THE EHLERS-DANLOS SYNDROME AND METASTATIC MEDULLARY THYROID CARCINOMA: A CASE REPORT

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INTRODUCTION:

The Ehlers-Danlos syndrome (EDS) classic type is a heritary disorder of connective tissue, characterized by fragility and hyperextensibility of skin, abnormal wound healing, and joint hypermobility, due to *COL5A1* or *COL5A2* genes mutations. The diagnosis of EDS is mainly clinical. Milder variants of the classical type of the EDS are common in the population and can be identified by a well-defined clinical scoring system [1–4]. Multiple endocrine neoplasia, type 2A (MEN2A) is a syndrome defined by a medullary carcinoma, pheochromocytoma, hyperparathyroidism, and occasionally cutaneous lichen amyloidosis, because of mutations in *RET* proto-oncogene [5–8]. *COL5A* and *RET* genes mutations are linked to conditions affecting the human integumentary system and may coexist.

CASE REPORT:

An 18-year-old Caucasian female was consulted by an endocrinologist in February 2014.

The patient was born by a full term normal delivery with any neonatal or perinatal morbidity. She was the only child in the family. Her psychomotor development was normal. Since childhood she was very flexible, attended rhythmic gymnastics classes. At age of 12 suddenly she felt discomfort, pain in the left hip during movement, started to limp. After few weeks the patient developed hip luxation and underwent internal fixation with screws. At age of 14 deformations of the pelvis and lumbar spine occurred, knee valgus position appeared. At 15 years patient was consulted at Toronto hospital, juvenile epiphysiolisis was diagnosed. She underwent left knee osteosynthesis followed by peroneal and tibial nerves damage, which caused impaired mobility at ankle and foot paresis.

In 2012 a small thyroid nodule was found and subclinical hypothyreosis was diagnosed; 25 mkg of levothyroxin were prescribed.

In 2014 at age of 18 during self-examination, she noticed hard neck nodules. Ultrasonography showed a hypoechoic 0.4 mm diameter lesion in the right lobe of thyroid and both sides neck lymphadenopathy. FNAC of thyroid nodule revealed medullary carcinoma. On 11 Apr 2014 total thyroidectomy and neck lymph node dissection was performed. Metastasis in 14 of 20 lymph nodes was found. 2.5 weeks after surgery calcitonin level was 1557.2 ng/l (normal range 0.5–7.8 ng/l), she had normal serum calcium and parathyroid hormone levels and negative urinary catecholamines. She received 34 cycles of neck radiotherapy course and vandetanib therapy. She has been taking replacement dose of 125 mkg levothyroxine per day. 23 Dec 2014 thyrotropin level was 0.195 mIU/l (normal range 0.27–3.75 mIU/l), free thyroxin – 20.98 pmol/l (12–22 pmol/l); 20 Jan 2015 calcitonin – 1755.4 ng/l.

Family history: the family history revealed no complaints on hyperextensibility of skin, abnormal wound healing or joint hypermobility in parents.

Her mother was diagnosed with primary parathyroid hyperplasia and MEN2A by mutational screening in all family members. She underwent total thyroidectomy and surgery for parathyroid adenoma. Father has multinodular goiter.

On physical examination: height 184 cm, body mass index 16 kg/m^2, long face, long palms and fingers, joints' hypermobility, scoliosis, soft, velvety skin, hyperelasticity of face and elbow skin, widened atrophic scars, atrophic striae at the back, piezogenic papules.

Investigations:

- Abdominal ultrasound and CT: no pathological changes were found.
- Left shoulder CT: sclerotic proximal growth line of left humerus.
- Body CT: multiple lymphnodes, lungs, pelvis bones and vertebrae metastases.
- Bone scan: active head, humerus and pelvis focuses, most probable metastases.
- Clinical geneticists' conclusion: Ehlers-Danlos syndrome; *RET* gene mutation at exon 13 (Y791F mutation), causing autosomal dominant MEN2A syndrome.

During our search for relevant literature on the web we did not find a similar case of co-occurrence of an aggressive form of MEN2A with Ehlers-Danlos syndrome. While there is a statistical chance that this rare combination of two syndromes may be incidental, genetic analysis may reveal the underlying genetic basis for the manifestations.

CONCLUSIONS:

If complicated growth and atypical phenotype is obvious, genetic counselling is desirable. Coexistent thyroid pathology might be inherited too. Careful patient's data collection and collaboration between health care specialists enables to achieve desirable outcomes.

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Clinical Cases - thyroid/others

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