PARTIAL HYPOPITUITARISM, PRESUMABLY OF HYPOTHALAMIC PATHOGENESIS, ASSOCIATED WITH DILATATION OF THE THIRD VENTRICLE

By

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It may be very difficult indeed for a clinician to prove that a case of hypopituitarism is of hypothalamic origin, without thorough post mortem examination. Even after the post mortem examination doubt may be expressed because of the frequently widespread damage suffered by the basal cerebral structures in cases of neoplasm, meningitis, etc. The accompanying symptoms such as sleep disturbances, peculiar behaviour, unusual types of obesity, disturbances in the temperature regulation, water metabolism and blood pressure, and in the sexual pattern, especially sexual precocity in the young, however, may give supporting evidence to such an assumption (Bauer, 1954).

Harris (1957) objects to the statement of Spurr & Stribling (1957) that the experimentalist is, in this field, far ahead of the clinician. Nevertheless it is up to the clinician to bring to fruition the results obtained by the neurophysiologists regarding the importance of the hypothalamic structures for pituitary functions. Not enough is known of the stimuli transmitted from the hypothalamus to the anterior part of the pituitary body, nor where they originate, though it is generally accepted that the message is conveyed by way of the portal vascular system between the tuber cinereum and the adenohypophysis.

A more or less selective atrophy of the hypothalamic structures necessary for adequate function of the distal hypophysis may occur, but the diagnosis is seldom made because of the inaccessibility of the hypothalamus to direct diagnostic procedures. If the atrophy is, however, of sufficient importance to cause dilatation of the third ventricle, it may be visualized by aeroencephalographic examination.

A dilatation of the third ventricle presumably due to atrophy of the wall structures (and not to their destructions by invasive disease or the obstruction
of the Sylvian aqueduct) important enough to be visualized aeroencephalographically, must be presumed to present a wide variety of symptoms (Engeset & Lönnum, 1957) and the almost selective failure of thyroidal and gonadal functions will presumably occur only rarely.

Hence the presentation of the following case.

_Case history._ A truck driver born 1905, entered the Medical Dept. A. Aker Hospital, Nov. 19, 1956.

No particular family history. His parents died at the age of 76 and 82. They had 10 children. Only one of them, a female, has had any endocrine disease, namely thyrotoxicosis at the age of 54 years.

The patient has three children, 26, 21 and 7 years old. His past history is irrelevant.

For some three months prior to admission to the hospital, he had been suffering from headache, initially only occasional, but increasing in intensity and constancy. The headache was mainly occipital, but occasionally it was felt frontally and periorbitally. During this period he also suffered from pains in the right lumbar region.

He grew tired, apathetic, and very somnolent. When driving his truck he was glad to be kept alert by difficult situations, lest he should fall asleep over the wheel. When coming home he ate heartily and then immediately went to sleep till the next morning. This was very much in contrast to his premorbid behaviour.

Furthermore he became very sensitive to cold. His working capacity was markedly reduced by lack of strength and endurance, as compared with workmates ten years his senior, and also suffered from breathlessness.

His voice became hoarse, he stopped sweating altogether. His weight increased from 86 to 101 kg., and his collar size increased from 43 to 47 cm., though he did not develop a goitre, fat being deposited over the shoulders and at the back of the neck.

He had to get up three times every night to urinate, which had never happened before, but he did not develop diabetes insipidus.

His sexual activity and urge stopped completely, and he noticed that the eye brows grew thinner, the axillary hair disappeared almost entirely, and the pubic hair became scantier than before. His testes became softer and insensitive to pressure, but they did not markedly decrease in size. His thyroid gland was not visible or palpable. The prostate was normal.

His hemoglobin values dropped from well over 100°/o to 80°/o of the Haldane standard, despite iron treatment. (His blood-values are under constant supervision since he is a blood donor).

The findings are shown in Tables 1 and 2.

His suspected myxoedematous state was confirmed by the lowered I^131 uptake, which was significantly raised by TSH. His cholesterol values were normal (normal range in our laboratory 200–350 mg. %) and so was his basal metabolic rate. Apart from the assessment of the 17-ketosteroid excretion (8.9 mg./24 hrs.) his gonadal and adrenocortical functions were not tested during this stay in the hospital.

From Dec. 15, 1956 till March 1, 1957 he was given 0.2 mg. I-thyroxine-sodium daily. His myxoedematous appearance was alleviated, and he lost altogether 14 kg. in weight, but despite this he did not feel better; all his subjective complaints persisted, even the sensitivity to cold, the lack of sweat, the hoarseness of the voice and especially the somnolence and the headache. He was completely unable to work.

He entered Med. Dept. B, Aker Hospital on March 1, 1957. Since he no longer was so obviously myxoedematous, we doubted the validity of the lowered uptake of I^131

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Table 1.

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<tbody>
<tr>
<td>Treatment</td>
<td>Dietary restriction</td>
<td>I-thyroxine 0.2 mg.</td>
<td>Dietary restriction</td>
<td>250 mg. bimonthly of Testosterone octanate</td>
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<tr>
<td>Weight (kg.)</td>
<td>99</td>
<td>88.5</td>
<td>87.3</td>
<td>83.6</td>
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<tr>
<td>Blood pressure</td>
<td>220/130 165/100 145/90</td>
<td>135/90 150/90</td>
<td>170/95</td>
<td>140/90</td>
</tr>
<tr>
<td>Sedimentation rate (mm.)</td>
<td>40 24</td>
<td>17</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Hemoglobin (%)</td>
<td>80</td>
<td>80</td>
<td>90</td>
<td>96</td>
</tr>
<tr>
<td>Cholesterol (mg. %)</td>
<td>224 240 188</td>
<td>228 219</td>
<td>213 314 293</td>
<td></td>
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<tr>
<td>B. M. R. (%)</td>
<td>94 86</td>
<td>86 95 87</td>
<td>87 87 100 %</td>
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Dec. 6 – 10**: Before TSH 3 %/6/2 hrs. 8.4 %/6/24 hrs.
131I: 13.8 %/48 hrs.
Plasma 131I 48 hrs. 0.1 %

After TSH
10 U. S. P. U. 33.8 %/48 hrs.

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<th>March 18–22*** April 5***</th>
<th>Oct. 15–18</th>
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<td>8.1 %/6/24 hrs. 27.7 %/6/48 hrs.</td>
<td>Plasma 131I 48 hrs. 0.09 %</td>
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* 20 microcuries.
** Urographic exam. Nov. 21.
*** Thyroxine stopped March 1.
found 5 months previously, mainly because it was assessed 19 days after a urographic examination (which was normal). Werner (1955), however, states that it is sufficient to wait 14 days after a urographic examination in order to get a correct result. The second assessment (Table 1) was made 18 days after thyroxine medication had been stopped, and the third, after a further 16 days. (Normal values in our laboratory for 24 days uptake decidedly above 20%.) Hence we felt convinced that he really was hypothyrotic. The good response to TSH injections proved that this was not due to primary thyroid failure.

His gonadal functions were evidently reduced, and this was confirmed by the assessment of the gonadotrophin excretion (Table 2). His adrenocortical functions seemed unimpaired. His sugar tolerance was augmented.

Repeated examination showed the sella turcica to be normal, as was his visual field, the ophthalmoscopic findings and his spinal fluid. His renal functions were unimpaired (creatinine in serum 1.1 mg. %, endogenous creatinine clearance 135 ml.). The uterine was normal except for a single finding of proteinuria in Nov. 1956. There were no signs of hepatic impairment judged either clinically or from the turbidity tests.

The electroencephalographic examination revealed no abnormalities.

The aeroencephalographic examinations too showed normal findings, except for a conspicuous dilatation of the third ventricle, measuring 12 mm. across (Fig. 1). The lateral ventricles were normal. The X-ray specialist suggested the diagnosis of central cerebral atrophy, though the headache and the somnolence still made us suspect the possibility of an obstruction by a tumour. However, additional findings and the subsequent course seemed to eliminate this possibility. As to the cause of the presumed central cerebral atrophy we strongly suspected an encephalitic process (Skouby, 1956) of unknown etiology, because of the prolonged elevation of the sedimentation rate, the sudden onset of the disease, its general symptomatology and subsequent course.
Course of treatment. Apart from general measures, our only means of treatment seemed to be adequate substitution therapy. He did not show any need for adrenocortical substitution and the thyroid substitution treatment had proved a failure. His gonadal insufficiency was evident, so testosterone was given as bimonthly injections of 250 mg. of testosterone enanthate in oily solution.

This treatment induced a remarkable improvement. He had his first injection on June 21. During July he gained in strength, felt very fit and able to work, he stopped being sleepy, lost his sensitivity to cold and his headache, and resumed his sexual activity.

During August he began to sweat when in a hot room, and in September he was glad to report that he sweated normally when working. He furthermore noticed growth of his axillary and pubic hairs, and also that his testes became sensitive to pressure.

Attempts have been made to lengthen the intervals between the injections, but the patient strongly asserts that an interval of more than a fortnight brings back his somnolence and lack of energy.
DISCUSSION

The arguments in favour of the author's interpretation of the case are as follow.

The selective and conspicuous dilatation of the third ventricle is evidence against an obstruction of the Sylvian aqueduct. The absence of papilloedema, dilatation of the sella turcica and symptoms from the chiasma opticum precludes the possibility of a pituitary tumour.

The sudden onset of the symptoms, especially the obesity and the marked somnolence, are not suggestive of a primary pituitary disease.

In conditions of pituitary hypothyroidism the uptake of iodine by the thyroid is more substantially and consistently reduced than in thyroidal failure of hypothalamic pathogenesis, as observed in this case, where the basal metabolic rate remained unaltered.

The absence of diabetes insipidus and of adrenocortical failure makes the possibility of a lesion of the supraoptical and paraventricular nuclei unlikely. It also is in favour of the hypothalamo-hypophysial tract, the portal hypophysial vascular system and the median eminence being intact.

The lesions responsible for the symptoms in the present case, namely marked hypogonadism, obesity, somnolence, apathy and increased sugar tolerance, thus may be located to the intermediate and posterior hypothalamic nuclei. The same lesions may also be responsible for the incomplete thyroidal failure, though the conspicuous dilatation of the third ventricle is suggestive of extensive damage to the wall structures.

SUMMARY

A report is given of a 50 years old man, suffering from secondary hypothyroidism and hypogonadism, with fat deposition, and a marked and long-lasting somnolence. The syndrome is thought to be due to a central cerebral atrophy as visualized by a conspicuous dilatation of the third ventricle, presumably due to an encephalitic process of unknown etiology.

Post mortem confirmation of the hypothesis is obviously lacking.

The patient became worse with thyroxine treatment, but when treated with testosterone only, the improvement was remarkable.

REFERENCES


