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HYPOPITUITARISM (SHEEHAN'S SYNDROME) FOLLOWING MASSIVE POSTPARTUM HAEMORRHAGE WITH AFIBRINOGENAEMIA

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The occurrence of pituitary necrosis is the most dreaded long-term after-effect following a delivery complicated by severe postpartum haemorrhage and collapse.

This case is reported because of the infrequent recording of Sheehan's syndrome following afibrinogenaemia, and because recent interesting observations on the aetiology of afibrinogenaemia after abruptio placentae[1] have a bearing on the aetiology of subsequent postpartum pituitary necrosis. Gold and Librach[2] (1957) first described a patient who developed panhypopituitarism after massive haemorrhage owing to hypofibrinogenaemia. She developed evidence of thyroid, adrenal and ovarian insufficiency. The authors considered this a case of amniotic fluid embolism, but this was not proved. Beischer[3] reported 2 cases of hypofibrinogenaemia; one was thought to have resulted from accidental haemorrhage, and she died 10 days after caesarean section. At autopsy anterior pituitary necrosis was almost complete and intra-arterial fibrin emboli were seen in pituitary vessels. Glatthaar[4] had a patient with uteroplacental apoplexy and afibrinogenaemia who died 19 days later of extensive renal cortical necrosis. Several small areas of anterior pituitary necrosis were present. Dingman *et al.*[44] reported symptoms and signs of pituitary deficiency in a patient whose delivery was complicated by afibrinogenaemia and acute renal failure.

Sheehan[5] has not had a case where he has identified afibrinogenaemia and also seen a pituitary necrosis.

Beischer[45] traced 32 out of 34 patients treated for hypofibrinogenaemia, and 5 of these had clinical evidence of hypopituitarism. He also found 3 cases of hypopituitarism in 115 patients examined, out of 165, who had 3 or more pints of blood transfused at the time of delivery, but none of these had coagulation failure.

INCIDENCE OF HYPOPITUITARISM

The incidence of clinical cases of severe chronic hypopituitarism was given as 1:2,500 in adult women by Sheehan,[6] but he expected the total number to increase after the advent of antibiotics, since these would diminish the number of puerperal deaths and therefore the number of pituitary necroses found at autopsy. Hall,[7] in a follow-up of all patients attended by the Radcliffe Infirmary Flying Squad for collapse from haemorrhage between the years 1944 and 1955, inclusive, found the incidence of hypopituitarism to be about 3·6%. The conclusions on incidence by Hornabrook and Caughey[8] were based on clinical evaluation only and they could trace less than half the number of patients who had suffered from severe postpartum haemorrhage during the period under review.

The 35 cases of Schneeberg *et al.*[9] were not a random sample; the incidence of hypopituitarism among them is therefore not valid for cases of postpartum haemorrhage and shock generally. It has been shown that the belief that hypopituitarism is very rare is probably due to the fact that most cases remain undiagnosed.[10] The patient does not bother to seek medical care and will not discuss her symptoms. If, after a few years, following a minor illness, she lapses into coma and recovers after treatment, hypopituitarism may be diagnosed, provided there is no misconception that these patients must have cachexia and progeria.

CASE REPORT

The patient, Mrs. I.R., a Coloured female, para 7, was admitted as an emergency to the Peninsula Maternity Hospital on 25 October 1960, with an antepartum haemorrhage. She had attended an outside clinic on the morning of 25 October, and an external cephalic version was performed. On rising from the couch she complained of pain on the right side of the abdomen. This occurred intermittently after she had left the clinic. The pain was more severe at home, and shortly afterwards vaginal bleeding commenced. The Flying Squad was summoned and, on arrival, the patient was found to be shocked with a blood pressure of 70/30 mm.Hg. The foetal heart was not audible. Two pints of blood were given and she was transferred to hospital. On admission she was pale, her pulse was 88 and regular. The blood pressure had risen to 140/90 mm.Hg, heart sounds were normal and the chest was clear. On abdominal examination the uterus was at term; it was rigid and foetal parts could not be felt. There were no foetal movements and the foetal heart could not be heard. The girth was 39½ inches.

Urine examination: Albumin +++. She was receiving the third pint of blood. The diagnosis was accidental haemorrhage. A specimen of venous blood taken on admission at 5 p.m. showed a clotting time of 7 minutes.

Artificial rupture of the membranes was performed with the cervix 2 fingers dilated and thick. At 11.15 p.m. there was a spontaneous vertex delivery of a stillborn infant. Intravenous ergometrine was given with the delivery of the shoulder. The placenta was expelled complete and there was a 12-oz. retroplacental clot. After the third stage there was marked bleeding and the uterus was not well contracted. Ergometrine, 0·5 mg., was repeated intravenously and 20 units of pitocin was given. The blood pressure and pulse were now not recordable in spite of 3 pints of blood having been given to date. Two transfusions were set up: 10 ml. of calcium gluconate was given and the administration of pitocin repeated. The patient was pale and sweating. There was a steady loss *per vaginam* and it was observed that the blood did not clot.

Blood was now pumped in and 2 G of fibrinogen was given intravenously. Calcium gluconate and ergometrine were repeated and 30 mg. of methedrine was given intravenously. Pitocin was inserted in the infusion. The uterus was now well contracted, but at 2 a.m. the patient was still pulseless and the blood pressure could not be recorded. No cause was found for the persistent bleeding — a small cervical tear was present, but did not require a suture. The uterus was packed without using an anaesthetic. Omnopon, methedrine and intravenous solucortef, 100 mg., were given. Hysterectomy was contemplated, but it was later decided not to do it. At 3.30 a.m. the first pulse was noticed and the blood pressure recorded again.

The total estimated postpartum blood loss was 16 pints + 12 oz. retroplacental clot. The total amount of blood transfused before and after delivery was 20 pints.

The patient's condition improved and in the puerperium the Hb. rose from 8 to 11 G/100 ml. The urinary output was satisfactory. Antibiotics were given for a staphylococcal and *E.coli* genital infection. There was no record of any oestrogens given to suppress lactation. The patient says she did not have a 'drop of milk' after the confinement. She was discharged on 6 November 1960.

On 14 November 1960 she was admitted to Groote Schuur Hospital after a secondary postpartum haemorrhage of 2-3 pints. On examination she was shocked, pale and cyanosed. Her blood pressure was 40 mm.Hg, systolic. Hb. 9 G/100 ml. Four pints of Group O Rh negative blood were given. On 19 November 1960 the Hb. was 10 G/100 ml. and 2 pints of packed cells were given. On admission her temperature was 103°F. Intravenous terramycin infusion was given and later erythromycin. She was discharged on 28 November 1960 and given a date to come in for a hysterectomy, but she did not return.

Present Admission

She was admitted to Groote Schuur Hospital on 5 September 1963 for investigation, having been seen by me at the gynaecological outpatients department. Her chief complaint was amenorrhoea since her last confinement. Following delivery she had also noted total absence of lactation and a feeling of coldness and tiredness. She received tablets from her own doctor, after which the 'cold' feeling decreased (?thyroid tabs.). Her pubic hair failed to regrow and all axillary hair was lost. There was decreased sweating since delivery. Loss of appetite and therefore some loss of weight had occurred. On questioning, she stated that loss of libido had persisted since the confinement and she had not had intercourse during the last year. She was able to carry on with housework, though not as vigorously as before. She was not keen to visit people. There was no history of fainting, hot flushes or a change in her voice.

Obstetric history. Para 8. Seven were normal vertex deliveries, all breast-fed. Menses returned 6-9 months after each confinement. The eighth confinement has been described above.

Menstrual history. Before the last pregnancy her cycle was 3/28 day, regular, with a moderate flow.

Frequency of micturition was present, but no dysuria. Her previous history and family history were negative.

On examination the patient was a thin, tired-looking female with a waxy pallor of the skin over the cheeks and forehead. Her skin was dry to the feel, but fairly smooth and soft, there was some loss of the outer third of both eyebrows and from the right parietal area of the scalp, head hair was thin and wispy, and there was a complete absence of axillary hair (Fig. 1). There was no sweating in the axilla, and there were only a few scanty hairs on the pubes and adjoining labia majora.

The mucosae were well-coloured. There was no oedema or adenopathy and the thyroid felt normal. The breasts appeared slightly atrophied, while the areolae showed some loss of pigmentation. Voice normal. Weight 105 lb. Temperature on admission 96·8°F; this never rose above 98·4°F.

Her pulse varied between 55 and 75 beats per minute in hospital and the rhythm was regular. Blood pressure 140/90 mm.Hg. Auscultation of the heart and lung fields revealed no abnormality. Abdominal examination negative.

Vaginal examination showed a marked shrinking of the vulva and vagina. The vagina was 'senile', with reddening around the urethral meatus. The cervix was atrophied and flush with the vaginal vault, while the uterus was small, anteverted and mobile, and the adnexae were not palpable.

Ward urine examination: Nil abnormal.

Special Investigations

Papanicolaou smear report: 'Almost completely atrophic—very little oestrogen effect.'

Blood Count: Hb. 13·0 G/100 ml., PCV 40%, MCHC 36%, WBC 8,760, and platelets 284,000. Smear normal.

Berger negative. Wassermann reaction negative.

Serum electrolytes: Sodium 138m.Eq., potassium 4·9m.Eq., chloride 104m.Eq., blood urea 34mg/100ml.

Serum cholesterol: 232mg/100ml.

24-hour steroid excretion tests were as follows:

	17 Ketosteroids	*17 Hydroxycorticosteroids*
Basic values	3·9 mg./24 hrs.	9·1 mg./24 hrs.
After ACTH (40 units)	5·1 mg./24 hrs.	21·4 mg./24 hrs.
Control, 24 hours after ACTH	5·4 mg./24 hrs.	10·9 mg./24 hrs.
Control, 48 hours after ACTH	7·6 mg./24 hrs.	15·8 mg./24 hrs.
On metopirone tablets	2·1 mg./24 hrs.	13·5 mg./24 hrs.
Control after metopirone	4·3 mg./24 hrs.	13·0 mg./24 hrs.

Follicle stimulating hormone: 24 mouse units/24 hrs.

After the first dose of metopirone (750 mg.) the patient felt tired and 'lame'. Following the next dose at 12 p.m. she felt 'as if she were in a trance' and refused food. On examination her pulse and blood pressure were normal. Her symptoms improved after bed rest. The successive 4-hourly doses of metopirone were thereafter reduced to 500 mg. per dose. There was no further untoward reaction.

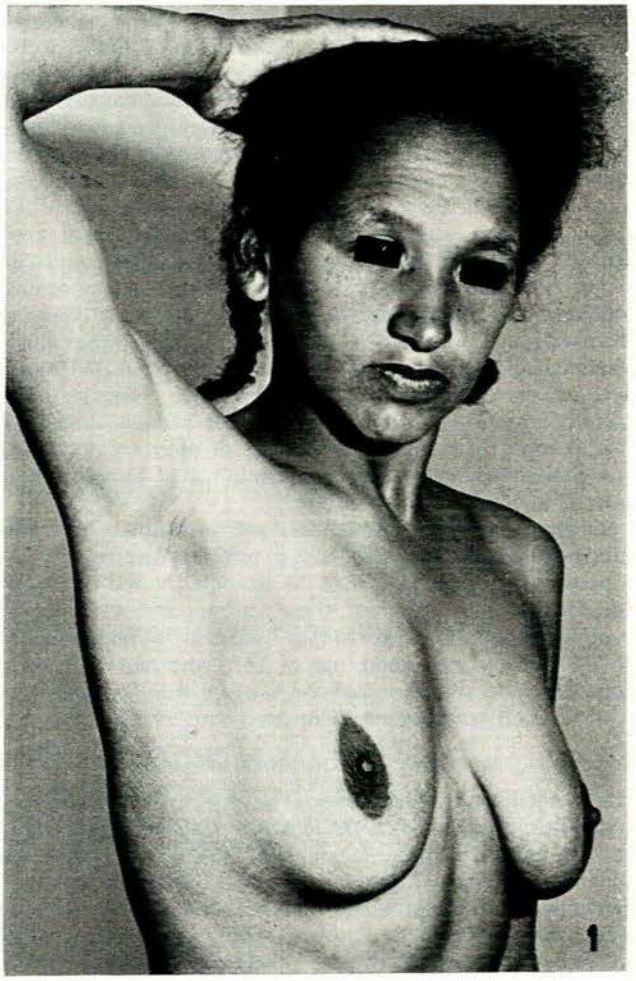

Fig. 1. See text.

Radio-iodine studies of thyroid function: A dose of 25 μC. ^{131}I was administered. At 6 hours thyroid uptake was 18% of the dose. At 24 hours thyroid uptake was 27% of the dose. RBC uptake was 12·9%. Comment: Low normal thyroid and RBC uptakes.

Insulin sensitivity test: Two units of insulin (·03 units/kg. body weight) were injected after a fasting blood-sugar specimen. The results were as follows: Fasting blood-sugar level 76 mg./100 ml. After 20 minutes the blood-sugar level was 76 mg./100 ml., after 30 minutes 87 mg./100 ml., after 45 minutes 82 mg./100 ml., after 60 minutes 82 mg./100 ml., after 90 minutes 65 mg./100 ml., and after 120 minutes 82 mg./100 ml.

X-ray of the skull and the pituitary fossa: No cranial or intracranial pathology.

Biopsy of the endometrium: No anaesthetic was given because of the risk in cases of pituitary insufficiency. The depth of the uterus was 1½ inches. The adnexae were not outlined. A biopsy curette was passed, but very little tissue was obtained. The histological report read: 'Specimen consists of a thin fragment of tissue, 0·3 cm. long. Histology is that of atrophic uterine endometrium in which only an occasional inactive gland is present.'

Treatment: Eltroxin, 0·2 mg./day; hydrocortisone, 10 mg. *b.d.*; stilboestrol, 0·5 mg./day.

Follow-up: When seen on 18 February 1964 there was a distinct improvement in her appearance. She was more lively, her speech was quicker and her answers to the point. She now felt inclined to visit friends and do housework. Her libido had improved but she was anxious not to conceive again! Menstruation had not returned, but she had recently noticed a pink discharge. She was eating well and her weight was now 117 lb. There has not been any sweating in hot weather and no regrowth of body hair.

DISCUSSION

The steady loss of blood which did not clot after delivery in spite of a contracted uterus and the repeated administration of oxytocics, and the absence of any local cause for the bleeding, warrant the clinical diagnosis of afibrinogenaemia. The clotting time on venous blood was presumably not repeated because it had been normal earlier and several pints of blood had already been given. A criticism is that insufficient fibrinogen was given, or triple-strength plasma could have been employed.

Postpartum pituitary necrosis, whether trivial or gross, is the result of collapse at delivery. Haemorrhage, with or without retained placenta, is the most important cause of the collapse. The incidence and size of the necroses are directly related to the severity of the circulatory collapse at delivery.[11] The duration of the collapse, though difficult to assess, is also important. The lesion, as exemplified in this patient, is not immediately fatal, but of course may be responsible for hypoglycaemia in the puerperium with its resultant complications.

In 6 cases of postpartum hypopituitarism Oelbaum[12] found a marked variation in the severity of the clinical picture and a dissociation in the degree of functional impairment of the thyroid, adrenal cortex, and the gonads. Even in the milder cases the clinical features were of paramount importance. Smith and Howard[13] found atypical endocrine function in 3 out of 7 cases of postpartum hypopituitarism. The use of metopirone has facilitated the endocrine investigation of the anterior pituitary gland. Sheehan and Summers[14] stated that there is no regular pattern in the development of symptoms (thyroid or adrenal) in hypopituitarism apart from the constant occurrence of genital atrophy and loss of body hair. Pubic hair may persist for a year or two.

Aetiology

According to Sheehan's original hypothesis[11] there was, in the presence of general circulatory collapse, such a reduction of blood flow in the vessels of the hypertrophied anterior pituitary that thrombosis occurred in these vessels, and this led to ischaemic necrosis. Because of the finding of fibrin thrombi in the vessels of the anterior pituitary (and in the posterior pituitary) by many workers,[3, 15, 16] there has been a division of opinion as to whether fibrin thrombi are the precipitating factor causing ischaemic necrosis or merely secondary associated findings.

Beernink and McKay[15] believe that haemorrhage and shock are not the cause of pituitary necrosis, but 'rather that all three are the result of an episode of disseminated intravascular coagulation.' The thrombi which lodge in the pituitary vessels, they claim, are part of a generalized intravascular clotting which results in thrombosis of small vessels of the kidney, spleen, liver, adrenal, gastro-intestinal tract, and the lungs. However, not all these organs are involved in every patient, and those factors causing the localization in certain organs are not known. These authors describe 6 cases which showed evidence of 'disseminated intravascular coagulation.' The first 5 also had associated evidence of infection in the genital tract, and in 3 of these there was evidence of infection in other organs also.

McKay *et al.*[17] demonstrated generalized intravascular coagulation in eclampsia and premature separation of the placenta. Although the mechanism is unknown, Schneider[18] had postulated that in these conditions there was a sudden acute injection into the maternal blood stream of thromboplastin derived from decidua or placenta. He also believed that the defibrination in human beings leading to severe haemorrhage was achieved by an 'auto-injection' of this thromboplastic material at the time of premature separation of the placenta. McKay *et al.*[17] developed this idea by suggesting that 'toxic material suddenly released into the maternal blood stream is responsible for the deposition of fibrin, the haemorrhages and necroses, and the acute clinical symptoms of shock, anuria and haemorrhage in toxaemic patients with premature separation of the placenta and in eclamptic patients, and that these conditions are manifestations of the generalized Schwartzman phenomenon in human beings'. Shock is said to result in the release of fibrinolysin which may lyse many or all of the fibrin thrombi. If the patient does not die suddenly, she may develop pituitary necrosis or bilateral renal cortical necrosis or extensive liver damage and may succumb later, but some patients may survive with marked pathological changes in one of these organs.

Reid[19] showed generalized intravascular coagulation in amniotic fluid embolism and McKay *et al.*[20] showed it in infections by gram-negative bacteria, including infected abortions and premature rupture of the membranes. This is more understandable since amniotic fluid contains thromboplastic material as well as foetal squames, hairs, and mucus, and these can produce intravascular coagulation. In animal experiments generalized clotting has been produced by endotoxins derived from gram-negative bacteria.

Intravascular coagulation has been particularly stressed by Schneider[18] to explain the pathogenesis of hypofibrinogenaemia in abruptio placentae. The fibrin formed is filtered out in the capillaries, especially in the lungs. Thromboplastin, an intracellular substance, may be released through laceration of the decidual plate of the placenta.[21] This theory has depended partly on the finding of fibrin plugs in the pulmonary vessels in patients who died from premature separation of the placenta.[22] Such cases are, however, rare, and moreover fibrin deposits have been found in the lungs in other conditions.[23]

Nilsen[1] rejects the theory of intravascular coagulation as the usual cause of defibrination in abruptio placentae, not

only for the above reasons, but also because shock owing to pulmonary complications and acute cor pulmonale should occur frequently in these cases. In fact, however, these are rarely, if ever, seen. The defibrination after intravenous injection of thromboplastin in animals has also been taken as evidence for the thromboplastin theory. Hartman *et al.*,[24] however, found it unlikely that the large amount of thromboplastin, which would be required for defibrination, could be released and enter the blood stream in abruptio placentae. In his own animal experiments Nilsen[1] found that the injection of thromboplastin did not give uniform changes and the changes did not correlate with the amounts of thromboplastin used. While the fibrinogen in most cases decreased to a moderate degree, extensive or complete defibrination did not occur.

Hypofibrinogenaemia of varying degree was found in 30 - 40% of Nilsen's cases of abruptio placentae, though a bleeding tendency only occurred in a proportion of these. Most reports indicate a lower incidence of hypofibrinogenaemia following accidental haemorrhage.[25,26] On the basis of clinical observations, blood clotting factors, lytic activity, fibrin in the retroplacental clots (estimated in 24 cases), and some animal and human experiments, Nilsen[1] concluded that the hypofibrinogenaemia in premature separation of the placenta is simply explained by extravascular clotting in the retroplacental space, and by serum reinfusion into the maternal circulation. This concept is based on the finding of fibrin in the retroplacental clots in sufficient amounts to account for the fibrinogen depletion.[1,27] The quantity of fibrin corresponded to a larger blood volume than the blood loss measured during labour and after delivery, indicating that a substantial quantity of serum from the retroplacental haematoma had entered the maternal circulation. This gave rise to raised proconvertin (factor VII) values and lowered proaccelerin (factor V) values. The prothrombin level was somewhat reduced and the fibrinogen level was reduced by dilution. Hence Nilsen deduced that it is unnecessary to postulate intravascular coagulation as a cause of hypofibrinogenaemia. He could detect no appreciable lytic activity in the cases investigated and fibrinolysis was not a causative factor. The rare possibility of intravascular coagulation could occur, but these cases would show far more serious symptoms than those usually observed. Retroplacental deposition of fibrin in the blood clots of patients with abruptio placentae who developed hypofibrinogenaemia has also been demonstrated by other workers.[28-31]

In the present case, if one accepts Nilsen's findings, there is no need to consider disseminated intravascular coagulation as a cause of the coagulation failure, and hence it can hardly be postulated as a cause of the pituitary necrosis. Moreover, despite large quantities of blood rapidly transfused in this patient, there was no evidence of acute right-heart failure as may be expected with pulmonary fibrin thrombi in disseminated coagulation.

Sheehan and Stanfield[32] reject the suggestion of intravascular fibrin deposition as a cause of pituitary necrosis. In those cases where renal cortical necrosis is associated with a pituitary necrosis the association is purely coincidental. They further state that the explanation by McKay *et al.*[17] does not account for the fact that most cases of pituitary necrosis after delivery are due to postpartum haemorrhage or retained placenta and they are not accompanied by cortical necrosis of the kidney or by toxaemic lesions in the liver or kidney.

The original hypothesis offered by Sheehan to explain postpartum necrosis has been withdrawn.[32] From a study of the histological changes that develop, Sheehan and Stanfield[32] conclude that initially there is a period of ischaemia of the anterior lobe and this is followed by an unsuccessful attempt at reflow of blood into the area. They reject as a cause of the ischaemia a simple haemodynamic change following the general circulatory collapse, because, if this caused an arrest of the portal blood flow or of the direct arterial flow in the pituitary gland, then it should affect blood flow to many other organs in the body as well. They conclude that the primary vascular disturbance is an occlusive spasm involving the arteries which supply the anterior lobe and the stalk. Both portal and direct arterial blood supply to the lobe are arrested, but some circulation continues in the stalk. If this spasm is relieved in a short while there is only transient parenchymal damage, but where spasm continues (over 2 hours) the tissues in the anterior lobe undergo extensive necrosis. Thereafter, when blood attempts to flow into the dead vessels, stasis and thrombosis occur. The extent of the necrosis will vary with the extent and duration of the spasm. In about 50% of cases the lesion involves 97 - 99% of the anterior lobe, but there is always survival of the pars tuberalis and a small portion of the pars interloralis.[32,33,42] The reason for the specific localization of the arterial spasm to the anterior lobe of the pituitary gland unfortunately remains obscure.

Older theories regarding causation, e.g. compression of the hypertrophied pituitary gland by the rigid stella tursica and the embolic theory, have been discarded.[6]

PREVENTION

Vigorous and rapid management of postpartum haemorrhage and shock is essential. This includes the ready availability of fibrinogen. Hornabrook and Caughey[8] had one case of severe hypopituitarism following a severe haemorrhage with collapse lasting 2 hours. Although they had at least 23 other cases with haemorrhage and collapse of comparable severity, there were no other cases of gross pituitary damage in the series, and this was ascribed to prompt resuscitative measures. Murdoch[34] states that in the presence of severe pre-existing anaemia a lesser degree of shock may be sufficient to produce necrosis of the anterior pituitary.

Hysterectomy is not a preventive measure in the presence of coagulation failure, which requires adequate blood transfusion and fibrinogen. Nor is it indicated because of haemorrhage into the uterus or loss of its contractile power. Nilsen[27] mentions that hysterectomy has been performed because decidua or placental remnants in the uterus (or uterine veins) are thought to contain thromboplastic or fibrinolytic material, and the activity of this material may persist after delivery. There is no proof in the present case that the secondary postpartum haemorrhage was due to this cause.

ASPECTS OF TREATMENT

Several authors[35,36] have shown that successful pregnancy is the best method of improving the patient's condition, but

this is only possible in the absence of genital atrophy. In this connection Sheehan and Murdoch[37] successfully enabled pregnancy to occur in a patient who had complete superinvolution of the uterus, by instituting hormone therapy. Though a pregnancy usually brings marked improvement and even a permanent cure of the symptoms of the pituitary insufficiency, the improvement is nullified if there is a repetition of haemorrhage or collapse at the delivery, since further anterior pituitary necrosis can then occur. Moreover, Israel and Conston[38] warned of the danger of sudden death at the end of pregnancy or in the puerperium in cases with a previously undetected massive anterior pituitary necrosis. They stress the importance of identifying the presence of hypopituitarism in all women who recover from a severe postpartum haemorrhage. If steroid therapy had been given previously, the dosage must be adjusted during pregnancy and labour.

It must be considered that some patients, because of their previous experience, the size of their family or other reasons, are averse to having another pregnancy, and this is certainly the case in this patient. Substitution therapy must then be continued indefinitely. The administration of oestrogen is regarded as justified, not only for the possible production of a withdrawal bleed at intervals, but as a protective factor against the onset of coronary heart disease.[39,40]

PROGNOSIS

While most patients live for 5 - 15 years, some may survive for as long as 40 years after the occurrence of pituitary damage.[14] Though secondary endocrine atrophy invariably follows massive pituitary damage, the time factor necessary for this atrophy to become clearly recognizable is not known. The constant threat of coma in these cases can result from infection or cessation of therapy.[41] In this patient one is tempted to speculate whether the pituitary remnant will atrophy later and thus lose any of its present function. On the question of a phase of regeneration after the initial necrosis followed later by atrophy, Sheehan[42] could find no difference in the microscopic appearance of pituitary remnants in patients who died within days, and those who died within years, of the original necrosis; however, there is no finality on this point.

THE NEUROHYPOPHYSIS

There is nothing in this patient's history suggestive of even transient diabetes insipidus. In a detailed study Sheehan and Whitehead[43] found a high incidence of neural-stalk lesions in their early cases of massive anterior pituitary necrosis, but lesions in the posterior lobe were much less frequent. They based their explanation of these lesions on the degree of vascular spasm at the time of collapse at delivery. In their late cases, i.e. many years after massive anterior-lobe necrosis, there was atrophy or scarring in over 90% of cases in the posterior lobe. These lesions could not be correlated with the clinical findings, and in particular there was no proof that the uncommon occurrence of diabetes insipidus is related to the posterior-lobe lesions.

SUMMARY

A case of severe hypopituitarism, presenting with amenorrhoea 3 years after a massive postpartum haemorrhage owing to afibrinogenaemia, is described in detail. The patient had an abruptio placentae at term. The literature is reviewed, especially in relation to aetiology. The mechanism of production of fibrinogen deficiency and its relation to the subsequent development of pituitary necrosis is discussed. The loss of fibrinogen by retroplacental coagulation, described by several authors, is evidence against intravascular clotting in cases of accidental haemorrhage with afibrinogenaemia.

It is concluded that the theory of 'disseminated intravascular coagulation' is not applicable in this case, or in a similar case, as a cause of pituitary necrosis, and the concept of vascular spasm followed by stasis and thrombosis is given credence. Aspects of prevention, treatment, and prognosis are discussed. Lesions involving the neurohypophysis are briefly mentioned.

I am indebted to the late Prof. J. T. Louw for his encouragement and for allowing me to investigate this case in his ward; and to Dr. W. P. U. Jackson (who is following-up this patient at the Endocrine Clinic) for his advice. I also wish to acknowledge the assistance of Prof. H. L. Sheehan, of Liverpool, who has supplied me with much helpful information.

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