Mosaic Turner Syndrome Presenting with Ambiguous Genitalia and Mixed Ovarian Germ Cell Tumor in a Filipino Adult

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Abstract

This report details the case of a 24-year-old Filipino individual born with ambiguous genitalia, assigned female at birth, and raised as such. Around the age of 13, the patient began to develop secondary male characteristics. Medical assessment was postponed until the onset of abdominal pain led the patient to seek consultation. Cytogenetic testing revealed a sex chromosome disorder of sexual development with a mosaic karyotype of 45,X/45,X,del(X)(q13). Imaging, surgical exploration, and histopathologic evaluation confirmed that a pelvoabdominal mass originated from the left ovary and was a mixed germ cell tumor containing yolk sac tumor and mature teratoma components. At presentation, the patient also reported symptoms consistent with gender dysphoria. This case highlights the wide phenotypic variability of mosaic Turner syndrome and reinforces the importance of accurate neonatal sex assignment in individuals with DSD. It further emphasizes the need for healthcare providers to remain vigilant for such presentations to enable prompt, tailored, and comprehensive management.

Key words: disorder of sex development, ambiguous genitalia, mixed germ cell tumor

Introduction

Disorders of sex development (DSDs) are a group of congenital conditions in which chromosomal configuration, gonadal structure, or anatomical sex traits develop in ways that deviate from typical patterns.[1] Globally, they represent a significant subset of congenital anomalies, with some reports estimating a prevalence of up to 7% among such cases. Ambiguous genitalia are identified in approximately one out of every 4,500 live births.[2]

Earlier classification schemes categorized DSDs based on the type of gonadal tissue present. Within this framework, "true hermaphroditism" denoted the presence of both ovarian and testicular tissue in a single individual. The term "male pseudohermaphroditism" was used for individuals with testes but primarily female- appearing external genitalia, while "female pseudohermaphroditism" referred to those with ovaries but external genitalia that were masculinized or virilized.[3]

This report describes an uncommon presentation of mosaic Turner syndrome with an atypical clinical progression, emphasizing the broad variability of manifestations in this chromosomal condition. It also stresses the importance of early diagnosis in facilitating coordinated, prompt, and comprehensive care for patients with disorders of sex development (DSD).

The Case

History of Present Illness

A 24-year-old individual, reared as female, presented to the Obstetrics and Gynecology

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Outpatient Department of Davao Regional Medical Center due to abdominal pain and was subsequently referred to the Reproductive Medicine service for assessment of ambiguous genitalia. Informed consent from the patient and parental assent were secured for the publication of medical information and photographs.

The patient was the third child of a Gravida 6 Para 5 (5-0-1-5) mother with no known comorbidities. Delivery was via spontaneous vaginal birth at home at full term, with no prenatal consultations or medications reported during pregnancy. The mother denied any illnesses during gestation. At birth, a phallus-like structure was noted, but the patient was assigned female and reared accordingly. No newborn screening or further investigations were conducted.

At 13 years of age, the patient developed secondary male characteristics, including coarse pubic and axillary hair, facial hair, and deepeningof the voice. No breast development or menarche occurred.

At age 20, intermittent lower abdominal pain and vomiting episodes began. Abdominal ultrasound revealed a pancreatic mass, for which surgery was advised, but patient was lost to follow-up.

At age 22, persistent symptoms prompted private consultation. Repeat imaging showed a midpelvic mass suspected to be ovarian in origin, but again no further work- ups were pursued.

At 24 years, worsening abdominal pain with weight loss, poor appetite, and fatigue led to re-presentation at our facility.

Clinical and Laboratory Findings

The patient measured 137 cm in height and weighed 27.5 kg (BMI 14.6, underweight), with an arm span of 145 cm. Blood pressure was 90/60 mmHg. Aside from short stature and a broad chest, no other classic Turner syndrome stigmata—such as webbed neck, low posterior hairline, lymphedema, or cardiac/renal anomalies—were evident. The patient had thick axillary and facial hair without a prominent laryngeal bulge. Breast development was Tanner stage I. Abdominal palpation revealed a soft, non-tender abdomen with a pelvo-abdominal mass extending three fingerbreadths above the pubic symphysis. Baseline blood work, serum chemistry, and urinalysis were unremarkable. Chest radiography revealed thoracic dextroscoliosis, and ECG was normal.

Genital Organs

External genital assessment showed Tanner stage V pubic hair, a phallus-like structure measuring 3cm from the base, a small vaginal opening, and a separate urethral orifice. Transrectal ultrasound demonstrated a midline pelvo-abdominal mass measuring 10.59cm × 10.44cm × 8.11cm (volume 469.57 mL). The lesion was thick-walled and mainly solid, with irregular cystic regions and grade 3 vascularity. No uterus, cervix, or normal-appearing ovaries were visualized. CT scan findings supported a malignant ovarian neoplasm with moderate adhesions, though the side of origin was unclear.

Chromosomal Analysis

GTG-banding karyotyping identified two abnormal cell lines in 31 examined cells. Twenty-eight cells showed monosomy X (45,X), while two cells showed an X chromosome deletion at band q13 (45,X,del(X)(q13)). One cell displayed a complex abnormality, 46,X,del(X)(q13),t(7;14)(p22;24), though its clonal origin was uncertain. The final report was mosaic 45,X[28]/45,X,del(X)(q13)[2].

Endocrinologic Tests and Tumor Markers

Preoperative labs showed low estradiol (<25 pg/mL), elevated FSH (54 mIU/mL), and elevated LH (49 mIU/mL). 17OH-progesterone, DHEA-S, testosterone, and TSH were within normal limits. AFP was markedly elevated (>332 mIU/L), CA-125 was 72.1 u/mL, and LDH was 622 U/L. β-hCG, CEA, and CA 19-9 were normal.

Based on karyotype and phenotype, the leading diagnosis was mosaic Turner syndrome (45,X/46,X,del(X)), characterized by short stature, dysgenetic gonads, primary amenorrhea, and hypergonadotropic hypogonadism. Mixed gonadal dysgenesis without a Y chromosome was considered due to ambiguous genitalia and the possibility of one functioning gonad. Androgen excess disorders such as partial androgen insensitivity syndrome and 17β-hydroxysteroid dehydrogenase type 3 deficiency were entertained but deemed less likely given hormonal patterns. The tumor marker profile

strongly suggested a yolk sac tumor, possibly with a mature teratoma component, and dysgerminoma was considered but less favored.

Surgical Management

The patient underwent exploratory laparotomy, peritoneal fluid cytology, adhesiolysis, left salpingo-oophorectomy with frozen section, biopsy of the right ovary, and random peritoneal biopsy by the gynecology service. Frozen section revealed consideration of yolk sac tumor. Intraoperatively, there was 100cc of sanguinous fluid suctioned. The left ovary was converted into a 14cm x 8cm friable mass. The capsule was noted to have a 3cm x 4cm point of rupture at the superior portion and was actively bleeding (Figure 4). It was densely adherent to the posterior wall of the uterus, rectosigmoid and occupied the cul de sac. The omentum was adherent to the posterior portion of the mass. The left fallopian tube was grossly normal. The right ovary was small measuring 1cm x 2cm with smooth and glossy white surface and with a corresponding normal looking fallopian tube. The uterus was small and densely adherent to the posterior bladder (Figure 5). Vaginoscopy and hysteroscopy were performed. Systemic survey revealed no resistance upon insertion of the scope. There were no vaginal and intrauterine masses noted. Left and right ostia were both identified (Figure 6).

The liver was smooth and grossly normal-looking. The pancreas was enlarged to 10cm x 12cm, movable, solid with nodulations, highly vascularized confined between the liver and the spleen. The appendix was grossly normal-looking. No palpable lymphadenopathies at the pelvic and aortic region. Pelvic lymph node dissection, partial omentectomy, distal pancreatectomy, splenectomy, en bloc segmental resection of the distal transverse colon, double-barreled ileostomy drain, and JP drain insertion were done by the Onco-Surgery service.

The specimen taken were sent to the Pathology section. The final histopathologic diagnosis were as follows: Left ovary: Mixed Germ Cell Tumor (90% Yolk Sac Tumor and 10% Mature Teratoma) 11cm in greatest dimension with lymphovascular invasion. Acute Salpingitis for the left fallopian tube. Right ovarian tissue consistent with ovarian tissue. Omentum, abdominal and pelvic peritoneal tissue, bladder reflection, bilateral pelvic lymph nodes specimen all revealed negative for malignancy. Postoperatively, the plan was to start standard

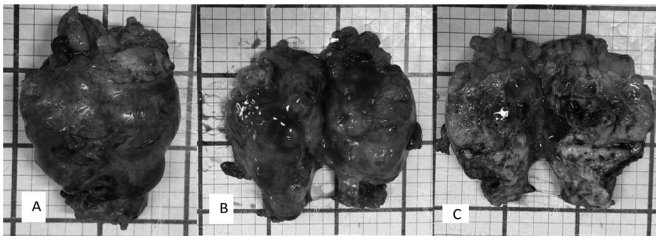

Figure 4. Gross, Left ovarian mass; **(A) & (B)** Cut-section **(C)**

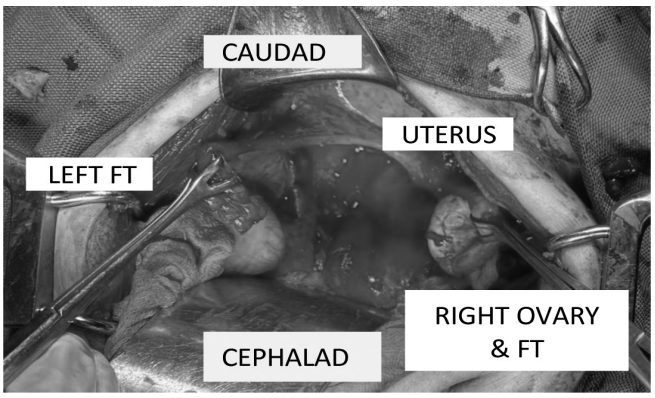

Figure 5. Uterus, Left fallopian tube post left ovarian mass removal, Right ovary & fallopian tube.

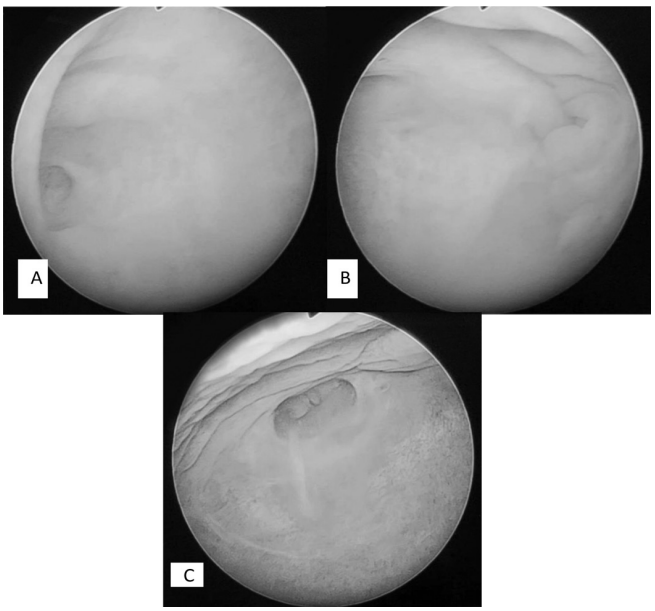

Figure 6. Uterus, Left fallopian tube post left ovarian mass removal, Right ovary & fallopian tube.

postoperative chemotherapy and hormonal replacement therapy with both estrogen and progesterone.

Final histopathologic diagnosis of the Pancreatic mass revealed: Well-differentiated Pancreatic Neuroendocrine Tumor, Grade 2. Congestion of the spleen and Segments of transverse colon with serosal acute inflammation.

Follow-up

Patient was followed up, and the postoperative plan included standard postoperative chemotherapy and hormonal replacement therapy with both estrogen and progesterone.

Psychosocial Issues

At the time of presentation, the patient was unemployed, attained secondary level with signs of gender dysphoria. The patient identified as female with sexual interest towards the male sex, but due to apparent masculinization over the years, the patient had already started to develop issues on gender identity and became more socially withdrawn. The patient denied any suicidal ideations. The patient was referred to Psychiatry service for evaluation and psychosocial support.

Discussion

Disorders of Sex Development (DSDs) encompass a heterogeneous group of congenital conditions in which chromosomal pattern, gonadal structure, and genital anatomy do not correspond in the usual way. The 2006 International Consensus Statement on the Management of Intersex Disorders organizes DSDs into three major categories based on chromosomal complement and etiology: sex chromosome DSD, 46,XY DSD, and 46,XX DSD. Cytogenetic analysis remains a cornerstone of initial evaluation, as it both confirms diagnosis and directs further investigation and management.

Our patient's karyotype—mosaic 45,X/45,X,del(X)(q13)—places the case in the sex chromosome DSD group, specifically as an unusual variant of Turner syndrome. Although Turner syndrome is classically characterized by monosomy X (45,X), mosaic forms may produce highly variable phenotypes, sometimes with partial sexual development or ambiguous genitalia, as in this case.

Sexual Differentiation and Pathophysiology

Sex determination begins between the 6th and 8th weeks of embryogenesis, when bipotential gonads commit to either ovarian or testicular differentiation. The presence of the SRY gene on the Y chromosome triggers testis formation through activation of SOX9, NR5A1, and other downstream factors. In its absence, ovarian differentiation is promoted by genes such as WNT4, RSPO1, and DAX1.[5] Disruption at any step can result in atypical gonadal and genital development.

In mosaic Turner syndrome, some cells lack a second sex chromosome altogether, while others may carry structural abnormalities of the X chromosome. This genetic variability explains the broad spectrum of physical and reproductive features, from complete gonadal dysgenesis to partial sexual maturation.[6,7]

Malignancy Risk in DSD

Individuals with DSD—particularly those with dysgenetic gonads and Y chromosome material—face a substantially elevated lifetime risk of gonadal tumors, with estimates up to 35% in some series.[8,9,10] The most common is gonadoblastoma, though other germ cell tumors such as yolk sac tumors, dysgerminomas, and teratomas can occur. Notably, despite the absence of detectable Y chromosome material on karyotyping, our patient developed a malignant mixed germ cell tumor—an unusual, though previously reported, phenomenon.

Yolk sac tumors are highly aggressive neoplasms, typically presenting unilaterally, but have favorable outcomes when identified early and treated with surgical intervention followed by platinum-based chemotherapy. The presence of a mature teratoma in this case is consistent with the presentation of mixed germ cell tumors typically observed in younger patients.

Psychosocial Considerations

The late diagnosis—occurring well into adulthood—had repercussions beyond physical health. Upon presentation, the patient showed

signs of gender dysphoria, characterized by distress stemming from a mismatch between the assigned gender at birth and the individual's experienced gender identity.[1,12] The combination of delayed recognition, masculinization at puberty, and tumor-related morbidity compounded psychosocial stress and social withdrawal.

Psychological support should be an integral component of DSD management, ideally introduced during adolescence. Counseling can help patients process gender identity, sexuality, body image, and interpersonal relationships, reducing the risk of long-term mental health complications.

Management Principles

Effective DSD care requires multidisciplinary coordination involving endocrinology, genetics, gynecology, urology, oncology, and mental health professionals. Geneticists assist in confirming diagnosis, counseling families, and identifying at-risk relatives.[13] Early evaluation of ambiguous genitalia is both a medical and social urgency—sex assignment decisions must weigh karyotype, gonadal type, genital configuration, potential fertility, need for hormone therapy or surgery, and family cultural context.

When tumor risk is high, as in dysgenetic gonads, prophylactic gonadectomy is recommended without undue delay. In this case, earlier recognition of Turner mosaicism could have prompted earlier intervention and possibly prevented advanced tumor development.

Conclusion

This case illustrates the diagnostic and therapeutic challenges posed by mosaic Turner syndrome with ambiguous genitalia, especially when diagnosis is delayed into adulthood. It underscores the necessity of early recognition, thorough karyotyping, and integrated psychosocial care in DSD management. Timely, multidisciplinary, and patient-centered approaches not only improve survival in tumor-associated cases but also enhance long-term quality of life.

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