

## Swyer Syndrome : A Case Report with Literature Review

Patnayak R<sup>1</sup>, Suresh V<sup>2</sup>, Jena A<sup>3</sup>, Rajagopal G<sup>4</sup>, Vijayalakshmi B<sup>4</sup>, Reddy AP<sup>4</sup>, Rukumangadha M<sup>1</sup>, Sachan A<sup>2</sup>

Department of Pathology<sup>1</sup>, Department of Endocrinology<sup>2</sup>, Department of Surgical Oncology<sup>3</sup>, Department of Radiology<sup>4</sup>, Sri Venkateswar Institute Of Medical Sciences, Tirupati, India

### ABSTRACT

Gonadoblastomas are known to develop in dysgenetic gonads, especially so, if Y chromosome material is present. A 20-years- old girl who noticed breast development since the age of 12 years presented with primary amenorrhoea, distension of lower abdomen and intermittent pain for two months. She had breakthrough bleeding with six months of estrogen replacement. Tanner breast stage was five and pubic hair stage was also five. Examination revealed a mass in the lower abdomen extending into hypogastrium, umbilical and lumbar regions. Her gonadotropin levels were grossly elevated. Karyotyping showed 46XY. CT scan of abdomen showed a 17X11 cm mass in the pelvis without visible gonads. Surgical excision of the mass along with bilateral salpingophorectomy was performed. Histopathology revealed the mass to be a dysgerminoma, while the right gonad lodged gonadoblastoma. She was diagnosed as a rare case of Swyer syndrome.

**Keywords:** *Dysgerminoma, gonadoblastoma, Swyer syndrome, XY gonadal dysgenesis*

### INTRODUCTION

In 1955, Swyer first described two phenotypic women with gonadal dysgenesis without the stigma of Turner syndrome (46XY pure gonadal dysgenesis, now known as Swyer syndrome).<sup>1,2</sup> The chance of tumor development in Swyer syndrome is 20–30% . The most common tumor described is bilateral gonadoblastoma, but also seen are dysgerminoma and even embryonal carcinoma.<sup>2,3</sup> Five percent of dysgerminomas are discovered in patients who are phenotypically females with abnormal gonads and 46XY karyotype.<sup>1,3</sup>

### CASE PRESENTATION

A 20-years-old lady, who still had not attained menarche presented with abdominal pain and distension of two month duration, more in lower part, dull and associated with two episodes of vomiting. Her height was 150 cm (mid parental target height was 152cm) and body mass index was 23.5 kg/m<sup>2</sup>. Patient had development

of breast from 12 years of age. She developed pubic hair from the age of 11 years. She did not have any history of anosmia, headache or disturbance in vision. There was no history of cyclical pain in the abdomen. There was no family history of delayed puberty. There was no history of change of voice. She was a product of non consanguineous marriage. She had been started on estrogen and had breakthrough bleeding within six months of estrogen replacement.

On examination she did not have Turner phenotype. Acanthosis nigricans was noted. Tanner breast stage and pubic hair stage was five. There was no acne, hirsutism or galactorrhoea. Abdominal distension was involving lower part extending upto midepigastria region. On palpation, a mass was felt arising from pelvis and extending to midepigastria and both lumbar regions, firm, mobile and nontender. There was clitoromegaly. Ultrasonography revealed normal sized uterus. CT scan of abdomen showed well defined heterogeneously enhancing mixed density lesion with calcification in

### Correspondence:

Dr. Rashmi Patnayak  
Department of Pathology  
Sri Venkateswar Institute Of Medical Sciences Tirupati  
Andhra Pradesh-517507  
Tel no. – 919493547727  
E-mail –rashmipatnayak2002@yahoo.co.in

pelvis and abdomen measuring 17x11.6 cm. (Figure 1).

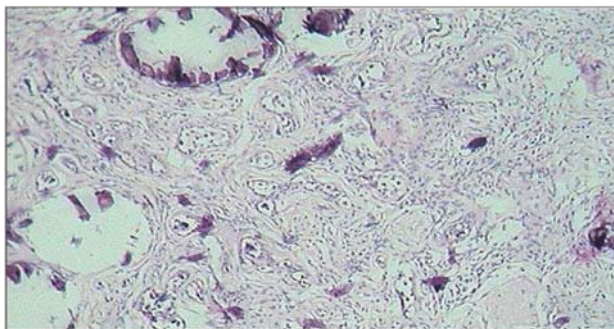


**Figure 1.** CT scan of abdomen—well defined heterogeneously enhancing mixed density lesion with calcification in pelvis and abdomen

Minimal free fluid was present. Small lymph nodes were noted in perigastric region measuring 1.8X1.5 cms. Gonads could not be visualized separately. While off estrogen therapy her gonadotropins were grossly elevated [FSH -110 IU/L) and LH 40 IU/L) respectively], consistent with hypergonadotropic hypogonadism. Her karyotyping was 46XY.

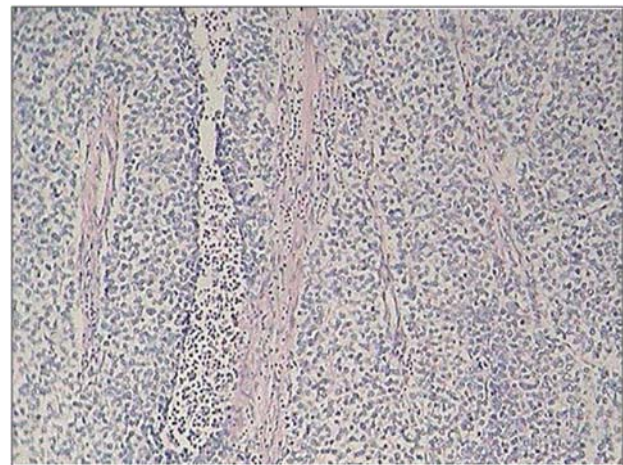
Patient underwent bilateral salpingo-gonadectomy. Intraoperatively a left gonadal mass with variable consistency was noted measuring 20X25 cm whereas on right side a streak gonad was present. The patient had no peritoneal or omental nodule. She also had no deposits over bowel, mesentery and liver surface.

Histopathological examination of the left gonadal mass revealed a well circumscribed lesion showing typical features of dysgerminoma characterized by the presence of neoplastic cells with prominent nucleoli arranged in lobules separated by thin fibrous septae infiltrated with lymphocytes. (Figure 2).



**Figure 2.** Gonadoblastoma with abundant calcified areas. (H&E X20)

Interestingly this lesion showed micro calcification, thus signifying the presence of burnt out gonadoblastoma. Sections from the right side gonad revealed normal ovarian stroma and a gonadoblastoma, which showed both tubular cells with secretions and germ cell component along with abundant calcified areas. (Figure 3). Immunohistochemically the tumor was CD 117 positive. Hence the final diagnosis was made as Swyer syndrome with dysgerminoma and gonadoblastoma. Both fallopian tubes showed normal histology. There was no lymph-nodal metastasis. Our patient received four cycles of combination chemotherapy of BEP regimen comprising of cisplatin, etoposide and bleomycin and responded well.



**Figure 3.** Dysgerminoma cells with prominent nucleoli arranged in lobules separated by thin fibrous septae infiltrated with lymphocytes. (H&E X20)

## DISCUSSION

Swyer syndrome (46XY, pure gonadal dysgenesis) is a rare condition of sexual abnormality seen in female phenotypic rare condition of sexual abnormality.<sup>2,3</sup> The etiology of 46XY, gonadal dysgenesis is believed to be deletion of short arm of Y chromosome involving the sex determining region of Y (SRY) gene, mutation in other genes leading to inhibition of SRY function, or mutation of SRY itself.<sup>3</sup> Genes which play active role in the testes determining pathway are located on other chromosomes like SOX9 (Sry box-containing gene 9), SF1 (steroidogenic factor 1), WT1 (Wilms' tumor 1), DHH (desert hedgehog) etc.<sup>3-6</sup> Most of the latter genes are associated with other phenotypic features apart from gonadal dysgenesis. However gonadal dysgenesis alone may occur due to a number of as yet unknown genes as well, all of which contribute to the determination and development of the initially undifferentiated gonad as testes.

In embryonic stage the bipotential gonads can differentiate either into the male or female direction,

depending on the correct and timely expression of specific genes.<sup>3,4</sup> With the expression of SRY male sex differentiation is initiated, resulting in the full masculinization of internal and external genital structures.<sup>3,4</sup> Thus testicular Anti-Müllerian Hormone (AMH) causes regression of the müllerian duct structures (uterus and fallopian tube) whereas androgens cause stabilization and development of the Wolffian duct structures (epididymis, vas deferens and seminal vesicles) and the formation of the prostate and the male external genitalia.<sup>3,4</sup> Thus when the testes are dysgenetic, as in our patient, the Müllerian duct derived structures remain (hence our patient had a uterus) and the Wolffian duct derived structures disappear and the external genitalia remain phenotypically female.<sup>3-5</sup> The incidence of Swyer syndrome reported in literature is 1:100 000.<sup>7</sup> Very few cases (less than 100) have been reported in the world literature.<sup>7-11</sup> It is characterized by a 46 XY karyotype, a female phenotype with normal female external genitalia, and a hypoplastic to normal uterus, streak gonads and primary amenorrhea.<sup>3,7-9</sup> Majority show minimal breast development.<sup>2,3,7</sup> However, in the present case the unique feature was well developed breast corresponding to Tanner stage five. This may be explained due to estrogen secretion from the gonadoblastoma as well as due to the action of exogenously administered estrogen.<sup>11,12</sup>

The reported incidence of Swyer syndrome is 1:100000. Less than 100 cases have been reported in the world literature so far.<sup>6</sup> Mostly it is characterized by a 46 XY karyotype, a female phenotype with normal female external genitalia, a hypoplastic to normal uterus, streak gonads and primary amenorrhea.<sup>7</sup> Major cases show minimal breast development. However, in the present case the unique feature was well developed breast corresponding to Tanner stage five. This may be explained due to estrogen secretion from the gonadoblastoma as well as due to the action of exogenously administered estrogen.<sup>8,9</sup>

Gonadoblastomas are benign tumours composed of germ cells and sex cord stroma.<sup>1,9,12</sup> Most of the patients in possession of gonadal dysgenesis and a Y chromosome develop gonadoblastoma or dysgerminoma.<sup>2,3</sup> In our case, we noted dysgerminoma associated with evidence of residual or burnt out gonadoblastoma in the same gonad and gonadoblastoma in the other. Since dysgenetic gonads have a very high risk of developing into malignant germ cell neoplasm, a prophylactic bilateral gonadectomy is strongly recommended.<sup>3,7</sup>

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