SIMMONDS' DISEASE

by

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Simmonds' disease is characterised by partial or complete destruction of the anterior pituitary lobe leading to failure of gonadal, thyroid and adrenocortical functions. It can occur at any age, varying from 20-60 years, and is twice as common in women as in men.

Amongst the various aetiological factors, the commonest cause is ischaemic necrosis due to severe postpartum haemorrhage or shock after childbirth. This peculiar reaction to haemorrhage and shock is hardly ever seen except in parturient women. The risk of injury depends on the speed with which blood is replaced. Nevertheless, even in those countries where maternity services are well developed, 4% of all women who lose more than 800 cc of blood during childbirth develop this syndrome. If the blood loss is severe and the condition untreated, it is said that 50% will develop ischaemic necrosis. This means that in a population of 1 million, there are 100-200 cases of Simmonds' disease. Yet many affected women are not discovered because the apathy which characterises the disease prevents them from taking medical advice. Patients may take 2-7 years before seeking medical advice.

As one expects, the incidence is more in our country where ignorance, poverty, superstition, long distances and lack of sufficient well-equipped hospitals play a great part. It is easy for one to miss the diagnosis if we are not on the look out for such cases; at the same time, the diagnosis should be easy, as the patient presents typical symptoms and signs at the time of seeking medical advice. The treatment is encouraging. The following case illustrates these points.

Case Report

Mrs. V., aged 25 years, attended the gynaecological outpatient department on 19th September, 1968, for increasing debility, loss of appetite and amenorrhoea of 2 years' duration. Menarche was at 14th year and her periods were regular till 5 years ago. She had been married for 9 years and had had 2 deliveries. The first was a normal delivery at term 7 years ago and the child is alive and well. The second delivery was by caesarean section elsewhere for placenta praevia, 5 years ago. A stillborn foetus was delivered and the patient had severe haemorrhage during the operation. No blood transfusion was given. Her periods started 1 year after the last childbirth and they were irregular for the first 2 years, occurring once in 3 months. She had complete amenorrhoea for the past 2 years. Apart from this, there was nothing relevant in her past history.

She was a small thin-built individual, weighing 88 pounds, and slightly anaemic.

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Her speech was slow, but there was no hoarseness or slurring. Abdominal examination was normal. She had scanty eyebrows and no axillary or pubic hair. Blood pressure was 90/70 mm. Hg. and pulse was normal, but of low volume; cardiovascular, respiratory and alimentary systems were normal. Bimanual examination revealed atrophy of the external genitalia, and the uterus was smaller than normal. The fornices were clear and the cervix healthy. Length of the uterine cavity was 2½". A diagnosis of Simmonds' disease was made.

The patient was advised admission, but came a month later (17-10-68).

The following investigations were done:

1. Hb. — 10.6 gms%.
2. Serum cholesterol — 190 mgs%.
3. B.M.R. — Minus 10%.
4. Glucose tolerance test — Flat curve (Values 65, 80, 80, 55, 55 mgs% of sugar).
5. Serum electrolytes—S. Na 136 me/1 K-4.6 me/1, Cl_2 102 me/1.
6. 17-ketosteroids in 24 hours 3.2 mgm% (Pre-ACTH), urine.
7. 17-ketosteroids in 24 hours 6.9 mgm% (Post-ACTH), urine.
8. 17-ketogenic steroids — 1.8 mgm% (Pre-ACTH), 17-ketogenic steroids — 1.7 mgm% (Post-ACTH).
9. Urine and stool examination were normal.
10. Exfoliative cytology showed slight oestrogen and progesterone effect.
11. Endometrial biopsy done during her first visit to the outpatient department was reported as inadequate and was repeated again after a course of treatment with stilboestrol. The report was endometrium in the oestrogen phase.

Treatment

She was prescribed cortisone acetate 12.5 mg once a day for one month and Thyroxin 0.1 mg twice a day for one month. It was decided to give her cyclical hormonal therapy with stilboestrol for a period of 3-6 months. She has had 4 courses so far and each time it was followed by withdrawal bleeding. Follow-up studies show that the patient feels much better after the therapy was started.

Discussion

The disease has an insidious onset. In the fully developed syndrome, seen when 95% of the pituitary is destroyed, all functions such as gonadotrophic, thyrotrophic and corticotrophic are impaired. The symptoms seem to follow a definite order. Symptoms of gonadal failure appear first, followed by symptoms of hypothyroidism and lastly those of adrenal failure. The symptoms are weakness, amenorrhoea, failure of lactation, loss of libido, loss of axillary and pubic hair, puffiness of face, dry skin and sensitiveness to cold, apathy, bradycardia, slurred speech, loss of axillary sweating and mental changes. Clinical evidence of adrenal failure is not usually marked. Pigmentation of Addison's disease is absent. These patients are very liable to get infection and are unable to stand physical and mental strain. There is usually no loss of weight in these patients. Skin is wrinkled and pale with a yellow tint. The pallor is a striking feature and is partly due to lack of the pituitary erythropoietic factor. Normochromic anaemia may also be present. Because of adrenal failure water concentration by the kidneys is poor. Insulin tolerance is reduced. Coma, which is very common in these patients, may be due to hypothermia, hypoglycaemia, hypothyroidism and due to water intoxication. Stress, strain, infection and surgery might also precipitate coma. All genital organs show an extreme degree of atrophy.

Diagnosis

When one or more target glands are affected together with a history of post-partum haemorrhage, amenorrhoea, weakness, failure of lactation, loss of axillary and pubic hair, all dating from the last delivery, and with the findings of extreme genital atrophy, low pulse pressure, low B.M.R. a flat glucose tolerance curve, low 17-ketogenic and 17-ketosteroid excretion, absence of oestrogen in Papanicolaou smear, and a low urinary excretion of pituitary gonadotrophins (F.H.S. and L.H.), the diagnosis is obvious. One should be careful in doing water load tests and insulin tolerance tests as these tests may precipitate coma. The low urinary 17-ketogenic steroid excretion will show a little increase with Metapirone administration, but normal increase with ACTH. Similarly, the low basal Iodine^{131} uptake values will show an increase with TSH administration.

An analyses of 8 cases of Simmonds' disease revealed the following facts. All of them gave a history of post-partum haemorrhage, 6 had vaginal delivery and 2 had caesarean section. All complained of extreme debility and amenorrhoea dating from the last delivery. Failure of lactation was present in 6, loss of weight in 5, gain in weight in 2, hoarseness of voice in 2, intolerance to cold in one, loss of sweating in one. Extreme genital atrophy was present in 6 cases, sallow complexion in 6, low pulse pressure in 7, dry skin in two, and associated T.B. in 2 cases. Flat G.T.T. curve was obtained in six, low B.M.R. (varying from minus 15 to minus 38) in six and low 17-ketosteroids in 5 cases.

Treatment

Treatment is mainly substitutional. Cortisone by mouth, 12.5 mg three times a day, and thyroid extract, ½-1 gr. once a day are given. Thyroxin can also be given instead of thyroid extract, starting with 0.1 mg once a day and to be increased every 2 weeks till a maximum dose of 0.3 mg once a day is given. Thyroid treatment eliminates fluid from tissues and may produce dehydration which in turn might precipitate adrenocortical crisis (Addisonian).

The treatment of coma depends on the cause. Intravenous hydrocortisone, 100 mg., is given stat and should be repeated 8 hourly, and 50% glucose is given. One should be careful not to overload the heart. The patient should be kept warm. Surgery in these patients might precipitate coma, which should be prevented by cortisone therapy. Treatment of amenorrhoea is difficult. Theoretically, pituitary gonadotrophins, like FSH and LH hormones, are indicated. Pituitary hormones are not available; they are expensive and their prolonged use might produce antibodies and diminish the response of the target organs. Amenorrhoea does not usually respond to ovarian hormones. Androgens are tried in some cases with varying results. Because of the danger of virilizing symptoms with androgens, non-virilizing, protein anabolic androgens like Durabolin, 25 mg, given intramuscularly once a week, are recommended.

As the case presented had with-

drawal bleeding following stilboestrol therapy, it is reasonable to presume that part of the anterior lobe of the pituitary was functioning.

The prognosis is fairly good if the patient takes the treatment regularly. In untreated cases, death can occur due to intercurrent infection or coma. Sterility is permanent.

Summary and Conclusions

1. Among the various aetiological factors in Simmonds' disease, the chief one is ischaemic necrosis following post-partum haemorrhage.

2. The symptoms of gonadal failure usually appear first, followed by symptoms of thyroid failure and lastly those of adrenocortical failure.

3. Because of extreme apathy, patients do not seek medical advice early. And because apathy is a common symptom of many diseases, the diagnosis is often missed.

4. Prognosis is good if treatment is taken regularly. Otherwise, death will occur due to bronchopneumonia or coma.