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Sheehan's Syndrome in Association with Diabetes Insipidus

Sheehan's syndrome and diabetes insipidus are both well-known conditions, but the combination of the two is unusual and is of considerable physiological interest. Only 17 cases of this association have been reported in the literature. These have been reviewed by Evans (1960). A further case is recorded here, not only because of the rarity of the association but also because the failure to recognize the hypopituitarism during the first two years after the onset illustrates a common cause of diagnostic error.

CASE REPORT

The patient, aged 30, was admitted to the obstetric department of the hospital for delivery at the end of a normal pregnancy. She was very obese, and weighed 103 kg. (16 st. 3 lb.). After the delivery there was atonic post-partum haemorrhage, which was so severe that she became unconscious and hysterectomy had to be performed to arrest the bleeding. Next day she drank 16 litres of water. She was forbidden to continue drinking such large quantities, but during the following night she was extremely thirsty and kept screaming that she would die unless she could get water to drink. Her condition distressed the other patients in the ward so much that they took her jugs of water to drink throughout the whole night. The acute phase of polydipsia gradually subsided, but from this time onwards she had gross polyuria and a correspondingly high fluid intake. Lactation failed to occur. She was extremely weak and could not even sit up in bed to wash herself. Her blood-pressure was 70/50. She was kept in hospital for the next five months, being quite unfit to be discharged home. During this time her weight fell to about 88.9 kg. (14 st.), her axillary and pubic hair fell out completely, and there was some loss of head hair.

The correct diagnosis was not made at this stage because the patient was so obese. Many physicians still believe the old concept of Simmonds's cachexia—that is, that the characteristic feature of hypopituitarism is emaciation without demonstrable cause—though Sheehan has given clear evidence since 1937 that significant loss of weight is an extremely rare sequel to post-partum necrosis of the pituitary.

After the patient was discharged from hospital she continued in the same very poor state of health, and was so weak that she could take only a few steps with assistance. She spent most of the next 18 months in bed. The systolic B.P. varied between 70 and 90. The intake of water and the output of urine were about 6 to 8 litres daily.

At the age of 32 she was readmitted to hospital for investigation. The most prominent clinical features were somnolence, a dry skin, and pallor. Laboratory investigations showed a slightly raised serum cholesterol level and a low basal metabolic rate. These findings led to an initial diagnosis of myxoedema, though the serum cholesterol level is characteristically high in genuine myxoedema and is often normal in cases of hypothyroidism of pituitary origin. However, there was also evidence of adrenal insufficiency: great physical weakness, hypotension at 95/70, and a low excretion of adrenal steroids. Further laboratory investigations gave the following results: glucose-tolerance test 70, 114, 119, and 75 mg./100 ml.; blood-sugar curve after protein-loading showed a decrease characteristic of adrenal insufficiency (Góth *et al.*, 1952), 88, 72, and 92 mg./100 ml.;

serum cholesterol, 260 mg./100 ml.; sedimentation rate, 20–27 mm.; blood count normal; urinary excretion of 17-ketosteroids, 2.3 mg./day; urinary excretion of 17-ketogenic steroids, 4.5 mg./day; B.M.R., minus 16%; urine specific gravity, 1000–1005; radiological measurement of the sella showed a normal area, 75 sq. mm.

The clinical condition and the laboratory findings finally led to the correct diagnosis—that is, that the patient was suffering from Sheehan's syndrome in association with diabetes insipidus. This diagnosis was confirmed by the excellent effects produced by substitution therapy. Treatment was begun with the daily administration of 50 mg. of cortisone, 75 mg. of thyroid extract, and 50 mg. of methyl androstenediol. This treatment produced a dramatic improvement. There was a rapid disappearance of the asthenia and somnolence, and she had a marked sense of well-being so that she was soon able to undertake her ordinary work again. Her blood-pressure rose to 140/80.

In the six years since this therapy was instituted she has remained very well and is able to work normally. The diabetes insipidus is basically less severe, but varies according to the treatment being given. The output of urine is 2 to 3 litres a day when all therapy is stopped experimentally, and rises to 5 to 7 litres a day when she is taking cortisone but no antidiuretic. The polyuria is well controlled by the injection of "pitressin" tannate twice a week. On the day of the injection the urinary output falls to less than 1 litre a day, and for the next two days it is 2 litres a day.

DISCUSSION

It is very difficult to explain how, in rare cases, diabetes insipidus can occur after severe post-partum necrosis of the anterior pituitary. The posterior lobe is seldom involved, and there is no necrosis in the hypothalamus, which is the probable source of the posterior pituitary hormones.

In experimental studies on animals the presence of the anterior lobe seems to be necessary for the development and continuance of diabetes insipidus. Thus removal of the posterior lobe alone causes diabetes insipidus. On the other hand, removal of the anterior and posterior lobes together does not do so; there is an initial polyuria and polydipsia, but this disappears in about 24 to 36 hours, when the effects of the loss of the anterior lobe become manifest.

When women have surgical hypophysectomy for carcinoma of the breast, about 50% of them develop mild diabetes insipidus (Lipsett and Pearson, 1957). This continues while cortisone therapy is being given, but disappears if the cortisone is omitted (Ikkos *et al.*, 1955; Baron *et al.*, 1958). The mechanism of this phenomenon is not yet fully explained, but Dingman *et al.* (1958) suggest that cortisol may have an inhibitory effect on the secretion of antidiuretic hormone.

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The British Council's *Annual Report 1961–1962* shows that of the 7,522 overseas visitors in Britain assisted by the Council 1,030 were studying medicine. Of the others 2,198 studied education, 1,717 science and technology, 1,535 social science, 864 arts and humanities, and 178 miscellaneous subjects.