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Case report

A CASE REPORT OF COMPLETE ANDROGEN INSENSITIVITY SYNDROME RISING A CONCERN ABOUT THE TIME OF SURGERY AND THE ROLE OF PARENTS' BEHAVIOR

Victoria Spasova[1], Liliya Koleva[2,3], Svetlana Shumarova[4,5], Diana Hristova[5,6], Ventsislava Pencheva[5], Anatoli Kolev[4], Bozhidar Karamishev[4], Daria Koleva[4], Vladislav Petkov[4], Svetozar Marangozov[7], Vesela Karamisheva[8,9],

1)Department of Medical Genetics, Medical University of Sofia, Bulgaria.
2)Operative gynecology clinic UMBALSM "N. I. Pirogov", Sofia, Bulgaria.
3)University Hospital "Sofiamed", Sofia, Bulgaria.
4) Department of Surgery, Medical Faculty, Medical University of Sofia, Bulgaria.
5)University Hospital "Aleksandrovska", Medical University Sofia, Bulgaria.
6)National Center for Infectious and Parasitic Diseases, Sofia, Bulgaria.
7)Military Medical Academy, Sofia, Bulgaria.
8)Second gynecology clinic SBALAG "Maichin dom", Sofia, Bulgaria.
9)Department of Obstetrics and Gynecology, Medical University of Sofia, Bulgariaa.

.**ABSTRACT**

Purpose: This case study refers to a case of complete androgen insensitivity syndrome, which presented with amenorrhea back in the past.

Case: After conformation of the diagnosis, parents decided not to reveal the condition's specifics to the patient. At the age of 34 years, she attended our hospital with abdominal swelling, and the following CT scan showed an abdominal mass arising from the ovary of 13 cm x 14 cm size. A laparotomy was done, and a mixture of solid and cystic mass of 20 cm in diameter was found and removed with the ovary. Histopathology of the tumor showed features of testicular seminoma.

Conclusion: The aim of this case report is to outline the difficulties in choosing whether and when to do the gonadectomy and whether and how to explain the condition to the patient.

Keywords: androgen insensitivity syndrome, surgery, malignancy, disorders of sex development, psychology impact,

INTRODUCTION

Androgen insensitivity syndrome (AIS) is an X-linked recessive condition that is the most common cause of disorders of sex development (DSD) in 46 XY individuals [1, 2]. The complete form of the disorder is characterized by a female phenotype with normal female external genitalia. Instead of female internal genitalia, these individuals have testes producing age-appropriate normal concentrations of androgens [2, 3].

The malignancy rate in AIS is considered lower than in other DSD [4]. Nevertheless, the risk of gonadal malignancy development in complete androgen insensitivity syndrome (CAIS) is reported to be 3.6% at 25 years and 33% at 50 years [5]. The most common neoplasms include germ cell neoplasia in situ and invasive germ cell tumors of the gonad (including seminoma/non-seminomas, dysgerminoma/non-dysgerminomas) [6]. Even though the risk of malignancy increases with age, there is no consensus on whether or not the gonadectomy should be performed and what is the optimal time for the procedure.

The CAIS lacks external signs of genital ambiguity, and it is not a life-threatening condition. Nonetheless, coping with this diagnosis is still a great challenge for the patients and their parents. The main cause for this is the large gap in understanding this condition among societies. In many cases, this results in insensitive reactions and stigmatization for patients with DSD [7]. It is not unusual for parents to find the DSD diagnosis distressing, and consequently, they may choose not to share the disease details with their affected children. Studies show that more than 60% of parents of children with DSD experience difficulties in discussing the issue with friends and relatives, 68%

worry that the disease would result in their child being stigmatized [8].

The case we present is an example of how misunderstanding of DSD from society rises severe physical and psychological problems for patients and their families.

CASE REPORT

A 34-year-old phenotypically female who presented with gradually increasing abdominal swelling and discomfort was diagnosed with a cystic formation of the right ovary. She was admitted to our hospital for surgical removal of the ovary mass. Her gynecologic history included primary amenorrhea. There was no history of other gynecologic disturbances. Her surgical history was remarkable for a bilateral inguinal hernia as a child. She had no relevant family history.

Our patient had well-developed breasts and sparse pubic hair. The vagina appeared normal with a blind end, and the cervix was not visualized on the gynecologic examination. No uterus was observed on the abdominal palpitation. The ultrasound examination revealed an absent uterus and a large, well-defined mass in the pelvis sizing 15 cm in diameter.

A private conversation was held with the patient's mother. She disclosed that cytogenetic analysis done in the past showed a normal male karyotype – 46, XY. The diagnosis of CAIS was established by undermusculinized external genitalia, normal testosterone levels, blind end of the vagina, absence of ovaries and a uterus, and 46, XY karyotype. The patient had never received hormone replacement during puberty and post-puberty. The family decided not to explain the precise features of the condition to the patient in order not to disturb her self-esteem and self-perception. They explained to their daughter that because of a congenital condition she will never menstruate and she will not be able to have children. However, they never revealed the details about the condition.

The following abdomen-pelvis CT (contrast) was suggestive of a large lesion with cystic and solid components arising probably from an ovary tissue. The lesion was reaching the rectum and the urinary bladder, sizing 13cm x 14cm (Fig. 1 and 2). No enlargement of the lymph nodes was detected.

Fig. 1. Contact-enhanced CT image of a large non-homogenous cystic formation in the right hemipelvis în the level of rectum

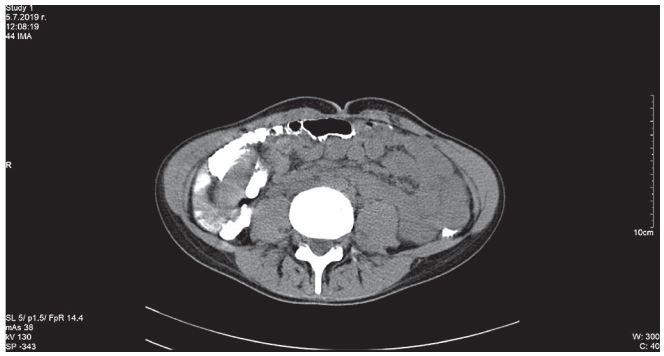
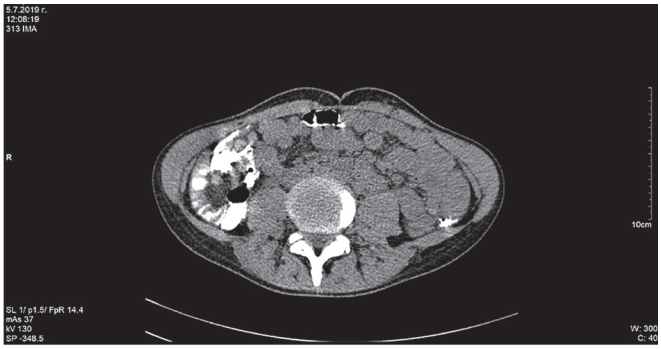


Fig. 2. Pelvic CT scan of the patient revealing a tumor with cystic and solid components on the level of urinary bladder



Laparotomy was conducted under general anesthesia. A tumor arising from the right testicle was totally removed along with the right testicle and part of the omentum. The left testicle was seen looking immature, and a biopsy specimen was obtained from it. The post-operative period was uneventful. Histopathological examination revealed: testicular seminoma of the right "ovary" and prepubertal testis morphology of the left "ovary". The patient was referred to an Oncology Department, but no further treatment regimen was prescribed.

The condition's specifics were discussed with the mother to make her rethink the decision not to reveal it to her daughter. However, she stuck to her thesis that the situation is too puzzling and revealing the details about the disease would cause extreme stress and confusion for the patient.

DISCUSSION

AIS, formerly known as Morris syndrome or testicular feminization, is a spectrum of androgen function defects. The incidence of this disorder is estimated to be approximately 1 case per 20,400 live-born males. [9] A loss-of-function mutation in the gene coding the androgen receptor (AR) is the cause of AIS. According to the amount of properly functional androgen receptors, this failure of virilization can be divided into three phenotypes: complete androgen insensitivity syndrome (CAIS), partial androgen insensitivity syndrome (PAIS), and mild androgen insensitivity syndrome (MAIS). [10] Patients with CAIS are often identified in their teenage years for the lack of menstruation. [11] Many of them have a medical history of hernia surgery and/or masses in the inguinal canals that are found to be testes during surgery. [12, 13] The majority of CAIS patients lack pubic and axillary hair, while breasts and female adiposity develop normally because of the conversion of testosterone to estradiol. [14]

A milestone in the management of CAIS is the decision of whether or not to remove the testes due to an increased risk of gonadal tumor development [15, 16]. The main causes for the development of germ cell tumors in patients with AIS include expression of early fetal germ cell factors (OCT3/4, PLAP, etc.) and TSPY (testis-specific protein Y-encoded) in germ cells in the DSD gonad. [15] Semi-

noma, the most common testicular tumor in CAIS, is usually presented after the age of 30 [6]. Given the malignancy risk, the recent consensus on the management of intersex disorders advocates early gonadectomy, taking into consideration the availability of estrogen-replacement therapy [17, 18]. On the contrary, some argue that the malignancy risk in early childhood is low and propose a removal of the gonads after puberty when feminization is complete [19]. The benefits of natural testosterone production for patient quality of life make the decision on the exact timing of surgery even harder [6].

The treatment of our patient was late according to both approaches, therefore, the malignancy process was already evident. Such a slow reaction is a consequence of various mistakes. Firstly, the interaction between the physicians who establish the diagnosis and the family did not work. The early and proper explanation of the condition to the parents is the key to a better understanding of the pathophysiology of DSD and CAIS, respectively. Most above all, it helps parents make timely decisions on the proper surgical and hormonal treatment of their child. Parents' trust should be gained after the diagnosis is established to allow their healthcare provider to make evidence-based steps toward their child's treatment. Secondly, the refusal of the mother to accept the diagnosis and disclose it to her daughter. Of course, parents react differently, and some of them feel personal discomfort discussing the issue of gender, sexuality, and genetic conditions. Moreover, some feel their child's condition is extremely difficult to explain, and they fear sharing information about DSD would lead to stigmatization [20]. The abovementioned raises the question of whether doctors should disclose information to patients after they reach lawful age against their parent's will. Lastly, society is still unaware of what exactly DSDs are, and the topic is "forbidden" for public discussions. This field is vast, and its bases should be put during school years so that later talking about it would not cause embarrassment.

The medical prognosis for patients with CAIS is excellent. However, psychological morbidity is common. The diagnosis of being genetic and gonadal male in a phenotypic female may have a serious physiologic impact on the patient. This may range from issues with identity to the assessment of one's gender. In our case, parents decided not to explain the medical condition to their child in order to protect her from the possible difficulties in the assimilation of the diagnosis. Unfortunately, that decision led to delayed treatment and the development of cancer.

CONCLUSION

The case we present illustrates the importance of early surgical removal of the abdominal gonads and the lack of societal awareness of DSD disorders. We want to emphasize the tough decisions parents and physicians should make regarding whether or not to reveal the underlying condition to the patients themselves. In conclusion, our case report illustrates the obstacles the doctors and families have to face and overcome when dealing with CAIS.

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Address for correspondence:
Victoria Spasova, MD
Department of Medical Genetics, Medical faculty, Medical University of Sofia;
2, Zdrave Str, 1431 Sofia, Bulgaria,
E-mail: vic.spasova@gmail.com,