ESSENTIAL TREMOR AND BRAIN METAL ACCUMULATION DISEASE IN KLINEFELTER SYNDROME: A CASE REPORT

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INTRODUCTION

Klinefelter syndrome (KS) [karyotype 47,xxy] is the most frequent sex chromosomal disorder in males and characterized by testosterone deficiency and increase of gonadotropins FSH and LH, with a prevalence of about 500-1000 subjects born alive. Patients affected by KS present with infertility and hypergonadotropic hypogonadism. A recent report has described the presence of tremor in patients affected by KS sharing similar features with essential tremor (ET).

OBJECTIVE

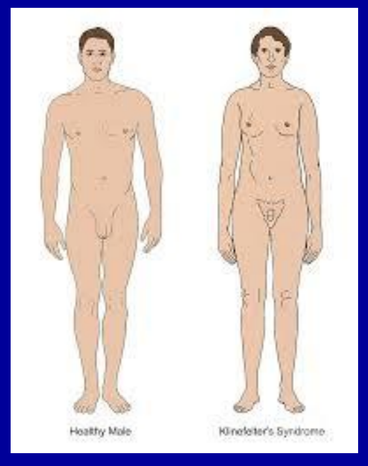
To report on a case of KS associated with tremor and concomitant brain metal accumulation disease.

MATERIALS AND METHODS

A 35-year-old man affected by hypergonadotropic hypogonadism (Klinefelter syndrome) presented with a history of upper limbs predominant postural tremor, more evident to the right side, with clinical features more evocative of an ET.

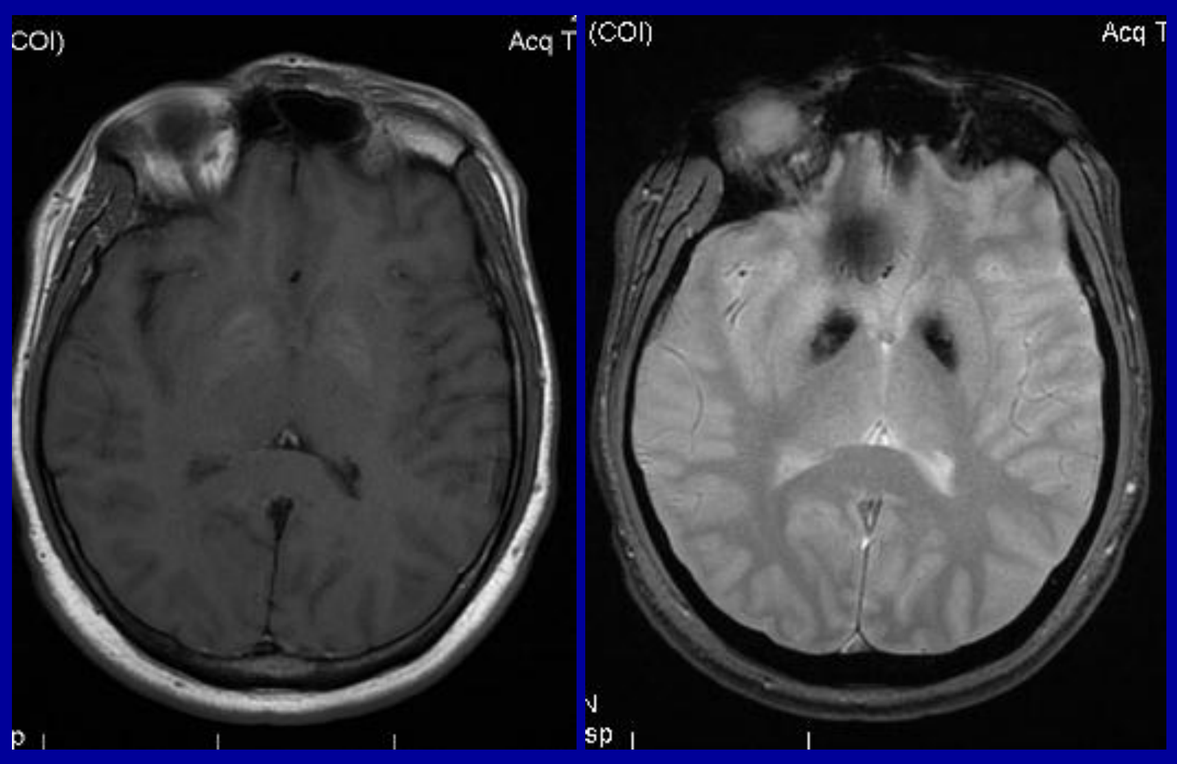
DISCUSSION AND CONCLUSIONS

To the best of our knowledge, this is the first case of a KS patient presenting with ET and brain metal accumulation disease. In this patient, the tremor was worsened by testosterone administration. The presence of a brain metal accumulation and the response to testosterone raise several issues about the definite correlation of the tremor with the hormonal disorder, the correct treatment of this condition and a hypothetical role of the PANK2 polymorphisms as modifiers on KS phenotype.



RESULTS

Brain MRI showed bilateral pallidal hyperintensity on T1-weighted and gradient echo images, and minor abnormalities on FLAIR and T2-weighted images, according to a brain metal accumulation. DAT-SPECT was normal. Screening for Wilson disease and neuroferritinopathy was negative, as far as PANK 2 gene sequencing did not identify any pathogenetic variant (PANK2 analysis showed in exon 1 two homozygous polimorphisms - rs71647828 CTG>CAG Leu111Gln ; rs3737084 GGG>GCG Gly126A - whose clinical significance is reported as benign). Treatment with testosterone administration worsened features of tremor.



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