

Fetal Phenotype of Wiedemann-Rautenstrauch Syndrome: A Rare Gem of Genetic Disorder

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BACKGROUND

- Wiedemann-Rautenstrauch Syndrome (Neonatal Progeroid Syndrome): an extremely rare, autosomal recessive genetic disorder.
- Caused by mutations in the POLR3A gene.
- Parents are typically asymptomatic carriers.
- High perinatal mortality, though rare cases surviving up to 20 years have been documented.
- Fewer than 20 cases reported worldwide.

<1:1,000,000

Estimated prevalence

25%

Recurrence risk per pregnancy

<20

Cases reported worldwide

POLR3A encodes the largest subunit of RNA Polymerase III, an enzyme essential for transcribing small non-coding RNAs required for normal cell growth, division, and development — explaining the multisystem impact seen in WRS.

CASE PRESENTATION

30-year-old primigravida at 29 weeks’ gestation (non-consanguineous, no prior antenatal complications) was evaluated for early-onset fetal growth restriction (FGR) and short long bones. She re-presented at 31 weeks with reduced fetal movements; ultrasound confirmed intrauterine fetal demise (IUFD).

Diagnosis: Amniocentesis (29 weeks) with Whole Exome Sequencing (WES) confirmed Wiedemann-Rautenstrauch Syndrome.

3D ULTRASOUND IMAGE



DISCUSSION

Wiedemann-Rautenstrauch Syndrome (WRS), or Neonatal Progeroid Syndrome, is characterized by a complex prenatal phenotype. In addition to severe early-onset intrauterine growth restriction (FGR) and hypo mineralization, children with WRS display a variety of skeletal anomalies as well as distinct craniofacial features including frontal bossing, craniosynostosis, and hypotelorism. However in our scan findings, the progeroid facies of the fetus was not able to detect in antenatally. WRS is caused by autosomal recessive mutations in the POLR3A gene, which encodes the largest subunit of RNA polymerase III, essential for cellular function. While the phenotypes in the different forms of WRS overlap with other forms of skeletal dysplasia as well as with growth restriction syndromes, conventional imaging is typically not sufficient for a definitive diagnosis. Instead, a detailed neurosonography and fetal skeletal survey, in combination with a Whole Exome Sequencing (WES) approach, can provide a definitive genetic diagnosis. This early genetic confirmation enables a precise multidisciplinary management approach, which in turn allows for an assessment of prognosis with regard to high perinatal lethality as well as for critical recurrence risk counselling for carrier parents (25% for subsequent pregnancies).

Key Prenatal Ultrasound Findings



1. Craniosynostosis & frontal bossing
2. Hypotelorism
3. Hypo mineralized distal long bones
4. Hands flapped inward
5. CTEV (clubfoot)
6. Prominent cauda equina (sacral bones)
7. Early-onset fetal growth restriction

CONCLUSION

- Consider WRS in fetuses with early-onset FGR, skeletal dysplasia, and dysmorphic craniofacial features.
- WES is crucial to differentiate WRS from overlapping disorders by identifying POLR3A variants.
- Early molecular confirmation enables realistic prognostic guidance and precise 25% recurrence-risk counselling.

Syndrome	Gene	Protein Function	Age of Onset	Prenatal Detection	Median Survival	Primary Organ Involvement
Wiedemann-Rautenst rauch (WRS)	POL3RA chr 17q25.1	RNA Polymerase III subunit	IN UTERO 18-20 weeks	✓ YES Detectable on US	4-6 months (rarely to 20 yrs)	Multi-organ (Prenatal growth)
Hutchinson-Gilford Progeria (HGPS)	LMNA chr 1q22	Lamin A/C (Nuclear envelope)	6-12 months early infancy	✗ NO Normal at birth	13-14 years	Cardiovascular (Atherosclerosis, MI/stroke)
Werner Syndrome (WS)	WRN chr 8p12	DNA Helicase (DNA repair)	20-30 years adulthood	✗ NO Completely normal	~48 years	Cardiovascular Cancer (55x risk)
Cockayne Syndrome (CS)	ERCC8/ERCC8	DNA repair factors (Transcription-coupled)	6+ years childhood	✗ NO Subtle findings	10-20 years	Neurological (Neurodegeneration, ataxia)
Dyskeratosis Congenita (DC)	DKC1/TERC/TER T	Telomerase components (Telomere maintenance)	Variable childhood/adult	✗ NO Normal at birth	30-40+ years	Hematopoietic (Bone marrow failure)

PROGEROID SYNDROMES : Clinical Classification