Mucinous cystadenoma in a female patient with 45,X/46,XY karyotype

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Summary

The mosaic karyotype of 45,X/46,XY has a wide phenotypic spectrum and there are substantial differences between prenatally and postnatally diagnosed cases. The phenotype varies between normal male to classical Turner syndrome. There is a high risk of gonadal tumor development in the dysgenetic gonads of patients with sex chromosome mosaicism. We report a case of a 24-year-old patient with a pelvic mass and amenorrhea referred to our laboratory for karyotyping. Peripheral blood chromosome analysis showed a mosaic karyotype of 45,X[17]/46,XY[83]. The tumor originated from the left ovary and the right ovary was found to be a streak gonad. The uterus was intact. Pathologic examination of the tumor revealed mucinous cystadenoma. Physical examination of the patient showed signs of Turner syndrome, as short stature (145 cm), short neck and asymmetric shoulders. Her mental state was normal. Y chromosome microdeletion screening involving SRY and ZFY genes was performed and no deletion was found. The patient was informed about the condition during the genetic counseling session.

Key words: Mucinous cystadenoma; Chromosomal mosaicism; Turner syndrome.

Introduction

Numerical abnormalities of the sex chromosomes are among the most frequent abnormalities cytogeneticists encounter during routine studies. Among these, cases with sex chromosome mosaicism are probably the most heterogeneous condition. Especially in postnatally diagnosed cases of 45,X/46,XY mosaicism is well-known to exhibit a wide spectrum of phenotypes, ranging from typical Turner syndrome to normal male [1].

Mosaicism is defined as the presence of two or more cell lines in the same individual. In most cases of 45, X/46,XY mosaicism, the cause is considered to be the loss of the Y chromosome by nondisjunction after normal disomic fertilization [2]. Gonad tissues have been studied in these patients, as mosaicism in the lymphocytes does not always display the same percentage in the gonads [3]. Whatever the phenotype, the presence of the Y chromosome is considered as an indicator of increased risk for the development of tumors in the dysgenetic gonads.

Case Report

A 25-year-old woman with a pelvic mass and amenorrhea was admitted to the Gynecology Department of our university hospital for diagnostic procedures. She was a twin, had another pair of older twin sisters and two younger brothers. Her parents were non-consanguineous and pedigree analysis was noncontributory. She was 145 cm tall and weighed 60 kg. She had a short neck and asymmetric shoulders. Pubic hair was present and the breasts were normal in size. Her mental state was normal and she had attended university. Her twin sister appeared normal and had no complaints.

The patient had primary amenorrhea and the pelvic mass was found to have originated from the left ovary, thus first suspected to be dysgerminoma. During surgery, the uterus was visualized and the right ovary appeared as a streak gonad (Figure 1). Left salpingo-oophorectomy was performed and pathological examination of the tumor revealed mucinous cystadenoma (Figure 2).

Concurrently, the peripheral blood of the patient was sent to our laboratory for chromosome analysis. Lymphocyte cultures were set up and analysis of the G-banded chromosomes revealed a 45,X/17 46,XY/83 karyotype. Fluorescence *in situ* hybridization was performed with CEPX-Y probes (chromosome X (DXZ1), chromosome Y (DYZ3) cocktail probe (Kreatech) to confirm the presence of Y chromosome material. In addition, Y chromosome microdeletion screening involving SRY and ZFY genes was carried out and no deletion was found. The presence of a XY cell line was demonstrated in the tumor tissue as well by FISH analysis with CEPX-Y probes of paraffin-fixed samples from the cystadenoma, though with a lower ratio (36% X, 64% XY) (Figure 3).

The patient was informed about her karyotype in a counseling session and was referred to different departments for further examination. Her hormone profile showed hypergonadotrophic hypogonadism (FSH: 48.14 mIU/ml, LH: 16.28 mIU/ml, E2: 17 pg/ml). She was offered gonadectomy and allowed time for her decision on request.

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Fig 1

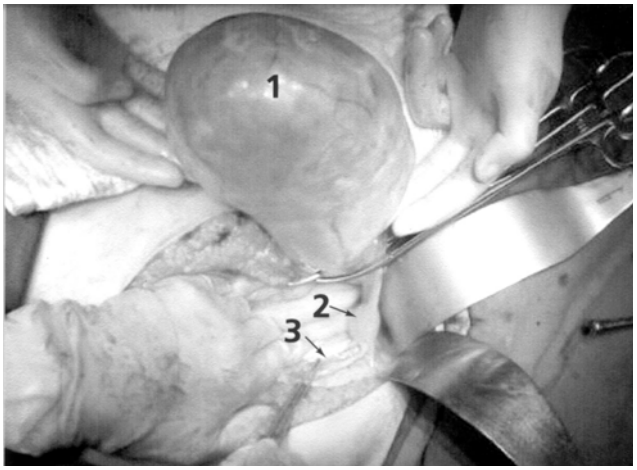

Fig 2

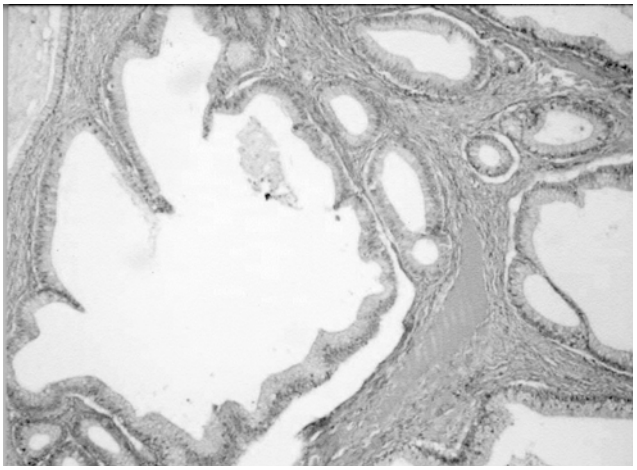

Fig 3

Figure 1. — Mucinous cystadenoma of the left ovary (1), the uterus (2) and right ovary appearing as a streak gonad (3).

Figure 2. — Histopathological appearance of the tumor; glands and cysts lined by a single layer of mucinous columnar epithelium (hematoxylin-eosin x 100).

Figure 3. — Presence of cells with one X signal and cells with one X and one Y signal, shown by FISH with XY cocktail probe (Kreatech) on paraffin-fixed samples of the tumor.

Discussion

Mosaic individuals with 45,X/46,XY karyotype manifest a variety of gonadal dysgenesis phenotypes; the external genitalia may be female, male or ambiguous. Most patients with female external genitalia are clinically indistinguishable from Turner syndrome, while some are tall in stature, some may manifest virilization and some show no somatic abnormalities. After karyotyping, further studies like FISH or PCR are suggested especially for these patients, to demonstrate the presence of Y chromosome material [4-6]. This is of utmost importance in terms of approximately 20% risk of ovarian tumor development, especially gonadoblastoma [4]. Neoplasia often develops in the first and second decades of life and is thought to be caused by a cancer predisposing locus on the Y chromosome (gonadoblastoma) [7-8]. Currently it is recommended to perform an ovariectomy in these patients [8].

Mucinous neoplasms of the ovary are classified to surface epithelial tumors and may be grouped into benign, borderline or malignant categories depending on their histopathologic features. Approximately 80% of these tumors are cystadenomas, which are usually large, multicystic, characteristically unilateral and benign [9]. These tumors often are heterogeneous and may contain borderline or malignant elements. They are not expected to recur after being surgically removed, though malignant transformation has been described as a sequential process [9].

The case reported here had an unusual type of tumor development in the ovary which led to the diagnosis of the sex chromosome mosaicism she harbored. Mucinous cystadenoma has rarely been reported in patients with turner syndrome or 45,X mosaic patients with a structurally abnormal Y chromosome [10-13]. To our knowledge this is the first report of mucinous cystadenoma in a patient with 45,X/46,XY karyotype.

The patient's contralateral ovary was a streak gonad; the chromosome constitution of this tissue has not been studied since the karyotype was determined after surgery and the patient has not yet decided to undergo a second operation.

Streak gonads of some 45,X/46,XY mosaic individuals were found to contain a homogeneous 45,X complement, thus the absolute necessity for gonadectomy is being argued [3]. These authors deduced that absence of the Y chromosome in the gonad would reduce the probability of neoplasia and suggested further extensive studies to better determine the risk before surgery. The proportions of cell lines in different tissues of a patient may determine their normal or abnormal development; therefore gonad karyotyping seems to be valuable in this context.

Conclusion

The association of the presence of Y chromosome in 45,X individuals and gonadoblastoma formation has been studied and is thought to be a mechanism of oncogene activation on Y [8]. The development of a benign cystic tumor in this patient, though unexpected, may be attributed to the Y chromosome, as the tumor was also shown to contain Y chromosome material.

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