Ascending cluster headache: a description of three cases and a review of the literature

Carmen Serna-Candel, M. Luz Cuadrado-Pérez, Ángel L. Guerrero-Peral, Sara García-Ptacek, Jesús Porta-Etessam

Headache Unit; Department of Neurology; Hospital Clínico San Carlos; Universidad Complutense; Madrid (C. Serna-Candel, M.L. Cuadrado-Pérez, S. García-Ptacek, J. Porta Etessam). Headache Unit; Department of Neurology; Hospital Clínico Universitario de Valladolid; Valladolid, Spain (A.L. Guerrero-Peral).

Corresponding author:
Dra. María Luz Cuadrado Pérez. Department of Neurology. Hospital Clínico San Carlos. Profesor Martín Lagos, s/n. E-28040 Madrid.

Fax:
+34 913 303 512.

E-mail:
mlcuadrado@med.ucm.es

Accepted:
15.11.10.

How to cite this article:
Serna-Candel C, Cuadrado-Pérez ML, Guerrero-Peral AL, García-Ptacek S, Porta-Etessam J. Ascending cluster headache: a description of three cases and a review of the literature. Rev Neurol 2011; 52: 412-6.

Versión española disponible en www.neurologia.com

Introduction. It has been previously shown that cluster headache (CH) can involve some extratrigeminal areas. Occipital pain has been recognized in several patients, even as the origin of the attacks. Nevertheless, the proposals of topographic variations of CH have been mainly focused on the location of pain in either supraorbital or infraorbital regions.

Case reports. We report three patients fulfilling International Classification of Headache Disorders criteria for CH whose attacks started with mild or moderate headache at the occipital region and gradually moved forward over 10 to 30 minutes, finally reaching the ipsilateral orbital area. There the pain acquired typical CH features, with severe intensity and ipsilateral autonomic accompaniments.

Conclusions. These descriptions of ascending CH probably reflect pathophysiological mechanisms involving the trigeminocervical complex, and also offer theoretical support for some new therapeutic approaches such as great occipital nerve blockades or occipital neurostimulation.

Key words. Ascending cluster headache. Cluster headache. Occipital pain. Trigeminal autonomic cephalalgias. Trigeminal spinal nucleus caudalis. Trigeminocervical complex.

Introduction

According to the International Headache Society (IHS) diagnostic criteria, cluster headache (CH) is characterized by attacks of severe, strictly unilateral pain in orbital, supraorbital or temporal locations, or in any combination of these sites [1]. Pain may also be felt in other trigeminal, and even extratrigeminal territories, although the maximum pain usually locates in the area supplied by the first division (V1) of the trigeminal nerve [2]. Pain attacks are associated with ipsilateral autonomic features reflecting cranial parasympathetic activation and/or sympathetic hypofunction. CH is encoded as a trigeminal autonomic cephalalgia (TAC). It is believed that pain arises as a result of the activation of the trigeminal system, and that autonomic craniofacial events appear due to the recruitment of a trigeminofacial (parasympathetic) brainstem reflex. In addition, current pathophysiological hypotheses point to the hypothalamus as a trigger or modulator of both pain and autonomic phenomena. Otherwise, upper cervical inputs may be allegedly involved through the trigeminocervical complex. Whether TACs are entirely brain disorders or whether a peripheral stimulus is necessary to trigger headaches is still unclear [3]

Here we report three patients fulfilling IHS criteria for CH whose attacks started with mild or moderate headache at the occipital region and gradually moved forward over several minutes, finally reaching the ipsilateral orbital area. There the pain acquired typical CH features, with severe intensity and ipsilateral autonomic accompaniments. This clinical picture seems to represent an ascending form of cluster headache, and might be revealing certain underlying mechanisms important for pain pathogenesis or modulation in CH.

Case reports

Patient 1

A 31-year-old woman related a 7-year history of headache attacks occurring yearly as a cluster. Her mother suffered from migraine, and her personal medical history was unremarkable. Headache attacks always occurred at evening once daily from October to November. Each episode started with mild, dull pain (intensity 3/10 in a visual analogical scale, VAS) and paresthesia at the right retroauricular region. Then the pain moved forward along a linear trajectory reaching the ipsilateral eye after

10-20 minutes. When periorbitally located, the pain became throbbing and excruciating (intensity 10/10 in the VAS), and was consistently associated with ipsilateral tearing, conjunctival injection, ptosis, rhinorrhoea and restlessness. Without treatment, the total sequence lasted from 40 minutes to 3 hours. No triggers or accompanying nausea or vomiting were identified.

A complete general and neurological examination was performed, including palpation of the main superficial arteries and pericranial nerves, with no abnormalities. Brain magnetic resonance imaging (MRI) excluded any underlying lesions. She had tried oral rizatriptan and zolmitriptan as symptomatic treatments at the beginning of some attacks with partial response.

Patient 2

A 24-year-old man presented with a 4-year history of headache attacks occurring twice a year as clusters. They occurred mainly at the beginning of summer and winter. His father had been diagnosed with both migraine and medication overuse headache, and he also had history of atopic asthma, pyloric obstruction surgery during early infancy, and a knife wound in his left hemithorax. He was an occasional tobacco and marijuana user. His headache appeared once or twice a day, usually around 3:00 p.m. or 8:00 p.m. Apart from a few right-sided attacks at the onset of this clinical picture, the headache was strictly left-sided. The pain always emerged at the left occipital region, with tightening quality and mild intensity (2/10 in the VAS). Then it shifted during 20 minutes following a linear trajectory through the temporal scalp towards the ipsilateral eye. While migrating, the pain acquired throbbing quality and increased in intensity up to 9/10. It remained fixed within the orbital area between 30 and 60 minutes, accompanied by concurrent restlessness, ipsilateral conjunctival injection, tearing and, occasionally, rhinorrhoea. Photo-, phono- and osmophobia, but no nausea or vomiting, could also be present. Fasting, stress, intense lights or smells and sleeplessness were identified as common triggers.

No abnormalities were detected at general and neurological examinations, including palpation of pericranial nerves. Brain MRI was obtained with normal results. The patient had noticed partial relief of the early occipital pain with acetaminophen.

Patient 3

A 54-year-old woman had a 14-month history of headache attacks with no remissions. She also reported past hysterectomy, surgery for right shoulder tendinitis, hyperlipemia and smoking. She suffered two headache episodes per day with no definite circadian pattern. They always started as a tightening pain of mild intensity (4/10 in the VAS) in the left occipital region. The pain moved lineally for the next 30 minutes towards the ipsilateral eye, where it eventually acquired stabbing quality and severe intensity, up to 8/10 in the VAS. It remained confined to the periorbital area between 60 to 90 minutes, and was then associated with ipsilateral conjunctival injection and ptosis, as well as slight photo- and phonophobia. No triggers were identified.

Physical examination only revealed tenderness of the left great occipital nerve (GON). A brain MRI excluded any underlying lesions. Nonsteroidal anti-inflammatory drugs (NSAIDs) were used as symptomatic drugs with partial relief of the early occipital pain. Indomethacin was used to no effect. Prednisone (60 mg/day) and verapamil (240 mg/day) led to a decrease in both the frequency and the severity of attacks.

Discussion

These three patients fulfilled diagnostic criteria for CH, but shared some particular features at the beginning of the attacks. The pain first appeared on the occipital scalp, and then gradually moved forward through a linear trajectory, reaching the ipsilateral orbital area after 10 to 30 minutes. While running back to front, the pain quality changed, its intensity increased, and parasympathetic autonomic features ensued. Once orbitally located, the headache could be classified as CH according to IHS criteria (episodic CH in the first two patients, and chronic CH in the last one) [1].

Pain location in CH is typically orbital, supraorbital and/or temporal. This location could be found in the first descriptions of CH [4,5], and stays in the current definition of the IHS classification [1]. Nevertheless, other pain locations have been previously recognized in large CH series. For instance, Manzoni et al [6] found that pain started in orbital and periorbital regions only in 70% of 180 CH cases. However, even when the pain stemmed from other regions (including cervical, occipital and others, such as maxillar, mandibular or zygomatic) it would eventually spread and mainly involve the typical orbital and periorbital regions, where pain intensity would increase. Later on, Solomon et al [7] found that 10 out of 100 CH patients experienced their

initial pain in the neck, sometimes heralding the onset of the orbital attack by a few minutes. The occipital pain was of mild or moderate intensity, whereas the orbital pain acquired typical CH features. This orbital pain could occur simultaneously or after a non-detailed spread from the neck. These authors pointed out that neck movements, especially flexion, could precipitate cluster headache in up to 9% of patients, and that the posterior pain was commonly overshadowed by the severity of the typical periorbital headache. Sanin et al [8] described three patients with CH characteristics according to periodicity and pain profile, but strictly confined to the posterior head and neck, where pain intensity, unlike previous descriptions, was extremely severe. In a prospective clinical study of 230 CH patients, Bahra et al [2] described pain as predominantly retro-orbital (92%) and temporal (70%), but the pain could be experienced over a wide area including the forehead, jaw, cheek, upper and lower teeth, and less frequently, the ear, nose, neck, shoulder, vertex, occiput and parietal scalp.

In 1968, Ekbom and Kugelberg [9] proposed the differentiation of CH into an 'upper syndrome' and a 'lower syndrome', based on the location of the headache. The upper syndrome would be located supraorbitally, while the lower syndrome would involve at least one infraorbital region, such as the upper teeth or the jaw. Although this proposal has not gained wide acceptance, some authors have focused their observations according to this upper-lower distinction. In 1975 Ekbom [10] published a series of 33 CH patients, 14 with the upper form and 19 with the lower form, and observed that a spread to the occipital area or the neck could be present in both types. Cademartiri et al [11] applied Ekbom and Kugelberg's classification criteria to 608 patients with CH. Among them, 278 were classified as upper forms, and 330 as lower forms. The occipital location was equally found in both upper and lower CH sufferers, but the nuchal location was more common in lower CH sufferers. The patients with lower CH also had a higher rate of autonomic symptoms. Verslegers et al [12] reported 7 patients (9.5%) out of 73 newly diagnosed CH who spontaneously located the source of their pain at the craniocervical margin. Interestingly, two of them had a clinical pattern quite similar to our three cases. They used the term 'lower syndrome' for these CH forms with upper cervical pain, but that was not the original sense of 'lower syndrome' in Ekbom and Kugelberg's classification.

So far the attempts of a topographic classification of CH have had more academic significance than practical value. Still, the observation of some CH patients with pain ascending from the posterior scalp –like our three patients- may have renewed interest as some new facts have come to light. First, a similar, yet brief, trajectory has been recently described in a novel clinical picture -epicrania fugax-. Second, cervical inputs to the trigeminocervical complex have been lately involved in the pathophysiology of CH. And finally, some new therapeutic approaches of CH are directed to the GON.

Epicrania fugax (EF) is a new headache condition, recently described as a paroxysmal electric or stabbing pain stemming from a particular focal area of the posterior scalp, and rapidly spreading forward along a linear or zigzag trajectory to reach the ipsilateral forehead, eye or nose in 1-10 s [13,14]. Parasympathetic autonomic symptoms –lacrimation, conjunctival injection or rhinorrhoea- have been identified in 40% of patients. Both clinical pictures differ as for the duration and the quality of the pain, but our CH patients show the same pain trajectory. The pathogenesis of EF is still unknown. A peripheral origin has been proposed, but the spread of the pain could be caused by central mechanisms, due to the anatomical overlap of cervical and trigeminal afferents at the trigeminal spinal nucleus caudalis. Perhaps both EF and CH share some pathophysiological mechanisms.

A posterior origin and a pain shift in some patients with CH may be reflecting certain pathophysiological phenomena occurring in the central nervous system. Indeed, there is a convergence of duramater and skin inputs from the trigeminal (V1) distribution with cervical afferents onto the same nociceptive second-order neurons in the trigeminocervical complex at the level of C2. It is known that the stimulation of the supratentorial duramater, which is innervated by V1, may be referred not only to the trigeminal territory but also to dermatomes supplied by the upper cervical roots. Similarly, it has been shown that an anterior spread or referral of the pain can be induced by stimulation of structures that are innervated by upper cervical roots [15,16]. An ascending form of CH might well be a clinical expression of this anatomic and physiologic overlap.

Posterior and ascending CH may also offer theoretical support for the use of occipital nerve blocks in CH treatment. Up to now well-established indications for GON anaesthetic blockade are cervicogenic headache and occipital neuralgia. Yet, several studies have found effectiveness of unilateral GON blockade in CH [17]. Variable combinations of anaesthetic or steroid injections in GON have led to clinical improvement in CH patients [18-22]. The

mechanisms why GON blockades may be effective in CH are not completely understood. Busch et al found that the nociceptive blink reflex response area decreased and the latency increased after GON blockade in both healthy subjects [23] and CH patients [22]. These findings support the hypothesis of functional connectivity between trigeminal and cervical afferent pathways in humans, raising a possible explanation for the effect of GON blockades in anterior head pain syndromes, including CH [15]. Finally, in some CH patients refractory to medical treatment, occipital neurostimulation is also providing a positive outcome [24-27].

In conclusion, we have encountered three patients with an ascending form of CH, starting as mild or moderate pain at the occipital region and gradually moving towards the orbital area, where the headache finally acquired typical CH features. This clinical picture may reflect some underlying mechanisms involving the trigeminocervical complex in the pathophysiology of CH. The effectiveness of new therapeutic approaches directed at the GON may also support the involvement of upper cervical inputs in the pathogenesis or modulation of CH.

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Cefalea en racimos ascendente: presentación de tres casos y revisión de la bibliografía

Introducción. Se sabe que la cefalea en racimos (CR) puede afectar a regiones extratrigeminales. En varios pacientes se ha descrito dolor occipital, incluso en el inicio de los ataques; sin embargo, las propuestas sobre variaciones topográficas de la CR sólo se han centrado, hasta el momento, en la distinción de localizaciones supra e infraorbitarias.

Casos clínicos. Presentamos a tres pacientes que cumplían criterios diagnósticos de CR de la Clasificación Internacional de las Cefaleas, cuyos ataques se iniciaban con dolor leve o moderado en la región occipital. En los 10-30 minutos siguientes el dolor se desplazaba hacia delante de forma gradual, para instalarse finalmente en la región orbitaria. Una vez localizada en la región periocular, la cefalea adquiría características típicas de CR, con dolor intenso y síntomas autonómicos acompañantes.

Conclusiones. La CR puede adoptar un patrón de progresión ascendente desde la región occipital. Es probable que este patrón clínico sea la expresión de ciertos mecanismos fisiopatológicos que implican al complejo trigémino-cervical. Estos mismos mecanismos podrían justificar la eficacia de determinados procedimientos terapéuticos en la CR, como el bloqueo del nervio occipital mayor o la neuroestimulación occipital.

Palabras clave. Cefalea en racimos. Cefalea en racimos ascendente. Cefaleas trigémino-autonómicas. Complejo trigémino-cervical. Dolor occipital. Núcleo espinal del trigémino.