Antenatal sonographic and genetic diagnosis of two cases of Bardet-Biedl - Syndrome

J. Hartung*, K. Ladig**, G. Thiel***, R. Chaoui*** (*Fetal Medicine Practice-Berlin, ** Fetal Medicine Practice-Kamenz, ***Center for Prenatal Diagnosis and Human Genetics, Berlin, Germany)

Introduction
Bardet-Biedl syndrome (BBS) belongs to the group of ciliopathies and has an autosomal-recessive inheritance with 22 genes known already. In the child it is associated with retinal dystrophy, obesity, neurological and psychic disabilities, hypogonadism, postaxial polydactyly and renal dysfunction. Antenatal diagnosis remains difficult due to the postnatal onset of most symptoms and the genetic heterogenicity. We present two cases of antenatal suspicion and genetic confirmation of BBS.

Case 1
On 22 weeks screening US of a primigravida, enlarged, hyperechoic kidneys were detected (Fig.1). The following detailed examination showed a hexadactyly of one foot (Fig 2); no other malformations were found. BBS was suspected and amniocentesis revealed a homocygotic mutation in the BBS 1 gene, both parents were heterocygotic carriers. Parents opted for TOP.

Case 2
On first trimester US of a primigravida, polydactyly of all extremities was detected. Amniocenteses revealed a normal karyotype. Follow up US at 18 gw showed hyperechogenic kidneys (Fig. 3) and polydactyly (Fig 4). BBS was suspected and confirmed by detection of a homozygotic mutation in the BBS1 gen. Both parents were heterocygotic carriers. Parents opted for TOP.

Conclusion
Given the incomplete clinical manifestation of BBS during fetal life, prenatal diagnosis remains challenging. Our two cases show, that antenatal sonographic diagnosis of enlarged, hyperechoic kidneys in combination with polydactyly should prompt targeted genetic diagnosis for BBS. Additional malformations (e. g. intracerebral or skeletal) could lead to the diagnosis of other ciliopathies, like Joubert or Meckel syndrome.

Genetic:
BBS1 gene
Exon 12
c.1169T > G
p.Met 390Arg

Genetic:
BBS1 gene
Exon 14-17
c.1285C < T
p.Arg 429