GENETICS AND GENODERMATOSES

ROTHMUND THOMSON SYNDROME WITH RECQL4 MUTATION PRESENTING WITH HYPERCORTISOLEMIA

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Background: Rothmund-Thomson syndrome (RTS) is a rare autosomal recessive genodermatosis, with specific clinical features. Herein, we report a case of RTS with RECQL4 mutation, unusually associated with hypercortisolemia.

Observation: An 18-year old girl, born to consanguinous parents, with a history of xeroderma pigmentosum (XP) in two cousins, has been followed-up for RTS, since the age of 3 years. The diagnosis of RTS was made based on photosensitivity, poikilodermatous rash, sparse scalp hair, eyelashes and eyebrows, verrucous hyperkeratosis of hands and feet, short stature and various skeletal anomalies (small hands, hypoplastic thumbs, hypoplasia of the patella, diffuse osteoporosis). Molecular analysis for RECQL4 mutations, revealed a nonsense homozygous p.GLN757X mutation. During a follow-up visit, the patient reported a secondary amenorrhea. Cushing's syndrome was suspected, since the patient displayed central obesity with high levels of cortisol and corticotrophin-releasing hormone. This diagnosis was however discarded given the negativity of dexamethasone suppression test in addition to the normality of thoraco-abdominal tomodensitometry and pituitary magnetic resonance imaging.

Key message: RTS is caused, in 65% of cases, by homozygous or compound heterozygous mutations in the RECQL4 helicase gene, determining a defect in helicases functioning, that is found in a number of genetic disorders with genomic instability and predisposition to cancer as common features. XP is one of these characteristic genodermatosis, which explains the family history of XP in our patient. The nonsense exon 14 mutation c.2269C>T (p.Gln757X) seems to be the second recurrent mutation shown on the world map. Cutaneous and skeletal manifestations noticed in our patient are common among RTS patients. However, hypercortisolemia with central obesity has not been previously reported. Given her genetic predisposition to cancer, our patient was suspected to have a paraneoplastic syndrome. The negativity of hormonal and radiological investigations

suggested the diagnosis of cyclic Cushing's syndrome.