status continued to deteriorate, with ultimate death. The adrenal gland at autopsy showed focal areas of infiltration of lymphoid cells in the cortex and medulla, with degeneration of the cortical cells. This may explain our failure with the use of ACTH stimulation. Cortisone and/or adrenal cortical extract may have been the drugs of choice as substitution therapy for the diseased adrenal gland.

SUMMARY

A death resulting from phenylbutazone (Butazolidin) therapy is reported. The patient died from the toxic and possibly hypersensitive effects of the drug.

BIBLIOGRAPHY


PANHYPOPITUITARISM AND HYPOCALCEMIC TETANY IN A MALE: CASE PRESENTATION *

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Lesions of the anterior pituitary gland which prevent the elaboration of the pituitary trophic hormones (adrenocorticotropic, thyrotropic and the gonadotropins) will produce hypothyroidism, hypoadrenocorticalism and hypogonadism, the syndrome of severe panhypopituitarism. This syndrome is rare. Ninety-five confirmed cases of severe panhypopituitarism have been collected from the world literature by Sheehan and Summers. In his monograph on extreme insufficiency of the adenohypophysis, Farquharson listed 92 cases collected from the world literature, of which 57 cases presented the typical syndrome.

The following lesions of the pituitary gland have been reported as causes of panhypopituitarism: postpartum necrosis, tumors and cysts, trauma, "spon-

* Received for publication May 20, 1953.
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taneous atrophy and fibrosis and granulomatous lesions such as tuberculosis and syphilis. Only three of the 57 cases reported by Farquharson were caused by spontaneous atrophy and fibrosis of the gland. In view of the rarity of reports of severe panhypopituitarism caused by spontaneous atrophy and fibrosis of the gland, we thought it worth while to report the case of a male who presented the typical syndrome of panhypopituitarism, and in whom autopsy revealed atrophy and fibrosis of the pituitary gland.

CASE REPORT

A 57 year old white unemployed farmer was admitted in February 1949 to the Medical Service for study of the cause of a refractory anemia. He had been well until 1940, when he developed symptoms of prostatism for which a transurethral resection was performed. The operative procedure was tolerated well and was followed by a remission of symptoms. One year later he noticed loss of libido and potencia, decrease in body hair, decrease in appetite, weakness, easy fatigability and intolerance to cold. Between 1941 and 1948 there was a gradual weight loss of 28 pounds. In the fall of 1948 the patient was admitted to another hospital because of bouts of nausea and vomiting. Studies performed during that admission failed to reveal any abnormality except for a severe anemia. Between October and December of 1948 he was given 10 whole blood transfusions and liver extract for the anemia which, however, proved to be refractory.

Physical examination revealed a white male who appeared older than his stated age of 57 years. The patient was neither malnourished nor cachectic. The head hair was normal, but facial, axillary and pubic hair were scant. There were no abnormal eye signs, and the funduscopic examination was normal. Examination of the heart, lungs and abdomen revealed no abnormalities. The skin was dry and not unusually thick. There was no myxedema. Depigmentation of the skin characteristic of vitiligo was present; there was no pigmentation of the buccal mucosa or of the creases of the hands or axillae. The testes were smaller than normal. The neurologic examination was normal.

Various laboratory studies gave the following results: hemoglobin, 65 per cent; red blood cell count, 2,900,000; leucocyte count, 2,900, with 12 per cent eosinophils; platelet count, 98,000. Repeated urinalyses were normal. A specific gravity of 1.026 was reached during a urine concentration test. The values for blood urea nitrogen, urea clearance and phenolsulphophthalein excretion were within normal limits. Plasma proteins were 7.84 gm. per cent, with an albumin-globulin ratio of 2.7/1. The results of various liver function tests were within normal limits. Repeated stool examinations did not reveal any occult blood. Gastric analysis showed the presence of free hydrochloric acid. Roentgenographic studies of the chest, upper and lower gastrointestinal tracts and skull were normal, as were the oral and intravenous glucose tolerance tests. The basal metabolic rate was minus 35. Serum cholesterol was 231 mg. per 100 ml. of blood. Urinary gonadotropins as determined by the mouse uterine weight method were absent at a level of six mouse units per 24 hours. The urinary excretion of 17-ketosteroids determined by the method of Holter and Koch was 0.8 mg. per 24 hours. In the salt deprivation test of Cutler et al.4 the value for the urinary chlorides was 461 mg. per 100 ml. of urine. The eosinophil count prior to the injection of 0.5 mg. of epinephrine was 575 per cubic millimeter; four hours later it was 515 per cubic millimeter. Perimetric studies of the visual fields were normal.

During the patient's hospitalization the blood pressure varied between 90/60 and 110/70 mm. of Hg, except for the period of the adrenal crisis (see below), when the blood pressure was as low as 50/30 mm. of Hg. After the completion of the
studies, treatment with testosterone propionate, 75 mg. daily by intramuscular injection, was started. The response to treatment was excellent. Appetite improved, a weight gain of seven pounds occurred over a three week period, and the patient was stronger and more alert. At this time the salt deprivation test was repeated in order to determine if part of this improvement was caused by salt retention resulting from testosterone medication. On the second day of the test the patient developed a typical adrenal crisis. He responded to treatment with desoxycorticosterone acetate, adrenal cortical extract, saline and glucose. Although the pulse rate, blood pressure, urinary output and blood sugar had returned to normal, the patient's general condition was not as satisfactory as it had been prior to the adrenal crisis. Three days after the adrenal crisis the patient developed generalized convulsions and carpopedal spasms. At the time of the convulsions the serum calcium was 4.5 mg. per 100 ml., serum phosphorus was 4.1 mg. per 100 ml., and alkaline phosphatase was 3.7 Bodansky units. Convulsions subsided immediately following intravenous injection of calcium gluconate. In spite of continued oral treatment with calcium gluconate the latent tetany, as evidenced by positive Trouseau's and Chvostek's signs and by blood calcium of 7.7 mg. per 100 ml. persisted until death. The patient died suddenly and unexpectedly seven days after the adrenal crisis and four days after the onset of hypocalcemic tetany.

The positive findings at autopsy were limited to the endocrine glands. There was atrophy, but no fibrosis, of the testes, the thyroid gland and the adrenal glands. The parathyroid glands were not identified. The atrophic pituitary gland showed diffuse fibrosis with a moderate amount of lymphocytic infiltration, with the lymphocytes collected in small foci. The gross and histologic findings of the rest of the tissues were normal.

**DISCUSSION**

This patient presented the signs and symptoms of severe panhypopituitarism: loss of sexual function with atrophy of the testes, loss of body hair, decreased appetite, weight loss, weakness, intolerance to cold, low basal metabolic rate, lethargy, adrenal crisis following salt restriction, and a refractory anemia with eosinophilia. The clinical picture was that of a multiglandular deficiency, and the various laboratory studies confirmed the diagnosis. The low basal metabolic rate pointed to hypofunction of the thyroid gland. The hypofunction of the adrenal glands was reflected in the low 17-ketosteroid excretion, adrenal crisis and positive salt deprivation test. The unusually low 17-ketosteroid excretion also suggested testicular failure, since a part of the urinary 17-ketosteroids is derived from the testicular androgens. The low values of the urinary gonadotropins suggested that pituitary failure was responsible for the testicular atrophy.

A refractory anemia is a frequent occurrence in patients with panhypopituitarism. This anemia may be of such severity as to dominate the clinical picture, causing it to be attributed to the anemia rather than to pituitary deficiency; such was the case in our patient. The cause of the anemia in panhypopituitarism is not known. In patients with pituitary failure the anemia can be corrected in part by testosterone medication, but it is not influenced by thyroid substance. The anemia of hypophysectomized rats can be corrected by cobalt or by an unidentified pituitary factor.

Four days prior to death the patient developed hypocalcemic tetany. As far as we are aware, hypocalcemic tetany has not been described in cases of severe panhypopituitarism. In some cases of panhypopituitarism the parathy-
roid glands have been found to be small and the cellular elements reduced in numbers. These changes probably reflect the decrease in general body weight, rather than the absence of a pituitary factor controlling the function of the parathyroid glands. There is very little evidence to support the hypothesis that the pituitary gland produces a parathyrotrropic hormone. According to Sheehan and Summers, blood calcium levels in cases of panhypopituitarism are normal. Blood calcium values were normal in five other cases of panhypopituitarism observed by the present authors. Neither the cause nor the mechanism of the hypocalcemic tetany which occurred in this patient is known. Although the parathyroid glands were not identified at autopsy, these glands probably were present and functioning normally until a few days prior to death, since the patient had no symptoms suggestive of hypocalcemia until after the adrenal crisis.

The cause of the pituitary fibrosis found in our case is not known. There was no history and no evidence of preceding trauma, no granulomatous lesions, or history of severe blood loss and shock such as occurs in patients who develop postpartum necrosis of the pituitary gland. The histologic picture of the pituitary was that described as spontaneous atrophy and fibrosis.

SUMMARY

A case is presented of panhypopituitarism in a male resulting from spontaneous atrophy and fibrosis of the gland. In addition to the manifestations of hypofunction of the thyroid gland, the adrenal glands and testes, the patient developed hypocalcemic tetany. The cause of neither the pituitary fibrosis nor the hypocalcemia could be determined.

BIBLIOGRAPHY