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## Abstract

A case of postpartum necrosis of the anterior lobe of the pituitary, known as Sheehan's syndrome, is presented. The patient has done well on a combined replacement therapy with cortisone and thyroid. It is hoped that increased awareness will be given to this clinical entity.

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## **SHEEHAN'S SYNDROME (POSTPARTUM HYPOPITUITARISM), REPORT OF A CASE**

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Simmonds' disease<sup>1</sup> follows the destruction of the anterior lobe of the pituitary gland. The underlying pathological lesions may be caused by postpartum hemorrhage<sup>2</sup>, tumors<sup>3</sup>, head injuries<sup>4</sup>, vascular disturbances, or surgical hypophysectomy. An obstetric difficulty complicated by excessive hemorrhage and collapse often results in Simmonds' disease. In 1937 SHEEHAN, in a series of brilliant papers<sup>5-8</sup>, clarified the causative relationship between the ischemic necrosis of the anterior pituitary and postpartum hemorrhage. As a tribute to his work, this type of Simmonds' disease has been called Sheehan's syndrome. The patient described below appears to be a typical case of the Sheehan's syndrome. The present paper is being presented, because of the rarity of reported cases of this syndrome in Japan.

### **CASE REPORT**

A 35-year-old housewife was admitted to the hospital on August 31, 1961, because of pallor and easy fatigability. In April 1959 she had her fourth delivery that was complicated by severe hemorrhage due to delayed separation of the placenta and went into profound shock. For the next half a year she remained bedfast because of generalized weakness, headache and tinnitus. Since she became able to be up and around, she slowly exhibited signs and symptoms of myxedema and anemia. She became intolerant to cold, and physically and mentally inactive. She had falling out of the scalp hair and gradually lost the pubic hair. Following delivery she failed to lactate and had amenorrhea, loss of libido and atrophy of the breasts. At one time she developed swelling of the left knee and a diagnosis of rheumatoid arthritis was made. Before she came to our hospital, she was seen by the practicing physicians who treated her with vitamin and iron tablets to no avail.

Family history was unremarkable except for her twin, second and third children.

Past history revealed that her menarche was at the age of 14, and she

married at the age of 24. Seven years previously she had a vague history of nephrolithiasis on the left. In the past she had undergone artificial abortions six times.

Physical examination on admission revealed a slow and soft speaking woman in no distress (Fig. 1). The temperature was 36.1°C., the pulse 88, and the

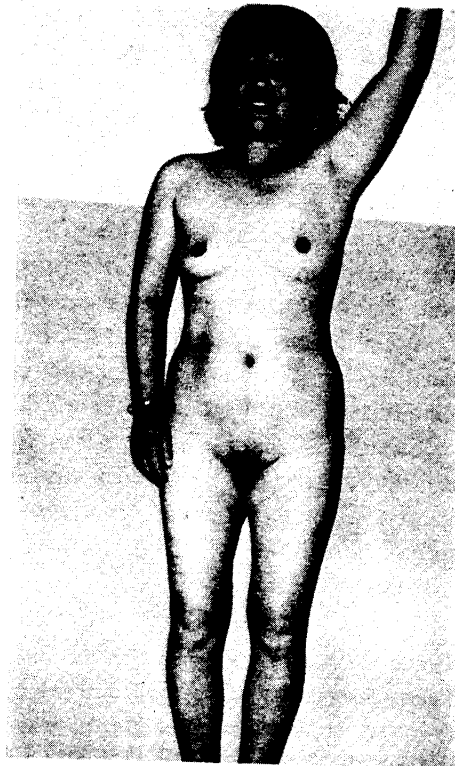


Fig. 1. Picture of patient with Sheehan's syndrome. Note the puffy face and almost complete absence of the axillary and pubic hair.

blood pressure 110 systolic, 76 diastolic. She was moderately well nourished and there was no sign of cachexia. There was puffiness of the face. The skin was dry, pale, coarse and cold. There was no abnormal skin pigmentation. The thyroid was not palpable. The heart and lungs were normal to percussion and auscultation. The abdomen was not remarkable. The palpebral conjunctiva was slightly anemic. The pupils were normal and reacted promptly to light and accommodation. The tongue was normal. The head hair was brittle. There was thinning of the lateral margins of the eyebrows. The axillary and pubic hair was almost absent. The breasts were atrophic. The tendon reflexes of the lower extremities were bilaterally hypoactive, but there were no sensory or

motor disturbances. Pelvic examination revealed atrophic vaginal mucosa and a small uterus.

Urinalysis was normal. A stool specimen was negative for occult blood and parasitic ova. The erythrocyte sedimentation rate was 51 mm. per hour. Serology for syphilis was negative. Examination of the blood showed a hemoglobin of 80 % (Sahli), a red-cell count of 3,570,000, and a white-cell count of 3,800, with 7 % band forms, 35 % segmented neutrophils, 52 % lymphocytes, 5 % monocytes and 1 % basophils. The platelet count was 275,000 and the reticulocyte count 1.1 %. The cholesterol was 278 mg., the fasting blood sugar 87 mg., the non-protein nitrogen 27 mg. per 100 ml. The sodium was 142.5 milliequiv., the potassium 3.45 milliequiv., and the chloride 104.5 milliequiv. per liter. The serum iron was 63 microgm., and copper 141 microgm. per 100 ml. Bromsulfalein retention was 13 % in 45 minutes. Other liver function tests were normal. The total serum protein was 7.0 g., with the albumin 45.7 % and the globulin 54.3 %, per 100 ml. Gastric juice analysis revealed hypoacidity. Insulin sensitivity test showed a moderate hypoglycemic response. Urinary 17-ketosteroid excretion was 0.9 mg., and 17-hydroxysteroid 3.2 mg. per 24 hours. A Thorn test caused no decrease of the circulating eosinophils. A Robinson-Kepler-Power water test gave a positive result with the quotient 'A' equal to 5.7. The basal metabolic rate was -37 %. The protein-bound iodine was 4.5 microgm. per 100 ml. Urinary estrogen excretion was 8.2 microgm. per 24 hours. An

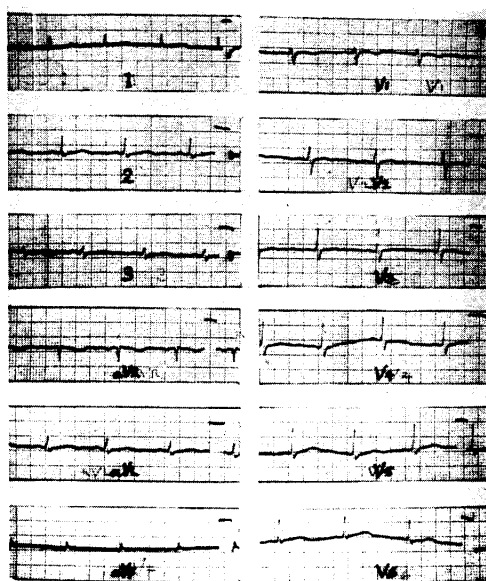


Fig. 2. EKG showing low voltage and flattened T waves in all 12 leads.

electrocardiogram demonstrated low voltage and flattened T waves in all 12 leads (Fig. 2). An X-ray film of the chest was normal. X-ray films of the skull showed no abnormalities of the sella turcica.

On the basis of her clinical history that dates back to her last delivery, the characteristic physical findings and the abnormal endocrine laboratory tests, a diagnosis of Sheehan's syndrome was considered most likely. She was then started on 2 mg. of dexamethasone initially and the drug was gradually decreased to the maintenance dose of 0.5 mg. daily. One week later, 0.1 gm. of thyroid was added to the steroid hormone. With this combined therapy, there were increase of her urinary output, elevation of her temperature and blood pressure, and improvement of her appetite. Prior to the therapy, her temperature and blood pressure tended to be subnormal. She appeared animated again and became active in speech and thought. One month later, there was a return of the pubic hair.

Dexamethasone was replaced with cortisone in the maintenance dose of 25 mg. daily because of the latter's superior carbohydrate-regulating effect. At one time, 10 units of ACTH-Z was administered together with cortisone for about 10 days. But because of urticaria she developed during the ACTH-Z therapy, the drug was discontinued. Gynecological work-up revealed severe gonadal insufficiency that failed to respond to the administration of 1,000 units of human chorionic gonadotropine for 6 days followed by 1,000 units of pregnant mare serum for 6 days. Despite atrophic endometrium, she once had a menstruation-like bleeding by the successive use of estrogen and progesterone. She was discharged on September 15, 1961 to be followed in the outpatient clinic.

#### DISCUSSION

SHEEHAN<sup>8</sup>, on the basis of many histologic observations, concluded that obstetric hemorrhage and collapse drastically cut down the amount of blood that circulates into the anterior pituitary, leading to the stasis and thrombus formation in the sinusoids of the anterior lobe of the pituitary. This sequence of events results in the ischemic necrosis of the anterior pituitary cells, and the severity of the hemorrhage determines the degree of cellular involvement, and consequently the clinical course of the patient. Since traumatic bodily hemorrhage and shock resulting in the ischemic necrosis of the anterior pituitary in either sex must be extremely rare, some other factors such as vulnerability of the hypertrophied pituitary to the decreased blood flow and increased coagulability of blood during parturition may be operating in the development of the Sheehan's syndrome.

European and American literatures are replete with case reports of the Sheehan's syndrome<sup>1, 5, 6, 8, 9-12, 16</sup>, but not many cases have been reported in the Japanese literature<sup>13-15</sup>. Indeed the lack of awareness of this condition might be

in part responsible for a small figure of the reported cases in this country.

As a matter of fact, Sheehan's syndrome is not so uncommon as has been generally believed. But in the early stage of the disease or in an atypical case, it is not always easy to make a correct diagnosis. Therefore, it is highly probable that many patients having the Sheehan's syndrome are treated by physicians as primary myxedema, Addison's disease, unexplained anemia, neurosis or anorexia nervosa.

Anorexia and cachexia erroneously associated with Simmonds' disease are seen uncommonly in the Sheehan's syndrome<sup>7</sup> and may be more pronounced in anorexia nervosa. Reference may be made to Escamilla's extensive review concerning differential diagnosis between Simmonds' disease and anorexia nervosa<sup>16</sup>. In Addison's disease there is a striking pigmentation in contrast to the Sheehan's syndrome.

As a sequel to anterior pituitary insufficiency, sexual atrophy is usually early and absolute<sup>11</sup>. While clinical evidence of thyroid and adrenocortical failure manifests itself slowly and partially. Our case reported herein appears to be no exception to this rule.

When endogenous adrenocorticotrophic hormone becomes deficient, of three representative adrenocortical hormones, 'N' hormone is the first to become deficient, followed by 'S' hormone. It is generally believed that salt-regulating hormone is not under the direct influence of the adrenocorticotrophic hormone<sup>17</sup>.

Since the pituitary lesion is irreversible, efforts should be made to restore as much functions of the target endocrine organs. At present, there is no pituitary extract that can completely substitute the anterior pituitary. Tropic hormones may be used effectively when the target organs are still in the state of responsiveness to the tropic stimulation. However, by the time the patient with hypopituitarism seeks medical help, the endocrine organs would have undergone considerable atrophy to the point where the effects of tropic stimulation are unpredictable. WHITTAKER *et al*<sup>19</sup>. reported advantageous use of ACTH, but the effect of ACTH does not usually last long after its withdrawal. In addition, a long-term use of ACTH may provoke allergic manifestations as in our case in which urticaria developed following its administration. It is for these reasons that replacement therapy is the treatment of choice in most of the patients. Cortisone is the ideal carbohydrate-regulating hormone for replacement and can be given in small dosages of 25 mg. daily by tablet<sup>18</sup>. Our patient is doing well on half a tablet of cortisone plus supplemental thyroid medication. It is dangerous to administer thyroid alone, because the drug would augment metabolic activity despite the associated adrenocortical insufficiency, precipitating the development of the Addisonian crisis<sup>3,20</sup>.

Many designations used in the earlier literatures such as 'pluriglandular in-

sufficiency,<sup>21</sup> 'multiple ductless glandular sclerosis,'<sup>22</sup> 'hypophysäre Magersucht,'<sup>23</sup> and 'cachexia hypophyseopriva'<sup>24</sup> are in all likelihood synonymous to Simmonds' disease.

#### SUMMARY

A case of postpartum necrosis of the anterior lobe of the pituitary, known as Sheehan's syndrome, is presented. The patient has done well on a combined replacement therapy with cortisone and thyroid. It is hoped that increased awareness will be given to this clinical entity.

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