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Headache in a patient with Klinefelter’s syndrome and hyperostosis frontalis interna

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Abstract Hyperostosis frontalis interna (HFI) has been reported in older women, but reports in men are rare. We present a novel case of migraine headache in a gentleman with Klinefelter’s syndrome and HFI, along with a discussion of possible pathophysiologic mechanisms underlying both the headache and the HFI.

Keywords Hyperostosis frontalis interna • Klinefelter’s syndrome • Headache • Migraine • Oestrogen

Introduction

Recently, several advances have been made in describing the pathophysiology of headaches, especially migraines. Hormonal influences are believed to play a large role in migraine headaches. We describe an interesting case of migraine headaches in a 47, XYY male with Klinefelter’s syndrome and hyperostosis frontalis interna (HFI).

Case report

History

A 30-year-old obese man presented to the outpatient clinic with several weeks of early morning throbbing, right-sided headaches lasting several hours each, associated with nausea and vomiting. There was no associated aura or other neuro-
logic symptoms with these headaches. He had no prior history of headaches. He had excessive daytime somnolence and knew that he snored when asleep.

Past medical history was significant for the diagnosis of Klinefelter’s syndrome (47, XYY) and a transient ischaemic attack in 1994, when he presented with acute onset vertigo and slurred speech. He was not currently on any medication.

On examination, he was a pleasant, obese gentleman in no acute distress. Mental status was alert and oriented. Cranial nerves two through twelve were intact. Detailed testing of motor strength, sensory exam, gait and coordination was also normal, as were his reflexes. Plantar responses were flexor bilaterally.

Although the clinical suspicion was of new onset migraine headaches without aura, neuroimaging studies were pursued due to his past medical history of transient ischaemic attack, as well as due to the recent onset of headache and the early morning nature of the headaches, which were concerning for increased intracranial pressure. Magnetic resonance imaging (MRI) showed hypertrophic frontal bone (Figure 1), with mild compression of underlying parenchyma (Figure 2). In addition, he had two small areas of T2 hyperintensity in the right occipital cortex, which were non-enhancing.

The patient underwent a lumbar puncture and cerebrospinal fluid (CSF) analysis for demyelinating disease; the CSF opening pressure was normal, with a protein level of 27 and glucose of 63. No other CNS disease process was found on extensive testing. Due to his excessive daytime somnolence, polysomnographic evaluation was conducted, which showed obstructive sleep apnoea, and he was started on continuous positive airway pressure (CPAP). The final diagnosis was new onset migraine headache without aura. Given the past history of a transient ischaemic attack, abortive therapy was contraindicated. Due to the frequency of his headaches and the disability associated with it, he was treated with a prophylactic medication: amitriptyline hydrochloride, with headache resolution.

Discussion

HFI is a descriptive finding of thickening of the inner table of the frontal bone. It is seen in 5%–12% of the population, and is most commonly an incidental finding on imaging ordered for other pathology [1, 2]. Although most commonly described in obese older women, HFI has also been described in men with testicular atrophy, suggesting underlying hormonal irregularities as the aetiologic basis [3].

HFI is clinically a benign process, and most often an incidental finding on radiologic studies. However, prominent HFI may compress soft tissues with resultant dural irritation and pressure atrophy of the brain, and surgical decompression...
is required to treat such cases [4, 5]. Historically, several papers have noted the strong association between HFI and headaches; the pathophysiologic basis was felt to be dural irritation from the bony compression [6, 7]. This view has persisted through to the present, and consequently, the characteristics of these headaches have not been well described [1, 2]. In our patient, the HFI did not appear flagrant enough to induce such symptomatology. Our patient’s headache met the characteristics of migraine headache without aura (1.1), as defined by the International Classification of Headache Disorders, 2nd edition (ICHD-II) [8]. The punctuate white matter hyperintensities in the occipital cortex are not uncommon findings in patients with migraine headaches [9, 10].

The novel aspects of this case report include (1) the first report of HFI in a man, due to underlying Klinefelter’s syndrome and (2) the occurrence of migraine headaches in such a patient, which has not been previously reported. The HFI and migraine headaches probably share a common causal aetiopathology in our patient. Patients with Klinefelter’s syndrome have reduced testosterone and increased circulating oestradiol, hormonal states that can predispose to the development of HFI. Migraine is suspected to be intimately connected with increased circulating levels of oestradiol, as reflected by 3-fold higher rates of migraine in postpubertal women compared to men, increasing migraine frequency as oestradiol increases in the first trimester in pregnant women and reduced frequency in their 3rd trimester when oestradiol levels fall, and reduced migraine frequency in post-menopausal women [11]. Oestrogen enhances neuronal excitability by elevating Ca²⁺ and decreasing Mg²⁺ concentrations, and it increases synthesis and release of nitric oxide and calcitonin gene-related peptide, leading to vasodilatation and thus potentially activating trigeminal sensory afferents [12].

In our patient, we believe the migraine headache was primary. We do not believe it was related to the HFI, as the process leading to the development of HFI takes years, and his headaches were abrupt in onset; also, his headache was resolved by medications and measures that do not impact HFI. For similar reasons, his Klinefelter’s syndrome cannot be the primary cause of his migraine headaches, other than providing the hormonal milieu to sustain it.

In conclusion, our case report of migraine headaches in a 47, XYY male with Klinefelter’s syndrome and HFI, supports the importance of hormonal influences in migraine headaches, while alerting physicians to consider unusual causes of hormonal dysregulation, such as Klinefelter’s syndrome, in their male patients presenting with new-onset headaches.

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References

1. She R, Szakacs J (2004) Hyperostosis frontalis interna: case report and review of literature. Ann Clin Lab Sci 34:206–208
2. Waclawik AJ. Hyperostosis Frontalis Interna (2006) Arch Neurol 63:291
3. Hershkovitz I, Greenwald C, Rothschild BM et al (1999) Hyperostosis frontalis interna: an anthropological perspective. Am J Phys Anthropol 109:303–325
4. Hasegawa T, Ito H, Yamamoto S et al (1983) Unilateral hyperostosis frontalis interna: case report. J Neurosurg 59:710–713
5. Chaljub G, Johnson RF II, Johnson RF Jr, Sitton CW (1999) Unusually exuberant hyperostosis frontalis interna: MRI. Neuroradiol 41:44–45
6. Edwards C (1950) Hyperostosis frontalis interna and calvariae diffusa with surgical relief of sever headache (also bilateral scalenus anticus syndromes). Proc R Soc Med 43:251–252
7. Bavazzano A, Del Bianco PL, Del Bene E, Leoni V (1970) A statistical evaluation of the relationships between headache and internal frontal hyperostosis. Res Clin Stud Headache 3:191–197
8. Headache Classification Subcommittee of the International Headache Society. (2004) The International Classification of Headache Disorders: 2nd edition. Cephalalgia 24[Suppl 1]:9–160
9. Pavese N, Canapicchi R, Nuti A et al (1994) White matter MRI hyperintensities in a hundred and 29 consecutive migraine patients. Cephalalgia 14:342–345
10. Swartz RH, Kem RZ (2004) Migraine is associated with MRI white matter abnormalities: a meta-analysis. Arch Neurol 61:1366–1368
11. Ahkenazi A, Silberstein SD (2006) Hormone-related headache: pathophysiology and treatment. CNS Drugs 20:125–141
12. Gupta S, Mehrrota S, Villalon CM et al (2007) Potential role of female sex hormones in the pathophysiology of migraine. Pharmacol Ther 113:321–340