Successful pregnancy outcome in a case of Swyer Syndrome with hypertension and morbid obesity

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ABSTRACT

To report a case of Swyer syndrome with hypertension and morbid obesity with successful pregnancy and live birth after assisted reproductive technology. 27 year old morbidly obese female with essential hypertension who had been on HRT for 10 years with well-developed secondary sexual characters with primary infertility. After adequate development of the uterus and the endometrial preparation, Patients with Swyer syndrome conceive with oocyte donation and ICSI. Caesarean section rate is high due to multiple pregnancies and other obstetric complications. Early detection of these cases would help in timely development of their secondary sexual characters and restoration of menses and gonadectomy for prevention of malignancy as its propensity is high. Multidisciplinary approach is required including counseling and management of long term health problems. Pregnancy is feasible but caesarean rate is high.

Keywords: Gonadal dysgenesis, Multidisciplinary care, Gonadectomy, Oocyte donation

INTRODUCTION

The term Swyer syndrome was coined by Gim Swyer in 1955 where he described two cases of sex reversal that differed from the known forms of what was then termed ‘male pseudo hermaphroditism’. The two women had a 46XY karyotype and had primary amenorrhea, tall stature, female external genitalia (although one had an enlarged clitoris) and normal albeit hypoestrogenised vagina and cervix.1 The condition was later linked to dysgenetic gonads and is also known as pure gonadal dysgenesis, a form of 46XY Disorder of Sexual Development. It is an unusual condition with an incidence of 1 in 80,000 and is characterized by the presence of an unambiguously female phenotype and Mullerian structures in the presence of a “Y” line.2 10 to 20% of women with the syndrome have a deletion in the DNA-binding region of the SRY gene while in the remaining 80-90% of cases, the SRY gene is normal and mutations in other testis determining factors are probably implicated.3 Early diagnosis is important, as gonadal neoplasm is common in these patients.

METHODS

A 27 year old lady presented to our centre with primary Infertility. She had visited a clinic at the age of 17 years with primary amenorrhea and no development of the secondary sexual characters. Since then she was put on Hormone replacement therapy. So when she visited our clinic she had regular periods and well developed secondary sexual characters. Her family history was unremarkable. On examination she was a tall female with morbid obesity 5ft 10 inches high, weighing 129 kg, BMI: 40.8. Arm span was 180 cm. Breast and pubic hair tanners 5 and external genitalia of a normal female. Internal examination revealed a small uterus with non-palpable ovaries. Her blood pressure was 190/100mm Hg and she was not a diagnosed case of hypertension.

Hormonal evaluation revealed FSH: 30 IU/L, LH: 7.16 IU/L, E2: 36 pg/ml, Growth hormone: 0.064ng/ml, TSH: 2microIU/ml and prolactin: 7ng/ml. Her Blood sugar (fasting and post prandial), kidney function tests, lipid
profile, Serum cortisol was normal. Anti-phospholipid antibody screen was negative. Echocardiography and renal Doppler were also normal. Karyotype 46XY. Ultrasonography revealed small uterus 4.7x2.0x3.1cm, ET: 5mm, with small gonads Cervix: normal. MRI revealed streak gonads 10x9mm and 10x11mm along the broad ligaments. Our case was diagnosed as 46 XY Disorder of sexual Development (DSD) namely pure gonadal dysgenesis or Swyer syndrome. On laparoscopy there were B/L streak gonads and gonadectomy was done as the propensity of malignancy is high. Patient was advised life style modifications for weight reduction, salt restriction and anti-hypertensives. Meanwhile the patient was on regular follow up and hormone replacement therapy (17b estradiol gel and progesterone) was continued. After 1 year when she had a controlled blood pressure and had lost 30 kgs we took her up for oocyte donation and ICSI with husband’s sperm. First cycle failed where 3 day 3 embryos were transferred. After two months in second attempt two day 5 expanded blastocyst transfer was done. Serum b HCG on day 16 after transfer was 813. Her first sonography revealed single live intra uterine pregnancy. Luteal support was with Estradiol valerate (vales) 2mg, 17B estradiol gel and micronized progesterone 800mg. In addition to luteal support and folate supplementation, Salicylic acid was given empirically. Patient was also heparinized after transfer. Her first trimester was uneventful. Uterine artery Doppler at 16 weeks revealed a dicrotic notch and she had an episode of bleeding per vagina at the same time. Salicylic acid and LMWH was stopped and restarted after 2 weeks. Patient developed super imposed pre eclampsia at 28 weeks and pregnancy was terminated at 34 weeks by LSCS due to severe pre eclampsia and a healthy girl child weighing 2.1 Kg was born.

### Table 1: Case reports of pregnancies in patients with Swyer syndrome.

<table>
<thead>
<tr>
<th>Study</th>
<th>No of patients</th>
<th>Single/multiple pregnancy</th>
<th>Pregnancy complications</th>
<th>Mode of delivery</th>
<th>Indication for CS</th>
</tr>
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<tbody>
<tr>
<td>Sauer et al&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1</td>
<td>twin</td>
<td>preeclampsia</td>
<td>CS</td>
<td>Severe preeclampsia</td>
</tr>
<tr>
<td>Cornet et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>3</td>
<td>single</td>
<td>Nil</td>
<td>CS</td>
<td>Android pelvis</td>
</tr>
<tr>
<td>Bardegues et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>1</td>
<td>triplet</td>
<td>Nil</td>
<td>CS</td>
<td>PTL, PPROM</td>
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<tr>
<td>Bianco et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>1</td>
<td>single</td>
<td>Nil</td>
<td>Not known</td>
<td></td>
</tr>
<tr>
<td>Kan et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>1</td>
<td>1st single 2nt twin</td>
<td>Gestational HTN</td>
<td>CS</td>
<td>Failed induction CS with twin</td>
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<tr>
<td>Dirnfield et al&lt;sup&gt;10&lt;/sup&gt;</td>
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<td>Single and twin</td>
<td>No</td>
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<td>No</td>
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<td>Failed induction</td>
</tr>
<tr>
<td>Chen et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>1</td>
<td>Twin</td>
<td>No</td>
<td>CS</td>
<td>Malpresentation of twin</td>
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<tr>
<td>Ko et al&lt;sup&gt;13&lt;/sup&gt;</td>
<td>1</td>
<td>triplet</td>
<td>1 hydatidiform mole and preeclampsia</td>
<td>CS</td>
<td>Preeclampsia</td>
</tr>
<tr>
<td>Plante and Fritz&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1</td>
<td>Single</td>
<td>No</td>
<td>CS</td>
<td>Occipito post position with arrest of head descent, Bwt 3.617</td>
</tr>
<tr>
<td>Siddique et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>1</td>
<td>Single</td>
<td>Reduced amniotic fluid</td>
<td>CS</td>
<td>Breech with oligohydramnios</td>
</tr>
<tr>
<td>Tulic et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td>1</td>
<td>Single</td>
<td>Reduced amniotic fluid</td>
<td>CS</td>
<td>Breech with oligohydramnios</td>
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<tr>
<td>Michala et al&lt;sup&gt;4&lt;/sup&gt;</td>
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<td>single</td>
<td>1-nil</td>
<td>1-VD</td>
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<tr>
<td>George Creatsas et al&lt;sup&gt;17&lt;/sup&gt;</td>
<td>1</td>
<td>Single</td>
<td>Chronic Hypertension</td>
<td>CS</td>
<td>IUGR with fetal distress</td>
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<td>Azamsadat et al&lt;sup&gt;18&lt;/sup&gt;</td>
<td>1</td>
<td>Single</td>
<td>Preeclampsia</td>
<td>CS</td>
<td>Preeclampsia</td>
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### DISCUSSION

Swyer syndrome is a sex-reversal disorder resulting from embryonic testicular regression sequences. Clinical diagnosis is difficult and usually made at later ages and as a result of clinical presentations such as primary amenorrhea and/or delayed development of secondary sexual characters. However, early diagnosis is important because of the risk of gonadal malignancy, the early institution of estrogen therapy for induction of puberty and to allow for adequate hormone replacement to improve bone mineral density. The patient was given HRT for primary amenorrhea but she was not evaluated further until she visited our centre for infertility when she was diagnosed and gonadectomy done. The delay from the primary visit being 10 years.

The patients with Swyers are considered sterile. However pregnancy is possible with allogenic oocytes after adequate development of the uterus and proper priming...
of the endometrium. The first pregnancy and delivery by ovum donation was reported in 1984. After extensive literature search we found 15 papers from 1989 to 2012 of 20 women with swyers with a successful pregnancy outcome. Out of which only 1 patient had pre-existing hypertension (Creatsas G et al) as in our patient (Table 1). As our patient had hypertension and was morbidly obese, it was important to use the lowest possible dose of hormones to get the desired effect. Hypertension per se is not a contraindication for HRT but obesity and HRT may increase the risk of venous thromboembolism. 17b estradiol is preferred over ethinyl estradiol in such patients.19 We gave the patient 17b estradiol gel and nor ethisterone during the interval period of 1 year before ICSI. The patient was managed in liaison with the endocrinologist and physician. Post transfer luteal support was given with 2mg ethinyl estradiol and 17b estradiol gel twice daily (normally for OD cycles we give 6mg ethinyl estradiol) up to 12 weeks and we also gave her Low molecular weight heparin.

The use of allogenic oocytes and the endometrial response to exogenous hormones has enabled these patients to successfully achieve pregnancy. However due to the increased incidence of multiple pregnancies, preterm labor, premature rupture of membranes, hypertension the caesarean rate in the number of cases reported is high. In the cases reported by Sauer at al, Bardeguez et al, Cornet et al, Chen et al, Ko et al, Plante et al, Tulic et al, Michala et al, Creatsas et al and Azamsadat et al Cesarean section was performed for various obstetric complications before spontaneous/induced labor as in our case.4,5,7,12-14,16-18 In the case report by Cornet et al Elective cesarean was done for android pelvis.6 Only Kan et al and Selvaraj et al reported failed induction while Siddique et al and Michala et al reported successful vaginal delivery in three cases.4,9,11,15 The hypoplastic uterus responds well to hormonal therapy and it may have anatomical ability to permit normal dilatation and labor however more reports with vaginal delivery would be required to support that.

We have documented a rare case of Swyer syndrome with primary hypertension and morbid obesity with successful pregnancy and delivery of a healthy baby. We adopted a multidisciplinary care approach for her along with counselling both psychological and genetic.

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REFERENCES
