hours of daylight.

Most cluster episodes have onset within the first 2 weeks surrounding the beginning and end of daylight savings time.

Attacks of cluster headache have a notable tendency to occur at night; an attack often will occur 90 minutes into sleep, corresponding with the first period rapid eye movement (REM) sleep. Cluster sufferers may try to avoid sleep, but eventually sleep deprivation develops. After a period of sleep deprivation, REM sleep begins even earlier after falling asleep; the longer the headache cycle lasts, the shorter the REM latency period becomes. At that point, even short daytime naps may precipitate a cluster attack [6].

Some patients suffer from chronic cluster headache, a form of the disorder in which no remission occurs or remissions occur, but there are fewer than 14 days between cycles. Chronic cluster is perceived to be more difficult to treat than the episodic form. In 10% of patients, cluster headache is chronic from the onset. Another 5% of patients evolve to chronic cluster headache from the more typical episodic cluster headache [6].

Some authors have commented on what they believe to be characteristic physical characteristics and facial features of the cluster patient. Characteristics described include the "leonine facies" described by Graham [7], consisting of deep nasolabial folds, peau d'orange skin, and nasal telangiectasias. Kudrow [8] reported that two thirds of patients in his study had hazel colored eyes and were of tall stature with a

rugged appearance. Patients usually are male; recent reports have emphasized a change in the male-to-female prevalence ratio from 6.2:1 in the 1960s to 2.1:1 in the 1990s [9]. However, it is unclear whether this change was caused by a true increase in the incidence of cluster headache in women or whether this reflects improved diagnosis and reporting of this syndrome in women.

The prevalence of cluster headache is difficult to determine because of its rarity. Kudrow [10] described a prevalence rate of 0.4% in men and 0.08% in women. There may be a genetic predisposition to cluster headache in some cases. The percentage of patients for whom this disorder is familial is estimated to range from 4% to 7% [11–13]. Twin studies have revealed 100% concordance in five pairs of monozygotic twins. In some families, an autosomal dominant gene may be involved in the inheritance of cluster headache [14–17].

Pathophysiology of Cluster Headache

Much still remains to be learned about the pathophysiology of cluster headaches. Initially, it was thought that cluster headache, like migraine, was a vascular disturbance. A study by Ekbom and Greitz [18] revealed ipsilateral dilation of the ophthalmic artery during a cluster attack. Magnetic resonance angiography perfusion during a spontaneous cluster attack confirmed marked dilation of the ipsilateral ophthalmic artery [19].

Subsequent studies hypothesized that the cavernous sinus was the cluster "generator" [20,21], given that this structure is the final common pathway for trigeminal, sympathetic, and parasympathetic innervation. Hardebo and Dahlof [22] theorized that cluster headache is an inflammatory process in the cavernous sinus and tributary veins. Resulting vascular engorgement would block venous outflow, leading to pain and sympathetic and parasympathetic neuronal injury.

The cavernous sinus vascular congestion/inflammation theory eventually was discarded after magnetic resonance imaging (MRI) studies did not reveal any specific abnormalities in the cavernous sinus [23]. Parasellar hyperactivity detected by single positron emission computed tomography was observed in migraine and cluster headache, indicating that this activated region is not exclusive to cluster headache [24]. Orbital phlebography findings of dilation also were detected in other conditions such as Tolosa Hunt syndrome [25], hemicrania continua [26], and SUNCT (short-lasting unilateral neuralgiform headache with conjunctival injection and tearing) syndrome [27], suggesting that vascular dilation probably is an epiphenomenon of trigeminal activation and not the cause of any one disorder.

More recent research points to the hypothalamus as the possible generator of cluster headaches. Initial interest in the hypothalamus stems from the notable circadian and circannual rhythms observed in cluster headache. The chiasmatic nucleus in the hypothalamic grey is a recognized pacemaker region in the brain. This pacemaker is involved in modulation of hypothalamic regulation of the endocrine system. Numerous studies have shown that the unique endocrine rhythms of hormone production often are altered in cluster headache. For example, testosterone levels are low during cluster cycles and interictally [28]. The secretory circadian rhythms of luteinizing hormone, cortisol, and prolactin are modified in cluster headache as is altered production of cortisol, growth hormone, luteinizing hormone, follicle-stimulating hormone, prolactin, and thyroid-stimulating hormone in response to various chemical challenges [29•].

In addition, melatonin, the hormone produced by the pineal gland in response to changing light stimulation of the retina, is chronically reduced during the cluster phase and interictally [30,31]. Ordinarily, melatonin levels increase at night and drop during the day. Melatonin is a sensitive marker of circadian function and is regulated by the suprachiasmatic nucleus.

Another factor pointing to the hypothalamus as a key area in the generation of cluster headache was the results of a recent positron emission tomography (PET) imaging study of the hypothalamus. The study was performed during an acute cluster attack induced by nitroglycerin [32]. Increased activity was noted in the ipsilateral hypothalamic gray during the attack.

This localized increased activity also is seen in other trigeminal autonomic cephalgias. It does not occur in migraine [33] or with experimentally induced first-division trigeminal pain through capsaicin injection [34].

Voxel-based morphometric analysis of MRIs of patients with cluster headache and control subjects revealed an increase in hypothalamic volume in those with cluster headache only, in the same vicinity activated during the PET study (during a cluster attack) [35].

More recently, Leone *et al.* [36] inserted stimulatory electrodes in the hypothalamic gray area of a patient with intractable chronic cluster headache. He successfully inhibited further attacks. Franzini *et al.* [37•] performed a similar procedure on six patients with chronic cluster headache with similar success. If the stimulators were turned off, the pain returned, suggesting that an overactive hypothalamus may be the source of cluster headaches.

The hypothalamus is thought to have direct communications with the C1-C2 spinal cord nociceptive neurons via the trigeminal system [38] by the nucleus caudalis and the locus coeruleus [39], which also is involved in central pain processing. A reflex is present between the trigeminal nucleus caudalis and the cranial parasympathetic superior salivatory nucleus when the trigeminal ganglion is stimulated [40,41]. Thus, it seems likely that if these two pathways are activated, pain and autonomic symptoms can result.

Biochemically, cluster headache and migraine result in increased production of calcitonin gene-related peptide (CGRP) in the cranial venous circulation [42]. However,

Table 1. Conditions that can mimic primary cluster headache

Infections
Aspergillus
Inflammatory disorders
Wegener's granulomatosis
Orbital myositis
Plasmacytoma
Multiple sclerosis
Head trauma
Vascular abnormalities
Arterial dissections
Arteriovenous malformations
Neoplasms
Pituitary tumors
Metastases
Other trigeminal autonomic cephalgias
SUNCT syndrome
Paroxysmal hemicrania
Hypnic headache

SUNCT—short-lasting unilateral neuralgiform headache with conjunctival injection and tearing.

only cluster headache is associated with the production of vasoactive intestinal polypeptide (VIP), a parasympathetic marker not typically seen in migraine [43]. In migraineurs who show evidence of autonomic symptoms, VIP usually is elevated [43].

Sumatriptan, a $5HT_{1B/1D}$ receptor agonist, inhibits the release of CGRP from the trigeminal system [44]. It also is an effective abortive headache medication in migraine and cluster headache. It would appear then that activation of the trigeminal system occurs in cluster headache, but that trigeminal activation probably is the final common pathway of migraine and cluster headaches.

Secondary Cluster Headache Etiologies

Differentiating primary cluster headache from the secondary headaches sometimes can be difficult, particularly if the headache has many features described in the IHS criteria for primary cluster headache. It is helpful to have a solid understanding of the diagnostic criteria for primary cluster headache to appreciate subtle discrepancies in the history. In addition, any focal findings on the neurologic examination, abnormal vital signs, or other abnormal physical findings should raise the level of suspicion that one may be dealing with secondary cluster headache.

In the case of a history of cluster headache, any deviation from the IHS criteria for cluster headache, such as the lack of autonomic symptoms, the non-cyclical nature of the headache, pain that is too brief or too protracted, sudden worsening of pain ("the worst headache ever"), atypical age, female gender, change in pain location, and failure to respond to medications are potential clues that the headache may not be a primary cluster and warrants further evaluation.

Some of the conditions to consider as causes of secondary cluster headache include vascular disease, infections, inflammation, neoplasia, glaucoma, dental disease, trauma, and trigeminal neuralgia. Table 1 summarizes some conditions that can mimic primary cluster headache.

Inflammation

Inflammation occasionally may produce symptoms resembling cluster headache. In 2002, Lee and Lessell [45] reported on a 24-year-old man with sudden onset of unilateral supraorbital pain. He also experienced lacrimation, nasal congestion, proptosis, and painful eye movements. His pain waxed and waned over the course of each day for approximately 1 month before a head computed tomography (CT) was performed. The CT revealed right medial rectus swelling. Between headache episodes, no proptosis or autonomic symptoms were noted. During an attack, proptosis was sometimes absent. Eventually, the headache switched sides and was accompanied by blurred vision and proptosis. An MRI and angiography revealed an enlarged left superior rectus muscle. Thyroid function tests were normal. A diagnosis of orbital myositis was made and the patient responded to a trial of steroids.

This particular case was atypical for cluster headache for the following reasons: proptosis, painful eye movements, changing sides of the headache (only 15% of patients may experience this) [6], and duration of pain, which waxed and waned throughout the day without a definite beginning and end.

This case highlights that orbital myositis (a subgroup of idiopathic orbital inflammatory syndrome) and Wegener's granulomatosis of the orbit are two conditions that may resemble cluster headache. Both disorders require urgent diagnosis and treatment to avoid permanent pathology. In this particular case, cluster headache would have been considered more properly as a diagnosis of exclusion because there were too many features that deviated from the criteria for the diagnosis of primary cluster headache and warrant further investigation.

Another inflammatory condition that frequently causes migrainous and, less commonly, cluster headache is multiple sclerosis. Leandri *et al.* [46] described a 42-year-old man who was experiencing the onset of excruciating right orbital pain radiating to the right maxilla and temporal areas. The pain began 15 days prior to medical consultation. Most of the attacks were nocturnal, occurring between 11 PM and 4 AM. The pain lasted for 2 to 3 hours and was associated with restlessness, lacrimation, rhinorrhea, and scleral injection. The physical examination revealed left optic disc pallor (the patient reported a 20-day episode of left eye blindness the year before this) and a right extensor reflex in the great toe and hyper-reflexia on the right.

Neuroimaging revealed plaques around the lateral ventricles and the right trigeminal root entry zone. Lumbar puncture showed elevated Immunoglobulin G (IgG) synthesis and the presence of oligoclonal bands. Based on

these findings, the patient was diagnosed with laboratory-supported definite multiple sclerosis. The patient had a partial response to nonsteroidal anti-inflammatory drugs and experienced complete relief of headaches with lithium carbonate. When the lithium was tapered, the cluster-like headaches recurred.

A remarkable feature of this case is the occurrence of cluster-like headache instead of trigeminal neuralgia, given the location of a plaque in the trigeminal root entry zone. Factors that signaled the possibility of a secondary form of cluster headache included the history of blindness, the abnormal findings on neurologic examination of hyper-reflexia and a Babinski sign on the right, and optic nerve pallor. The headache itself conformed closely to the criteria for primary cluster headache and lithium carbonate, a cluster medication, controlled the patient's pain effectively. This case illustrates one of the pitfalls in interpreting a positive response to traditional treatment as confirmation of diagnosis

Other types of infections occasionally may present as cluster-like headache. A report by Heidegger *et al.* [47] described an aspergillus sinus infection, which initially presented as an abrupt-onset severe 3-hour long left orbitotemporal headache. The attacks occurred during the early morning hours and had been ongoing for 2 months. Five weeks before hospitalization, the patient experienced transient diplopia lasting approximately 10 days. Associated symptoms included conjunctival injection, left eye meiosis, and slight proptosis. The physical examination revealed a questionable finding of slightly reduced sensation in the left supraorbital branch of the trigeminal nerve. The patient had a history of a plasmacytoma stage III and had already received 20 cycles of melphalan. Testing, including MRI, magnetic resonance angiography, electroencephalogram, and lumbar puncture showed no abnormalities other than an IgG κ paraprotein that was present but stable, with nearly normal immunoglobulin levels.

In view of the unremarkable testing, the patient was treated for cluster headache with oxygen, which only gave transient relief. Ergotamine was ineffective. Indomethacin and steroids also gave incomplete relief. The patient's pain intensified and his vision deteriorated in the left eye. Repeat MRI of the superior orbital fissure and cavernous sinus/orbital CT revealed a small lesion of the apex and optic nerve in the left orbit, with perforation to the left sphenoid sinus. Biopsies of the left ethmoid and sphenoid sinuses revealed aspergillus fungal organisms.

This report suggests that whenever subtle focal findings are present (*eg,* the decreased trigeminal sensitivity noted in this patient) in combination with a disturbing history of diplopia/loss of vision in an immunosuppressed patient are present, headaches probably should be regarded as secondary until proven otherwise and aggressive evaluation undertaken. Another aspect of this case, the patient's failure to respond to a variety of frequently effective cluster headache medications, also should raise suspicion as to the origin of the head pain.

Vascular abnormalities

Case reports also exist of vascular abnormalities that produce cluster-like headache. Rosebraugh *et al.* [48] described a 34-year-old man who experienced sudden onset of severe right hemicranial pain, which became retro-orbital over a 2-hour period. The headache was associated with right-sided nasal stuffiness, lacrimation, and conjunctival injection. A right Horner's sign was present. A CT radiologic evaluation revealed a right venous pool. Subsequent MRI showed a right internal carotid artery dissection and occlusion, which was confirmed by angiography.

This patient's symptoms closely resembled primary cluster headache. However, because this was the first time the patient had ever experienced such an event, it was appropriate to perform neuroimaging. This case highlights the tension between managed care cost containment measures and the small but real risk of missing a catastrophic cause of headache such as arterial dissection. From a pathologic standpoint, the carotid artery is richly innervated with trigeminal, sympathetic, and parasympathetic nerve endings that were presumably stimulated by the dissection, producing cluster-like pain.

In 2001, another case report by Leira *et al.* [49] described a 45-year-old man with a history of hypertension and occasional headaches without aura who awoke with right-sided ptosis and right-sided visual scotomata followed by a severe right fronto-orbital headache.

The patient used a 50-mg sumatriptan tablet for the first time and experienced 90% pain relief. The headache recurred later that evening; redosing with another sumatriptan tablet helped almost as much as the first time. However, MRI revealed a right midcervical carotid artery dissection that was confirmed by angiography along with a pseudoaneurysm. The patient was treated with warfarin and then was switched to aspirin without further sequellae.

The significance of this report is threefold; the patient had pre-existing headaches, but this particular headache was accompanied by the additional features of scintillating scotoma and right-sided ptosis. Visual aura in cluster headache has been reported but is very rare [50]. Visual symptoms resembling aura have been reported more frequently in arterial dissections.

A second issue is that the patient's pain was relieved with oral sumatriptan, a rescue agent effective in cluster headache and migraine. This case highlights the dangers of making a diagnosis based on a positive response to medication. It also underscores the importance of careful evaluation, sometimes including neuroimaging, whenever a patient reports a sudden severe or new headache.

In 1995, Cremer *et al.* [51] described a 67-year-old man who developed new onset cluster headache after falling out of bed and wedging his neck between the bed and a locker. Immediately after the fall, he complained of severe neck pain and vertigo on upward gaze. The headache began 2 days later, originating in the neck with radiation to the left temporal area. Associated symptoms included left-sided

lacrimation, nasal stuffiness, and a left Horner's syndrome. The pain duration ranged from 30 minutes to 12 hours, averaging approximately 30 minutes. He experienced up to five attacks daily.

A cerebral angiogram revealed a right-sided vertebral artery dissection. The first cluster-like episode lasted for 3 months. An initial period of 2 days of relief occurred with a left greater occipital nerve block. This was followed by a C2 facet block, which provided pain relief for 6 months. The patient was treated with a variety of oral medications with good success during his active cycles. Cluster medications included subcutaneous sumatriptan, methysergide, valproate, and oxygen. Only oral ergots were ineffective.

The patient responded well to subcutaneous sumatriptan despite clear evidence of a secondary headache.

Cluster headache is associated with activation of the trigeminoneuropeptide marker CGRP; sumatriptan inhibits the production of CGRP, thus blocking head pain. This report describes one of the few instances in which sumatriptan was used deliberately to treat a secondary form of cluster headache and demonstrates that response to medication should not be interpreted as diagnostic of a particular form of headache.

Other vascular malformations have been associated with secondary forms of cluster headache, including aneurysms, subclavian steal syndrome, and arteriovenous malformations, but are not reviewed in this article in detail.

Neoplasms

Neoplasia also may present as cluster headache. Benign pituitary tumors perhaps are the most commonly reported neoplastic causes of secondary cluster headache. A typical example of this was described by Porta-Etessam *et al.* [52] in 2001. They described a 30-year-old man with a 2-year history of left retro-orbital excruciating headache lasting less than 120 minutes that was associated with ipsilateral lacrimation, rhinorrhea, ptosis, miosis, and scleral injection. The headaches occurred once daily for 20 days and remitted for several months. When they returned and were refractory to unspecified medications, the patient consulted a specialist. The neurology examination was unremarkable. A head CT revealed a parasellar and suprasellar mass with invasion into the left cavernous sinus. The prolactin level was 4759 ng/mL. The patient was treated with 1 mg/week of cabergolide, which resulted in complete resolution of his head pain within 1 week.

In this instance, the patient met diagnostic criteria for primary cluster headache. The only unusual sign was his failure to respond to medication that typically is helpful for cluster headache.

A high clinical index of suspicion was needed to warrant neuroimaging. It is likely that the cavernous sinus mass was impinging on the innervation (sympathetic, parasympathetic, and trigeminal) of the final common pathway for cluster headache generation.

Occasionally, metastatic disease may present as primary cluster headache. A case report by Tajti *et al.* [53] described a 55-year-old man with a 5-week history of excruciating left retro-orbitotemporal headache that lasted for 30 to 60 minutes. At onset, the attacks occurred once daily, but increased in frequency over time [53]. Associated symptoms included ipsilateral conjunctival injection, lacrimation, and nasal congestion. Over-the-counter medications were ineffective. The neurology examination was significant only for hypesthesia in the left V1 distribution of the trigeminal nerve. CT was performed in view of the new-onset severe headache and multiple metastatic lesions were noted. CT-guided biopsy indicated a probable lung source for this malignant epithelial tumor. Within 1 week of diagnosis, the patient experienced a dense right hemiparesis and ultimately died of a pulmonary embolus (from bilateral femoropopliteal thromboses).

This patient had a focal neurologic examination in the left trigeminal distribution, which warranted further evaluation. Although this patient did not experience Horner's syndrome, oat cell carcinomas of the lung may cause this finding and such a result should prompt suspicion of a secondary cause of cluster headache.

Head trauma

Another condition that has been associated with cluster headache is head trauma. In 1992, Turkewitz *et al.* [54] performed a review of the literature and found that 16.5% of patients with cluster headache have a history of head injury, higher than that expected in a general population sample. The temporal relationship between headache onset and the original injury was variable, ranging from immediate onset to 30 years after head trauma. [54].

Turkewitz *et al.* [54] also presented a case report of a 31-year-old woman who sustained a minor head injury without loss of consciousness during a car accident. Her periorbital headache occurred 6 days later (she had never had any headaches before the accident and had no other conditions that could contribute to headache). She described the pain as a spike going through her right eye and reported head banging behavior in her attempt to obtain relief. Associated symptoms included lacrimation and injection of the eye. The pain lasted for 30 to 45 minutes and occurred every afternoon. A contrast CT of the head and orbits was normal. A Minnesota Multiphasic Personality Inventory and Beck Depression Inventory suggested only situational anxiety resulting from her symptoms. The patient was taking eight acetaminophen and oxycodone tablets daily. Sodium valproate provided only marginal relief. She also had not responded to propranolol, methysergide, naproxen sodium, and antihistamines. Inpatient hospitalization with intravenous dihydroergotamine, oral lithium carbonate, and divalproate sodium and discontinuation of the narcotics resulted in total relief of her pain. Over time, her preventative program was discontinued after 6 months, without pain recurrence.

This case describes an intriguing temporal association between the head injury and the onset of cluster-like headache. It appears possible that some cluster headaches are caused by head trauma and suggests that questions about recent head trauma may be a useful part in evaluating new-onset cluster-like headache.

Orbital exenteration also may produce cluster-like pain. As with head injury related to accidents, there may be a time lag between the exenteration and the onset of cluster headache, ranging from 3 weeks to 18 years [55]. Evers *et al.* [55] described the case of a 37-year-old man who lost his right eye during an accident at work. Because he developed secondary glaucoma and bulb shrinkage, he eventually underwent enucleation of the right eye. There was no personal or family history of headaches. Within 3 weeks of the surgery, the patient developed a severe intermittent right orbital headache accompanied by ipsilateral lacrimation and rhinorrhea. Examination of the residual ipsilateral eye muscles revealed hyperemia during the headache attack. The patient experienced one to two attacks daily, each lasting for 60 to 120 minutes. The cluster cycles would occur once or twice a year, lasting for 3 to 4 weeks at a time. The patient responded well to oxygen, sumatriptan, and verapamil alone and in combination with lithium, valproate, or prednisone.

Cluster headache after exenteration probably is rare, with only seven case reports in the literature. It is a reasonable diagnostic consideration in patients who are missing an eye and present with cluster-like headache.

Trigeminal autonomic cephalgias

Occasionally, it can be difficult to distinguish other forms of trigeminal autonomic cephalgias (TACs) from cluster headache.

The three main headaches in this category that can be confused with cluster headache are SUNCT syndrome, hemicrania continua, and paroxysmal hemicrania.

The TACs and cluster headaches involve autonomic features and pain that localizes to the orbital region in the V1 distribution of the trigeminal nerve.

Paroxysmal hemicrania differs from cluster headache in several respects. The frequency of attacks usually is greater than five daily, with a range of one to 49 daily. There is no nocturnal predilection for pain onset and the duration of headaches is brief, lasting from 10 to 30 minutes, with a range of 2 to 45 minutes. Another difference from cluster headache is that mechanical movements of the head (flexion or rotation) may trigger an attack. External pressure on the C2 root or C4-C5 transverse processes also can precipitate attacks. The latter feature may explain why paroxysmal hemicrania frequently responds completely to treatment with indomethacin [56].

SUNCT syndrome is characterized by extremely brief episodes of pain that last anywhere from 5 to 250 seconds. Patients describe the pain as electric shock-like, burning, stabbing, or pricking and of moderate to severe intensity. Attacks may occur anywhere from one to 30 times an hour. There is a male predominance, but less so than in cluster headache, with a 2:1 male to female ratio. Exact prevalence and incidence statistics do not exist in this rare condition. Headaches may be precipitated or aborted by mechanical motion of the neck. There is similarity to trigeminal neuralgia in that patients describe trigger zones within the area of trigeminal innervation (and sometimes outside of it), which when activated by various activities (*eg*, chewing, talking, washing or touching the face) will trigger a headache. However, unlike trigeminal neuralgia, there is no refractory period following a pain episode and there is only a partial response to carbemazepine [56].

Hypnic headache occasionally may be confused with cluster headache because of its exclusively nocturnal onset (around 1:00 to 3:00 AM and up to three attacks each night). Differences include a female predominance (2.3:1 female to male ratio), older age at onset (mean, 66 years), pain that is more commonly bilateral than unilateral, and lack of autonomic symptoms. Similar to cluster headache, hypnic headache responds to lithium carbonate; unlike cluster headache, hypnic headache also may respond to caffeine and indomethacin if administered at bedtime [57].

Conclusions

When assessing a patient with apparent new-onset cluster headache, it is important to be aware of specific characteristics of primary cluster headache and carefully investigate headache patterns that differ even slightly from these characteristics or in which there are even subtle historic inconsistencies or focal findings on the neurologic examination. Response to medication should never be the sole basis for a diagnosis of primary cluster headache. Similarly, even in a patient with well-established cluster headache, a change in headache pattern or the development of new headache characteristics or associated features should be evaluated thoroughly.

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