Early prenatal diagnosis of Wolf-Hirschhorn syndrome

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Case:
• 32 y/o G0P0 patient, IVF-ICSI due to male factor – single embryo transfer
• 1st trimester morphologic scan at 12 weeks – absent nasal bone (high suspicion, poor examination due to fetal movements), slight growth restriction (fig.1). Patient declined CVS.
• At 15 weeks – clearly absent nasal bone, high forehead, increasing growth restriction, decreased amniotic fluid (fig.2,3 and 4).
• Karyotype – 46,XX, del(4)(p14)
• TOP at 20 weeks

The Wolf-Hirschhorn syndrome. Key points:
• Synonyms - 4p-syndrome, Pitt-Rogers-Danks syndrome, monosomy 4p, partial deletion 4p
• Incidence – very rare 1:50000 births, female: male ratio 2:1
• Causes – deletion in the terminal region of the short arm of chromosome 4 (classic band 4p16.3, variants), de novo deletions (50-60% of cases)
• Clinical signs: Craniofacial - specific phenotype “Greek warrior helmet” appearance of the nose (wide nasal bridge continuing to the forehead, hyperelorism, proeminent glabella), epicantal , short philtrum, downturned corners of the mouth, microcephaly, clefts (90%), muscular hypotonia (90%), IUGR (77%), mental retardation (75%), skeletal – kyphosis, scoliosis, clubfeet, split hand (50-75%), short stature (25-66%), congenital anomalies (30%), genital anomalies (30%), deafness (23%), renal anomalies (23%), GE and lung anomalies (20%)
• Differential diagnosis – Seckel syndrome, CHARGE, Smith-Lemli-Opitz syndrome, Malpuech syndrome, Angelmann syndrome
• Early antenatal diagnosis is possible. WHS should be suspected in case of abnormal ultrasound scan: a peculiar craniofacial profile associated with early IUGR +/- decreased fetal movements. Karyotyping (including additional FISH or microsatellite analysis) is compulsory and TOP should be offered after proper counselling.
• Life expectancy of WHS patients ranges between 18 and 34 years, depending on the extent of the genetic deletion.