SIMMONDS' DISEASE FOLLOWING CHRONIC SCLEROSING HYPOPHYTIS

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Summary. A case of Simmonds' disease following chronic sclerosing hypophytis is described in a moderately confused, 54-years-old woman in an extremely advanced cachexia. The patient died four days later in cardio-respiratory failure. The anterior lobe of the hypophysis showed dense, interlacing bands of fibrosis delineating small areas of atrophic pituitary cells. More than five-fifths of the anterior hypophyseal lobe was replaced by fibrosis or dense scarring. A scarce lymphocytic infiltrate between the fibrous bands was noted. The liver showed advanced fatty changes. An interesting finding was the presence of a chronic lymphocytic infiltrate in the adrenals. The association of chronic adenitis and sclerosing hypophytis could be interpreted as an autoimmune endocrinopathy.

Key words: Simmonds' disease, panhypopituitarism, chronic hypophysis, chronic adenitis, autoimmune endocrinopathy.

The failure of the whole anterior hypophyseal lobe is described as panhypopituitarism, or Simmonds' disease. The most common cause of panhypopituitarism is postpartum necrosis and its residual state. That is followed in frequency by tumors and cysts of the hypophysis. The inflammatory processes are very seldom responsible for Simmonds' disease. Purulent inflammation usually arises from inflammatory processes in the surroundings (meningitis, osteomyelitis of the sphenoid bone and thrombophlebitis of the cavernous sinus). Granulomatous inflammations such as tuberculoid giant cell granuloma, tuberculosi, syphilis, sarcoidosis and certain mycoses may lead to hypophyseal destruction as well. More recently, a diffuse non-purulent chronic pituitary inflammation reminiscent of an autoimmune process has been described as a possible cause of panhypopituitarism. We present herein a case of Simmonds' disease following a chronic sclerosing hypophysis.

CASE REPORT

S.C., 54-year-old female, was admitted to the 3rd Clinic of Internal Medicine on 29.1.1982. From the patient's history it resulted only that for several months she had been anorexic. The clinical examination revealed her to be moderately confused with a stiff neck, abdominal pain and tenderness, generalized moderate muscle hypertonus, cyanotic lips, dry-indurated skin and edema of the lower limbs. No significant symptoms originating in other systems were present. The laboratory data, X-ray examination and ECG were not relevant. The most striking feature was an extreme cachexia with almost complete disappearance of the adipose tissue. The clinical evolution declined rapidly, the patient lapsed into a deep, irreversible coma and died 4 days later in cardio-respiratory failure. The final
clinical diagnosis was: hypophysary cachexia, cardiopulmonary failure. The neurological symptoms also suggested an anorexia nervosa which was soon excluded, as this disease is a disorder appearing usually in a previously healthy adolescent girl which becomes emaciated as a result of voluntary starvation.

Pathological diagnosis: extreme cachexia, bilateral bronchopneumonia, pulmonary sclero-emphysema, fatty liver, renal arteriolosclerosis, low grade atherosclerosis.

Microscopic picture. The most important lesions were found in the anterior lobe of the hypophysis, consisting of dense, interlacing bands of fibrosis of variable width, delineating small areas of atrophic pituitary cells (Fig. 1). In other regions we noted an almost complete absence of hypophysal tissue, replaced by dense scarring (Figs 2 a, b), thus resembling true "hypophysal cirrhosis". A small inflammatory infiltrate of lymphocytes and histiocytes with a ribbon-like distribution between the fibrous bands was found (Fig. 3 a). Much of the outflow tract especially its smaller radicles was obliterated by extensive fibrosis. Small calcified areas were also present (Fig. 3 b). The posterior hypophysis was intact but surrounded by a dense rim of collagenous tissue (Fig. 3 c).

The thyroid gland showed follicles of variable size filled with a dense colloid, delineated by a flat nonfunctional cuboid epithelium. The capillary network separated by bands of sclerosis was reduced. Both adrenals were atrophied, with narrowed cortices especially with partial disappearance of the glomerular zone (Fig. 4). Inflammatory lymphocytic infiltrates of unequal extension were distributed among cortical cells (Fig. 5). The endometrium was thin and inactive. The myometrium showed fibromatous changes with frequent thickwalled blood vessels. In the ovaries a somewhat thicker corticalis and frequent corpora albicantia were present. An important lesion was the fatty liver: hepatic cells were filled with coalescent lipid vacuoles, sometimes resembling adipose cells (Fig. 6). We also noted bronchopneumoniaal lesions with leucocytic alveolitis. No other relevant lesions were found.

DISCUSSION

Panhypopituitarism occurs with a low incidence. Sheehan and Davis (1968) estimate an incidence of 100 cases of the most common variant of the disease, namely postpartum pituitary necrosis in 1 to one million women. They found hypopituitarism in 8% of the patients with mild blood loss during delivery and in 53% of patients with severe hemorrhage. The first cases described by Simmonds in 1914 were due to septic necroses (Simmonds, 1914 a), postpartum necroses (Simmonds, 1914 b) and also to tuberculous hypophysitis (Simmonds, 1914 c). The postpartum pituitary necrosis is caused by vascular spasms and also by thrombosis. It should be noted, however, that necroses of the anterior pituitary lobe without endocrine symptoms can occur in almost 10% during the systemic pathoanatomical examination of postmortem cases (Plaut, 1952). Sometimes only scars are detectable and their cause can no longer be found. Inflammatory processes are, in contrast, relatively seldom respon-
pneumonic failure.

Sheehan and Davis reported the most common variant of postpartum hypophysitis to occur in 1 to 5 cases. The condition is characterized by severe hemorrhage, consolidation of the terminal pituitary lobe, and partial destruction of the posterior pituitary lobe.

Fig. 1. — Chronic sclerosing hypophysitis with bands of dense fibrosis and small areas of atrophic pituitary cells (×50). Fig. 2 a. — Chronic hypophysitis with dense fibrosis (×250).

Fig. 2 b. — Dense scarring with atrophy of pituitary cells (×250). Fig. 3 a. — Chronic hypophysitis with scanty inflammatory and lymphocytic infiltration (×450).

Fig. 3 b. — Calcium deposition surrounded by bands of fibrosis (HE × 450). Fig. 3 c. — Posterior hypophyseal lobe without lesions, surrounded by a rim of dense fibrosis (×250).
Fig. 4. — Atrophied adrenal cortex with almost complete disappearance of the glomerular zone (× 150).

Fig. 5. — Chronic lymphocytic adrenalitis. (HE × 250).

Fig. 6. — Fatty liver with advanced dystrophic lesions (HE × 250).
sible for pituitary insufficiency. A case of Simmonds' disease following polyarteritis nodosa with hypophyseal involvement was described by Tasca and Petraiani in 1968. More recently, diffuse nonpurulent chronic inflammation of the anterior hypophyseal lobe has been described (Egloff and Fischbacher, 1969; Lack, 1975); Goudie and Pinkerton (1962) and Hume and Roberts (1967) have seen lymphocytic hypophysitis in a female patient with Hashimoto's thyroiditis. Lack (1975) noted the association of lymphocytic hypophysitis and lymphocytic parathyroiditis.

In our case we consider that sclerosis is the consequence of a slow-growing inflammatory process, because on the one side no sign of necrosis could be found, and on the other side, some residual inflammatory elements still persisted. The sclerosing process was very extensive, approx. four-fifths of the hypophysis being replaced by fibrosis. It is very difficult to ascertain the beginning of the disease, having in view that sometimes months or even years may elapse between the onset of pituitary inflammation or necrosis and the clinical appearance of hypopituitarism (Labhart, 1978). The impairment of consciousness leading finally to coma could be correlated with the psychosyndrome which, as known, is often present during the failure of the adrenohypophysis and may progress to paranoid hallucinations, delirium and coma. It seems probably that in the thanatogenesis of our case an important role was played by the hepatic failure due to the fatty liver. The fatty liver could be explained by the long period of lack of appetite when adipose tissue fats are mobilized and more fatty acids are brought to the liver, where they are synthesized into triglycerides. Moreover, starvation produces a decreased apoprotein synthesis which is necessary for the conversion of triglycerides to lipoproteins, the only form in which lipids are excreted from the liver (Alberti, 1972; Rotschild, 1972).

An interesting finding was the presence of the lymphocytic infiltrate in the adrenals, which constitutes the substrate of the immune adrenitis or primary cytotoxic nontuberculous atrophy of the adrenal cortex. The association of immune adrenitis and chronic sclerosing hypophysitis could be interpreted as an autoimmune endocrinopathy (Heitz and Steiner, 1981).

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