An unusual cause of short stature in a phenotypic male with Type I Diabetes Mellitus due to an unexpected deletion of the Y chromosome

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Introduction

- SHOX (short stature homeobox) gene, located on the pseudoautosomal region of the sex chromosome plays an important role in the development of skeleton[1]
- Mutations/deletions of *SHOX* can cause skeletal dysplasias[1]
- We report a male, with Type I Diabetes (T1DM) with Y chromosome deletion and short stature due to the concurrent loss of *SHOX*

Case

- 15-year-old boy with T1DM for 6 years was referred for short stature assessment (Height:148.1 cm, -2.62SDS)
- T1DM was managed by continuous subcutaneous insulin infusion(CSII) pump
- The initial poor control of TIDM (HbAIC 90mmol/mol), thought to be contributing to short stature, subsequently improved (HbA1C 58mmol/mol)
- Further investigations to look for any other underlying chronic illness were normal
- A mild body disproportion with upper and lower segment ratio of 1.3 was noted
- He was pubertal with testicular volumes of 8-10 ml
- IGF1 was normal and the bone age was advanced at 17.5 years

Investigations

- Skeletal survey showed subtle madelung deformity with mild relative shortening of both the ulnar bones and epiphyseal ossification
- Microarray analysis showed loss of most of the Y chromosome
- Fluorescent in Situ Hybridisation studies using specific centromere probes for X and Y chromosomes showed no Y chromosome in 73% of the cell lines and presence of isodicentric Y chromosome, i(Y) with SRY gene in 23% of the cell lines, giving rise to the karyotype 45,X/46,X,i(Y)
- The clear male phenotype and short stature in our patient is probably due to degree of mosaicism with higher distribution of i(Y), in the gonads and 45,X in the growth plates

Conclusion

- Loss of Y chromosome and resultant deletion of a copy of *SHOX* in a patient with T1DM has not been previously reported
- Infertility can be an associated problem
- Skeletal deformities can be subtle in the radiographs with typical bone age advancement. Microarray is helpful as an initial test to detect SHOX deletion

Reference

1.Deletions of the homeobox gene SHOX (short stature homeobox) are an important cause of growth failure in children with short stature. Rappold GA et.al. J Clin Endocrinol Metab. 2002 Mar;87(3):1402-6.

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