CASE REPORT

A ray of hope for a woman with Sheehan's syndrome

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SUMMARY

A 25-year-old woman presented with a history of secondary amenorrhoea for the last 3 years, coinciding with her delivery. She delivered at home and had massive postpartum haemorrhage. She was brought in a state of circulatory collapse to the nearest teaching hospital, where she was resuscitated. She developed anaemia, septicaemia and extradural empyema. The complications were managed and the woman improved. Presently, she approached us for infertility. She was investigated and diagnosed with postpartum hypopituitarism, that is, Sheehan's syndrome. Her gonadotrophin levels, luteinising hormone/follicle-stimulating hormone, were normal, serum oestradiol was low and serum prolactin was also on the lower side. She had started with genital atrophy and was given three cycles of cyclic oestrogen +progesterone combination. Ovulation was induced. She conceived and her antenatal period was uneventful. She delivered a full-term baby vaginally. However, she had inadequate lactation after delivery and lost the baby at one-and-a-half months' age due to gastroenteritis.

BACKGROUND

Postpartum haemorrhage is still a very significant cause of maternal mortality and morbidity, both in the developing and the developed world.¹ The sequelae considered for postpartum haemorrhage in *Global burden disease 1990* were Sheehan's syndrome and postpartum anaemia. However, *Global burden disease 2000* considers only postpartum anaemia as a sequela of postpartum haemorrhage.² Sheehan's syndrome is now obsolete in the developed world. Occasionally, rare cases are being witnessed in developing countries. The case is being presented to educate fellow gynaecologists so that Sheehan's syndrome is still kept in mind during follow-up of a woman with severe postpartum haemorrhage and is diagnosed early. Sheehan's syndrome, if discovered late, can result in significant morbidity in terms of amenorrhoea, infertility, premature ageing, osteoporosis, eventually genital atrophy and extreme weakness (figure 1).

The case also retails the extremely simple manner in which genital atrophy was reversed and infertility was treated,

the nearest tertiary care centre, a teaching hospital about 100 km away. She was wheeled into the emergency ward almost pulseless. She was resuscitated and given 12 units of O Rh-negative blood transfusion. Her shock was reversed, and after 3 days, she was shifted to the medical intensive care department. Here she was investigated further. She was found to be severely anaemic (haemoglobin 5.5 g %). She had disturbed liver function (S. bilirubin 6.6 mg %), uraemia (blood urea 124 mg %), leucocytosis (total leucocyte count 18 000, polymorphs (85%). Her blood sugar was normal and coagulation profile was not disturbed.

A diagnosis of severe anaemia with septicaemia with altered sensorium was made.

CT scan revealed an extradural collection of size 3×1.5×2 cm abutting the right parietal cortex. No other abnormality was seen.

MRI revealed an extradural empyema of the right parietal region.

There was orbital cellulitis causing proptosis.

The empyema was drained in a neurosurgical unit and the process of recovery began. During the stay in the medical ward, she was given Inj. glycerol, Inj. mannitol and high-dose antibiotics. The discharge notes do not mention the long-term use of corticosteroids.

She presented in 2011 with complaints of amenorrhoea and infertility.

An ultrasonogram performed in August 2009 revealed an atrophic uterus with a normal contour. Both ovaries were normal. There was no adnexal mass. Endometrial thickness was 2 mm.

Endometrial assays were performed to discern the cause of amenorrhoea.

Hormones	Values	Normal values
Serum oestradiol	24.94 pg/ml	>40 pg/ml
Luteinising hormone (LH)	3.78 miu/ml	1.90–12.50 (follicular phase)
Follicle-stimulating hormone (FSH)	8.29 miu/ml	2.50–10.00 (follicular phase)
Serum prolactin	1.50 ng/ml	2.80–29.20 ng/ml
Thyroid-stimulating hormone (TSH)	1.59	0.35–5.50

CASE PRESENTATION

A 25-year-old woman presented with amenorrhoea for the last 3 years, when she delivered a stillbirth baby at home. She recounted that her delivery occurred on 3 June 2008, and about after 2 h when she tried to get up, she found herself in a pool of blood. After that, according to her husband, she lost consciousness and was rushed to

INVESTIGATIONS

Given in the case presentation.

DIFFERENTIAL DIAGNOSIS

The history dated back to delivery when there occurred a massive postpartum haemorrhage.

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Figure 1 Sheehan's syndrome (courtesy of Shiv Prasad⁴).

There was no history of removal of placental bits or curettage, and so Asherman's syndrome or Synechiae was ruled out. There was no evidence of haematometra on ultrasound.

Endocrine assays reveal a low oestrogen level with normal LH/FSH, thus suggestive of hypogonadotrophic hypogonadism. An atrophic uterus implied that genital atrophy had already begun. A low prolactin level was also present.

A history of amenorrhoea following severe postpartum haemorrhage, requiring blood transfusion, a low oestrogen level, a low prolactin level and a normal LH/FSH despite oestrogen deficiency, led us to the diagnosis of postpartum hypopituitarism or Sheehan's syndrome.

TREATMENT

As the woman's thyroid status was normal and there is no known treatment for hypoprolactinaemia, sequential oestrogen + progesterone combination was started. She was given ethinyl estradiol 2 mg twice daily for 21 days, and after 11 days, medroxy progesterone acetate 5 mg was added for 10 days. She menstruated after the first cycle. Supplemental calcium was also prescribed. She was given two more cycles of oestrogen and progesterone.

After 2 months, she reported on day 2 of her menses. Ovulation induction was planned with human menopausal gonadotrophins (HMG) from day 2. She was given 75 IU HMG daily for 5 days. Oral ethinyl estradiol 2 mg twice daily was started. On day 7, the ultrasonogram showed no dominant follicle and the endometrial thickness was 3 mm.

From the 7th day, the HMG dose was increased to 150 IU and continued for 5 days. On the 12th day, two follicles were visualised measuring around 10–11 mm, and the endometrial thickness was 5 mm. From the 13th to 17th day, 225 IU HMG was given. On the 18th day, two follicles with a mean diameter of 15 and 18 mm, respectively, were seen, and the endometrial thickness was 7.3 mm (figure 2). The ovulation trigger was given with 10 000 IU human chorionic

gonadotrophin. She was advised to have intercourse on the same night and two successive nights. Luteal phase support was given with micronized vaginal progesterone for 10 days. The woman reported on 3 November 2011, that is, 41 days after her last menstrual period with a positive ELISA test for pregnancy. An ultrasonogram performed on 20 November showed a 6-week viable fetus (figure 3). An anomaly scan at 18 weeks reported a healthy fetus (figure 4). Her antenatal period was uneventful and she delivered at 37 weeks.

OUTCOME AND FOLLOW-UP

Around 37 weeks, the woman presented with leaking per vaginum. She was advised caesarean section considering the preciousness of the pregnancy but opted for a vaginal delivery. Labour was initiated with oxytocin drip. She delivered a male

L.M.P. : 23.09.2011					
Uterus: uterus is normal in size and echotexture.					
Date	Day	Right ovary	Left ovary	ET	Remarks
29.09.2011	7 th	No dominant follicle seen	No dominant follicle seen	3 mm	No free fluid seen
04.10.2011	13 th	11.2 x 9.1 mm	11.2 x 9.8 mm	5.5 mm	No free fluid seen
07.10.2011	16 th	13.7 x 13.1 mm	15.9 x 13.6 mm	6.9 mm	No free fluid seen
09.10.2011	18 th	16.9 x 14.7 mm	19.3 x 16.7 mm	7.3 mm	No free fluid seen

Figure 2 Chart showing the pattern of follicle development.

Figure 3 First trimester ultrasound scan.

baby vaginally. However, there was a slight delay in the second stage because of a loop of cord around the neck and poor bearing down efforts. The baby weighed 2.75 kg, had mild birth asphyxia and was shifted to the neonatal intensive care unit. The baby recovered and was discharged after 5 days. After a few days, we received a phone call from the patient reporting failure of lactation. She was prescribed Tab. Metoclopramide and Cumin, a popular Indian lactagogue. However, milk production did not improve, and due to faulty feeding practices, the baby developed gastroenteritis. The baby was not brought for hospitalisation, and to our great despair, the baby succumbed to dehydration. A precious life brought with great care and diligence was lost.

DISCUSSION

Sheehan's syndrome is diagnosed on the basis of the following criteria:

- ▶ Typical obstetrical history of severe postpartum bleeding.
- ▶ Severe hypotension or shock for which blood transfusion or fluid replacement is necessary.
- ▶ Failure of postpartum lactation.
- ▶ Varying degrees of anterior pituitary failure and partial or panhypopituitarism.
- ▶ Failure to resume menses after delivery.
- ▶ Empty sella on CT scan or MRI.³

Our patient presented with a history of profound haemorrhagic shock, amenorrhoea, marked oestrogen deficiency, and genital atrophy had begun. Empty sella appearance occurs due

Figure 4 Second trimester anomaly scan.

to ischaemic necrosis of the enlarged pituitary gland of pregnancy, followed by atrophy and finally empty sella. This picture on MRI develops after a variable period. The MRI and CT scan do not show an empty sella picture in our patient because MRI and CT scan were obtained in the acute phase.

Women with Sheehan's syndrome may present with panhypopituitarism or selective hormone deficiency.

Growth hormone and prolactin deficiency is seen in 90–100% of cases, and cortisol, gonadotrophin and TSH are decreased in 50–100% of cases.⁴ Gonadotrophin and prolactin deficiency were seen in the present case.

The treatment of Sheehan's syndrome lies in the replacement of deficient hormones. This woman was given pretreatment with cyclic oestrogen and progesterone to improve the uterine size. Other authors, too, have reported better ovulation rates in women with hypopituitarism when pretreated with oestrogen and progesterone.⁵ Our patient was put on oestrogen therapy along with HMG injections. Other authors have witnessed successful outcome after cotreatment in the seventh cycle with conjugated equine oestrogen in a woman of craniopharyngoma who

had taken six cycles of follicular development with HMG therapy alone.⁶

Ovulation induction was performed using HMG (HMG is FSH+LH ratio 1:1). HMG injections are easily available, inexpensive and were thus preferred. In other studies, authors have used 150 IU recombinant FSH combined with varying doses of LH ranging from 0 to 25, 75 or 225 IU rhLH.⁷

The dose was adjusted with follicular monitoring alone, and repeated serum oestrogen estimations were not performed, thus reducing the cost of treatment.

Luteal phase support after ovulation has been recommended by many because of inadequate endogenous gonadotropin secretion.⁸

Growth hormone therapy is also suggested in women with infertility secondary to hypopituitarism.⁹

However, our patient conceived in the first cycle with HMG, and hence adjuvants like growth hormone were not required.

Cyclic oestrogens and progestones to achieve a near normal uterine size, followed by ovarian stimulation with HMG, oestrogen supplementation, LH surge with HCG and luteal phase progesterone support, can be used as a method of choice for treatment of infertility associated with hypopituitarism.

Multifetal pregnancy is a frequent complication of gonadotrophins but can be avoided by careful ultrasonic follicular monitoring.

Lactation failure was seen even after a successful pregnancy and delivery. It should be managed vigorously, and that is where we fumbled and lost the baby.

Competing interests None.

Patient consent Obtained.

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Learning points

- Postpartum haemorrhage should be tackled with great skill and haste to avoid possible sequelae.
- Every woman after severe postpartum haemorrhage should be reviewed early for signs of hypopituitarism to prevent morbidity.
- Cyclic oestrogens+progesterone combination should be given to maintain bone mass and prevent genital atrophy in a woman with Sheehan's syndrome.
- Human menopausal gonadotrophins are a good and relatively inexpensive modality for induction of ovulation in hypopituitarism.

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