UNUSUAL CASE OF PATIENT WITH KLINEFELTER SYNDROME WITH SHOX DELETION BORN TO THE MOTHER WITH LERI-WEILL DYSCHONDROSTEOSIS

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P2- 179 Growth and syndromes

INTRODUCTON: Klinefelter syndrome (KS) describes the phenotype of the most common sex chromosome abnormality in humans. About 80% of KS patients have 47,XXY karyotype, while rest of the patients can have mosaicism or other numeric or structural sex chromosome abnormalities. Tall stature is one of the hallmarks of KS and it is thought to be due to supernumerary X chromosome leading to SHOX gene overdosage. Deletion of SHOX gene, on the contrary, has been related to impaired growth in patients with Leri-Weill dyschondrosteosis (LWD), Langer mesomelic dysplasia and Turner syndrome, but also in some cases of idiopathic short stature.

CASE REPORT: The proband is 14.6 year old boy evaluated for obesity (height 170.6 cm, + 0.4 SDS, weight 91.5 kg, +2.41 SDS, BMI 31.4 kg/m2, + 2.19 SDS). At examination he had penis buried in fat tissue, with testes size Prader 4-5, pubic hair Tanner 3 and adipomastia with enlarged areolas. His laboratory finding revealed elevated gonadotropins (LH 11.9 IU/L, ref. 0.2-5; FSH 25.5 IU/L, ref. 1.2-5.8; testosterone 7.9 nmol/l, ref. 3-27) and subsequently KS was suspected. The karyotyping revealed 46, XXY/46, XY mosaicism with one derivated X chromosome and 3.5% 46,XY cells (mos 47,X,der(X)del(Xp)dup(Xq)(Xq28-Xq27.2::Xp22.32-Xq28), Y/ 46,XY) (Figure 1). Further cytogenetic analysis with FISH proved deletion of pseudoautosomal region 1 of X chromosome including SHOX gene.

Proband was in custody of his grandmother (on father's side), so his parents were invited for further genetic evaluation. His father has 46, XY, normal male karyotype and normal phenotype. His mother is disproportionately short (height 155 cm, – 1.3 SDS, arm span 152 cm) and has phenotypic features of LWD (mesomelic limb shortening, Madelung deformity). Her karyotyping revealed complex rearrangement of one X chromosome with duplicated Xq27.2-qter, deleted Xp22.32 region and subsequent one SHOX deletion (46,X,der(X)del(Xp)dup(Xq)(Xq28-Xq27.2::Xp22.32-Xq28) (Figure 2).

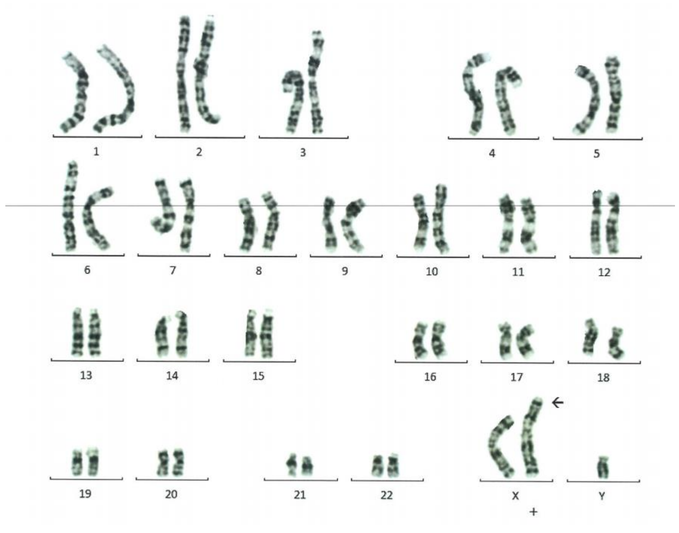
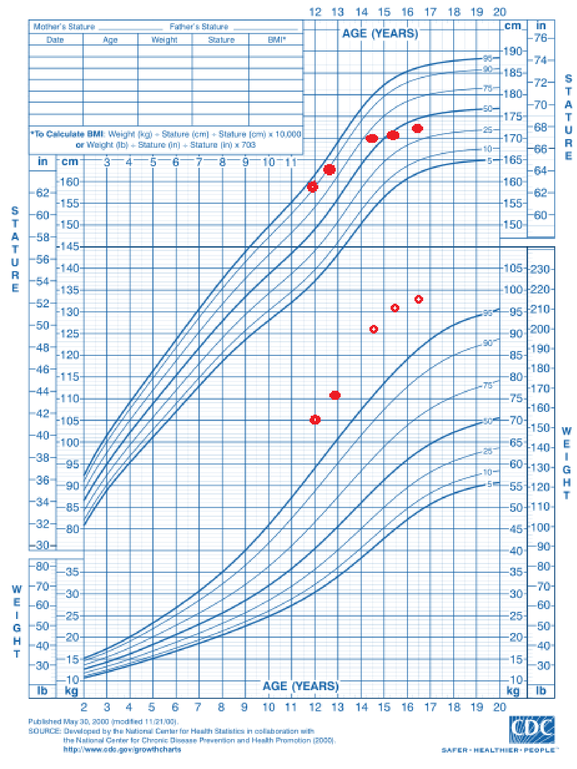


Figure 1. Proband's karyotype



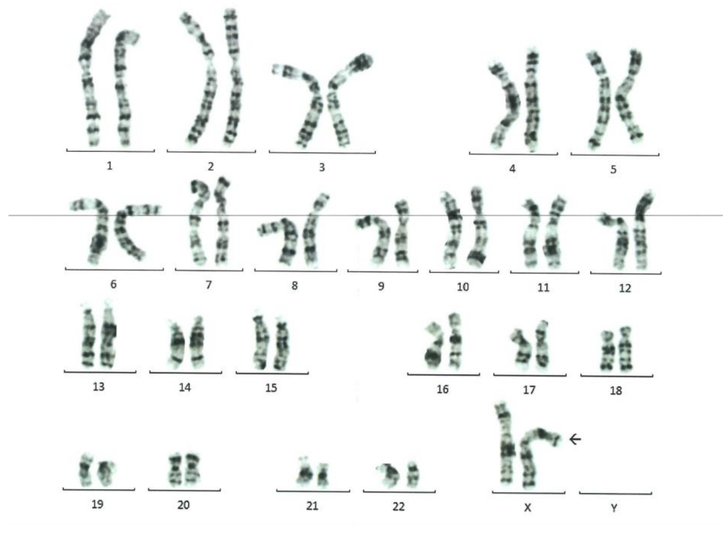


Figure 2. Karyotype of proband's mother

CONCLUSION: To the best of our knowledge this is the first report of the patient with KS born to the mother with LWD. Although tall stature would be expected, SHOX gene deletion might have contributed to normal stature of our patient. In KS patients carrying complex chromosomal rearrangements, detailed cytogenetic evaluation is indicated in patient and his parents. This might explain spectrum of phenotypes in patient, detect unrecognized disease in parents and provide correct genetic counseling regarding possibility of transmitting monogenic disorders in further parental pregnancies or in case of option for proband's fertility preservation.

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