A teachable moment: Identifying hyperostosis frontalis interna in a gross anatomy cadaver laboratory

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Hyperostosis frontalis interna (HFI) is a condition in which newly formed cancellous bone is deposited on the inner lamina of the cranium forming irregular thickening of the cranial bone. HFI is often found through scans ordered for other possible diseases [4]. Sometimes, however, the hypertrophy of the frontal bone can be extensive and may result in compression of brain tissue [5].

INTRODUCTION

Hyperostosis frontalis interna (HFI) is a condition with limited bone remodeling of the neurocranium. In HFI, newly formed cancellous bone is deposited on the inner lamina of the cranium forming irregular thickening on the internal surface of the frontal bone. Such thickening has been long documented in the literature, beginning in the early 1700’s with books written by Giovanni Batistta Morgagni, the father of anatomical pathology. This disease was further documented and detailed in the early 20th century [1-3]. HFI is usually not the primary cause of death for an individual and is often found through scans ordered for other possible diseases [4]. Sometimes, however, the hypertrophy of the frontal bone can be extensive and may result in compression of brain tissue [5].

Despite the wide-ranging literature on HFI, the etiology of this disease remains largely unknown [6]. Some authors have suggested insanity or dementia may cause this physical change in the cranium [1,5] while others have suggested hormonal causes [7-10] or metabolic disorders [4,11]. The literature is clear that there is marked female predominance in the epidemiology of this disorder, especially in post-menopausal elderly women [12-15]. However, HFI has also been reported in males with severe hypogonadism and testicular atrophy [9]. HFI is distinguished from other conditions, including acromegaly, Paget’s disease and bone cancer of the skull [4,10].

Gannon University teaches cadaver-based human gross anatomy to undergraduate college students in biology, chemistry, pre-physical therapy, and physician assistant majors [16]. These high volume high intensity courses involve both prosected cadavers and cadavers dissected by enrolled students [17]. One of the challenges of teaching cadaver-based anatomy is the extensive memorization students must achieve in order to be successful. Using pathological discovering during dissection of the cadavers to supplement and enhance lecture material is one method used by course instructors to engage students in anatomical and clinical discussions. These discussions enhance what is often a learning experience dominated by extensive memorization.

CASE REPORT

An 80 year-old woman who was diagnosed with Alzheimer’s disease/vascular dementia at the time of death was found to have HFI with dural fusion to the calvarium during dissection in the Gannon University human gross anatomy laboratory (Figure 1). The examination of the internal side of the skull cap revealed that the inner table (lamina) of the calvarium was covered with large, irregular nodular bony thickening that was predominantly localized to the region of the frontal bones (Figure 1). Consequently, the frontal lobes were found to be compressed and subdural space was decreased by the nodular thickness of the frontal bones. The bony thickening was not present on any part of the parietal or occipital bones. The thickness of the frontal bones was more marked and exceedingly dense than that of parietal or occipital bones, being apparently due to overgrowth of cancellous bony tissue (Figure 1). The diploe of the frontal bones was slightly reduced in amount. The dura mater was thickened and was adhered to the inner table of the skull and fused with, in particular, the frontal bone (Figure 2). The anterior end of falx cerebri contained a large bony plate, nearly a quarter of an inch thick and two inches long. The brain weight was less than the age-matching typical normal brain from another decedents without HFI (Table 1). The coronal sections of the brain described in this study revealed that both cerebral hemispheres were filled with a relatively larger amount of white matter composed of shallow sulci and atrophied gyri (Figure 3). In addition, the decedent’s brain showed atrophy of the frontal gyr, and the cerebral ventricles were found to be reduced in size (Figure 4).

DISCUSSION

HFI was first described by Morgagni more than 300 years ago in the early 1700’s, and since then HFI has been associated with frontal headaches, psychoneurosis, obesity, pregnancy, acromegaly, virilism, hypertrichosis, diabetes, and other hormonal and metabolic disorders [19-22]. Based on these case reports and studies, HFI has been included in Morgagni’s

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syndrome (HFI, obesity, virilism), Stewart-Morel syndrome (HFI, obesity, mental disturbances), and Troell-Junet syndrome (HFI, acromegaly, toxic goiter, and diabetes mellitus) [19,22]. However, at present, HFI is viewed as an independent condition representing a phenomenon itself rather than related to any specific syndrome as suggested in the past [12]. HFI has been reported in 5-12% of the general population, but the magnitude of manifestation and frequency of HFI are much higher in the female population [12,23]. It is now accepted that HFI by itself does not cause a significant clinical disease and is usually an incidental finding, however, the bone growth can be exuberant and cause compression of the underlying brain tissue [5]. Past archeological investigations have shown that HFI was rarely present in historic populations regardless of geographical origin; however, on the other hand, the skulls from modern times have been found to develop HFI, predominantly in the post-menopausal female population [12]. Currently, the etiology of HFI remains uncertain, and therefore, several hypotheses have been proposed to explain HFI. One hypothesis proposes that during human evolution, a wider availability of food favored an increased metabolic rate which may have caused a higher incidence of HFI via increased levels of leptin, a satiety peptide that increases sympathetic tone and energy expenditure [24]. Another explanation for detecting HFI more...
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frequently in elderly population is that greater longevity has allowed HFI to become more prevalent and detectable in the aging population [15]. Another hypothesis is that prolonged high levels of estrogen during the reproductive period of life may be the primary triggering factor contributing to the greater frequencies of HFI seen in post-menopausal females [25], and therefore, the incidence in the female population has been reported to be much higher than in male population [12]. While HFI is found predominantly in females, it is not a purely female phenomenon. Males with hormonal irregularities, such as atrophic testis and/or feminism were found to have HFI of variable severity [9,12]. On the other hand, it has been shown that HFI is related to elevated androgen levels in pre-menopausal women [26]. At present, the most acceptable hypothesis regarding HFI pathogenesis is hormonal imbalance of the gonads.

HFI is usually not the primary cause of death for an individual and is often found through scans ordered for other possible diseases, and therefore, upon recognition of prominent HFI in imaging, it is important to distinguish it from other pathologic processes, such as leptomeningeal metastasis, hemorrhage, or infection [5]. While HFI is a benign process, prominent HFI may cause compression of the underlying soft tissues, inflammation and irritation of the meninges and pressure atrophy of the brain, for which surgical decompression is the treatment [27]. Cases of HFI, with or without neuropsychiatric disorders, have been reported by several authors [1,4,5,9,11]. These studies report that the obesity, diabetes, dyslipidemia and other metabolic disturbances, hormonal imbalance, post-menopausal state, and female gender are considered to be the risk factors of HFI. The only known risk

### TABLE 2

Review of literature for the brain weight observed in the cases of HFI with neurological symptoms.

| Gender | Age (Years) | Pathology | Post-mortem brain weight (g) |
|--------|-------------|-----------|-----------------------------|
| Female | 48          | Melancholia, Loss of Memory | 1150                        |
| Female | 47          | Dementia, Disorientation in time and place | 1247                        |
| Female | 62          | Recurrent melancholia, dementia | 1169                        |
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