"WHEN AN AGEING WOMAN IS GENETICALLY MALE"

A CASE OF ANDROGEN INSENSITIVITY SYNDROME WITH INTRA-ABDOMINAL TESTES IN A 62 YEAR OLD WOMAN: A CASE REPORT

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ABSTRACT

Androgen Insensitivity Syndrome (AIS) is a disorder wherein a patient presents with a female phenotype but genetically male with an XY karyotype. Typically, AIS is diagnosed at the beginning of second decade, when a phenotypically female patient complains of amenorrhea. It is extremely rare to make a first diagnosis of AIS after the fifth decade of life. This case report presents a 62-year old female who consulted because of primary amenorrhea and intra-abdominal mass. Patient was diagnosed as Complete Androgen Insensitivity Syndrome based on PE findings, imaging studies, endocrine tests and karyotyping. She underwent laparoscopy followed by exploratory laparotomy, adhesiolysis and bilateral orchiectomy done under general anesthesia. This report will discuss diagnosis and appropriate management of patients with Complete Androgen Insensitivity.

Key words: Androgen Insensitivity Syndrome, elderly, intra- abdominal testes

CASE REPORT

This is a case of R.R, a 62 year old female, married, retired school teacher who consulted at the Outpatient Department with a chief complaint of hypogastric pain of two months duration. Patient had thelarche at 13 years old, nulligravid and no menarche. Coitarche was at age 28, with one lifetime partner and married for 32 years.

Figure 1 (left). Index patient with normal habitus, phenotypically female.

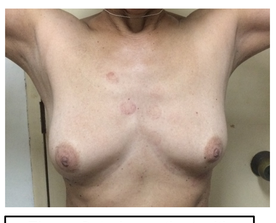

Figure 2. Index patient with Tanner stage 4 breast development.

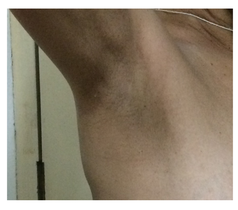

Figure 3. Index patient with absent axillary hair.

On PE, patient appeared phenotypically female, normal built, with average weight and height (Figure 1). Breasts are symmetrical, areola and papilla form a secondary mound above level of breast (Tanner Stage 4). No breast mass nor lesions, no nipple discharge (Figure 2). The axillary area had smooth skin, no lesions and no axillary hairs noted (Figure 3). The abdomen was flat, with normoactive bowel sounds, soft and nontender. There was a movable, non-tender, cystic mass, measuring 8x6 cm.

On pelvic exam, external genitalia was grossly normal with sparse growth of long, thin, straight, pigmented pubic hair along mons pubis and labia majora; (Tanner stage 2) with presence of a vaginal orifice. Speculum exam revealed a smooth vaginal wall, blind pouch, no cervix visualized, no masses, lesions, erosions, discharge. On internal examination, the vaginal canal measured 6cm in length and ends in a blind pouch. No palpable cervix, uterus, adnexal mass were noted.

At the Outpatient Department, patient was referred to the Reproductive Endocrinology and Infertility (REI) service. Laboratory tests were done and results showed: Whole abdomen ultrasound; visualization of bilateral kidneys with note of nephrolithiasis on the left, and Pelvic Mass probably Ovarian in origin. Transvaginal ultrasound revealed absent uterus, cervix and ovaries; occupying the pelvic cavity a unilocular, cystic structure measuring 10.27 x 10.8x 10.27cm with low to medium level echoes within. TVS impression was pelvic mass consider ovarian new growth probably benign by IOTA subgroup and Sassone Score 6 (Figure 4). Serum level determination were as follows: elevated FSH and LH levels (28.4 mIU/ml and 79.1 mIU/ml respectively), and testosterone of 9.2 nmol/L, normal for male and elevated for female; Additional test are as follows: serum LDH 200.22 U/L, Serum B-HCG of 3.96, CA-125 of 21.36 U/ml, AFP of 1.26 IU/ml. All tumor markers are within normal range. Karyotyping showed 46, XY. Abdominal CT scan showed a 9.5 x 9.2 cm, non enhancing cystic lesion in the pelvis above the urinary bladder without enhancing solid component. This may represent a large Mullerian duct cyst (Figure 5).

Assessment then was Primary Amenorrhea secondary to Androgen Insensitivity Syndrome; Pelvic Mass rule out Gonadoblastoma versus Seminoma.

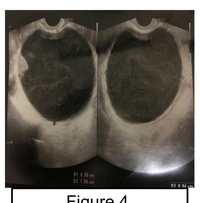

Figure 4. Transvaginal ultrasound showing pelvic mass with benign sonologic features.

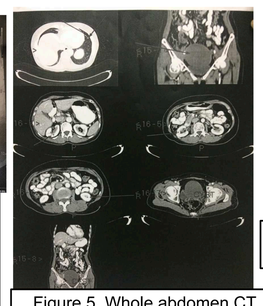

Figure 5. Whole abdomen CT scan showing mass in the pelvis with no solid lesions.

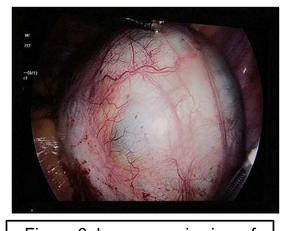

Figure 6. Laparoscopic view of pelvoabdominal mass.

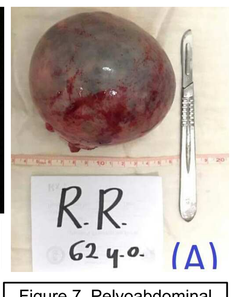

Figure 7. Pelvoabdominal mass, serous cyst

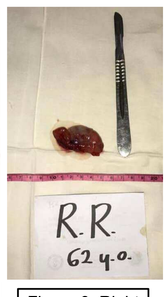

Figure 9. Right atrophied testis

On laparoscopy, the pathology was identified, located at the abdominal cavity, midline, with smooth white external surface, measuring 10x10 cm (Figure 6). The cyst had filmy adhesions to the bowel and pelvic sidewalls. On referral to urologist on board, the cyst was probably malignant. Hence, laparoscopy was converted to exploratory laparotomy followed by bilateral orchiectomy. On laparotomy, urology intraoperative findings noted a probable left testicular mass (Figure 7) and atrophied right testis (Figure 8). Specimen were removed and sent for histopathology.

The patient tolerated the procedure well and was subsequently discharged on her third post-operative day. Histopathologic examinations revealed: (a) Pelvoabdominal mass identified as Serous Cyst (Figure 9); (b) Right testis, consistent with cryptorchid testis; (c) Cyst fluid: negative for malignant cells.

DISCUSSION

Androgen Insensitivity Syndrome (AIS) is a condition wherein affected individuals have an XY chromosome and secrete normal levels of testosterone. However, there is lack of receptor activity in their targeted end organs resulting to deficient male internal and external genitalia. Individuals with Complete Androgen Insensitivity Syndrome (CAIS) present with phenotypically female external genitalia. AIS is inherited in an X-linked recessive fashion, although 30% are de novo mutations.

In the Philippines, there have been six published cases of AIS (Landines, 1982; Cruz, Morales and Bongala, 2000; Alday-Atienza, 2002; Ang-Sy, Tan-Garcia, Garcia, 2007; Lipana, Tanangonan, 2009; Villafuerte, Soriano- Estrella, 2016). All cases were diagnosed when the patients were in their second or third decades of life. Internationally, there was one case from The International Journal of Surgery Case Reports 2013, who presented with CAIS in a 70-year old patient with inguinal testes. This case presents a locally diagnosed elderly patient having an intra-abdominal testes, with a benign pathology.

The most common presentation of CAIS is primary amenorrhea in a female adolescent, usually during the second decade of life. It can also present as inguinal hernia in an infant or child with an incidence rate of 1.1%. The testes may be located as labial swelling or found intra-abdominally. The first diagnosis of CAIS after the fifth decade of life is rare and that the risk of malignant transformation increases with age. With 3% occurring malignancy at age 20, and increases to 30% at age 50.9. In the index patient, malignancy was considered because of age and location of the testes.

Aside from the clinical findings in CAIS of absent uterus, short blind ending vagina, scant or absent pubic and/or axillary hair, Individuals show a pattern consistent with an X- linked trait with reports of other family members exhibiting the same clinical findings. Pelvic ultrasound, CT scan and the gold standard MRI should be obtained to document the internal anatomy. The patient in this case report was diagnosed with CAIS based of the following findings: phenotypically female, primary amenorrhea, elevated FSH, LH, and a normal level of testosterone for male, XY karyotype, with significant addition of an intra-abdominal testis.

The management of patients with Androgen Insensitivity Syndrome requires a multidisciplinary approach. The Multidisciplinary team (MDT) is composed of gynaecologist, endocrinologist, urologist, psychologist and clinical geneticists.

The standard surgical management for CAIS is orchiectomy. This should be performed after puberty because of the risk of malignant transformation of up to 30%. Also, the patient has reached breast and height development. Sex identity is already established. Sexual identity and sexual rearing was not a problem in the case of our patient. At the age of 62, our patient has a solid foundation of her femininity. She is married for 32 years has 2 adopted children and 2 grandchildren. Medical management for patients with AIS is composed of Hormonal Replacement Therapy (HRT) and psychological support. Estrogen therapy is needed to initiate puberty, maintain feminization and to prevent osteoporosis.

Based on Beauchamp and Childress ethical principles of beneficence, non-maleficence, autonomy and justice, it is integral to disclose the genotype of AIS at the time of diagnosis. If the diagnosis was made during infancy or soon after, together with a psychotherapist, the parents are responsible in making the decision when to disclose the diagnosis to the patient. In the index patient, she was informed of her diagnosis as soon as the karyotyping result was obtained. She exerted autonomy in her decision to give full disclosure about her condition to her husband. This knowledge of her condition did not seem to harm their marital relationship. Her spouse was very emotionally supportive and continued to be her caregiver throughout her stay at our institution. Regardless of age at diagnosis, CAIS often cause psychological distress for the patient and her family. Long term counselling is strongly encouraged.

CONCLUSIONS

We report a rare case of Complete Androgen Insensitivity Syndrome with intra- abdominal testes in a 62 year-old phenotypically female who presented with a pelvic mass and primary amenorrhea. Karyotyping showed 46, XY chromosome. Surgical intervention was immediately done due to the high risk of malignancy. Fortunately, result showed a benign cystic mass histopathologically, and confirmed the diagnosis of intra-abdominal testes. Aside from gonadectomy, part of her long term care was counselling, her condition was explained to her and her husband. In this case, there was a holistic approach to the condition of the patient, her interaction with her family and peers, medical and psychological complications were undertaken.

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