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Hyperostosis Frontalis Interna

ABSTRACT

Hyperostosis frontalis interna is the thickening of the inner layer of the frontal bone due to the formation of cancellous bone. In hyperostosis frontalis interna, nodular protrusions occur due to the formation of cancellous bone in the inner table of frontal bone. These nodular protrusions may be unilateral or on both sides of the midline but spare midline. Hyperostosis frontalis interna is associated with aging, obesity, menopause, or other endocrinopathies such as diabetes mellitus. The prevalence is shown to be 5%-12% in autopsy series or imaging-based studies. It may be classified according to the extensiveness and appearance of the lesion. The clinical significance is not clear, and hyperostosis frontalis interna is generally an incidental finding detected by imaging methods. But, sometimes headache, dural irritation, or brain atrophy may occur. Neurological or mental signs may be associated with hyperostosis frontalis interna. Underlying endocrinopathies (acromegaly, primary hyperparathyroidism, osteopetrosis, fibrous dysplasia, or Paget's disease) or malignancies should be excluded. Treatment is supportive and needs to be planned against the underlying disease.

Keywords: Bone, frontal, hyperostosis, hyperostosis frontalis, Morgagni

Introduction

Hyperostosis frontalis interna (HFI) is the thickening of the inner layer of the frontal bone due to the formation of cancellous bone. It was first defined by Morgagni in 1719 as a part of a more general syndrome characterized by virilism and obesity.[1]

The frontal bone consists of 3 layers: the inner table, the diploe layer in the middle, and the outer table. In HFI, nodular protrusions occur due to the formation of cancellous bone in the inner table. These nodular protrusions may be on both sides of the midline, but the midline is preserved. Symmetrical or asymmetric involvement can be observed.

In clinical practice, HFI can be detected incidentally in cranial imaging performed for different reasons. It is difficult to have a clear information about the prevalence of HFI. The prevalence of HFI in autopsy series or retrospective analyses of radiological imaging methods is thought to be between 5% and 12%. The frequency of HFI increases with age and may reach as high as 44.2% in people aged >80 years.[2] In a study conducted in Japan, the frequency of HFI was reported to be much lower (0.13%).[3]

Hyperostosis frontalis interna is within the field of interest of different disciplines due to the clinical conditions it may be associated with. Various studies on HFI have been published in the journals of endocrinology and metabolic diseases, anatomy, radiology, pathology, nuclear medicine, craniofacial surgery, oncology, paleopathology, and anthropology.

Concepts and Classification

Sherwood Moore et al have published many studies on HFI. The first classification was made by Moore in 1936 based on radiographic images (XR).[4,5]

The terms hyperostosis Frontalis and hyperostosis frontalis interna are generally used synonymously. It defines cancellous bone formation in the inner table of the frontal bone.

- Hyperostosis calvaria diffusa (also called hyperostosis calvaria interna and hyperostosis cranialis diffusa): Defines the thickening of all calvarial bones.
- Hyperostosis frontoparietalis: Defines the thickening of the inner table of the frontal and parietal bones.
- Nebula frontalis: A flatter uniform thickening of the frontal bone.

Ömercan Topaloğlu[1,2]

Taner Bayraktaroğlu[1,2]

Sakin Tekin[1]

Seda Nur Topaloğlu[3]

İbrahim Şahin[4]

Zeynep Cantürk[5]

[1]*Department of Endocrinology and Metabolism, Zonguldak Bülent Ecevit University Faculty of Medicine, Zonguldak, Turkey*
[2]*Obesity and Diabetes Practice and Research Center, Zonguldak Bülent Ecevit University, Zonguldak, Turkey*
[3]*Department of Internal Medicine, Zonguldak Bülent Ecevit University Faculty of Medicine, Zonguldak, Turkey*
[4]*Department of Endocrinology and Metabolism, İnönü University Faculty of Medicine, Malatya, Turkey*
[5]*Department of Endocrinology and Metabolism, Kocaeli University Faculty of Medicine, Malatya, Turkey*

Corresponding author:
Ömercan Topaloğlu
✉ drhomercan@hotmail.com

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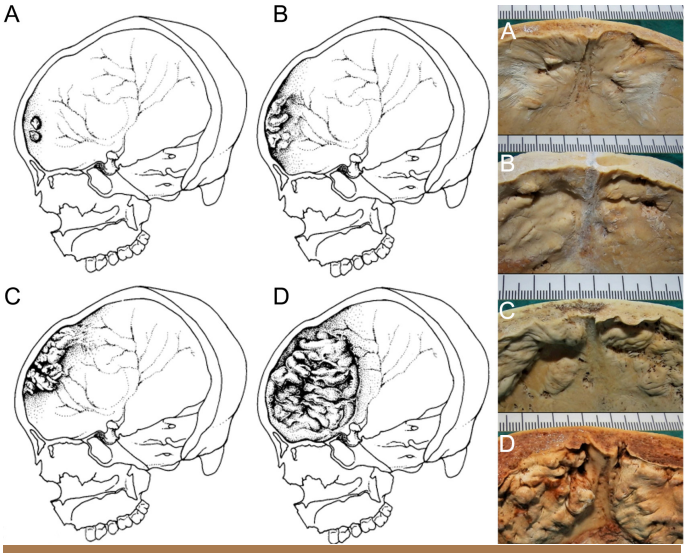

Figure 1. According to the classification proposed by Hershkowitz: (A): Type A, (B): Type B, (C): Type C and (D): Type D (Hershkovitz et al[6]).

Hershkovitz et al[6] proposed a new classification method for HFI in 1999:

- Extensiveness of the lesion: diameter, thickness, size
- Appearance: isolated or continuous
- Borders: well defined, or the borders are not exactly clear
- Shape: round or lobular or elongated
- Location on the frontal bone: anterior or posterior or orbital floor
- Involvement in other bones: parietal or sphenoid or temporal bone

According to these findings, the HFI is macromorphologically examined in 4 types (Figure 1):[6]

Type A: Isolated islets of elevated bones; single or multiple, unilateral or bilateral; sharply limited. It is <10 mm in size and is usually located anteromedially of the frontal bone.

Type B: Nodular growth is present; its borders are not sharp; there is slight elevation; it occupies <25% of the frontal bone.

Type C: Diffuse nodular growth is present; it can occupy up to 50% of the frontal bone area.

Type D: There is bone growth of more than 50% of the frontal endocranial surface and irregular elevation.

Ethiopathogenesis

Published case reports and results from studies have shown that HFI is more common in postmenopausal women with obesity (Table 1).[1,3,5-7] In addition, it has been suggested that the frequency of HFI is increased in individuals with oral contraceptive use, hormone replacement therapy, or breast cancer.[7] It has been also shown that the frequency of HFI is increased in men receiving androgen deprivation therapy.[8] The fact that it is associated with hormonal factors (postmenopausal estrogen deficiency or androgen deprivation) and is more common in older ages suggests that HFI may occur as a result of vascular dysregulation. There are publications suggesting that "VEGF" plays a role in the necessary neovascularization during the formation of HFI.[3] However, the ethiopathogenesis of HFI has not been fully elucidated.

Clinical Manifestations

Hyperostosis frontalis interna is usually asymptomatic and does not cause clinical symptoms or findings. There are publications in which it is associated with headache, dural irritation, and brain atrophy due to pressure.[2,5,7,9]

It is frequently detected incidentally on radiological imaging. Hyperostosis frontalis interna can be detected in cranial imaging (direct X-ray, magnetic resonance imaging, tomography) taken for headache or other reasons (Figure 2A and 2C). According to the findings obtained from radiological imaging and autopsy studies, HFI does not exceed the sagittal sinus line in the midline and the middle meningeal artery in the posterior.[2]

Hyperostosis frontalis interna has some features on tomography distinguishing it from other possible etiological factors, such as continuity with the inner table and diploe, being medially limited to the sagittal sinus, bifrontal symmetry, expansion over the frontal endocranial surfaces.[7]

Hyperostosis frontalis interna can accompany the underlying clinical conditions. Morgagni-Stewart-Morel Syndrome has been defined as the occurrence of virilism, obesity, and neurological and mental disorders (e.g., psychosis) together with HFI.[10] It has also been called metabolic craniopathy. There are case reports of HFI detected in patients with schizophrenia.[11] Troell-Junet Syndrome describes the association of HFI with acromegaly, diabetes, and toxic goiter.[12]

Although the association of HFI with psychosis, brain atrophy, or dementia was reported, we could not achieve any information regarding the association of HFI with mental retardation or decreased intelligence quotient.[13,14]

Hyperostosis frontalis interna can also be detected as an incidental finding in bone scintigraphy scans performed to investigate unexplained elevation of alkaline phosphatase level (Figure 2B).

MAIN POINTS

- Hyperostosis frontalis interna (HFI) is the thickening of the internal table of the frontal bone and spares midline.
- Hyperostosis frontalis interna is generally an asymptomatic incidental finding detected by imaging methods.
- Hyperostosis frontalis interna may be associated with headache, neuropsychiatric symptoms, or endocrinopathies.
- Differential diagnosis should include other pathologies affecting frontal bone or calvarium such as Paget's disease, fibrous dysplasia, metastasis, acromegaly, or primary hyperparathyroidism.

Table 1. Factors That Are Considered to be Associated with Hyperostosis Frontalis Interna

Old age
Being female
Obesity
Menopause
Diabetes mellitus
Androgen deprivation (in males)
Virilism
Neurological, mental disorders, and psychosis
Lifestyle change (modern lifestyle; more often in the last century)

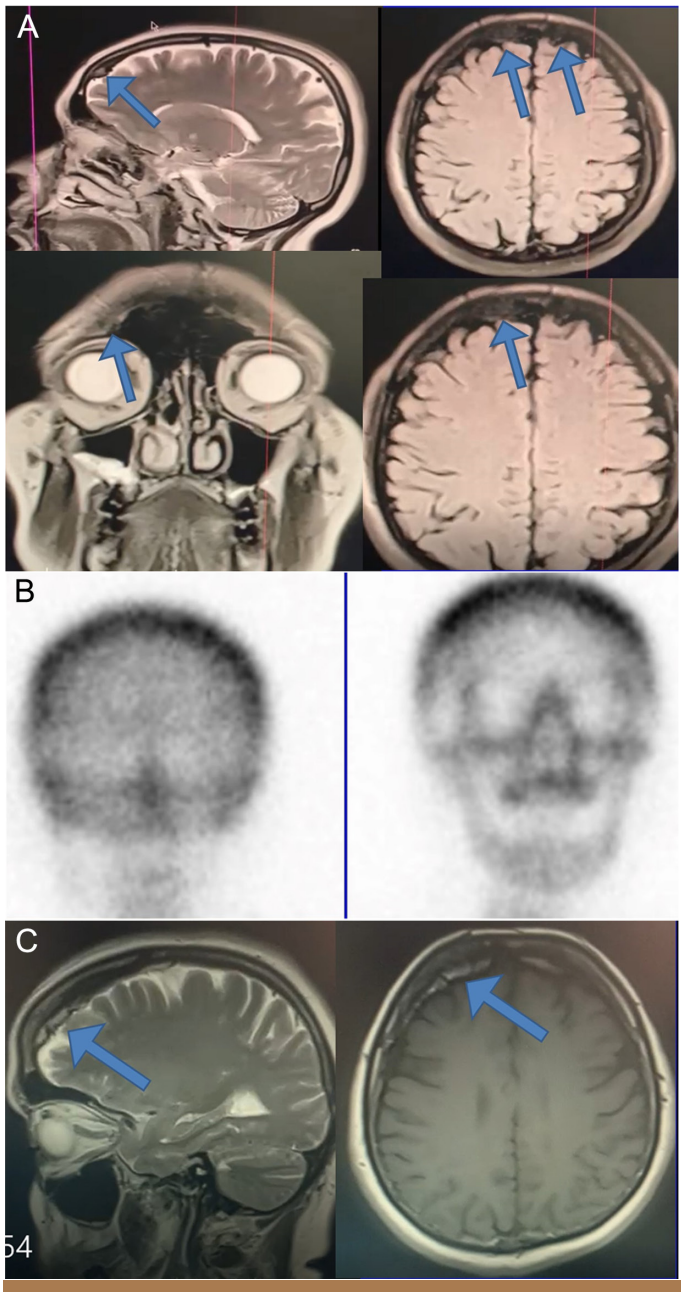

Figure 2. (A) HFI is demonstrated (arrow) on cranial MRI of a 37-year-old obese female patient presented with headache. (B) HFI is demonstrated on bone scan of a 52-year-old female patient with type 2 diabetes, obesity, hypertension, and adrenal Cushing syndrome (adrenalectomized) who was evaluated for unexplained alkaline phosphatase elevation. (C) HFI is demonstrated (arrow) on cranial MRI of a 65-year-old postmenopausal woman. HFI, hyperostosis frontalis; interna MRI, magnetic resonance imaging.

On tomographic imaging of a cadaver, diploization of the inner table was clearly demonstrated.[3]

Diagnosis and Differential Diagnosis

The clinical conditions and distinctive features that should be considered in the differential diagnosis of HFI are summarized in Table 2. The history and physical examination of a patient with HFI detected by imaging methods should be evaluated for obesity, menopause, diabetes, or another endocrinopathy. Measurement of biochemical parameters, parathyroid hormone, insulin-like growth factor-1 levels are guiding in the differential diagnosis. In cases where direct

Table 2. Differential Diagnosis of Hyperostosis Frontalis Interna

Diseases That Can Involve the Calvaria	Distinctive Feature
Primary hyperparathyroidism	The appearance of "salt-pepper" on the cranial bones Due to the destruction of the trabecular bone, the separation of the inner table, outer table, and diploic cavity becomes difficult
Acromegaly	New bone formation in the periosteum Thickening of the inner and outer tables Bilateral frontal bossing
Paget's disease	Lytic phase: well-limited radiolucent lytic lesions mainly in the frontal bone, cortical thickening, osteosclerotic changes in the inner and outer tables and diploe layer Osteoblastic phase: marked thickening of the diploe layer, increased sclerosis, "cotton wool spots" appearance Mixed phase: coexistence of lytic and sclerotic phase
Metastatic tumors	Coexistence of lytic metastases (thyroid or renal cell cancer) or sclerotic metastases (breast or prostate cancer) or lytic-sclerotic metastatic lesions may occur
Multiple myeloma	"Punched-out" lytic lesions Small, diffuse lytic lesions with unclear boundaries
Fibrous dysplasia	Inner and outer tables are thinned Sclerotic form: "ground glass" appearance, matrix expansion in the diploe layer Lytic form: radiolucent appearance Pseudopagetic form: lytic and sclerotic areas
Osteopetrosis	The entire cranium thickens progressively There is an intense sclerosis Thickening of the inner and outer tables and enlargement of the diploe layer is present The "hair-on-end" appearance
Ossifying fibroma (OFD)	The external surface of the cortex may be enlarged or thinned Intracortical osteolysis is monitored Osteolytic areas appear in the form of blisters
Van Buchem's Disease (cortical hyperostosis generalizata)	It is an autosomal recessive disease characterized by endosteal hyperostosis with osteosclerosis of the calvarium, skull base, mandible, clavicles, and ribs
Thalassemia major, sickle cell anemia, G6PD deficiency, iron deficiency anemia, hereditary spherocytosis	Marked enlargement of the diploic cavity; thinning of the inner and outer tables: "Hair-on-end" appearance

radiography is insufficient, tomography can be performed to better evaluate the inner and outer table and diploic space. In suspected cases, radiographs of the costa and vertebrae and other long bone radiographs may be taken. Hyperostosis frontalis interna can also be detected in bone scintigraphy performed for unexplained elevation alkaline phosphatase level.

Hyperostosis frontalis interna may lead to variable appearances due to differences in tracer uptake on bone scan; therefore, it may be difficult to differentiate it from bone metastases.[7] In a previous case report, SPECT CT: single-photon emission computed tomography was successfully used to differentiate HFI.[15] Awareness of HFI and the unique features on imaging modalities are so important. PET/CT: positron emission tomography/computed tomography was found to detect increased osteoblastic activity in an older patient which may be an early sign of HFI.[16] In 1 study, computed tomography imaging adjusted by three-dimensional volume rendering protocol for bone was used in the diagnosis of HFI and found to be reliable and prevent delay in the diagnosis.[17]

Treatment

If an underlying disease has been detected, it should be treated. Symptomatic treatment of headache can be done with acetaminophen or NSAIDs: non-steroidal anti-inflammatory drugs. If there is a vitamin D deficiency, replacement should be done.

Case reports have been published of symptomatic improvement with surgical removal of the thickened bone fragment in patients with severe headache, dural irritation, brain atrophy, and neurological symptoms.[2]

In a view of the scant current literature regarding HFI, we tried to synthesize the clinical knowledge about and differential diagnosis of HFI. We evaluated major important articles published. As we reviewed the reports, we showed that there was not an exact treatment of HFI. Therefore, we think that future studies, either case reports or retrospective analyses, will indicate whether therapeutic intervention in HFI is really necessary or not.

Conclusion

Hyperostosis frontalis interna is often asymptomatic and is an incidentally detected finding on imaging of the cranium. In some patients, it may be associated with headaches and, rarely, neurological symptoms. Differential diagnosis should be made with underlying endocrinopathies (acromegaly, primary hyperparathyroidism, osteopetrosis, fibrous dysplasia, or Paget's disease) or malignancies. Treatment of the underlying disease, symptomatic treatment, and vitamin D replacement are suggested.

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