

**Right ovarian Endodermal sinus tumor and left ovarian Gonadoblastoma in a young female of Turner's syndrome: a case report.**

Manju Pandey<sup>1</sup>, Hemnath Subedi<sup>1</sup>, Nirmal Lamichhane<sup>2</sup>, Greta Pandey<sup>3</sup>, Binuma Shrestha<sup>1</sup>

<sup>1</sup>Gyneoncology Unit, Department of Surgical Oncology, B. P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal

<sup>2</sup>Urology Unit, Department of Surgical Oncology, B. P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal

<sup>3</sup>Department of Pathology, B. P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal

**Abstract**

Gonadal dysgenesis includes variety of clinical condition due to abnormalities of sex chromosomes. The most frequent of this condition is Turner's syndrome, affecting 1 in every 2000 to 2500 live births. Gonadoblastoma is a benign lesion mostly detected in individuals with dysgenetic gonads with Y chromosome and has potential for malignant transformation; or may be associated with malignant germ cell tumors, most commonly dysgerminoma or occasionally immature teratoma, endodermal sinus tumor, embryonal carcinoma, or choriocarcinoma. We report a 22-year-old girl with primary amenorrhea and physical stigmas of Turner's syndrome presented with huge abdominopelvic mass and abdominal pain. She underwent laparotomy with TAH with BSO with appendectomy with omentectomy with resection of portion of terminal ileum with ileoileal anastomosis with resection of sigmoid colon with colorectal anastomosis and right pelvic lymph node dissection. Patient had anastomotic site leak with sepsis with multi organ dysfunction syndrome and could not be revived. Final histopathology was consistent with endodermal sinus tumor in right ovary and gonadoblastoma in left ovary. Her karyotype analysis revealed 45, X0. Endodermal sinus tumor is a highly malignant germ cell tumor with poor prognosis.<sup>4</sup> Gonadoblastoma associated with endodermal sinus tumor in Turner's syndrome is very rare and challenging for the clinical management.

*Keywords:* Endodermal sinus tumor, Gonadoblastoma, Ovarian dysgenesis, Turner's syndrome.

**Introduction**

Gonadal dysgenesis consists of a variety of clinical condition characterized by abnormal development of fetal gonads due to

alteration in sex chromosome number or structure or mutation in gene involved in development of the gonads.<sup>1</sup> Turner's syndrome is classified as partial gonadal

**Correspondence:** Dr Manju Pandey , Gynecology Oncology Unit, Dept. of Surgical Oncology, BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal. Email: [drmanju921@gmail.com](mailto:drmanju921@gmail.com)

dysgenesis with incidence between 1/2000 to 1/2500 live births among girls.<sup>2</sup> Approximately 40-60% of patient with Turner's syndrome have an X chromosome completely missing with 45, XO karyotype. Remaining cases have a structurally abnormal X chromosome or mosaics with 45X/46, XX cell lineage or 45X/47, XXX cell lineage or 45X/46XY mosaic encountered rarely.<sup>2, 5</sup> The streak gonads of Turner's patients are at greater risk of developing variety of ovarian neoplasm.<sup>5</sup> Gonadoblastoma is a benign mixed tumor seen in patients with dysgenetic gonads and have high potential for malignant transformation. In majority of cases, gonadoblastoma is associated most commonly with dysgerminoma and occasionally with immature teratoma, endodermal sinus tumor, embryonal carcinoma or choriocarcinoma.<sup>3</sup> Endodermal sinus tumor are highly malignant and lethal germ cell tumor with poor prognosis.<sup>4</sup> Several case reports of dysgerminoma and gonadoblastoma have been published till date in patients with gonadal dysgenesis. Gonadoblastoma with ovarian germ cell tumor other than dysgerminoma coexists very rarely. Because of this rarity, we report a case of gonadoblastoma and endodermal sinus tumor in young female with Turner's syndrome.

### Case report

- A 22 years unmarried girl presented in Gynecology OPD of BPKMCH with complaints of lower abdominal pain for 3 months and mass per abdomen for 2months. She was a referred case from outside hospital

with a provisional diagnosis of primary amenorrhea with Germ cell tumor. She was from a lower socioeconomic status. She was born to parents of non-consanguineous marriage, delivered at term with an uneventful birth history. She was the third child of her parents and has two normal elder sisters and one normal younger brother. Developmental history throughout the infancy and childhood was normal. She has passed her 10<sup>th</sup> standard with average marks four years back and left her further study due to financial problem. There was no history of tuberculosis and other chronic illness, no history of any drug or radiation exposure. She had not attained her menarche yet. On examination her height was 136cm and weight was 37 Kg. She had Tanner stage 1 breast development with widely separated nipples, shield chest as shown in picture 1.



Picture 1: Shield chest, widely separated nipples, tanner stage 1 breast development

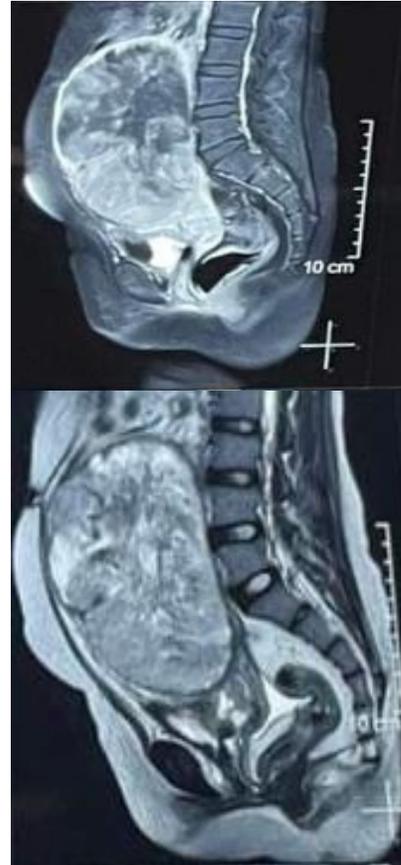
Pubic and axillary hairs were absent. On abdominal examination there was a firm tense mass felt with distinct border up to just

above the umbilicus, around 20 x 15 cm without tenderness, with restricted mobility. On local examination of external genitalia, there was depigmentation and fusion of labia minora. On per rectal examination, rectal mucosa was free, POD was free, and it was difficult to access the uterus. She had a follicle stimulating hormone level of 151.83 IU/L, luteinizing hormone(LH) level of 51.4 IU/L, an Estradiol level of 11.86pg/ml and serum Progesterone level of 0.22 ng/ml showing hypergonadotropic hypogonadism feature. She had an alpha-fetoprotein value of > 1210 and LDH value of 1664.3U/L, CA125 value of 58.2U/L, rest Serum  $\beta$  HCG, CEA, CA19.9 were normal. Her serum Prolactin value was normal. On the thyroid function test her TSH value was 10.62 with normal T3, T4.

- Magnetic resonance imaging revealed approximately 15.3 x 14.7x 10.5cm well defined heterogeneous, hyper intense lesion noted in the pelvic cavity. Multiple foci of cystic degeneration were noted within the lesion. Left ovary was not visualized separately and a hypoplastic uterus of 4.35 X 2 X 1.9 cm with high signal thin endometrium was present. Mild right hydroureteronephrosis was also noted.

She had a normal Echocardiography study. She had pallor with hemoglobin value of 7.7 gm/dl, total count – 13,700 with neutrophil – 85. She had hyponatremia with serum sodium – 117mmol/L and hypokalemia with serum potassium – 3.15mmol/L. Her blood urea, serum

creatinine, liver function test were within normal limit. She had total protein of 6.17g/dl and albumin of 3.55 g/dl.



Picture 2: Sagittal image showing well defined heterogeneous, hyper intense lesion noted in the pelvic cavity. Multiple foci of cystic degeneration were noted within the lesion.

USG guided FNA from pelvic mass was done outside which showed cytomorphological features of malignancy, possibility of germ cell origin. She was started with tablet thyronorm 50  $\mu$ g daily, two pint of whole blood transfusion IV fluid NS, along with KCL supplementation

and analgesic SOS. Karyotyping was sent. Hemoglobin was corrected to 10.6 gm/dl after transfusion. Serum potassium was corrected with serum sodium value of 128mmol/L. TFT was repeated which showed TSH – 8.97. High risk informed consent was taken for staging laparotomy along with consent for bilateral salpingoophorectomy, and if needed hysterectomy. Her mother was persistently requesting for hysterectomy also as she had a fear that if disease recurs she can't afford another surgery.

- TAH with BSO with appendectomy with omentectomy with resection of portion of terminal ileum with ileoileal anastomosis with resection of sigmoid colon with colorectal anastomosis and right pelvic lymph node dissection was done.

During staging laparotomy she was found to have a huge ovarian mass approximately 35 x 25cm arising from right adnexal region completely fused with 40cm portion of terminal ileum and on left side around 25cm of sigmoid colon. Uterus was hypoplastic around 4cm length. Right fallopian tube was not separately visualized. Left fallopian tube was normal looking. She was found to have streak gonad on left side. Right ovarian mass was adherent to anterior abdominal wall, during dissection tumor mass was cut open with plenty of friable necrotic tissue and dark altered blood. Mass was also adherent to posterior wall of urinary bladder densely. Bilateral ureters were dilated due to pressure effect of mass. Pelvic lymph nodes mostly

on right side were enlarged. Multiple tumors present on the mesentery of small bowel around 2x2cm.



Picture 3: Left streak ovary with left fallopian tube with hypoplastic uterus and right ovarian mass with plastered bowel.

She started developing fever from second postoperative day; antibiotics were upgraded to inj meropenam with continuation of metronidazole. She deteriorated on 4<sup>th</sup> postoperative and suspected of leakage of anastomotic site. Exploration done, small leak at ileoileal anastomotic site was present. Loop ileostomy was done. Patient shifted to postop kept on ventilator. Patient did not improve, had multiorgan dysfunction and expired on 5<sup>th</sup> postoperative day.

## Discussion

Gonadoblastoma is a benign mixed germ cell tumor, histologically composed of two cell lineages namely germ cells similar to dysgerminoma cells and sex cord cells that are similar to immature sertoli cells or granulosa cells, presence of micro calcification also helps in diagnosis.<sup>5</sup> Gonadoblastoma is a tumor that is relatively specific for individuals with dysgenetic gonads who have Y chromosomes in their genome. 46XY genotype is found in most cases, with mosaic 45X/46XY karyotype in some cases. Very few case reports of

gonadoblastoma in individuals with normal karyotype have been published. Gonadoblastoma has high potential to undergo malignant transformation or in majority of cases are associated with malignant germ cell tumors most commonly dysgerminoma and less commonly immature teratoma, endodermal sinus tumor, embryonal carcinoma or choriocarcinoma.<sup>3</sup>The prognosis with gonadoblastoma is uniformly good if they do not contain any elements of the more aggressive germ cell tumors and are completely removed, but can be lethal when associated with aggressive malignant germ cell tumors as four lethal cases reported by Scully and three lethal cases reported by Gallager, Talerman and Ito. Some individuals who appear to be non-mosaic 45, X using standard metaphase karyotyping may contain cryptic Y DNA and the frequency varies from 0% to 9.3% in published literature. <sup>6</sup>In present study histopathology from left ovary which appeared macroscopically streak come to be Gonadoblastoma, whereas karyotype was 45, X0. Screening of all non-mosaic 45, X patients (30-50 metaphases) using newer molecular methods like interphase FISH (Fluorescent In-Situ Hybridization) or more sensitive real time polymerase chain reaction in tumor tissue and peripheral blood is recommended to determine Y chromosome sequence.<sup>3,6</sup>

Endodermal sinus tumor is the second most common malignant germ cell tumor of the ovary. It is highly malignant and lethal germ cell tumor with tendency of early metastasis and rapid invasion of abdominal and pelvic structures and has very poor prognosis.

High alfa-fetoprotein in serum indicates endodermal sinus tumor, diagnosis confirmed with final histopathology. Surgery plus combination chemotherapy is the best treatment for this disease.<sup>4</sup>Approximately 50-60% gonadoblastoma are associated with malignant germ cell tumors commonly dysgerminoma.<sup>3</sup>Doger et.al. (2015) reported a phenotypically turner-like-girl of 13 years with 45X/46XY karyotype for whom exploratory laparotomy with bilateral gonadectomy were performed, histopathology revealed dysgerminoma in right ovary and gonadoblastoma in left ovary. She was started with hormone replacement therapy and doing fine in follow up.<sup>1</sup>Hasanzadehet. al. (2018) reported a case of 18-year-old girl with gonadoblastoma and dysgerminoma presented with primary amenorrhea, pain abdomen and abdominal mass with karyotype 46, XY who underwent bilateral salpingoophorectomy followed by BEP regimen chemotherapy as pelvic lymph nodes were involved by dysgerminoma. No evidence of recurrence has been reported.<sup>7</sup>Kota et.al. (2012) reported a case of 17 year-old-girl presenting with primary amenorrhoea with stigmas of Turner's syndrome with karyotype 46X inv (Y) who was adviced for prophylactic bilateral gonadectomy due to potential risk of malignancy but refused surgery. She was treated conjugated estrogen. After 12 months of diagnosis she presented with adnexal mass and underwent laparotomy with removal of right ovarian mass which came out to be dysgerminoma.<sup>2</sup>

Gonadoblastoma with ovarian germ cell tumors other than Dysgerminoma coexists very rarely. Etem et.al. (2009) reported a case of bilateral endodermal sinus tumor in a female of 21-year-old with Turner's syndrome who presented with primary amenorrhea with pelvic mass with karyotype 45X/46XY. She underwent TAH + BSO, omentectomy, lymphadenectomy. Pathology report showed endodermal sinus tumor in both ovaries. Pleural fluid and peritoneal cytology was positive for malignancy. Postoperative recovery was excellent and she received BEP and is under follow-up.<sup>4</sup>Gelincik et.al. reported a rare case of 18-year-old girl with coexisting gonadoblastoma and yolk sac tumor in left ovary. <sup>8</sup> Ono et.al. reported a case of ovarian endodermal sinus tumor in a 15-year-old girl with 45,X0/46,X,dic(Y) mosaicism. The patient's external genitalia was female; her left gonad consisted of a solid/cystic tumor, right ovary was replaced by streak and uterus immature.<sup>9</sup>

## Conclusion

As in present study, we could not follow the case, still the importance of karyotyping, early detection of Y chromosome sequence with new techniques like FISH, PCR; role of prophylactic gonadectomy in patient with Y chromosome to be highlighted based on literature review.

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