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A Rare Cause of Primary Amenorrhea: Swyer's Syndrome: A Case Report

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Abstract **Case Report**

Swyer syndrome is defined as pure XY gonadal dysgenesis (PGD). The phenotype is unequivocally female with a clinical history of primary amenorrhea and impuberty. We present a case of primary amenorrhea for which the etiological investigation revealed a 46XY karyotype. The patient was 34 years old and was admitted to the hospital for the development of primary amenorrhoea. On clinical examination, the patient had an adult female morphotype with a normal vulva. Hormonal work-up revealed hypogonado-hypergonadotropic, pelvic MRI: showed normal vagina and uterus with bilateral hypotrophic ovaries without follicles, complemented by a karyotype which showed 46XY on all metaphases analysed. The patient was put on oestrogen and vitamin supplementation and psychological counselling. A prophylactic gonadectomy was indicated for the patient. Swyer's syndrome remains a rare condition, even less so in the hierarchy of etiologies of primary amenorrhea. The performance of a karyotype in primary amenorrhoea has made this diagnosis possible. The risk of malignant transformation of undifferentiated gonads is high, requiring discussion of prophylactic gonadectomy as soon as the diagnosis is established. Complications of hypoestrogenism and psychological counselling are the other main areas of treatment. Up to now, egg donation remains the only alternative for infertility.

Keywords: Primary amenorrhea- Swyer's syndrome- XY gonadal dysgenesis.

INTRODUCTION

Swyer's syndrome is defined as pure XY gonadal dysgenesis (PGD) resulting from premature destruction of the fetal gonads which are reduced to an undifferentiated stroma with absence of germline and endocrine secretion. The phenotype is female without sexual ambiguity with a clinical picture associating primary amenorrhea and impuberty [1]. We present the case of a patient in whom a karyotype allowed us to clarify the etiological horizon of a primary amenorrhoea by showing 46XY on all the metaphases analysed.

OBSERVATION

A 34 year old female patient initially consulted a gynaecologist for primary amenorrhoea at the age of 16, where a check-up had been requested but not clarified and subsequently lost sight of. A few years later, the patient saw us again for clarification of the primary amenorrhea. The clinical examination of the patient had noted a female morphotype with a normal aspect of the vulva, a Tanner S5P5, a height of 1.72 m without real dysmorphic syndrome. The hormonal assessment revealed a hypogonado-hypergonadotropic with FSH: 118.20 mIU/l; LH: 17.89mIU/ML; estradiol: 10pg/ml; she had a normal prolactin, a collapsed AMH of 0.10ng/ml. The assessment of the bone consequences of hypoestrogenism noted a vitamin D deficiency with 13.60ng/ml as well as osteopenia on the bone densitometry (ODM). On imaging, pelvic MRI: showed a normal vagina and uterus with bilateral hypotrophic ovaries 12x7mm on the right and 11x9mm on the left without follicles. The investigation was completed by a karyotype which showed 46XY on all the metaphases analysed. This was therefore an unambiguous sexual differentiation disorder with a female phenotype suggesting pure gonadal dysgenesis (PGD) XY. The patient was put on oestroprogestogen treatment and vitamin supplementation. She received psychological counselling regarding the disclosure of her genetic sex. The patient was referred to gynaecology for diagnostic laparoscopy of the gonads and possibly prophylactic bilateral gonadectomy in view of the risk of gonadoblastoma in this field.

DISCUSSION

The first description of Swyer's syndrome was made in 1955 by Swyer, who identified it as a new form

of hermaphroditism where, unlike the more common forms, the Mullerian structures were normal in place. These patients had a genetic XY sex with dysgenic gonads not producing sex hormones responsible for the lack of virilisation but without sexual ambiguity with a female phenotype [2, 3].

It is caused by a mutation in the SRY gene (testicular determinism gene located on the distal short arm of the Y chromosome), the expression of which is essential for the activation of other testicular-specific genes: SOX9, which ensures cell migration and proliferation, thus engaging the gonad in the testicular differentiation pathway [4].

Ieuan A. Hughes [5] in his study on sex determination and differentiation published in 2004, showed a transformation to male phenotype in XX female mice after introduction of an SRY transgene. In the same study, a mutation in the SRY gene and in the SRY homologous autosomes, as well as in the SOX9 gene, were reported in a group of 46 XY females with pure gonadal dysgenesis. Such patients most often present in adolescence with primary amenorrhoea due to their non-functioning gonads.

The endocrine evaluation usually shows hypergonadotropic hypogonadism with elevated basal LH and FSH, as the gonads are not functional. Imaging studies, including pelvic ultrasound or MRI, demonstrate the presence of a uterus and may show bilateral striated gonads. If a gonadectomy or gonadal biopsy is performed, gonadal histology reveals bilateral striated gonads with dysgenesis. The diagnosis of pure XY gonadal dysgenesis is made based on a physical examination assessing the female phenotype, hormonal evaluation showing elevated FSH and LH gonadotropins, imaging studies showing Mullerian structures with bilateral undifferentiated striated gonads, genetic studies showing an XY karyotype with SRY gene study and gonadal histology [6].

Our patient presented with an unambiguous female appearance with hyper gonadotropic hypogonadism, XY genetic sex, mullerian structures were well present on imaging. The imaging described hypotrophic ovaries without germ cells which could be interpreted as undifferentiated gonads, the study of the SRY gene had not been performed. All these arguments allowed us to make a diagnosis in accordance with the literature.

The undifferentiated gonads in these patients have an estimated 30% risk of cancerous transformation, making prophylactic bilateral castration advisable [1]. A meta-analysis of patients with pure XY gonadal dysgenesis anomalies with SRY revealed a 52.5% incidence of gonadal tumours [7].

The question of the appropriate timing of gonadectomy in these patients: Thirteen (13) observational studies from 1970-2013 were identified with information on the indications for performing gonadectomy and/or advice regarding the timing of performing gonadectomy in patients with XY gonadal dysgenesis [6-8]. Most cases of gonadoblastoma or dysgerminomas have been discovered at the time of diagnosis of XY gonadal dysgenesia, usually occurring in adolescence. The consistent recommendation in the literature is to perform bilateral gonadectomy as soon as possible after the diagnosis is made, given the high risk of gonadoblastoma with progression to dysgerminoma [6, 8].

Our patient was 34 years old, a rather advanced age far from adolescence and therefore at higher risk of gonadoblastoma as described in the literature. Based on these data, the patient was referred to gynaecologists for prophylactic gonadectomy. In addition to the risk described above, these patients also present a bone and cardiovascular risk due to the hypoestrogenic climate, requiring oestroprogestogenic hormone replacement therapy [9]. For the problem of infertility, egg donation remains the only therapeutic option to date [1].

Our patient had been treated with hormone replacement therapy (HRT), had osteopenia and vitamin D deficiency, and was taking vitamin supplements. A psychological follow-up was recommended.

CONCLUSION

The syndrome of Swyer or pure gonadal dysgenesis XY remains a rare pathology even less in the hierarchy of the etiologies of primary amenorrhea. Karyotyping in primary amenorrhoea has made this diagnosis possible. It is a pathology that should be explored as fully as possible with molecular biologists to make progress on the complex path of sexual determinism. The risk of malignant transformation of undifferentiated gonads is very high, making it necessary to discuss prophylactic gonadectomy. The complications of hypoestrogenism and psychological care are the main therapeutic issues. Oocyte donation is still the only alternative for infertility.

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