46 XY Gonodal Dysgenesis

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ABSTRACT

46,XY disorder of sex development (46,XY DSD) is characterized by a 46,XY karyotype, ambiguous genitalia with mild to severe penoscrotal hypospadias ,dysgenetic testes, reduced to no sperm production, and müllerian structures that range from absent to presence of a fully developed uterus and fallopian tubes. 46,XY complete gonadal dysgenesis is characterized by a 46,XY karyotype, normal female external genitalia, completely undeveloped streak gonads, no sperm production, and presence of normal müllerian structures and often not diagnosed until puberty when secondary sexual characteristics fail to develop. The diagnosis of 46,XY DSD and 46,XY gonodal dysgenesis relies on clinical findings, gonadal histology, chromosome analysis testing to detect changes in genes.Because of increased risk for gonadal tumors(most commonly dysgerminoma) abdominal streak gonads should be surgically removed . Typically, hormone replacement therapy (HRT) is required from puberty onward. Here we describe the clinical, endocrinological and molecular data of a patient with complete 46, XY gonadal dysgenesis.

Key words: *46, XY, gonadal dysgenesis, primary amenorrhea*

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ÖZET

46,XY cinsiyet gelişim bozukluğu(46,XY CGB) 46,XY karyotip ile karakterize hafif yada ağır penoskrotal hipospadias, azalmış sperm üretimi ,disgenetik testisin olduğu ambigus genitalyadan matür uterus ve fallop tüplerinin olduğu geniş bir kliniğe sahiptir. 46, XY komplet gonadal disgenezi 46, XY karyotip ,normal kadın dış genitaldan sperm üretiminin olmadığı testis, streak gonad, yada normal müllerian yapıların varlığı ile karakterizedir.Sıklıkla seconder sex karakterilerinin gelişiminin geçiktiği puberte dönemine kadar tanısı gözden kaçabilir. 46,XY cinsiyet gelişim bozukluğu ve 46,XY gonodal disgenezi tanısı klinik bulgular,gonodal histoloji ve kromozom analizine dayanır.streak gonadlar artmış tümör riski(sıklıkla disgerminoma) nedeniyle cerrahi olarak çıkarılmalıdır. hormon replasman tedavisi puberteden itibaren gerekmektedir.bu yazıda 46, XY gonadal dysgenesizi olan bir vakanın klinik ,endokrinolojik ve genetik bulguları sunulmuştur.

Anahtar kelimeler: *46, XY, gonodal disgenezi, primer amenore*

INTRODUCTION

46,XY gonadal dysgenesis is characterized by abnormal testicular determination. This clinical condition can be divided into three histologic forms; 46,XY complete or pure gonadal dysgenesis , 46,XY mixed gonadal dysgenesis , partial gonadal dysgenesis (1). 46 XY pure gonadal dysgenesis is a rare condition of intersexuality described by Swyer in 1955. It arises from an abnormality in testicular differentiation and is thought to be due to a deletion or mutation involving the sex determining region of the Y chromosome (2). The incidence of Swyer syndrome is 1 : 100 000. It is usually characterized by a 46 XY karyotype, a female phenotype with normal female external genitalia, a hypoplastic to normal uterus, streak gonads and primary amenorrhea. In this article we report a patient diagnosed with 46,XY pure gonadal dysgenesis. Our aim

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was to evaluate the accuracy of diagnoses in XY female patients in the light of current knowledge.

CASE

We report a 16-year-old female who presented with primary amenorrhea. The phenotype of the patient was feminine without any dysmorphic feature, with infantilism of secondary sexual characters (lost puberal development of mammary tissue). Height was 162.7 cm(-0.09), weight was 50 kg(-0.48). Outer genitals are clearly feminine, without sign of Wolf structure's derivatives. Mullerian structures (uterus and fallopian tubes) were in normal status, as resulted from pelvic echography. Fluorescent in situ hybridization studies showed an XY karyotype, and polymerase chain reaction for sex determining region of Y chromosome was positive Pelvic magnetic resonance imaging showed a severe hypoplastic uterus regularly connected to the vaginal cervical channel and gonods were not seen.Endocrine evaluation was performed. Thyroid and adrenocortical function was normal The patient had abnormally elevated baseline levels of serum FSH >200.00 mIU/ml,(normal range 3.4–15.8 mIU/ml)and LH (52 mIU/ml(normal range 1.6–12.5 mIU/ml), Testosterone 21 ng/100 ml (normal range 20–50 ng/100 ml) was in the normal range . Briefly described a picture of primitive gonadal insufficiency. A hCG stimulation test was performed, no significant risein the level of testosterone (28 ng/100 ml) after hCG stimulation.Laparotomy revealed ,normal vagina, infantile uterus, and indistinct streak gonads .Bilateral gonadectomy was done and sent for a histopathological examination. Histologic examination revealed fibrovascular ovarian tissue containing of endometrium tıssue.These findings were suggestive of pure gonadal dysgenesis. Gender assignment was female. The patient currently assumes hormonal therapy.

DISCUSSION

A defining point during embryogenesis is the commitment to develop as male or female. In males this is initiated by the Y-linked SRY gene, which leads to testis development. Ovarian development occurs in the absence of the Y-linked SRY gene, and eventually results in a female phenotype. these developmental pathway have a vital importance for the correct development of gonads and associated anatomical structures (5). Any disruption of these pathways can lead to DSD, which are congenital conditions with atypical development of the chromosomal, gonadal or anatomical sex (6). DSD can be analyzed in three etiological subclasses, namely syndromic, disorders of androgen action, and gonadal dysgenesis (7). 46,XY gonadal dysgenesis is characterized by abnormal testicular determination. This clinical condition can be divided into three histologic forms. Individuals affected with 46,XY complete or pure gonadal dysgenesis female phenotype, lack testicular development, have bilateral streak gonads, well-developed Mullerian structures, absent Wolffian structures. In the 46,XY mixed gonadal dysgenesis, the usual gonadal pattern is a streak gonad on one side and a dysgenetic or normal-appearing testis on the other side of the abdomen. Mullerian and Wolffian duct development usually correlates with the character of the ipsilateral gonad. The term partial gonadal dysgenesis describes individuals who have bilateral dysgenetic testis and a mix of Mullerian and Wolffian structures usually correlated with the extent of testis differentiation. Ambiguity of the external genitalia is variable. The dysgenetic gonadal histology consists of poorly formed seminiferous tubules in combination with ovarian-like stroma(1)

Pure XY gonadal dysgenesis (Swyer syndrome) is an extremely rare endocrine disorder. This disorder was first identified in a 46, XY male, reared as female due to abnormal testicular differentiation (Swyer 1955). there are normal female genitalia at birth, but breast devolepment and menarche fail to occur at puberty.The uterus and fallopian tubes are present,but wolffian duct remnants are not found.Patients present at puberty with hypergonodotropic primary amenorrhea.familial cases suggest an X –linked or asex limited dominant autosomal transmission.Most of the patients examined have had mutations of the SRY gene.None had a SOX9 gene mutation.Histolology shows streak gonads indicating no morphological definition of testis development.The sterak gonads may undergo neoplastic changes,such as gonodoblastomas and dysgerminomas and should be removed shortly after diagnosis,regardless of age (8). Our patient admitted to our hospital with primer amenorrhea. She had normal statute and a female phenotype,inculiding vagına,uterus, and fallopian tubes but breast devolepment was fail to ocur.Chromosome analysis showed a 46 XY karyotype. Gonodotropin levels were markedly elevated. Briefly she was characterized by complete phenotypic sex revarsal in a XY female.then she was diagnosed as pure gonodal disgenesis.As there is a high risk of tumor development gonadectomy was done. In conclusion, this was a rare pre-

sentation of XY gonadal dysgenesis. In patients presenting with primary amenorrhea, gonadal disgenes should be to keep in mind .

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