Family name, name:

Study group:

Contact email:

Scope 1. Syndromology

In a genetic department, a 4-year-old girl is examined for her short stature. Her current height is 95 cm. She is the first child of healthy, unrelated parents (mother measures 166 cm, father 164 cm), the girl's prenatal and perinatal history is uncomplicated. Her psychomotor development is normal, and her phenotype is (except for a noticeably smaller stature) without clear abnormalities.

1) Evaluate the girl's current height using percentile graphs (in bilingual version they are available, for example, on the NIPH/SZÚ website http://www.szu.cz/uploads/documents/obi/CAV/6.CAV_5_Rustove_grafy.pdf)

2) What genetic laboratory tests would you indicate? Explain why.

Scope 2. Prenatal diagnostics

Two pregnant women came for genetic counseling, details of their referral follow (**pregnant 1** and **pregnant 2**). Evaluate their medical history (anamnesis) and previous results, and decide what are the options for further action.

Pregnant 1 is still healthy, without permanent medication. This pregnancy, currently 13 + 6 weeks, is her first; she will be 33 years old at the time of the expected birth. 1st trimester prenatal screening was positive (PAPP-A: 0.303 MoM, free-beta-hCG: 1.574 MoM, NT 3.05 mm, recalculated risk of T21 is 1:95).

What group of fetal diseases will we focus on next?

What options will you suggest for this pregnant woman?

Pregnant 2, now 37 years old, is allergic and asthmatic; she uses inhalation beta-2-mimetics in case of difficulties. This is her 3rd pregnancy (1x healthy son, 1x MAB in 7th week). She is currently in 16+8 weeks; Her first-trimester prenatal screening could not be evaluated (because of late blood sampling due to incorrect pregnancy dating); therefore, second-trimester screening is separately evaluated – it is positive (MS-AFP: 8,123 MoM, total-hCG: 0,978 MoM, uE3: 1,117 MoM, recalculated risk of T21 is 1:9500, risk of NTD computed as 1:5).

What group of fetal diseases will we focus on next?

What options will you suggest for this pregnant woman?

Scope 3. <u>Reproduction genetics</u>

A couple with a reproductive disorder came to the genetic outpatient department; the referral states that the couple's unsuccessful reproductive history lasts for two years. Women, now 37 years old, otherwise healthy, had three miscarriages, always in the first trimester of pregnancy. Her partner, 46, has arterial hypertension and hypercholesterolemia; oligospermia was detected. The family history of both members of the couple is insignificant, they do not report birth defects or reproductive losses in the extended family.

What options for further action would you suggest to this couple?

Will you indicate any genetic laboratory tests? If so, then which and for which of the partners?

Scope 4. <u>Oncogenetics</u>

Family 1: A healthy, 22-year-old girl (proband) comes to the clinical geneticist for a consultation. Her mother (now 49 years old) was diagnosed with breast cancer a week ago. Proband's grandmother (mother's mother) died at the age of 89 of the same disease, and the proband now fears that she has inherited the same predisposition and is asking for a genetic test for herself. Apart from the above-mentioned cases, the proband does not mention other cases of oncological disease in the family; no one in the family has yet been (onco)genetically tested.

Is molecular genetic diagnosis of hereditary forms of breast cancer indicated in this family? What procedure do you choose? Who and what genes will you investigate?

Family 2: Proband, 57-year-old, comes to the clinical geneticist for consultation; she is currently after the treatment for unilateral ovarian cancer. This is the first occurrence of oncological disease in the nuclear (immediate) family of proband. Based on molecular genetic testing of DNA isolated from a tumor tissue sample that showed a deletion of the *BRCA2* gene in a homozygous combination, the patient was treated with Lynparza (Olaparib). According to current recommendations, proband DNA isolated from peripheral blood sample was tested, targeted at gene mutations associated with hereditary tumor syndromes. However, this test was completely negative - the above or other mutations were not detected. What will be your comment and explanation?

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