Hyperostosis Frontalis Interna: Case Report and Review of Literature

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Abstract. Hyperostosis frontalis interna (HFI) has been reported in high frequency among post-menopausal elderly women. Although it was widely discussed in the past, this entity is rarely mentioned in the current pathology literature. We report a postmortem case of a 56 yr-old post-menopausal woman with irregular thickening of the internal surface of the frontal bone. Histology revealed an organized trabecular pattern with overall thickening of the cancellous bone. The periosteum and cortical bone were unaffected. The finding was considered to be unrelated to her death. HFI should be recognized as a benign entity and distinguished from other disorders that involve the frontal skull bone, such as Paget’s disease, acromegaly, and malignancy. The etiology of HFI is unknown, but current hypotheses implicate hormonal stimulation.

Keywords: hyperostosis, skull, Paget’s disease, acromegaly, rickets

Introduction

Hyperostosis frontalis interna (HFI), first described in 1765 by Santorini and Morgagni, has been defined as “a disorder of the endocranial plate which remodels into a more cancellous phenotype” [1]. It was initially found in association with virilism and obesity, but is now considered an independent entity.

HFI is characterized by sparing of the midline; bone deposition is usually limited to the inner table of the frontal bone. Histologically, there is a widened zone of lamellar bone and there may be remodeling of the endocranial plate [1]. HFI does not cause significant clinical disease and is usually an incidental finding, although the growth can be exuberant and cause compression of brain tissue [2].

Case Report

The decedent was a 56 yr-old woman with a medical history significant for type II diabetes mellitus, morbid obesity, coronary artery disease, and hypertension. She had no history of neurological disorders or headache. At 2 mo prior to hospital admission, the patient developed exertional chest pain; after cardiac catheterization, she underwent the placement of 2 stents in the left anterior descending artery. One mo later, the patient had a ground-level fall that injured her right knee. She was managed with physical therapy, but knee pain became more severe during the following mo. On further evaluation, a tibial plateau fracture was found in the vicinity of a right knee arthroplasty that was done 12 yr previously. The patient was admitted to the hospital for revision of the arthroplasty. On the 2nd post-operative day, the patient developed hyperkalemia, decreased urine output, and decreased hematocrit. Despite blood transfusions and iv fluids, the patient died on the 3rd day after surgery.

Postmortem examination revealed an obese female with Pickwickian syndrome, systemic atherosclerosis, and diabetic nephropathy. Death was caused by myocardial infarction attributed to stenosis of the left anterior descending artery. The ovaries and uterus showed the decedent to be post-menopausal; renal sections showed diabetic changes.

On gross inspection, the skull was of average thickness, except for the frontoparietal bone, which
displayed areas of irregular thickening. The thickening was bilaterally symmetrical and consisted of multiple smooth bony ridges and nodules protruding from the internal skull surface (Fig. 1). The midline was spared and the external surface of the skull was unaffected. The dura was normal. The brain was of average weight and showed no evidence of compression by the bony ostosis.

The skull tissue was decalcified and embedded in paraffin. Decalcified sections of the frontal bone showed marked trabecular thickening of cancellous bone (Fig. 2). Examination under polarized light showed the bony lamellae to be well organized in a concentric pattern about Haversian canals; the interstitial lamellae coursed in a linear pattern (Fig. 3). The periosteum was unremarkable.

**Discussion**

HFI has been reported in 5-12% of the general population [3], but is far more common in women than men [4]. There is an association between HFI and elderly post-menopausal women; the incidence in this population has been reported to be 40 to >60% [3]. HFI has been associated with many conditions, including frontal headaches, psychoneurosis, obesity, pregnancy, acromegaly, virilism, hypertrichosis, and diabetes [5-8]. HFI has been included in Morgagni’s syndrome (HFI, obesity, virilism), Stewart-Morel syndrome (HFI, obesity, mental disturbances), and Troell-Junet syndrome (HFI, acromegaly, toxic goiter, and diabetes mellitus) [5,6,9]. These associations were mostly based on case reports. Several studies found no significant differences in the association of these factors with HFI vs control groups [4,5,10]. HFI is now viewed as an independent entity, rather than part of a syndrome, since the only clear association is with elderly post-menopausal women. By itself, HFI does not generally cause significant clinical disease [3].

The etiology of HFI is uncertain. Archeological investigations of skulls of historic populations rarely reveal HFI, compared to modern populations. Hershkovitz et al [1] examined approximately 2000

**Fig. 1.** Internal surface of the decedent’s frontal bone. Note bilateral nodular thickening of bone with sparing of the midline.

**Fig. 2.** Frontal bone, cross section. Thickening is due to increase in cancellous bone deposition (20x, H&E stain).

**Fig. 3.** Frontal bone, cross section, polarized light. Lamellae are in concentric and linear patterns (100x, H&E stain).
skulls from various geographic locations and ethnic groups, extending from the 4th millennium B.C. to the 7th century A.D., as well as a large group of European skulls prior to the 19th century. None of these skulls displayed HFI. On the other hand, 24% of female skulls and 5% of male skulls showed HFI in a group of 1706 skulls from the 20th century.

Several hypotheses have been proposed to explain HFI. One hypothesis involves leptin, a peptide that signals the feeling of satiety to the hypothalamus and helps to control the metabolic rate [11]. Serum leptin levels are correlated with body mass index, and leptin is believed to increase sympathetic tone and energy expenditure when body fat is increased. Leptin has effects on various hormone levels, but its relationship to bone metabolism is debated. Ruhli [11] hypothesized that during human evolution, a wider availability of food favored an increased metabolic rate and increased leptin levels, which may have caused a higher incidence of HFI. Another explanation is that, since HFI occurs more frequently in elderly persons, greater longevity has allowed HFI to become more prevalent. Another hypothesis is that prolonged estrogen stimulation is related to HFI. While HFI is found predominantly in women, men with hormonal irregularities, such as those with atrophic testes, have been noted to have HFI of variable severity [1]. The etiology of HFI remains unknown, but it is generally considered that an endocrine imbalance may be responsible.

Based on conventional radiographs, Moore [6] classified HFI under the broad category of metabolic craniopathy, which also included nebula frontalis, hyperostosis calvaria diffusa, and hyperostosis frontoparietalis, named according to the location of the lesion. Hershkovitz et al [1] classified HFI into types A-D, based on involvement of other bones and the extent, appearance, border type, shape, and location of the lesions. The HFI lesions ranged from isolated, elevated bony islands to continuous hyperostosis involving more than half of the internal surface of the frontal bone.

The obesity, diabetes, post-menopausal state, and female gender of the present patient are consistent with the reported risk factors of HFI. Gross examination showed the characteristic bony nodular overgrowth of HFI that is not typically seen in other disease entities. Limitation of the lesion to the inner table of the skull and lack of pathology on the external contour of the skull were uncharacteristic of rickets, acromegaly, Paget’s disease, or leontiasis ossea. Paget’s disease was also excluded based on the organized thickening of bone in a lamellar pattern, rather than chaotic bone formation and prominent cement lines. Calvarial masses such as endosteal osteoma or osteosarcoma were excluded as they are unlikely to be extensively multifocal [1,3].

In summary, HFI is a common phenomenon among elderly post-menopausal women. HFI is a unique and benign clinical entity unrelated to other diseases of bone. The cause of HFI is unclear, but may involve hormonal influences on bone growth in the skull.

References