A clinical report case of Smith–Lemli–Opitz syndrome
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Objective
To report a case of Smith–Lemli–Opitz syndrome. Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive disorder affecting approximately 1 in 20,000 to 30,000. Prenatal and postnatal growth retardation, microcephaly, moderate to severe intellectual disability and multiple major and minor malformations characterize it. The malformations include distinctive facial features, cleft palate, cardiac defects, underdeveloped external genitalia in males, postaxial polydactyly, and 2-3 syndactyly of the toes. The clinical spectrum is wide and individuals have been described with normal development and only minor malformations. Severe cases can involve profound intellectual disability and major physical abnormalities. It is caused by homozygous or compound heterozygous mutation in the gene encoding sterol delta-7-reductase (DHCR7) (chromosome 11q13.2) The affected gene codes for the enzyme dehydrocholesterol reductase. This enzyme is responsible for the final step in the production of cholesterol. Cholesterol has numerous functions in the embryonic and postnatal development. It is a major component of cell membranes and myelin, and is a precursor of steroid hormones and bile acids. The development of the blood brain barrier likely around 12-18 weeks of human gestation makes the developing brain dependent on endogenous cholesterol synthesis so enzyme defects along the cholesterol biosynthetic pathway result in a host of neurodevelopmental and behavioral findings along with CNS structural anomalies.

Methods
Case report.

Results
DFTL, 27 years old; first pregnancy; no relevant in the personal or in the family history. The couple was non-consanguineous and both Caucasians. She was referred to our center at 31 week because of defects on the third trimester scan, there had been an unconfirmed suspicion of toxoplasmosis infection on the first trimester. Morphologic second trimester scan was apparently normal. At our initial evaluation at 31 weeks we identified a globally small fetus, with ambiguous genitalia, mild renal pelvis dilatation and polyhydramnios. Serial follow up scans showed profound fetal growth restriction most notable in the long bones. Amniocentesis was performed at 32w with amniodrainage (400cc), the karyotype reported as male, 46XY, PCR for toxoplasmosis was negative. At 34 week a second amniodrainage was performed because of maternal dyspnea - with the redraw of 1200 cc of amniotic fluid. She underwent spontaneous labor at 35 weeks and delivered an alive male neonate of birth weight 1930 grams by vertex presentation with Apgar 7 to 9. At clinical examination there was typical facial features with microcephaly, left eye ptosis and micrognathia. Limb findings include single palmar creases and syndactyly of the second and third toes. Genitalia examination showed hypospasias a small penis and right testicle cryptorchidism. Abdominal scan confirmed mild renal pelvis dilatation with no other malformations. Transfontanelar ultrasound scan showed various hemorrhagic choroid plexus cyst but no major abnormality. The neonate presented hypotonia and feeding difficulties. The clinical findings raised suspicions of SLOS. Clinical analyses confirmed low total cholesterol and elevated 7-dehydrocholesterol. The couple were later confirmed to be carriers.

Conclusion
Prenatal diagnosis of SLOS is infrequent unless parental carrier status is known or there is a family history. In our reported case unfortunately the second trimester scan was apparently normal as a suspicious of an ambiguous genitalia could have prompted the diagnose. The carrier frequency for SLOS mutations is higher than the documented incidence suggesting missed diagnoses probably because of the wide clinical spectrum with normal development and only minor impairment, females, and spontaneous miscarriages. In this case the couple were later confirmed to be carriers, so, prenatal gene testing can be offered in a future pregnancy. In the future prenatal testing maternal urine or serum steroid measurements may be a screening option.