

Metachromatic leukodystrophy identified through preconception genetic screening: a case report



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A 26-year-old nulligravid patient with no relevant family history underwent preconception expanded carrier screening without clinical indication. The results revealed heterozygous pathogenic variants in ARSA and WFS1. Her partner had identical findings. After genetic counseling, the couple opted for spontaneous conception with planned fetal investigation.

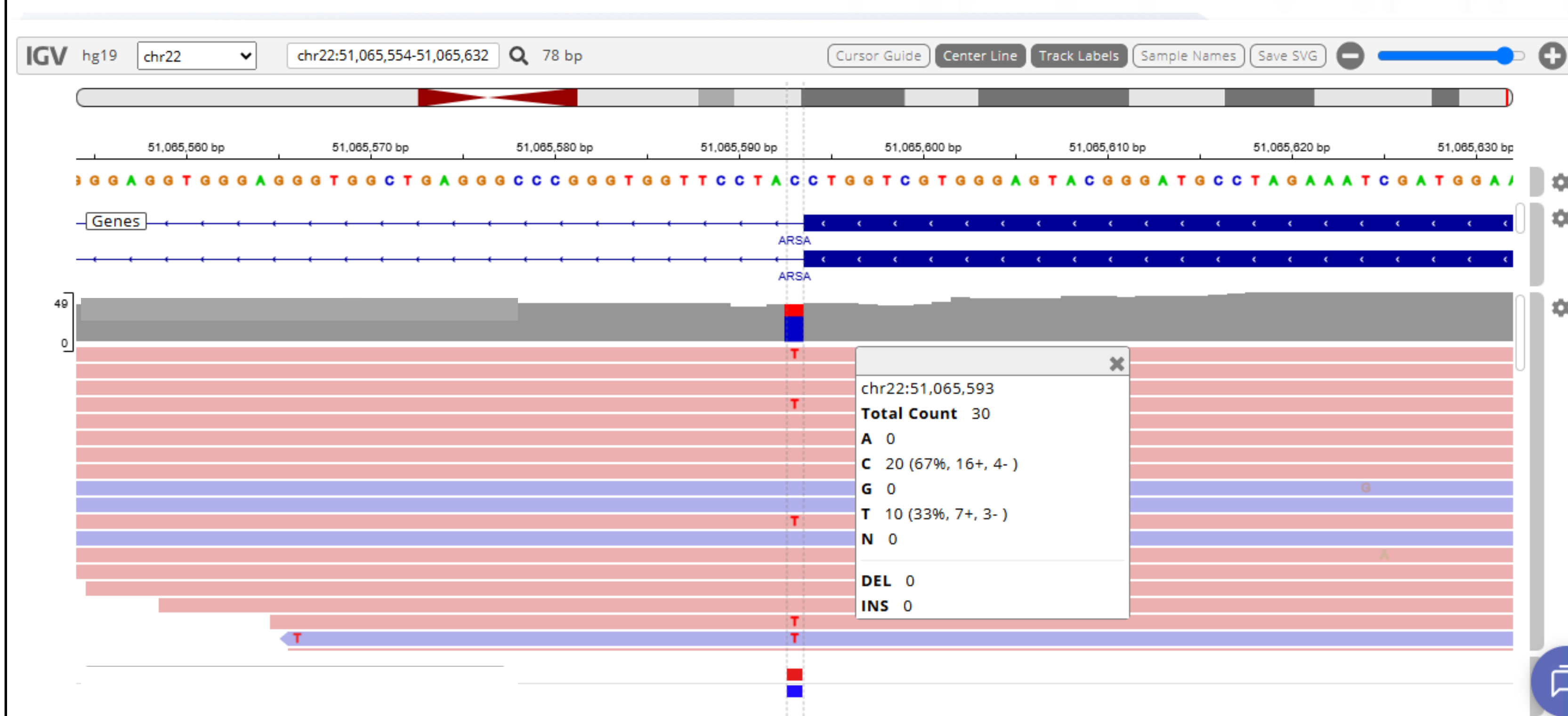
Ultrasound at 13+6 weeks demonstrated a singleton fetus with normal anatomy, a nuchal translucency of 1.5 mm, and no abnormal markers. Amniocentesis at 16+1 weeks showed a normal karyotype (46,XX). Whole exome sequencing identified 2 pathogenic ARSA variants in heterozygosity (in trans), confirming the molecular diagnosis of metachromatic leukodystrophy. Isolated heterozygosity for WFS1 was also identified, and the patient was referred for post-test genetic counseling. Discussion: This case demonstrates that expanded reproductive genetic testing, even when performed without clinical indication, may result in the fetal diagnosis of a severe recessive disorder with late onset and complex management.

Prenatal diagnosis of ARSA significantly impacts postnatal planning, allowing for:

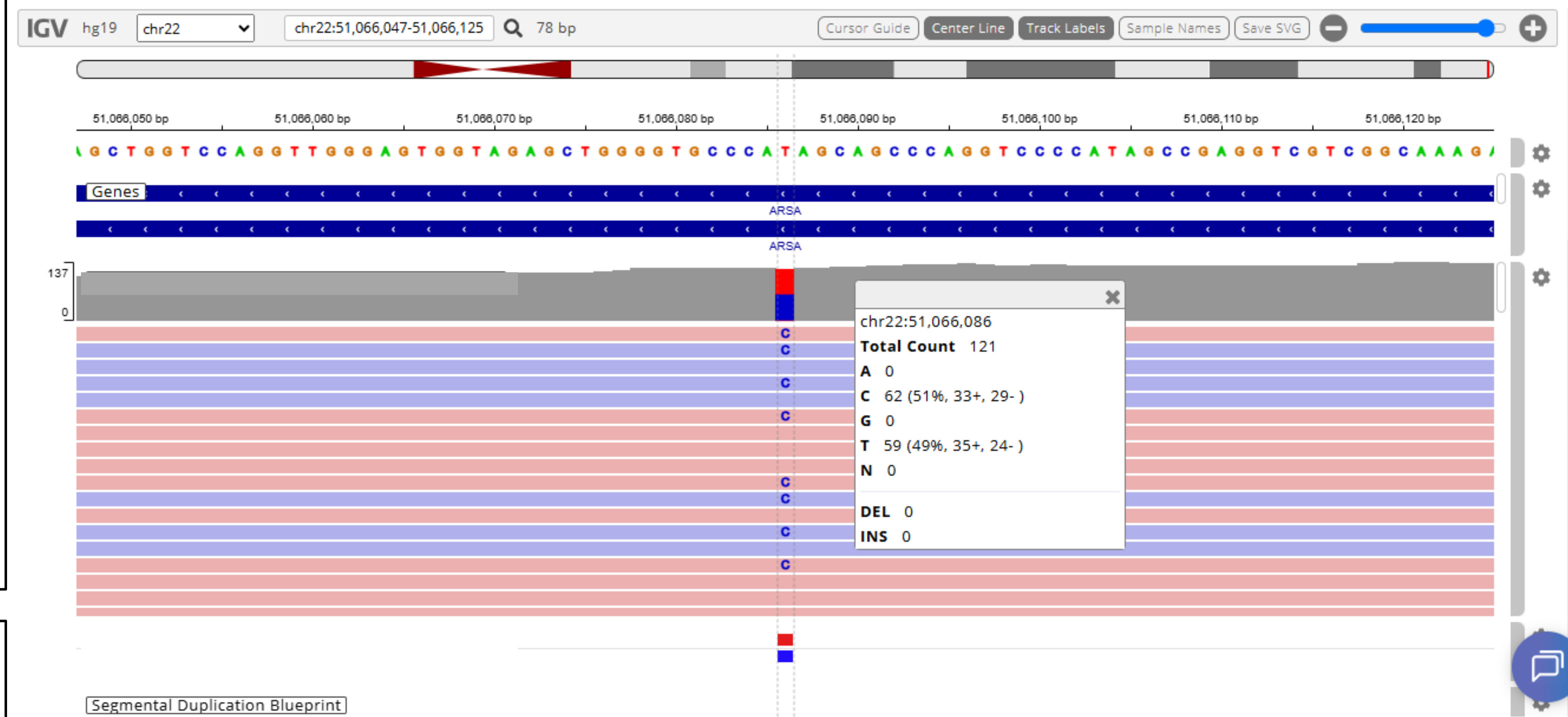
- (a) referral to a specialized multidisciplinary team;
- (b) emotional preparation of the parents;
- (c) early discussion of emerging therapies and clinical trials.

Guidelines from the American College of Obstetricians and Gynecologists (ACOG) emphasize that both pre- and post-test genetic counseling are essential for appropriate interpretation of results.

Incidental findings from reproductive genetic screening may lead to fetal molecular diagnosis of recessive disorders without an intrauterine phenotype. This case highlights the need for structured genetic counseling, given its important ethical and prognostic implications for the family



ARSA: NM_000487.6:c.465+1G>A in heterozigosity



ARSA: NM_000487.6:c.122A>G: p.(Tyr41Cys) in heterozigosity