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A case of *hyperostosis frontalis interna* from Deir el-Bahari, Egypt

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Abstract: Hypertosis frontalis interna *(HFI) is a condition of unknown etiology characterized by excess bone growth that is manifested on the inner table of the frontal bone. We present here a case of HFI in a female cranial vault found in the Temple of Hatshepsut at Deir el-Bahari, Egypt. This cranium was discovered in a secondary context and cannot be securely dated. HFI is rarely discovered in archaeological contexts, and this is one of the very few cases identified so far in Egypt and Nubia.*

Key words: cranium; bone growth; frontal bone; differential diagnosis

Introduction

Hyperostosis frontalis interna (HFI) is a condition that usually occurrs bilaterally on the endocranial surface of the frontal bone, presenting as an irregular thickening of the bone tissue. It is asymptomatic and is usually discovered accidentally during radiological examination (Waldron 2009). This pathological lesion can manifest as irregularly occurring, isolated nodules, or as more regular and continuous overgrowth of bone (Rühli & Henneberg 2002). Some authors believe that the condition may also affect the parietal, occipital (Mulhern et al. 2006), sphenoid, and temporal bones (Hershkovitz et al. 1999). There is a lack of agreement on the appearance and nature of HFI leading to the term being used to describe multiple similar conditions. Sometimes HFI is included among other hypertrophic changes in the skull (such as HCD – *hyperostosis cranii diffusa* and HCI – *hyperostosis calvariae interna*). However, since overgrowth of bone tissue in the skull can have different etiologies depending on location, only cases limited to the frontal bone (with possible extension to the neighbouring bones) should be classified as HFI (Hershkovitz et al. 1999).

HFI was first described by Morgagni (1719) after the autopsy of an elderly woman who additionally suffered from obesity and hirsutism (excessive hair growth). Based on individual cases, HFI has been associated with various syndromes (e.g., Morgagni's Syndrome, Morgagni-Morel Syndrome, and Troell-Junet Syndrome), which

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are, among other symptoms, characterized by overgrowth of the frontal bone (Hershkovitz et al. 1999; Raikos et al. 2011). Although the condition is more common in older women and can be linked to almost every ailment affecting this population subset (Hershkovitz et al. 1999), it does not necessarily indicate a real correlation between HFI and other ailments. As a result, HFI is considered as a separate condition and not as a symptom of any one syndrome (She & Szakacs 2004; Win & Aparici 2012).

Henschen (1949) found that only about 1% of individuals affected by HFI were males, suggesting that HFI can be used for sex assessment. The lower frequency of males affected by HFI can also be a result of underestimation as the early stage of the condition is more common among males but is also difficult to detect using X–ray examination (Hershkovitz et al. 1999). HFI was also associated with obesity and diabetes. The link between diabetes and new bone formation is still unclear but Joslin et al. (2005) state that 25% of studied patients with diabetes had some kind of hyperostosis (including HFI). Studies by Verdy et al. (1978) confirmed that sugar levels are higher in patients with HFI and that the condition occurs more frequently in obese individuals.

There is a disagreement among researchers concerning the histological background of the condition. There are three models of how HFI develops, termed the American, European, and global models (Hershkovitz et al. 1999). The first explains HFI as a process of proliferating trabecular bone and increasing diploic volume by expansion of the inner surface of bone. The second model describes the condition as a process taking place only in the dura and being activated by amplification of the intradural vasculature. The third model implies that the formation of HFI is a four-stage process beginning with disorganized diploization of the inner surface of the frontal bone followed by new lamellae being superimposed on the inner table by the dura, then blood vessels permeating the lamellar bone from the dura causing bone expansion (Hershkovitz et al. 1999).

Researchers remain unsure as to the cause of HFI and many hypotheses regarding the etiology of the condition have been proposed. Among the possible factors causing this lesion, include:

- **Genetic background**. Close relatives having HFI are known and may suggest that HFI is at least to some extent hereditary (Knies & Le Fever 1941, McKusick 1978, Rosatti 1972, Watrous et al. 1993).
- **Disorders of the skeletal system**. Individuals diagnosed with HFI have increased levels of alkaline phosphatase in their blood plasma indicating bone disease (Gegick et al. 1973).
- **Hormonal disorders**. Hormonal disorders caused by changes in the body that occur during menopause (Hershkovitz et al. 1999) as well as birth defects such as hypogonadism and testicular atrophy (Murczyński 1952) can be hypothetical

causes of HFI. According to some researchers, changes in frequencies of alleles regulating sex hormone levels that occur over time within a population might have an impact on the formation of the condition (Rühli et al. 2004). May et al. (2010a) also noted that the level of androgen, naturally higher in males, hampers the formation of HFI, while lower androgen levels in women foster the formation of the condition.

- **Metabolic disorders**. A correlation between the occurrence of HFI and metabolic conditions, such as disorders in the function of the diencephalon (which regulates the body's metabolism) (Gładykowska-Rzeczycka 1990) or disturbances in glucose regulation commonly known as diabetes (Armelagos & Chrisman 1988) have been observed. It is hypothesized that insulin can cause bone overgrowth as patients with HFI have high insulin levels (Littlejohn 1985) and diabetes is a common co-morbidity with frontal bone hyperostosis (Flohr & Witzel 2011). May et al. (2011) observed that during the last century there has been a significant increase in HFI occurrence and severity in industrial populations. New dietary habits, hormonal treatments, and changes in fertility patterns are likely to blame for this increase in occurrence.

To date, several methods for diagnosing and determining the degree of changes associated with HFI have been developed based on morphological (Hershkovitz et al. 1999; Perou 1964) or radiological characteristics (Littlejohn et al. 1986; May et al. 2010b). Perou (1964) proposed a four-stage scale of characteristic changes for all hypertrophic cranial disorders including HFI. Another four-stage scale was developed by Littlejohn et al. (1986) based on radiological features. Another system allowing for the classification of morphological changes associated with HFI was developed by Hershkovitz et al. (1999). Special attention was given to the following morphological criteria: extent of involvement; appearance; border type; shape; location on the frontal bone; and appearance of changes on other bones (Hershkovitz et al. 1999). May et al. (2010b) modified this scale, adapting it to study the images obtained from CT scans. However, Flohr and Witzel (2011) noted that these classification systems are difficult to adopt in cases of incomplete skulls.

The occurrence of HFI in archaeological remains is comparatively low in contrast to modern populations with a ratio of up to 70% of women after 40 years of age affected in modern times and 1-4% in archaeological crania (Barber et al. 1997). This can be, at least partially, explained by underestimation related to diagnostic issues and because the endocranium is not often inspected in complete crania. In cases of skeletons with complete crania no CT or RTG are used in standard examination and therefore HFI is mostly observed in fragmented remains.

There are only 12 published cases of HFI from Egypt and Nubia including the remains of both females and males of different ages and social statuses (Armelagos &

Chrisman 1988; Baker 2013; Mant 2014; Nielsen 1970; Rösing 1990; Dequeker et al. 1997; Jakob 2007; Shahin et al. 2014; Watrous et al. 1993). The aim of this paper is to present a new case of HFI from Hatshepsut's temple at Deir el-Bahari (erected in the 15th century BCE) and to compare it with other instances of the condition in the region.

Description of the case from Deir el-Bahari

The skull from the temple of Hatshepsut at Deir el-Bahari was found in 2006 and may have derived from burials dating to the XXVI dynasty, ca. 664-525 BCE (Dr. Zbigniew E. Szafrański, personal communication; cf. Hornung et al. 2006). Due to a lack of archaeological context, it is not possible to date the remains nor is it possible to determine the social status of the individual. The skull was preserved only in one large fragment (frontal and parietal bones, squama, and a fragment of the basilar part of the occipital bone, see **Figure 1**). Along with HFI, *cribra orbitalia* were also observed (**Figure 2**). The skull was examined following standard protocols (Buikstra & Ubelaker 1994). It was also examined macroscopically to determine the stage of HFI alteration using the scale by Hershkovitz et al. (1999).

Figure 1. The preserved part of the cranium, right medial view (photo by Vitali Kazlouski).

Figure 2. Endocranial surface of the frontal bone with visible HFI (photo by Vitali Kazlouski).

Sex was assessed as female basing on preserved morphological features (supraorbital ridges, supra-orbital margins, external occipital protuberance, inclination of the frontal squama, and nuchal crest). Age-at-death was difficult to estimate, but the sutures were partially obliterated and therefore the individual was determined to be adult.

The cranium bears signs of severe endocranial bony buildup. Overgrowth of the bone on the skull from Deir el-Bahari is severe and affects almost the entire inner surface of the frontal bone (>75%). The character of the overgrowth is irregular, largely elevated, and the borders of the alteration are sharp and clearly demarcated, which corresponds to the very advanced type of HFI in all grading systems, e.g. type D according to the method developed by Hershkovitz et al. (1999).

Discussion and conclusion

There continues to be uncertainty among researchers regarding what conclusions can be drawn concerning the occurrence of HFI in archaeological contexts. While some authors suggest that the condition can be helpful in determining age-at-death, sex, and social status (Belcastro et al. 2006; Henschen 1949), the etiology of HFI is not clear and therefore any conclusions would be premature.

HFI may be confused with other hypertrophic diseases. Among them, Paget's disease, in contrast to HFI, affects the ectocranium and is characterized by a partial

or complete loss of the diploe (Hershkovitz et al. 1999). The changes associated with acromegaly also appear on both the endo- and ectocranium, and include enlargement of the frontal sinuses and mandible (Hershkovitz et al. 1999), whereas *leontiasis ossea* affects the facial bones (Perou 1964). Osteomas usually occur unilaterally and have clearly defined borders (Antón 1997). Pregnancy osteophytes (PO) appear predominantly on the endocranial aspects of the frontal and parietal bones, but they can also occur on the facial portions of the cranium (Perou 1964). These disorders, while also manifesting as hyperplasia in the skull, have a number of characteristics that do not appear in HFI.

Possible differential diagnoses for the female from Deir el-Bahari include Paget's disease and acromegaly, but in both cases the endo- and ectocranium are affected by hypertrophic changes (Perou 1964), thus based on the macroscopic appearance of the cranium both diseases were excluded. *Leontiatis ossea* affects the facial skeleton (Perou 1964); however, due to a lack of preservation we could not exclude this disease. In the case from Deir el-Bahari osteomas were excluded since they are usually unilateral, are single, and circumscribed (Antón 1997). Also PO were excluded as they are generally small and are located on both the frontal and parietal bones and are occasionally found on the ectocranial surface of the vault and facial portions of the cranium (Perou 1964).

Table 1. Archaeological cases of HFI in Egypt and Nubia.

Site	Date	Sex	Age	Reference
Abydos, Egypt	ca. 3000 BCE	?	?	Baker 2013
Tarkhan, Egypt	ca. 2890-2630 BCE	male	25 yrs	Shahin et al. 2013
Giza, Egypt	ca. 2630-2350 BCE	male	35 yrs	Watrous et al. 1993
Giza, Egypt	ca. 2630-2350 BCE	male	45 yrs	Watrous et al. 1993
Giza, Egypt	ca. 2630-2350 BCE	female	30 yrs	Watrous et al. 1993
Mendes, Egypt	ca. 2592-2152 BCE	female	adult	Mant 2014
Qubbet el Hawa, Egypt	Old Kingdom (?)	male	40-54 yrs	Rösing 1990
4-K-203, Nubia	ca. 2500-2000 BCE	?	adult	Jakob 2007
Lisht, Egypt	ca. 1990–1786 BCE	female	50 yrs	Dequeker et al. 1997
Deir el-Bahari, Egypt	ca. 664-525 BCE (?)	female	adult	this study
Naga el-Deir, Egypt	ca. 220-180 BCE	female	elderly	Watrous et al. 1993
6B16, Nubia	ca. 0-300 CE	female	40 yrs	Armelagos & Chrisman 1988
280 (Serra), Nubia	ca. 0-350 CE	female	middle aged	Nielsen 1970[1]

[1] Nielsen (1970) wrote that this skeleton (site 280, grave 241) belonged to a middle aged woman, but Säve-Söderbergh (1981) noted that the skeleton found in the grave 241, cemetery 280 was headless and of unknown sex. Here also the date of the grave is more accurate: 200-350 CE.

Of the published HFI cases from Egypt and Nubia (**Table 1**), including the one presented here, there are 7 affected females, 4 males, one adult of unknown sex, and one of unknown age-at-death and sex. There is only one HFI case in a female under the age of 40 and 6 cases of females over 40 years; affected males were between 25

and 54 years of age. The small sample size and issues with adult age-at-death estimation should be kept in mind, however, when interpreting these data. A majority of HFI cases (7/13) in the literature date to the 3rd millennium BCE and there are no visible regional or social status patterns (there are both simple burials as in those from Tarkhan and Abydos and rich burials as in those from Qubbet el Hawa).

Although some researchers (Devriendt 2005; Henschen 1949) believe that the occurrence of HFI is strictly correlated with the female sex and older age, there are cases that contradict this relation. Ortner (2003) therefore recommends caution in diagnosing sex and age on the basis of the presence of HFI alone, and suggests using information about the presence of the condition only as an aid and not as a determinant. Also, the still undetermined etiology of the condition does not allow us to clearly connect HFI with high social status. For this reason, caution must be used to not assign other co-morbid states (e.g., obesity, diabetes or other hormonal or metabolic disorders) that can coexist with this lesion to individuals with HFI.

The majority of known cases of HFI from Egypt and Nubia occur in women (7/13), 4 of 7 were over 40 years old (and two more were described as adults), which may support the hypothesis that HFI affects mostly women after menopause. More than a half of all cases are dated to the 3rd millennium BCE, but this may be a consequence of more interest by archaeologists in cemeteries from this period. Considering the aforementioned cases, it is not possible to determine the specific regional pattern of HFI occurrence in Egypt and Nubia. It is also unlikely that HFI should be considered as an indicator of sex, age-at-death, or social status in Egyptian and Nubian populations. Given this limited evidence, the new case from Deir el-Bahari (despite the discovery itself) cannot bring us closer to the lifestyle, social status, and other potential diseases that this female may have presented.

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