CORTISONE INDUCED RECURRENCE OF DIABETES INSIPIDUS BY TOTAL DESTRUCTION OF THE HYPOPHYSIS

By

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The production of diabetes insipidus not only requires a lesion of the nucleus supraopticus in the hypothalamus, or of the stalk of the hypophysis or its posterior lobe, which reduces the production of antidiuretic hormone (ADH), but also some functional activity of the anterior lobe of the hypophysis. Experiments on animals have shown that total hypophysectomy does not produce diabetes insipidus but only a transient polyuria (Selye, 1949, Spence, 1953). Thyroidectomy can abolish this increased diuresis. Long after hypophysectomy, administration of thyroid hormone, cortisone or corticotrophin may once again produce polyuria.

Total hypophysectomy in man induces a polyuria, the persistence of which after the third postoperative week is dependent on cortisone administration (Ikkos et al., 1955).

ADH acts on the distal tubules of the kidney so that water is actively re-absorbed, whilst the excretion of sodium and chloride is also possibly increased. The hypothesis has been put forward that the effect of cortisone as well as of thyroxin is antagonistic to ADH by increasing water diuresis and possibly retaining sodium and chloride (Engstrom et al., 1953). Severe exacerbations of diabetes insipidus have been observed after treatment with moderate doses of thyroid hormone (Year Book of Endocrinology 1953/54). One case of simultaneous thyrotoxicosis and diabetes insipidus in the same patient has been reported, in which both diseases were apparently cured by a single dose of J 131 (Rieber & Silver, 1952).

At the Medical Department B of the Aker Hospital we have recently had the opportunity of observing a man, in whom metastases from a tumour...
destroyed the hypothalamus and the hypophysis, and in whom the course of his diabetes insipidus clearly showed the pathogenesis of the disease previously discussed.

**CASE REPORT**

A 59-year-old man was admitted to the Department on the 16th of August and stayed until October 19, 1954.

In the middle of April 1954 a malignant naevus cell tumour was removed from the left breast. The axillary glands were also removed, and he had X-ray treatment. Two months later it was necessary to remove metastases from the skin.

From July 1954 he experienced increasing anorexia, fatigue and for some weeks excessive thirst and considerable polyuria.

On admission on August 16 numerous metastases were found on the skin. In other respects nothing noteworthy was found.

Specific gravity of urine 1008. Volume of urine 1500 ml./24 hours. The excretion of 17-ketosteroids was 2.0 and 1.4 mg./24 hours. There were no signs of insufficiency of the thyroid gland or the gonads. Cholesterol 284 mg./100 ml. serum. Basal metabolic rate 108%.

The investigation with J131 could not be carried out because of the poor

![Graph](https://example.com/graph.png)

**Fig. 1.**

The 24-hours output of urine in the present case, before and during the administration of cortisone and pitressin.
condition of the patient. The glucose tolerance curve was normal. The hair growth and the secondary sexual characteristics were normal. Blood pressure 120/80 and 140/80.

Cortisone orally 25 mg. three times a day was given from August 21 to try and reduce the production of melanotrophic hormone. After ten days treatment the weight of the patient had increased by 3.4 kg., and he was put on a saltfree diet. The output of urine then increased from 2000 to 6000 ml./24 hours with a specific gravity of 1005. He suffered from excessive thirst and polyuria. Injections of pitressin tannate in oil 5 pressor units reduced the urine output to the normal level for three days at a time.

An attempt to discontinue cortisone brought about reduction of the daily output of urine from 5000–6000 ml. to 2800 ml. But after two days the cortisone treatment had to be repeated because of collapse and increasing temperature. Symptoms of collapse were taken to show failure of the suprarenal cortex. The volume of urine then increased once more. By successive reduction of the cortisone dose from 50 to 12.5 mg. a reduction of the urinary output was evident. But the dose had to be increased after one day because of signs of failure in the suprarenal cortex. By administering pitressin snuff the volume of urine was kept at 2000–2500 ml. in spite of the fact that he was being given 37.5 mg. cortisone daily.

When 75 mg. cortisone daily was administered, the excretion of 17-ketosteroids in the urine rose from less than 2 mg./24 hours to a maximum of 4 mg. indicating that practically the total 17-ketosteroid excretion was derived from the cortisone administered.

He died on October 19.

At autopsy (Knut Høeg) a dark-coloured metastasis the size of a hazelnut was found in the hypothalamus. The hypophysis was a little larger than a pea. Most of the anterior lobe consisted of a dark-coloured metastasis, while the posterior lobe was yellow. In the hemispheres and the basal ganglia there were several metastases as large as a bean. The suprarenal glands were smaller than usual. The cortex was yellow and of normal thickness, while the medulla was dark grey with a few nodules.

The microscopic description ran: »Microscopically in the hypophysis there is seen a tumorous infiltration which occupies the anterior-, intermediate- and posterior lobe, so that only peripheral areas of hypophyseal tissue are retained. The tumorous tissue shows no definite structure. The cells are irregular in shape. The cytoplasm is abundant and contains numerous brown-coloured granules, which are stained as melanin-pigment. The nuclei are also irregular in size and shape, and many mitoses are seen. The metastases in the hypothalamus and the suprarenal glands have the same structure.

D: Metastases from malignant melanoma. Knut Høeg. (Sign.).

DISCUSSION

Retrospectively we can assume that the patient at first had metastases of the hypothalamus and/or the posterior lobe of the hypophysis in July 1954. We may assume from the anamnesis that the polyuria arising from that lesion, lasted only for a few weeks, since the anterior lobe was also affected by metastase. These did not give rise to pluriglandular insufficiency, but the excretion of 17-ketosteroids was distinctly reduced.

After cortisone treatment for ten days his diabetes insipidus once more became evident. Discontinuation of the cortisone treatment and reduction of
the dose reduced his symptoms of diabetes insipidus but gave rise to severe symptoms and signs of insufficiency of the suprarenal cortex, which made any further attempt to reduce the dose impossible.

This case supports the assumption that the effect of the anterior lobe of the hypophysis on the diuresis in diabetes insipidus (the hypothetical diuretic hormone from the anterior lobe), is caused by the influence of the hypophysis on the hormone production of the suprarenal and thyroid glands.

**SUMMARY**

The author describes a case of diabetes insipidus produced by metastases in the hypothalamus. The symptoms seemed to disappear as metastases destroyed the anterior lobe of the hypophysis, but returned during cortisone therapy. The data support the assumption that the effect of the anterior lobe of the hypophysis on the diuresis in diabetes insipidus is caused by the influence of the hypophysis on the hormone production of the suprarenal and thyroid glands.

**REFERENCES**