HYPEROSTOSIS FRONTALIS INTERNA

BY

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It was in 1765 that Morgagni first described the triad of hyperostosis frontalis interna, obesity, and virilism. More than 150 years later Stewart (1928) and Morel (1930), on examining hyperostosis frontalis interna in psychiatric cases, suggested that the combination of hyperostosis and endocrine and neuropsychiatric disturbances was a definite syndrome. This came to be called the Morgagni, or Morgagni-Stewart-Morel, syndrome.

Hyperostosis, discovered at necropsy or radiologically, is not very uncommon in psychiatric conditions, and this may have tempted many authors to assume a causal relationship, for in many papers there is no clear definition of the syndrome and the bony changes are loosely spoken of as if they constituted the syndrome itself. Grollman and Rousseau (1944) have even stated that the diagnosis could be made without x-ray confirmation of bony change. Sherwood Moore (1936b) found hyperostosis frontalis interna in 1.44% of 6,650 skulls examined radiologically, and calvarial hyperostosis of all sorts in a total of 3.48%, from which he defined a symptom complex which he referred to as "metabolic craniopathy".

Medical literature is replete with accounts of the condition, e.g., van Bogaert (1930), Fracassi and Marelli (1936), Roger (1938), Notkin (1953). Grollman and Rousseau (1944) found calvarial hyperostosis in 78 or 4.1% of 1,620 skulls of mental patients in North Carolina. No authors have so far described a consistent or specific neuropsychiatric picture which they found associated with hyperostosis frontalis interna in a significant number of cases. Isolated cases have been described in which cerebral atrophy has been demonstrated by pneumo-encephalography (Moore, 1944), and some authors have suggested, without very much evidence, that hyperostosis damaged the brain directly. This may occur in very rare cases. Roth (1941), who discusses this question, believes that the cranial bone changes and the psychiatric disturbances are of separate origin.

Some authors (Mortimer, 1938, and André Calamé, 1951) believe in an endocrinopathic

aetiology. Calamé refers to 60 personally observed cases and considers that the syndrome is a real entity and due to a lesion of the adrenal cortex involving pituitary relationships and associated with increased intracranial tension.

Since hyperostosis frontalis interna has been looked for and demonstrated chiefly in mental patients, some case can be made for associating with neuropsychiatric disturbances, and the literature as a whole inclines to a belief in a syndrome called variously hyperostosis frontalis interna, the Stewart-Morel syndrome, l'hyperostose frontalis interne, metabolic craniopathy, or Morgagni syndrome. There is, however, some difference of opinion as to whether any association of skull change with neuropsychiatric, metabolic, or endocrine disturbances is fortuitous. It also seems well established that similar bony changes can be found in association with other conditions, such as dystrophia, myotonica, certain tumours of the brain and its coverings, and even after encephalitis in childhood (Wakeley and Orley, 1938).

Pedersen (1947) estimated that hyperostosis occurs in the skulls of 5% of normal people before 40 and 12% after 40; and other workers (e.g., Schneeberg, Woolhandler, and Levine, 1947) regard cranial hyperostosis as a not uncommon incidental skull abnormality in women, coincidental with various clinical conditions.

From examination of a considerable and varied psychiatric case material, we have been unable to suspect the existence of this syndrome or hyperostosis frontalis interna without radiological evidence, and we have not been satisfied that we could associate the radiological evidence with psychiatric or endocrine symptoms with sufficient confidence to make a diagnosis of the syndrome. We have observed that prognosis did not seem to be affected by hyperostosis frontalis interna and the clinical outcome in our cases was in accordance with the psychiatric diagnosis, irrespective of skull change.

We have followed up a case previously referred to by Hemphill and Stengel (1940) which is relevant to the question. These authors investigated

familial craniopathy and described post-mortem findings in the mother of the patient. At that time the patient showed a paranoid psychiatric picture. She was thick-set, obese, with some degree of hirsutism. Her physical constitution resembled that of her father. After the publication of the paper, the patient, who had been married, was divorced and re-married. Hyperostosis frontalis interna was demonstrated by radiography in her first child, who appears to have had a normal development and schooling, and is now believed to be normal, aged about 15, but she has not been available for examination since the divorce. There are four normal children as a result of the re-marriage, in whom radiological examination shows normal skulls. The patient is supervised by her husband; she has an extensive system of paranoid delusions with thought disorder, and manages her home very badly. There is now (15 years after the condition was diagnosed) no evidence of endocrine disturbance (other than what appears to be a constitutional or familial obesity); no evidence of an organic dementing process suggesting interference with brain; no hypertension; and no neurological disorder. In this case, the fairly confident diagnosis of Morgagni's syndrome that was made in 1940 could not now be accepted, according to the definition of the syndrome then agreed on, and the case must now be regarded as chronic paranoid schizophrenia, with a fortuitously associated, non-progressive familial craniopathy.

There is clearly, therefore, a fundamental divergence of opinion on this matter, and with this in mind we attempted the present study, in order to clarify this problem, if possible, by clinical and laboratory means.

We here present 11 female psychiatric cases in which a variety of biochemical, endocrine, and neuropsychiatric investigations were made.

Methodology

Eleven female cases were studied. Four of these were discovered by the routine skull radiography of 120 chronic mental patients, the remainder (seven) during the investigation of acute psychiatric admissions. Five major investigations were made: neuropsychiatric, electroencephalographic, endocrine, metabolic, and a miscellaneous group.

The miscellaneous group of investigations consisted of blood pressure, blood count, blood Wassermann reaction and analysis of C.S.F., and the results were all within normal limits; the maximum and minimum blood pressures were 150/85 mm. Hg (Case 3) and 105/70 mm. Hg (Case 9). Hypertension has been described in many reports. Grollman and Rousseau (1944) found it in 16 out of 40 patients, and Roth (1941) in five out of eight. It was not, however, present in our series.

The results of the other investigations are shown in the Tables.

Results

Neurological abnormalities were present in Case 1 only (presenile dementia). The remainder were normal and none of the findings of Moore (1935) (cranial nerve defects, aphasia or apraxia, ataxia, narcolepsy, etc.) were present. Psychiatrically there was no specific diagnostic picture and no evidence of the intellectual slowness with depression and anxiety, or disturbances of temperament and character, which could be associated with hyperostosis, as emphasized by Schiff and Trelles (1931). The electroencephalographic results were in agreement with the clinical diagnosis. The literature reports few air-encephalographic investigations; in six out of our 11 patients, air-encephalography was performed, and of these only one (the case of presenile dementia) showed the anticipated atrophy of the frontal and temporal regions.

No anomaly was noted in either the present state of menstruation or the time of menopausal cessation.

TABLE I
NEUROPSYCHIATRIC, ELECTROENCEPHALOGRAPHIC, AND AIR-ENCEPHALOGRAPHIC FINDINGS

No.	Age	Neurological State	Psychiatric State	Electroencephalogram	Air-Encephalogram
1	42	Transitory phases of apraxia, aphasia, and dyslexia. Nil else	Dementia, probably presenile	Abnormal, typical of diffuse organic change	Cortical atrophy frontal and left temporal lobes
2	42	Normal	Depressive stupor	Non-specific dysrhythmia	Normal
3	53	"	Neurotic depression, epilepsy	Diagnostic of epilepsy	Not done
4	26	"	Reactive depression, intellectually subnormal, epilepsy	" " "	Normal
5	59	"	Neurotic depression	Some immature and epileptiform features	Not done
6	38	"	Chronic paranoid schizophrenia	Normal	Normal
7	42	"	"	"	"
8	77	"	Chronic depression, intellect normal	"	Not done
9	73	"	Chronic depression, intellect normal	Dysrhythmia, with some lowering of convulsive threshold	Normal
10	74	"	Senile depression, minimal intellectual failure	Non-specific dysrhythmia. Just outside normal limits	Not done
11	66	"	Recurrent agitated depression, intellect normal	Normal	Normal

TABLE II
ENDOCRINE FINDINGS

No.	Age	Menses	Secondary Sex Characteristics	*Keto-steroids (total/24 hours)	†Adrenal Response	‡Thyroid Activity
1	42	Regular	Normal	9.4	Positive	Normal
2	42	Ceased 2½ years ago	Slight moustache. Diamond formation pubic region	13.6	Positive	Normal
3	53	Ceased 2 years ago	Normal	16.4	Positive	Normal
4	26	Regular	Normal	15.0	Positive	Normal
5	59	Ceased 3 years ago	Normal	14.6	Positive	Normal
6	38	Regular	Slight moustache	9.0	Positive	Normal
7	42	Regular	Normal	8.6	Positive	Normal
8	77	Ceased many years ago	Normal	2.9	Positive	Normal
9	73	Ceased many years ago	Much facial hair	5.4	Positive	Normal
10	74	Ceased many years ago	Normal	8.4	Positive	Normal
11	66	Ceased 16 years ago	Normal	8.6	Positive	Normal

* Ketosteroids: Normal values, age 16 to 40, 5.1 to 19.6 mg./24 hours urine (Dorfman, 1948).

† Adrenal response: This is indicated by a drop in eosinophils of 30%, and increases in uric-acid/creatinine ratio of 20% and in ketosteroid/creatinine ratio of 5% (Reiss, Hemphill, Early, Maggs, Cook, and Pelly, 1951).

‡ Thyroid activity was measured by radio-iodine (Haigh, Reiss, and Reiss, 1954).

TABLE III
METABOLIC FUNCTIONS

No.	Age	Obesity	*Plasma Cholesterol (mg.)	†Serum Calcium (mg.)	‡Serum Phosphate (mg.)	§Alkaline Phosphatase	Glucose Tolerance Test
1	42	Nil	216	9.6	4.0	5.95	Normal
2	42	Nil	212	9.5	4.2	5	Normal
3	53	Nil	180	10.4	5.1	6.4	Normal
4	26	Nil	210	10.4	4.5	6	Normal
5	59	Slight abdominal	224	9.46	4.8	4.2	Normal
6	38	Nil	190	9.2	4.4	6	Normal
7	42	Nil	132	9.6	3.1	4.1	Normal
8	77	Slight abdominal	170	9.8	3.6	5.4	Normal
9	73	Nil	220	10.6	4.0	9.95	Normal
10	74	Nil	179	10.5	3.5	6	Normal
11	66	Nil	200	10.8	4.1	7.4	Mildly diabetic

Normal values: * Plasma cholesterol, 140 to 215 mg./100 ml.
 † Serum calcium, 9.6 to 10.9 mg./100 ml.
 ‡ Serum phosphate, 2 to 5 mg./100 ml.
 § Alkaline phosphatase, 5 to 10 units/100 ml. (King, 1951)

Three of the 11 patients showed slight masculine distribution of hair—facial, chest, pubic. None of these, however, demonstrated any other associated endocrine dysfunction. Grollman and Rousseau (1944) observed that the principal endocrine disturbances in their cases were amenorrhoea and hirsutism, and in two of the current group under review (aged 42 and 38) the amenorrhoea and hirsutism might possibly be important, but more

likely are related to an early menopause. The low ketosteroid value (2.9 mg.) in Case 8 is attributable to old age (77).

These findings are substantially within normal limits. The results of metabolic investigation have hitherto varied. Grollman and Rousseau (1944) considered the principal metabolic anomaly to be obesity of the rhizomelic type, but in this group only two patients showed obesity to a slight degree. Roth (1941), on the other hand, found that six out of eight patients showed obesity, and, unlike Grollman and Rousseau's patients, all his eight cases gave a diabetic type of curve on glucose tolerance test; also two of Roth's patients gave increased values for serum calcium. In the present group only one gave an abnormal sugar tolerance curve. None gave calcium values outside normal. In the case of the patient with the abnormal curve, no glycosuria was found to be present and the high renal threshold might well represent a state of affairs not uncommon in the old.

Discussion

In view of the essentially normal or negative findings and the varying psychiatric pictures it seems impossible to be able to identify a definite syndrome. It is felt that the above results show that thickening of the internal table of the frontal bone in psychiatric cases does not imply any regular association of pathological deviations in endocrine, metabolic, biochemical or neurological fields. They agree with the view of Schneeberg and his colleagues (1947) that hyperostosis is incidental and may on occasion be associated with other signs and symptoms so as to produce an apparent Morgagni's syndrome, but that it may occur independently or in combination with other skull anomalies in association with conditions such as dystonia myotrophica (Caughey, 1952).

The statement of Grollman and Rousseau (1944) that although "x-ray changes need not be present . . . they remain the most constant and reliable characteristic of the disorder" must be qualified, in spite of the large number of cases they have investigated. Clinical and laboratory investigations in our series have shown that a definite condition of hyperostosis need *not* be associated with a definite syndrome and the occurrence of the bony changes may be entirely coincidental.

Summary

Eleven female patients suffering from various psychiatric disorders with associated hyperostosis frontalis interna were investigated. Ketosteroids, adrenal response activity, thyroid activity, physical development, and endocrine state were within

normal limits. There was no hypertension and no obesity. Electroencephalographic and neurological tests, when abnormal, were in keeping with the psychiatric diagnosis.

No relationship of symptomatology was found to suggest a diagnosis of Morgagni's syndrome.

It is concluded that hyperostosis frontalis interna may occur fortuitously with psychiatric or endocrine disorders, but it seems probable that Morgagni's syndrome—if it exists as a psychiatric identity—is very much rarer than hyperostosis frontalis interna in psychiatric patients.

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