A CASE OF CONTIGUOUS GENE DELETION SYNDROME

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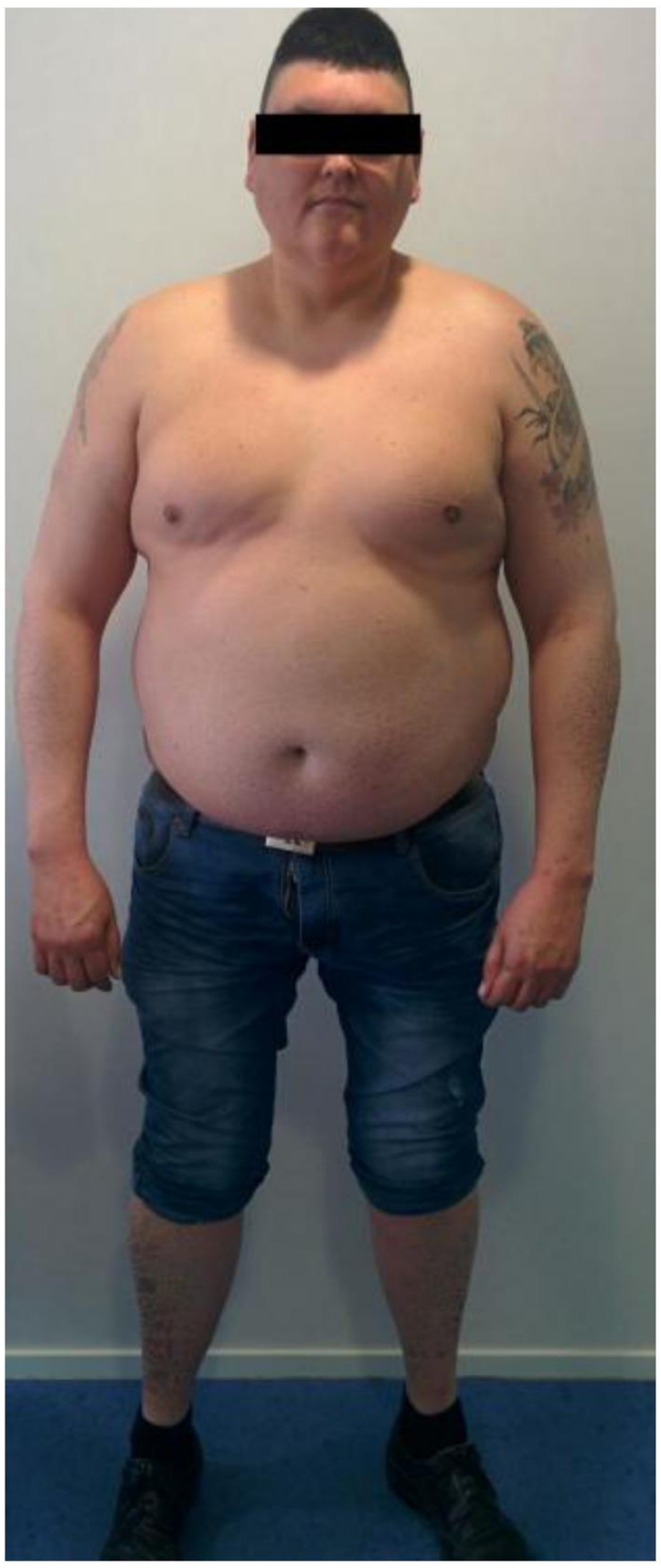
INTRODUCTION

Kallmann Syndrome (KS) is a genetically heterogeneous disease characterised by hypogonadotrophic hypogonadism with anosmia or hyposmia. Patients can develop osteoporosis, infertility and testis cancer. It can be associated with X-linked ichthyosis (XLI) in a contiguous gene syndrome related to a Xp22.3 region deletion, which include KAL1 and STS genes.

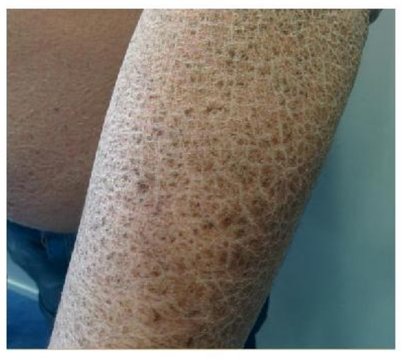
CASE REPORT

We report a case of a 32 –year-old male with ichthyosis referred for evaluation of high height (2,07m), overweight (BMI 29,6kg/m2) and microgenitalia. He had absence of secondary sexual characters. Baseline plasma levels of testosterone were 0,12 ng/mL (2,49-8,36) ,FSH 0,25 mUI/mL (1,5-12,4) and LH<0,1 mUI/mL (1,7-8,6). Prolactin levels were 7,67 ng/mL (4,04-15,2). MRI showed hypoplastic hypophysis, ultrasound showed small testes and a bone densitometry revealed osteoporosis (spine T score -3,55). Karyotype was 46 XY. He was diagnosed of hypogonadotrophic hypogonadism associated to ichthyosis. Therefore, we extracted Genomic DNA samples looking for a related genetic condition between these diseases. A microarray-based comparative genomic hybridisation test (aCGH) was performed.

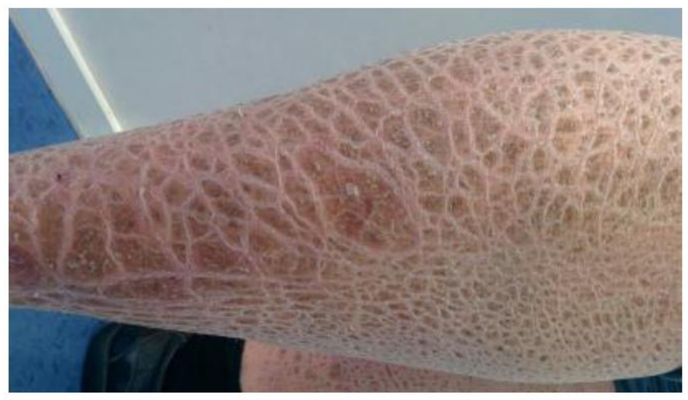


The result was a pathogenic copy number DNA variant: arr(hg19)Xp22.32p22.31 (4,699,972-9,427,600)xo which contains 12 genes: NLGN4X, VCX3A, HDHD1, STS, VCX, PNPLA4, MIR651, VCX2, VCX3B, KAL1, FAM9A, FAM9B. Among these genes, STS is responsible for XLI and KAL 1 gene I s responsible for the X-linked form of KS. Further studies revealed that the deletion was inherited from his mother. Females with similar Xp22 deletions are phenotypically normal except for short stature, because they need only one copy of this region to be normal.

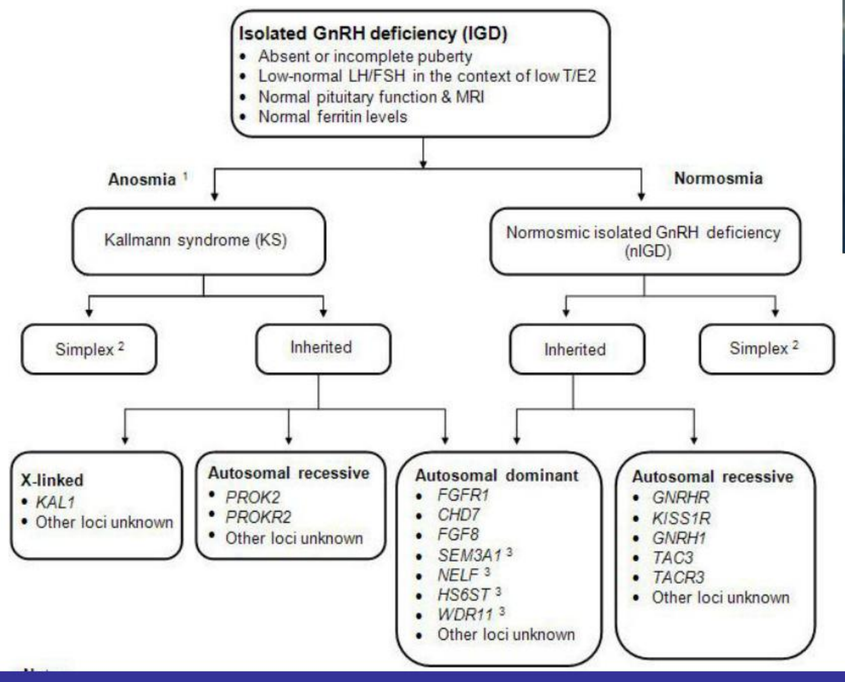
He started intramuscular testosterone undecanoate supplementation in progressive doses to achieve secondary sexual character development and continued with substitutive treatment. Three years later bone densitometry improved (spine T score -2,78 SD).

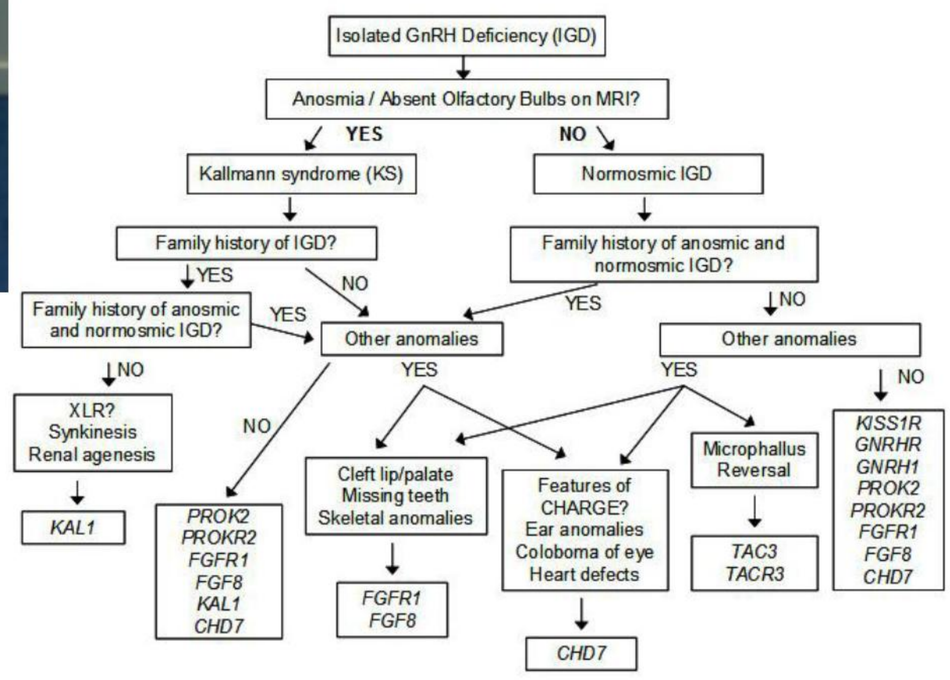


Patient' s arm with ichthyosis skin lesions



Patient' s leg with ichthyosis skin lesions





CONCLUSIONS

KS is a genetically heterogeneous disease that can be associated with other diseases in a contiguous gene syndrome. Therefore, it's very important to investigate related conditions and diseases to provide additional information to arrange the most accurate tests to stablish a diagnosis. New genomic tests provide a better understanding and knowledge of genetic diseases, diagnosis and management. Special attention has to be drawn to complications like osteoporosis, infertility and testis cancer.

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