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Case Report

Cluster headache with perimenstrual trigger mimicking chronic migraine: a case report and diagnostic challenge

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Introduction
Cluster headache (CH) is a trigeminal autonomic cephalalgia known for its excruciating unilateral pain and strong male predominance. Its triggers are rarely hormonal, contrasting with migraine, which is frequently modulated by the menstrual cycle. This discrepancy creates a potential for diagnostic confusion in female patients.

Case report
A 28-year-old woman presented with a two-year history of excruciating, right-sided periorbital attacks lasting 60-90 minutes. Bouts occurred for 4-6 weeks, exclusively triggered premenstrually. She exhibited prominent psychomotor agitation and ipsilateral autonomic symptoms. Initially diagnosed as refractory menstrual migraine, she was unresponsive to standard migraine treatments. A detailed anamnesis led to a revised diagnosis of episodic CH.

Discussion
The menstrual trigger, typical of migraine, masked a classic CH presentation, leading to a diagnostic delay. The correct diagnosis was established by focusing on attack phenomenology, particularly the patient's behavior (agitation *vs.* rest) and autonomic signs. The patient achieved complete resolution of attacks with high-flow oxygen and verapamil. This case highlights how gender and trigger-related biases can impede correct diagnosis and reinforces the need to consider CH in women with cyclical headaches.

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Introduction

Cluster headache (CH) represents the most common form of trigeminal autonomic cephalalgia (TAC) and is universally recognized as one of the most severe pain conditions to affect humans (1). Its clinical presentation is pathognomonic: strictly unilateral attacks of excruciating pain, located in the orbital, supraorbital, and/or temporal regions, lasting between 15 and 180 minutes. The attacks are accompanied by ipsilateral cranial autonomic symptoms - such as conjunctival injection, lacrimation, nasal congestion, rhinorrhea, facial sweating, miosis or ptosis - and a sense of restlessness or psychomotor agitation (2).

Epidemiologically, CH exhibits a marked male predominance (2,3). Although more recent studies suggest a decrease in this disparity, the condition remains significantly less prevalent in women, a finding consistent with epidemiological data from Brazil (2–4). Physiopathologically, activation of the posterior hypothalamus is considered the central generator of attacks, explaining the remarkable circadian and circannual periodicity of the disease (2,4).

In contrast, migraine is a highly prevalent primary headache that disproportionately affects women. The influence of sex hormones is a cornerstone of its pathophysiology, with menstrual migraine being a well-established clinical entity, as recognized in international classifications and national consensus guidelines (1,5–7).

The overlap of triggers between these two primary headaches is rare. This fundamental discrepancy can create a significant diagnostic bias when a woman presents with a cyclical headache following a menstrual pattern, almost invariably leading to the suspicion of migraine. This case report describes a rare presentation of episodic CH in a young woman, whose bouts were strictly triggered in the perimenstrual period. The objective is to highlight the diagnostic pitfalls that led to initial mismanagement and to underscore the semiological red flags that enabled the correct diagnosis.

Case report

A 28-year-old female patient presented to the neurology outpatient clinic with a two-year history of what had been diagnosed as "refractory menstrual migraine". Her initial history described a strictly right-sided headache with onset two to three days before each menstruation. She had been treated with multiple non-steroidal anti-inflammatory drugs (NSAIDs) and oral triptans, with minimal and inconsistent relief.

Given the refractoriness, a more detailed anamnesis was conducted. The patient refined her description of the pain as a "stabbing" and "piercing" sensation that reached a 10/10 intensity in under 10 minutes, lasting 60 to 90 minutes. The most revealing aspect was her behavior. Instead of seeking a dark, quiet room, as is typical in migraine - a condition with known neuropsychological impacts - the patient reported an overwhelming inability to remain still, pacing incessantly (8,9). Furthermore, she confirmed prominent ipsilateral autonomic symptoms.

Her headache diary confirmed a classic episodic pattern: attacks occurred 1 to 2 times per day for a period of 4 to 6 weeks, followed by months of being asymptomatic. The onset of each bout consistently coincided with the premenstrual phase. A neurological examination and brain magnetic resonance imaging were normal.

Based on the attack phenomenology, the diagnosis was revised to episodic Cluster Headache (1). The therapeutic approach was drastically modified. For acute attacks, inhalation of 100% oxygen at 12 L/min was prescribed, resulting in complete pain abortion. For prophylaxis, Verapamil was initiated (360 mg/day). After years of incapacitating pain and ineffective treatments, the correct diagnosis and therapy brought a transformative relief, allowing the patient to resume her daily and social activities.

Discussion

This case encapsulates a diagnostic challenge founded on two pillars: the presentation of a predominantly male disease in a woman and an atypical trigger. The initial misdiagnosis of migraine, a condition where central sensitization is a key fator (8,9), can be attributed to "anchoring bias," where the menstrual trigger - a well-known factor in migraine alongside others like specific foods - steered the clinical reasoning (8,10).

Studies demonstrate that women with CH face a significantly longer diagnostic delay than men (2,3,6). In this case, the overvaluation of the hormonal trigger to the detriment of the attack's phenomenology was the main source of error. The description of psychomotor agitation and prominent autonomic symptoms are the most robust clinical differentiators (8,11).

An intriguing aspect of this report is the menstrual trigger, and this case invites a deeper reflection on hormonal influences in TACs. While hormonal modulation is central to menstrual migraine (5,12), its association with CH is rarely described. This rarity is quantitatively supported by a large study by van Vliet et al., which investigated hormonal factors in 196 women with CH. They found that only 9% of participants reported increased attack severity

during menstruation, and the mean attack frequency was not increased (3.0 attacks/day *vs*. 3.1 in the non-bleeding period) (3). This contrasts sharply with migraine patients, of whom 67% reported menstruation-related migraine, highlighting how uncommon this trigger is in CH (3,13).

The pathophysiology of CH points to the posterior hypothalamus as the key generator of attacks. The hypothalamus, in turn, is a vital center for regulating the menstrual cycle via the hypothalamic-pituitary-ovarian axis. Although the link remains speculative, it is biologically plausible that cyclical hormonal fluctuations, particularly the premenstrual drop in estrogen, could act as a modulator of hypothalamic activity in an individual predisposed to CH, lowering the threshold for initiating a cluster bout (10,11). This hypothesis - regarding the modulation of the trigeminal system or the hypothalamus by estrogen and progesterone fluctuations - adds a layer of scientific depth and delineates a new avenue for future research into the pathophysiology of CH in women, although it requires further investigation.

The clinical implications are pragmatic. A detailed clinical history remains the most powerful diagnostic tool. The dramatic and specific response of CH to therapies like high-flow oxygen and Verapamil, in contrast to its refractoriness to standard migraine treatments, reinforces the vital importance of an accurate diagnosis (8,14).

In conclusion, this case report expands the known phenotypic spectrum of cluster headache. It serves as a crucial warning against diagnostic bias, underscoring that pain semiology must always prevail over demographic characteristics or apparent triggers in the differentiation of primary headaches.

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