Hypogonadotropic Hypogonadism Associated with Hereditary Hemorrhagic Telangiectasia

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INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant angiodysplasia. HHT is characterized by spontaneous nosebleeds, mucocutaneous telangiectases, visceral AVMs. Male idiopathic hypogonadotropic hypogonadism (MIHH) is characterized by partial or complete lack of pubertal development. About 60% of patients with MIHH have anosmia, such association being known as Kallmann syndrome. Herein, we report the first case of association of two rare genetic diseases, HHT and MIHH.

METHODS

A 65-year-old man presented with right hemiparesis as a result of a recent lacunar stroke. His past medical history was positive for frequent nosebleeds and hypogonadism. Laboratory investigation were performed to assess his hormonal profile. Olfactory function was studied by University of Pennsylvania Smell Identification Test (UPSIT). Brain MRI was performed to disclose cerebral AVMs and hypothalamic-hypophyseal anomalies. Pulmonary and hepatic AVMs were detected by Thoracic CT and Doppler US, respectively.

RESULTS

At medical examination, the patient showed tall stature, eunuchoid habitus, gynecoid fat deposition, scarce body hair, and hypogonadism. However, Klinefelter's Syndrome, the most frequent cause of male hypogonadism, could be ruled out in light of testicular phenotype (soft testes at clinical examination), normal karyotype (46, XY), as well as his hormonal profile (consistent with hypogonadotropic rather than hypergonadotropic hypogonadism). Prostatic hypotrophia and osteopenia were found by prostatic US and DEXA evaluation, respectively. Olfactory function fell in the range of hyposmia. These findings were consistent with a diagnosis of MIHH. Numerous telangiectases were visible on face, fingers, tongue. Brain MRI showed ischemic lesions, with no abnormalities in hypothalamic-hypophyseal region and no AVMs. Chest CT revealed a large pulmonary AVM, with AVMs also detected in the liver. Based on clinical criteria, the patient was diagnosed with definite HHT. Molecular analysis identified a mutation in the *ENG* gene.

CONCLUSIONS

Both HHT and MIHH are rare genetic disorders, with a similar prevalence, ranging from 1 : 4–5,000 to 1 : 10,000, the latter affecting only males. Our patient was affected by both of these conditions, likely due to a coincidence of two infrequent events.