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SCIENTIFIC LETTERS

Mosaicism XXY/X0☆

Mosaicismo XYY/X0

Thanks to the development of new techniques such as polymerase chain reaction (PCR), extensive banding, and fluorescent *in situ* hybridization, there have been important advances in the study of human chromosomes. Many abnormalities have been described, most of them consisting of altered numbers of chromosomes, but there have also been cases of mosaicism in the same person.[1] Mosaicism was first described in humans in 1959 by Ford et al.,[2] who noted that patients with Klinefelter syndrome could present 47,XXY/46,XX mosaicism. Later, Fraccaro et al. and Ford almost simultaneously observed 45,X0/46,XX mosaicism in women with Turner syndrome.[3,4] Other authors have subsequently reported other types of mosaicism, such as XY/XO, XXX/X0, XXX/XX, XXY/XY.[5,6] In 1962, Cooper et al.[1] published a description of XYY/X0 mosaicism, which had not previously been reported. This was the case of a highly intelligent 16-year-old female with no relevant personal history, who complained of amenorrhea and the lack of development of secondary sexual characteristics.

A 14-year-old female attended our clinic complaining of delayed puberty. Physical examination revealed a Turner-like phenotype, 52.3 kg of weight, 1.47 m of height, and a BMI of 22.9 kg/m^2. She had acne and hirsutism (over 14 points in the Ferriman-Gallwey scale). Her breasts had not developed, but she had had incipient public hair (Tanner stage II) since the age of 11 years and clitoromegaly. Hormone tests, genital ultrasound, and karyotyping were requested. Gonads were not visualized in ultrasonography. Laboratory tests revealed hypergonadotropic hypogonadism (FSH 23.5 IU/L, LH 12.9 IU/L, estradiol 33.5 pg/mL, total testosterone 0.275 μg/mL, and HCG < 0.6 IU/L). A cytogenetic analysis with a 400-band resolution showed two cell lines; one (6 metaphases: 17%) had karyotype 47,XYY; the second line (29 metaphases: 83%) had karyotype 45,X0. In short, it was a 47,XYY/45,X0 mosaicism.

In view of these results, and as gonads were not seen in ultrasonography, an exploratory laparotomy was performed, during which gonads consistent with testes were found and excised as a preventive measure, because of the increased risk of germ cell tumor (gonadoblastoma or dysgerminoma).[7]

Microscopic examination of the right gonad showed a testis with seminiferous tubules with thickened tunica propria; intraluminal contents consisted of abortive spermatogonia with a 30% fertility index and a predominance of pre-Sertoli cells. The interstitial space was wide, fibrous, and contained some pre-Leydig cells. The left gonad consisted of connective-adipose tissue, with lumina lined with epithelium consistent with epididymal ducts. It was decided to maintain her female sex assignment, as she had been considered a girl since birth, with a female role for herself and her family. Estrogen therapy was started, with a very good response. Follow-up continues at the clinic, and has been uneventful.

Chromosomal mosaicism is a genetic disorder in which two or more cell populations with different genotypes, supposedly originating from a single zygote, coexist in one individual. This is usually attributed to an accident during mitosis, which may be of two types[1]:

1. During the anaphase, a chromosome is delayed at the time of chromosomal replication. When nuclear membranes are formed, this chromosome is excluded. The result is one cell with a normal chromosome, and another cell with a deficiency of one chromosome. If the loss of the chromosome does not interfere with cell viability and replication, both cells will continue to replicate, and the new individual will present mosaicism of both cell types. It must be kept in mind that one of the two cell types is normal.
2. The second type of accident is mitotic nondisjunction. In this case, a chromosome replicates during anaphase but does not adequately divide into two parts moving toward opposite poles; instead, the two halves move toward the same pole. The result is a cell with one extra chromosome and one cell with one chromosome too few.

Mosaicism of the XYY/X0 type is extremely rare. Isolated cases have been reported in the literature by Chang et al. in 1990[8] and Farrugia et al. in 2013.[9] The latter described three individuals with the same chromosomal change; the final outcome was one male and two females. In 2015, 45,X0, 46,XY, 47,XYY mosaicism was reported[10] in a 13-year-old girl who, as in our case, consulted for short stature. After a complete work-up, including karyotyping, an exploratory laparotomy found a dysgerminoma in the right ovary and a gonadoblastoma in the left ovary. Both gonads were excised. Fetal sexual differentiation is the result of the joint interaction of hormonal events and an intracellular signaling complex.[11] When hypogonadism is seen in children or adolescents, genetic testing is essential. Karyotyping should be

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performed first, and will reveal the etiology if abnormal. If the result is normal, and a genetic cause is suspected, genetic testing could involve the analysis of multiple genes implicated in sexual differentiation.[12]

References

1. Cooper HL, Kupperman HS, Rendon OR, Hirschhorn K. Sex-chromosome mosaicism of type XYY/XO. New Engl J Med. 1962;266:699–702.
2. Ford CE, Polani PE, Briggs JH, Bishop PM. A presumptive human XXY/XX mosaic. Nature. 1959;183:1030–2.
3. Fraccaro M, Gemzell CA, Lindsten J. Plasma level of growth hormone and chromosome complement in four patients with gonadal dysgenesis (Turner's syndrome). Acta Endocrinol. 1960;34:496–507.
4. Ford CE. Human chromosome mosaics. In: Conference on human Chromosomal Abnormalities: Proceedings, London, 1959. Editores: Davidson WM, Robertson Smith D. 148 pp. London: Staples Press; 1961. p 23–27.
5. Hirschhorn K, Decker WH, Cooper HL. Human intersex with chromosome mosaicism of type XY/X0: report of case. New Eng J Med. 1960;263:1044–8.
6. Jacobs PA. Abnormalities involving X-chromosome in women. Lancet. 1960;1:1213–6.
7. Coyle D, Kutasy B, Han Suying K, Antao B, Lynch SA, McDermott MB, et al. Gonadoblastoma in patients with 45 X0/46XY mosaicism: a 16-year experience. J Pediatr Urol. 2016;12, 283.e1-283.e7.
8. Chang HJ, Clark RD, Bachman H. The phenotype of 45X/46 XY mosaicism: an analysis of 92 prenatally diagnosed cases. Am J Hum Genet. 1990;46:156–67.
9. Farrugia MK, Sebire NJ, Achermann JC, Eisawi A, Duffy PG, Mushtaq I. Clinical and gonadal features and early surgical management of 45 X/46 XY and 45 X/47 XYY chromosomal mosaicism presenting with genital anomalies. J Pediatr Urol. 2013;9:139–44.
10. Yüce O, Döger E, Celik N, Emeksiz HC, Camurdan MO, Bideci A. Gonadoblastoma with dysgerminoma in a phenotypically turner-like girl with 45X/46XY karyotype. J Clin Res Pediatr Endcorinol. 2015;7:336–9.
11. Morel Y, Roucher F, Malet D, Plotton I. Genetic of gonadal determination. Ann Endocrinol (Paris). 2014;75:32–9.
12. McCabe MJ, Bancalari RE, Dattani MT. Diagnosis and evaluation of hypogonadism. Pediatr Endocrinol Rev. 2014;11 Suppl. 2:S214–29.

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Restricted diet in fruits causes scurvy in a child of 7 years old☆

Dieta restrictiva en frutas como causa de escorbuto en niño de 7 años

Scurvy is a disease caused by vitamin C deficiency. Humans do not synthesize this vitamin, so it needs to be taken in the diet. Scurvy is very rare in industrialized countries; cases reported in children may be caused by inadequate diet in patients with neuropsychiatric disorders such as autism or infantile cerebral palsy. Some cases have also been reported in children with celiac disease[1] and in infants given inadequate diets such as almond beverages instead of adapted formulas.[2]

We report the case of a boy with multiple allergies, multiple food intolerances, and fructose malabsorption-intolerance who had scurvy despite not being on a vegetable-and fruit-restricted diet.

This was a 7-year-old Caucasian boy diagnosed two years previously with an allergy with anaphylaxis to nuts and stone fruits, in addition to intolerance to other food such as tomatoes, kiwis, oranges, milk and dairy products (which the child refused to eat due to abdominal pain). As he had been diagnosed with fructose malabsorption and intolerance by a hydrogen breath test, his diet also restricted the intake of fruit juices, honey, baked goods and manufactured products containing fructose. During monitoring at the clinic, malabsorption diseases such as celiac disease and inflammatory bowel diseases had been ruled out, and there was no relevant family history of the disease.

At his yearly nutritional check-up, the boy had normal body measurements as follows: weight, 22 kg (p50–85); height, 123 cm (p85–97); BMI, 14.2 kg/m^2 (p85–97), with no weight or height stagnation. The mother reported that the boy was tired and complained of severe bone pain in his lower limbs and lumbar region, for which reason the pediatrician had referred him to the orthopedic surgeon. She also mentioned gum bleeding and small perifollicular ecchymoses on the legs and arms, which led the pediatrician to request coagulation tests and a complete blood count, which were normal. The physical examination was unremarkable except for the small ecchymoses on his legs. A very low vitamin C level of 1 mg/L (4.6–14.9 mg/L) was seen in the tests requested for the check-up at the clinic. Levels of all other vitamins were within normal ranges: folic acid, 11 ng/mL (2.8–20 ng/mL); vitamin B_{12}, 545 pg/mL (239–931 pg/mL); vitamin E, 8 mg/L (3–9 mg/L); vitamin A, 0.25 mg/L (0.2–0.4 mg/L); vitamin D, 32 ng/mL

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