Case Report

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Pregnancy following Sheehan's Syndrome

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Abstract

Sheehan Syndrome is a rare entity with an incidence of around 3% described from the Indian Subcontinent. It has a variable presentation from an acute catastrophic event like an adrenal crisis to more subtle symptoms like fatiguability. It is invariably associated with deficits in gonadotropic hormones leading to secondary infertility and assisted reproduction. Such pregnancies are considered high risk and require high medical vigilance. The present article discusses similar patient who developed the syndrome following events of her first pregnancy and later conceived with gonadotropin induced ovulation induction.

Keyword: Sheehan's Syndrome; gonadotropin induced ovulation induction.

Sheehan's Syndrome is characterized by postpartum necrosis of the anterior pituitary gland which occurs as a consequence of ischemia after severe puerperal hemorrhage. It is named after Harold Leeming Sheehan who described the syndrome being an aftermath of postpartum events in 1937. Morris Simmonds, a diagnostic pathologist, in 1914 described pituitary atropy in the autopsy of a 46 year old woman who had a history of puerperial sepsis 11 years back and had developed features of hypopituitarism and later lapsed into coma and died because of chronic hypopituitarism. Sheehan however, later concluded that pituitary necrosis is an infarction caused by arrest of blood flow to the adenohypophysis, and clarified that ischaemia, rather than puerperal sepsis or mycotic bacterial emboli, caused the necrotic process. Increased incidence of pituitary necrosis has also been reported in diabetes mellitus, acute haemorrhagic fever, after cardiac surgery, and in patients who were ventilated before death. Though, an epidemiological study from the Kashmir valley of the Indian subcontinent estimated the prevalence to be about 3% for women above 20 years of age, it is a rare entity in the developed countries with advanced maternal health care facilities.

Case report

A 27 year old woman presented to the outpatient department with complaints of cessation of menses since 2 years. Patient was apparently doing fine till her last pregnancy in 2014 when she had preterm labor and diabetic ketoacidosis at 28 weeks gestation. She had a preterm vaginal delivery following which she developed postpartum heamorrhage and

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puerperial sepsis. She developed pleural effusion and pyonephritis. She subsequently underwent pigtail drainage of the same and received 8 cycles of hemodialysis in consequence of the acute renal insult inflicted by the postpartum hemorrhage and sepsis.

Patient had one menstrual cycle 6 weeks after delivery. However after that cycle, menses were abrupted. Thereafter in April 2016, she had a complaint of early fatiguability and lethargy. On examination at a peripheral centre, she was found to have hypotension and dull reflexes and was started on hisone and levothyroxine suspecting Sheehan Syndrome. On examination, her pubic hair were found to be decreased. Hormonal profile suggested low normal levels of cortisol (169nmol/L), prolactin levels 2.6 ng/ml. Her MRI sella was suggestive of pituitary hypoplasia. She was continued on thyroxine replacement and prednisolone(5mg-25mg-25mg) orally. She received a few cycles of oral contraceptive pills following which she was given ovulation induction with gonadotropins in view of the hypogonadotropic hypogonadism. Intrauterine insemination was done for the patient after which she conceived a twin pregnancy (diamniotic monochorionic twins) . Patient received micronized progesterone support thoughout her pregnancy. She was admitted in the hospital for safe confinement and for the management of blood sugars. She was on insulin for management of blood sugars(regular insulin 21-28-28 and isophane 40) and simultaneously she was receiving her requisite dose of steroids and thyroxine supplementation. During her hospital stay her blood sugars were monitored and insulin doses were titrated accordingly. She was also evaluated for any secondary changes associated with diabetes. The growth parameters of both the fetuses was monitored carefully and the babies were detected to have intrauterine growth retardation. Therefore patient was planned for an elective cesarean section at 36 weeks gestation in view of intrauterine growth retardation, precious pregnancy and the associated comorbidities. She delivered girl children of 2.1 kg and 2 kg respectively with good apgars. She was given stress dose of glucocorticoids in the perioperative period. She received inj hydrocortisone 100mg before commencement of the surgery, followed by 50 mg i/v 8 hourly following the surgery and 25 mg 8 hourly on the following day. Her postpartum period was uncomplicated and she was given insulin in the postpartum period and later shifted over to oral hypoglycemic agents (glimepiride and metformin) at one month postpartum. The babies were on mixed feeds (breast feed + top feeding). Her levothyroxine supplementation and prednisolone supplementation was continued at 88 micrograms and 5-5-2.5 mg respectively.

Discussion

Sheehan syndrome occurs as a result of postpartum necrosis of pituitary following postpartum haemorrhage.

The weight of the gland increases by approximately one-third during pregnancy [1]. Mean height of normal gland as measured by magnetic resonance studies is 9.6-10 mm during pregnancy, 10.2-12 mm in immediate postpartum period and regains normal pre-pregnancy size in about 6 months post-partum [2,3].

Pituitary enlargement during pregnancy results in compression of superior hypophyseal artery, any hypotension around childbirth causes arterial spasm in smaller vessels, apoplexy and subsequent pituitary necrosis [4]. There is no correlation between the degree of *postpartum* pituitary necrosis and the severity of clinical expression [5].

It has been reported that disseminated intravascular coagulation (DIC) can cause postpartum hypopituitarism [6,7]. Our patient had a history of preterm labor and diabetic ketoacidosis followed by sepsis and disseminated intravascular coagulation which might have led to pituitary ischemia followed by necrosis. Vasospasm and autoimmunity are other factors which are given consideration in etiopathogenesis of the syndrome in literature. However role of these factors in our patient cannot be defined.

This syndrome usually presents late in its course. It may present from months to years after the inciting event. Our patient presented 2.5 years after her delivery.

The presentation may vary from subtle symptoms like fatiguability to catastrophic events like adrenal crisis.

Hormones secreted by the anterior pituitary gland are adrenocorticotrophic hormone, thyroid stimulating hormone, prolactin, follicle stimulating hormone, leutinising hormone and growth hormone. The pituitary necrosis associated with the syndrome results in variable loss of one or more of these hormones secreted from the anterior pituitary gland with patients manifesting symptoms of the hormonal deficit. The most common involvement is in the secretion of growth hormone (GH) and prolactin (90–100%), while deficiencies in cortisol

secretion, gonadotropin and thyroid stimulating hormone (TSH) range from 50 to 100% [9-15]. At least 75% of pituitary must be destroyed for the clinical manifestations to become evident.

Most common presentation is agalactorrhea. Another common presentation is amenorrhea or oligomenorrhea after delivery [8]. In some cases, a woman with Sheehan syndrome might be relatively asymptomatic, and the diagnosis is not made until years later, with features of hypopituitarism [8]. Such features include secondary hypothyroidism with tiredness, intolerance to cold, constipation, weight gain, hair loss and slowed thinking, as well as a slowed heart rate and low blood pressure.

Our patient presented with secondary amenorrhoea. She had menstrual bleeding only once after her first delivery and came with a chief complaint of inability to have menses since the last two years. Also she had symptoms of early fatigability and lethargy.

In the peripheral centre where she first consulted, she was found to be hypothyroid and started on levothyroxine and prednisolone. When patient came to our centre, her hormonal profile was done and she was found to have low normal levels of gonadotropins and estradiol levels. Her hormonal profile was - cortisol 169 nmol/L, FSH levels of 5.5 mIU, LH levels of 4.11 mIU, serum estradiol levels of 26, prolactin levels 2.6 ng/ml. MRI sella was suggestive of pituitary hypoplasia.

The criteria suggested for the diagnosis of SS are as follows: i) typical obstetric history of severe *postpartum* vaginal bleeding; ii) severe hypotension or shock for which blood transfusion or fluid replacement is necessary; iii) failure of *postpartum* lactation; iv) failure to resume regular menses after delivery; v) varying degrees of anterior pituitary failure and partial or panhypopituitarism; vi) empty sella on CT scan or MRI [16].

Our patient had all these features thus confirming the diagnosis.

She was continued on her levothyroxine and prednisolone supplementation.

Hypogonadotropic hypogonadism caused by pituitary necrosis is one of the rarer causes of female infertility. The present patient also desired conception. She was started on oral contraception pills for a few cycles on which patient had her cycles ruling out any endometrial cause for amenorrhoea and infertility.

Owing to the deficiency of endogenous gonadotropins in patients with sheehans, it is not possible to induce ovulation in these patients with drugs like clomiphene citrate and letrozole which act through the feedback mechanism. Therefore direct ovulation induction with gonadotropins and menotropins is required in these patients. Our patient, was thus given ovulation induction with gonodotropins followed by intrauterine insemination. Patient conceived a twin pregnancy following the procedure.

Her pregnancy was supervised in the present institute and she was admitted at 30 weeks for sugar control and safe confinement. Elective cesarean section was done at 36 weeks in view of small for gestational age babies and precious pregnancy and delivered twin girl babies of 2 kg and 2.1 kg.

She was not able to lactate adequately after delivery and the babies were on mixed feeds.

After this she was continued on her usual doses of steroid and levothyroxine and oral hypoglycemic drugs for diabetes.

The maximum number of cases with pregnancy in hypopituitarism have been reported by Kubler et al. They analysed 31 pregnancies in 27 such women and concluded that these women were at an increased risk of obstetrical complications; postpartum hemorrhage occurred in 5.26%, transverse lie occurred in 15%, and 38% of the newborns were small for gestational age. The high small for gestational age rate was attributed to poor placentation. In our patient, both the babies were small for gestational age though we did not have any postpartum hemorrhage or malpresentation. High rate of cesarean delivery was also noted and was attributed to obstetricians recommendations rather that medical necessity. In our case also an elective cesarean section was done owing to the – precious nature of the preganancy and small babies and these cannot be regarded as absolute medical necessity as indications for cesarean section [17].

Overton et al published an audit of 18 pregnancies in nine women with hypopituitarism who underwent ovulation induction over 20 years. They demonstrated a live birth rate of 61%, miscarriage rate of 28% and midtrimester death rate of 11% with no survivors from four sets of twins. The Caesarian section rate was 100% and half of the live births were on or below the 10th centile for weight. Only one woman successfully breast-fed [18]. The authors concluded that such pregnancies are high risk and attributed it to uterine defect secondary to hormonal deficits and suggested avoidance of twin pregnancies and early elective cesarean sections for successful pregnancies in such patients.

Thus published data on pregnancies with Sheehan syndrome are very less. Most of these women require gonadotropin induced ovulation induction for conception though spontaneous conceptions in women with Sheehan's have been reported. Published literature suggests taking appropriate measures to avoid multifetal pregnancies. These pregnancies are invariably considered high risk and need adequate hormonal supplementation of the deficient hormones and progesterone support for the maintenance of the pregnancy. Regular monitoring of the deficient hormones and fetal monitoring by ultrasonography for early detection of fetal growth retardation should be done. All attempts should be made to prevent postpartum hemorrhage.

Conclusion

In summary, we report a patient who developed Sheehan syndrome following her first pregnancy which manifested years later with subtle findings of panhypopituitarism. After initial hormonal supplementation patient conceived a twin pregnancy after ovulation induction and intrauterine insemination. Elective cesarean section was done for her at 36 weeks. Need for ovulation induction by gonadotrophins, adequate replacement of the deficient hormones, progesterone support during the pregnancy and prophylaxis of postpartum hemorrhage need to be emphasized.

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