

EP10.08 First prenatal case of homozygous HPDL gene variant in Lithuania in the fetus with CNS anomalies

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Introduction

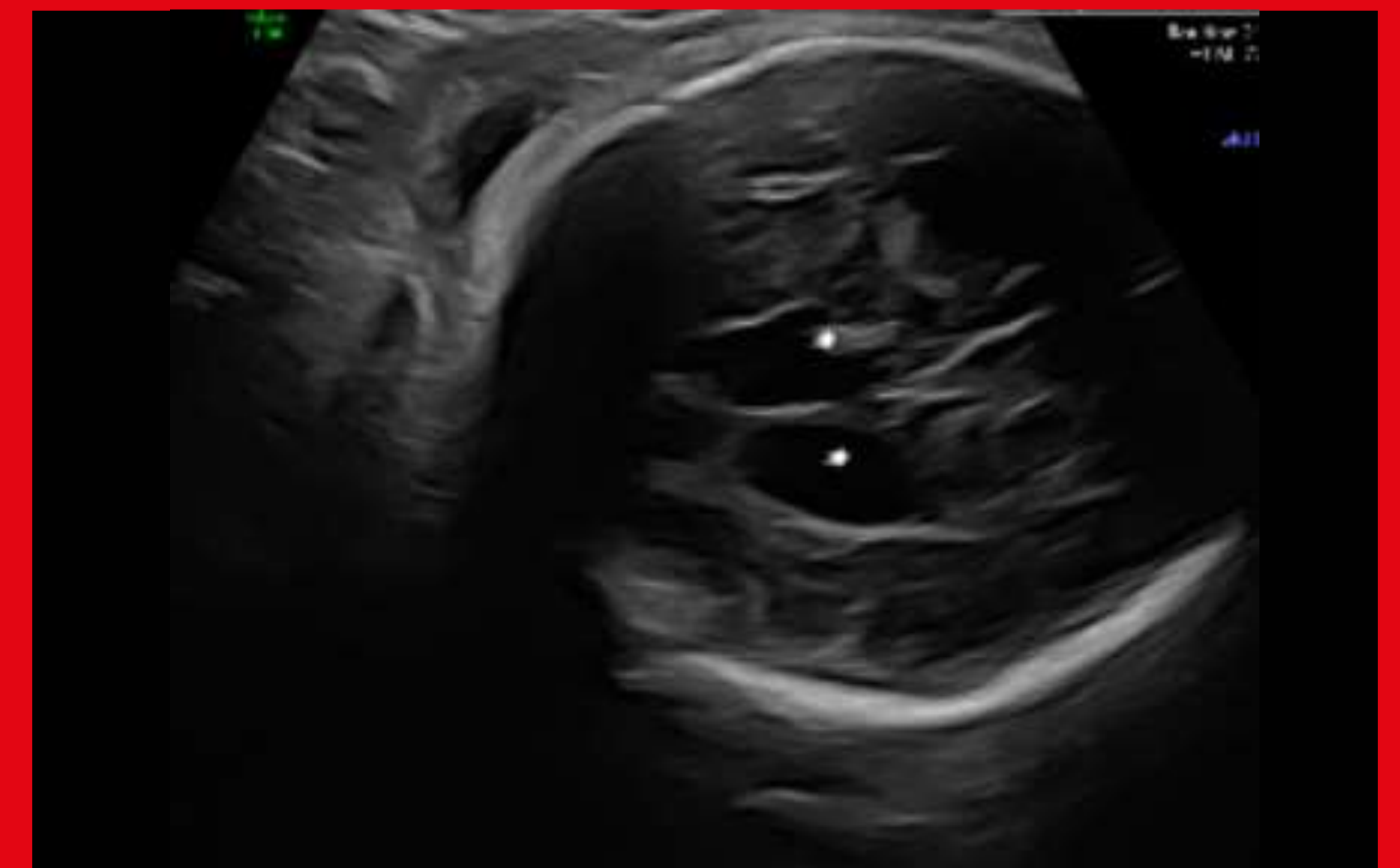
Central nervous system anomalies (CNS) can be found during prenatal ultrasound examination, in ~1–2% of fetuses in the 2nd trimester. Most of them are transient and isolated, resolve by the 3rd trimester. We report a case of prenatal CNS anomalies resulted in homozygous variant in *HPDL* gene.

Case report

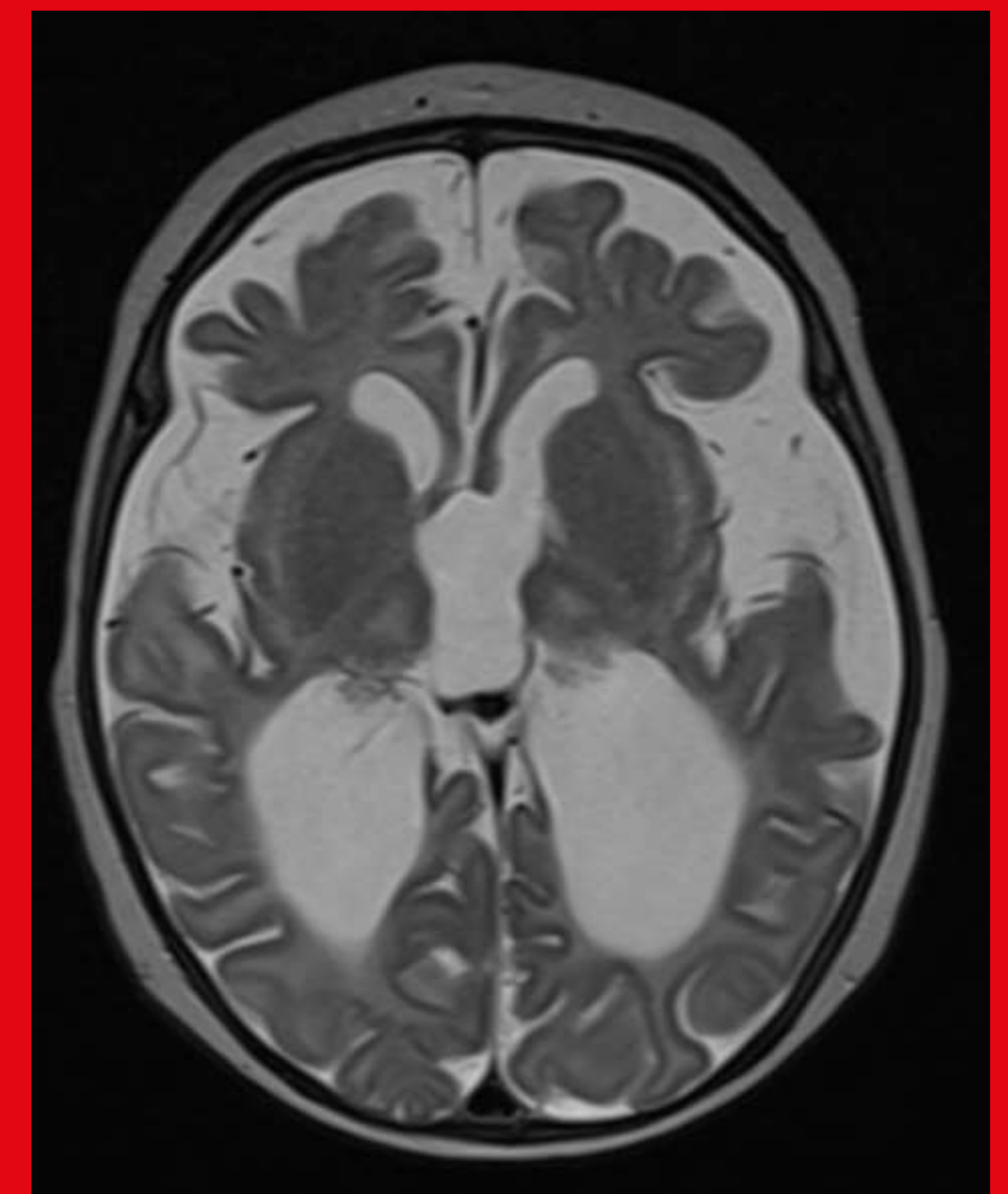
- Patient – 35 year old 2nd time pregnant woman;
- Reason of consultation – **choroid plexus cysts** in **19 weeks ultrasound**;
- **Amniocentesis** results – normal female karyotype, **46, XX**;
- Follow up – at **31+2 weeks fetal growth retardation, unilateral moderate ventriculomegaly**;
- Fetal magnetic resonance imaging – asymmetric communicating **hydrocephaly**, **hypoplastic corpus callosum**, **cyst** on the right at the **frontal horn**, **wide interhemispheric space**, lower part of ***vermis cerebelli*** hypoplasia, slightly **enlarged *cisterna magna***;
- Genetic testing – extended to the Whole exome sequencing (**WES**), found **likely pathogenic frameshift homozygous** variant in *HPDL*: ***NM_032756.4:c.[599del];[599del] (p.Gly200Alafs*4)***, classified based on ACGS2024/ClinGen criteria (PVS1_strong; PM2_supporting; PM3_moderate);
- **Unilateral ventriculomegaly** enlarged to **severe** (18 mm);
- Delivery – **41st week of gestation, 3210 g, Apgar score 6-8**;
- **Neonatal** period – **resuscitated**, severely **hypotonic**, **no swallowing reflex**, **discharged with tube feeding**.
- Neurosonogram – asymmetric **hydrocephalus**, ***corpus callosum*** hypoplasia, **brain cyst**.

Discussion

HPDL gene, found in mitochondria, encodes a protein, functioning as a 4-hydroxyphenylpyruvate dioxygenase. It is involved in coenzyme Q10 synthesis. *HPDL* gene variant cause Neurodevelopmental disorder with progressive spasticity, brain white matter abnormalities. Patients display cortical atrophy, ***vermis cerebelli***, brainstem, ***corpus callosum*** hypoplasia, ventriculomegaly that result in severe neurologic disability.



Fetal ultrasound. Ventriculomegaly present



Postnatal brain magnetic resonance imaging

Conclusion

WES is important tool to find cause of CNS anomalies in prenatal ultrasound.