## CASE REPORT

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# Hyperostosis Cranii *Ex Vacuo* in Adults: A Consequence of Brain Atrophy from Diverse Causes

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**ABSTRACT:** Hyperostosis cranii *ex vacuo* is diffuse thickening of the bones of the cranium occurring after successful ventricular shunting in hydrocephalic children, presumably as a compensatory phenomenon. We present three adults with severe brain atrophy and correspondingly severe skull thickening. In each, the cause of cerebral atrophy was well defined, and none had undergone ventricular shunting. In two, brain atrophy resulted from different temporally discrete insults sustained in adult life, ischemic in one and traumatic in the other. In the third case, progressive brain atrophy resulted from a primary neurodegenerative disorder, Hallervordan Spatz disease. Our observations suggest that hyperostosis cranii *ex vacuo* is a more general phenomenon than has been previously recognized, and point to a relationship between dynamic changes in brain size and skull thickness. We suggest that such relationships should be taken into account in anthropometric evaluation of the skull.

**KEYWORDS:** forensic pathology, forensic anthropology, physical anthropology, skull thickness, hyperostosis cranii, brain atrophy, anthropometric

Cranial thickness is influenced by a variety of factors, including hormonal balance, metabolic state, and mechanical forces. Diffuse or localized abnormal thickening of cranial bones may occur because of many different underlying derangements. The underlying causes may include: primary metabolic diseases of bone, such as Paget's disease; hormonal imbalances affecting bone growth such as acromegaly; hematopoieitic abnormalities such as sickle cell disease; and idiopathic causes probably including a genetic component or a combination of factors.

Hyperostosis cranii *ex vacuo* is diffuse thickening of the bones of the cranial vault which occurs in children following successful ventricular shunting for hydrocephalus (1–3). The decrease in brain size, from a previously hydrocephalic state, presumably exerts a physical influence on the surrounding calvarium through diminution of pressure on the inner table by the underlying brain or cerebrospinal fluid. We have noticed adult individuals with marked brain atrophy, and who also have strikingly severe thickening of the calvarial bones. In many of these cases, brain atrophy is the result of a temporally discrete insult, occurring in adulthood, and the individuals have no history of ventricular shunting procedures.

Anthropometric and radiologic assessment of skull thickness in relation to age and sex has yielded conflicting results. A positive correlation of cranial thickness with age has been observed in some studies (4,5), but not in others (6,7). Ross et al. (1998) have shown a slight negative correlation of frontoparietal thickness and age in males, and a slight positive correlation of age and frontal thickness in females (8). They suggest the positive correlation in females may be related to the onset of hyperostosis frontalis interna. Our observations suggest that skull thickness is influenced to a great extent by dynamic changes in brain mass and volume, and that measurements of skull thickness should be interpreted in light of brain findings. To illustrate this premise, we present three adults with markedly thickened cranial bones, and correspondingly atrophic brains. The etiology of brain atrophy in each case was different, and in two, the brain atrophy resulted from a temporally discrete insult which occurred during adult life.

### Case Histories and Postmortem Findings

*Case 1*—A 30-year-old Hispanic male fled from police during a routine traffic stop on 11 August 1988. Following the chase, cocaine in powdered form was observed on the subject's nose and pants, and on the vehicle floorboard. He was arrested, and approximately 1 h after his arrest, he began having generalized tonic clonic seizures and became unresponsive. A drug screen on transfer to the hospital was positive for cocaine, benzoylecgonine, and phenylpropanolamine. A CT scan the day after admission demonstrated diffuse cerebral edema, and changes suggestive of diffuse cerebral ischemia. Skull thickness was not mentioned on the CT scan report. The patient remained in a persistent vegetative state until his demise on 6 October 1998, at the age of 40 years.

Autopsy findings included generalized muscle atrophy and other stigmata of a persistent vegetative state, an epithelialized tracheostomy, and necrotizing tracheobronchitis with aspirated blood in the proximal and distal respiratory tract. The 800 g brain was atrophic, with extensive cortical laminar cavitary necrosis, diffuse white matter loss, atrophy of the descending tracts, and hydrocephalus *ex vacuo,* consistent with a remote hypoxic-ischemic insult and persistent vegetative state (Fig. 1*A*). The cranial bones were markedly thickened, with attenuation of the normal furrows and ridges of the orbital plates of the frontal bone, obliteration of

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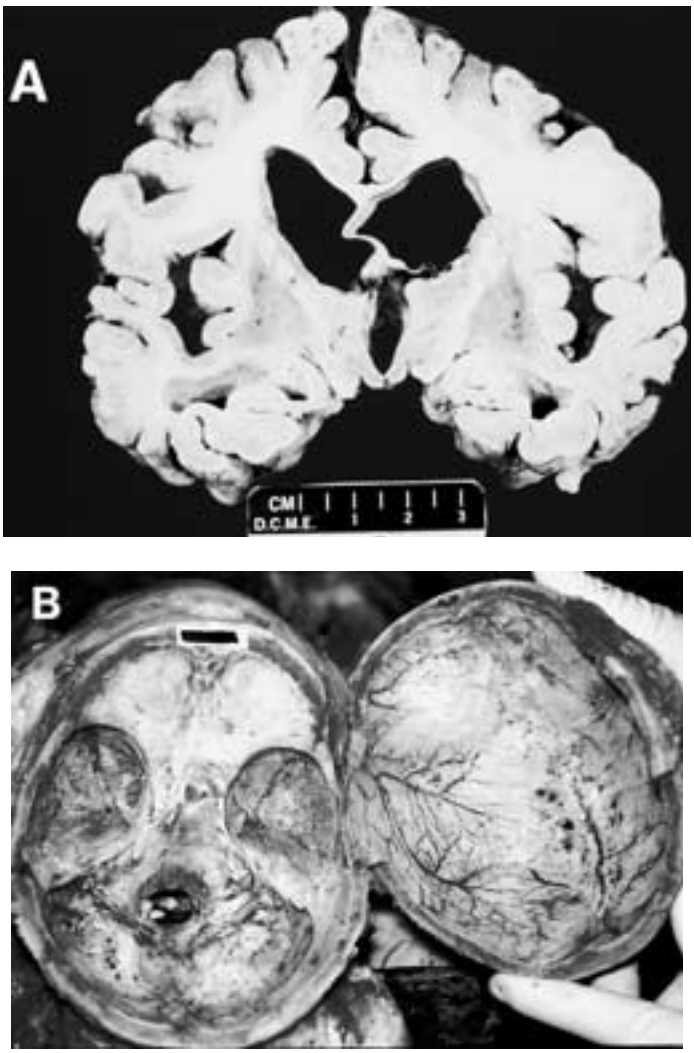


FIG. 1—*Case 1.* A: *Coronal view of brain; remote hypoxic-ischemic changes, including severe atrophy, hydrocephalus* ex vacuo, *and cavitary cortical laminar necrosis.* B: *Marked thickening of the skull, with attenuation of digital markings of the endocranial surface of the anterior cranial fossa and prominent vascular grooves on the inner table of the convexity skull.*

the frontosphenoid endocranial suture, and accentuation of the vascular markings of the inner table of the skull convexity (Fig. 1*B*).

*Case 2*—A 28-year-old black female was involved in a motor vehicle accident on 7 January 1988. The patient was comatose upon transfer to the hospital. She remained in a vegetative state until her death 11 years later on 10 February 1999.

Autopsy findings included the stigmata of a persistent vegetative state, including decubitus ulcers and muscle atrophy; she also had pulmonary congestion and pneumonia. The 640 g brain was markedly atrophic, with cortical cavitary laminar necrosis, and focal remote cortical contusions, with bilateral cavitary lesions in the superior parasagittal frontal white matter. Extensive white matter loss and atrophy of deep nuclei were also noted. The hippocampal formations were relatively less devastated. Territorial remote cavitary lesions were in the medial occipital lobes, in the distribution of the posterior cerebral arteries. The findings were consistent with remote residua of a traumatic insult, with superimposed ischemic changes (Fig. 2*A*). The bones of the skull were diffusely thickened, with striking obliteration of the normal digital markings of the floor of the anterior cranial fossa; the endocranial frontosphenoid suture was also obliterated (Fig. 2*B*). The maximal thickness of the frontal and parietal bones was 2 cm (Fig. 2*C*). Microscopic sections did

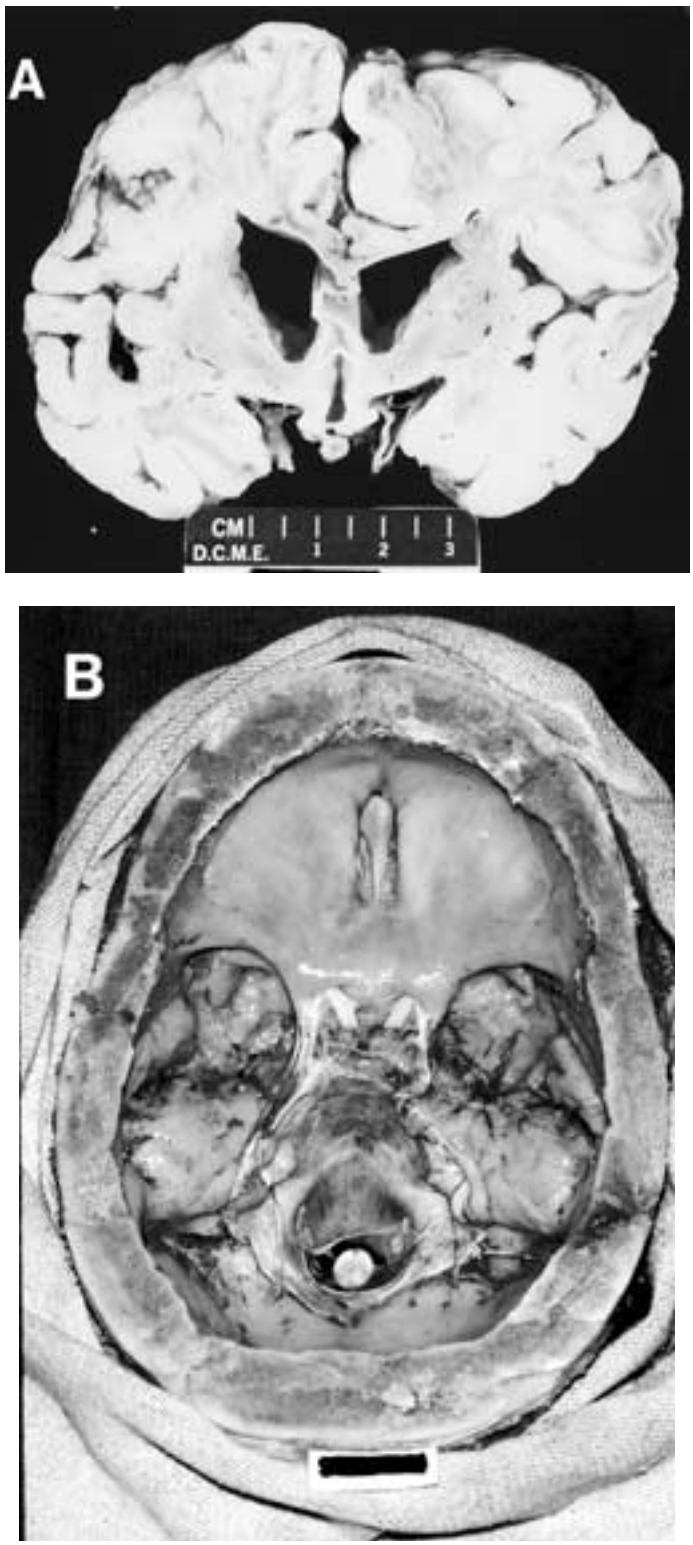


FIG. 2—*Case 2.* A: *Coronal view of brain; remote traumatic injury, with severe atrophy, hydrocephalus* ex vacuo, *and cavitary parasagittal white matter lesions.* B: *Marked thickening of the bones of the calvarium, with a smooth contour of the floor of the anterior cranial fossa.*

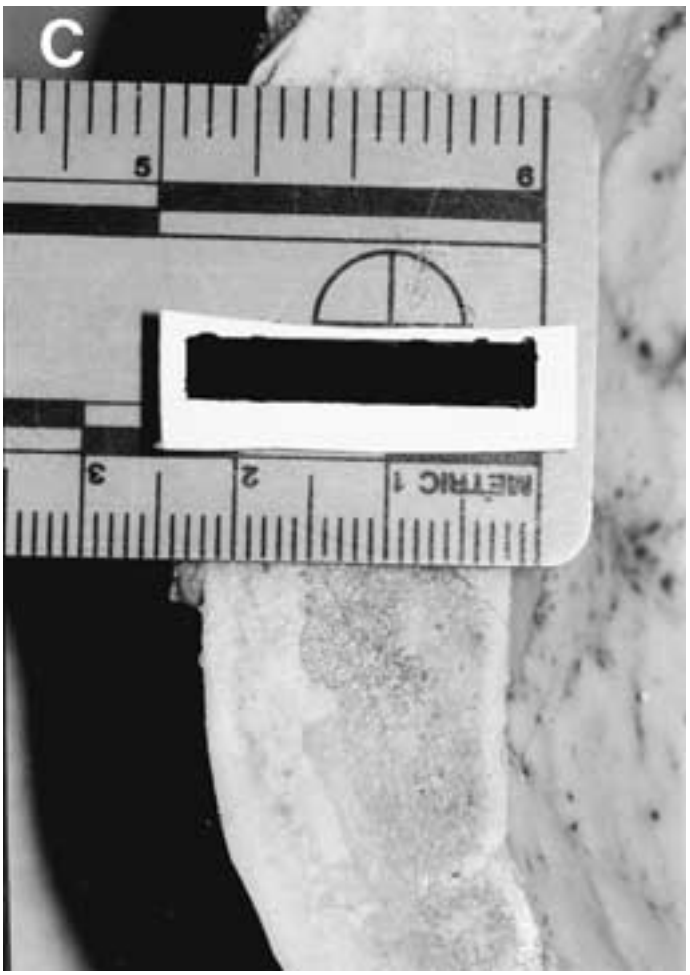


FIG. 2—*(Continued).* C: *Maximal thickness of the skull bones is nearly 2 cm. Outer table and marrow space are thickened at this level.*

not reveal abnormal osteoclastic or osteoblastic activity, or evidence of infiltrative processes.

*Case 3*—A mentally retarded white female had a history of progressive spasticity, with occasional seizures. Her condition deteriorated and she required institutionalized assistance with all activities of daily living since the age of 14. She expired on 2 July 1998, at the age of 39 years.

Autopsy revealed muscle contractures, decubitus ulcers, and fecal impaction. The 860 g brain was atrophic, with diffuse cerebral white matter loss, hydrocephalus *ex vacuo,* and an intense rust-brown discoloration of the substantia nigra and subthalamic nuclei. Microscopy of the brain confirmed diffuse cerebral neuronal loss, dystrophic axons, and abundant iron positive pigment deposition in neurons, astrocytes, microglia, and in perivascular spaces. The clinical and neuropathologic findings were consistent with Hallervorden-Spatz disease. All bones of the calvarium were markedly thickened. In addition, the frontal bones had a nodular surface contour, consistent with superimposed hyperostosis frontalis (Fig. 3).

## Discussion

Hyperostosis cranii *ex vacuo* is diffuse thickening of all bones of the neurocranial vault occurring in children as a response to successful ventricular shunting for hydrocephalus (1–3). The bone changes are probably a physiologic response of the skull to a reduction in outward pressure exerted by the abnormally increased volume of cerebrospinal fluid. We illustrate three examples of marked cranial hyperostosis in adults accompanying brain atrophy due to diverse causes. We suggest the mechanism of hyperostosis in these cases may be a physiologic response of the skull to diminution of the normal outward pressure, similar to the childhood cases of hyperostosis cranii *ex vacuo.*

The underlying cause of brain atrophy in each of our cases was different, suggesting that thickening of the cranial bones is a consequence of brain atrophy, and is unrelated to the nature of the underlying initial insult. In Case 1, brain atrophy followed a temporally discrete drug related hypoxic-ischemic episode. Although skull thickness was not specifically assessed antemortem, a head CT scan report generated ten years before death did not mention unusual cranial features. Brain atrophy in Case 2 was a sequela of traumatic brain injury sustained in a motor vehicle accident. The remote cerebral changes in Case 1 and Case 2 had overlapping neuropathologic features, owing to the presence of superimposed ischemic damage in Case 2. Brain atrophy in Case 3 resulted from a primary neurodegenerative process, unrelated to trauma or ischemia. It is interesting that not all cases of brain atrophy are accompanied by noticeable hyperostosis. One possible explanation is that other factors are involved. Further, the examples given here are

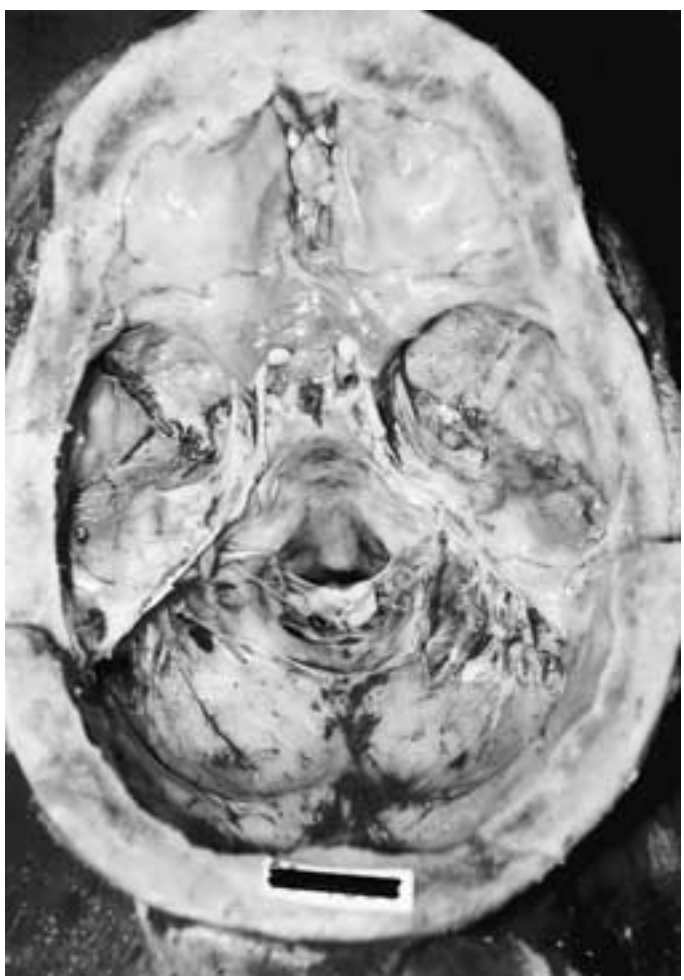

FIG. 3—*Case 3. Marked thickening of the calvarial bones. The anterior endocranial surface of the frontal bone is nodular, as seen at the level of the horizontal saw cut.*

extreme, with brain weights less than 900 g. In lesser degrees of brain atrophy, more quantitative measures of skull thickness may be necessary to perceive a correlation. In contrast, in instances of microencephaly due to defects of brain development, hyperostosis is often not a feature, even in severe cases. This indicates that a dynamic change in brain size, or in cerebrospinal fluid volume, or both, rather than a small brain size per se, is the underlying stimulus.

One crucial goal of forensic anthropologic analysis of human skeletal remains is identification of the decedent, accomplished by retrospective deduction of characteristic antemortem medical or historical features by analysis of atypical skeletal features. Although our sample size is small, our observations suggest that diffuse skull thickening in adult skeletonized remains may indicate that the individual had brain atrophy in life. As shown here, diverse causes of brain atrophy must be considered, but acquired causes (such as hypoxic-ischemic insult or trauma) would be likely. Further, if the thickening is severe, a degree of antemortem neurological impairment may be suggested. Therefore, this skeletal feature may give important clues to significant antemortem characteristics.

Our observations indicate that skull thickness is a dynamic parameter, and is influenced to a great extent by changes in the volume of the brain, even in adult life. Although only a small sample has been presented here, these effects appear to be independent of sex or age. We therefore suggest that anthropologic research of skull indices should include, when possible, assessment of at least basic neuropathologic features such as brain weight.

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