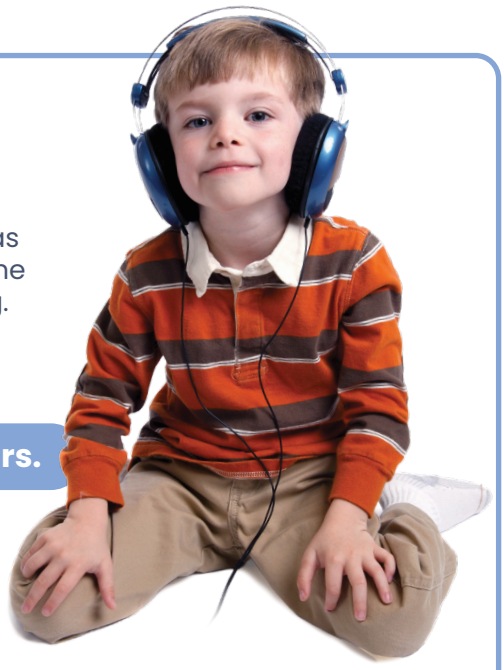
CASE STUDY

Implications to clinical practice

Meet Oliver†

Shortly after his birth, routine newborn assessment identified that Oliver exhibited mild hypotonia. Without additional findings, Oliver was discharged. But by 15 months of age, Oliver's parents started noticing he wasn't meeting the normal milestones and wasn't speaking or walking. They brought their concerns to Oliver's pediatrician.



Oliver's journey to a genetic diagnosis took almost 7 years.

15 months old

Oliver's pediatrician referred him for a hearing test and a consultation with a speech and language pathologist based on his speech delay. His hearing test was normal, but he was identified to have expressive language delay.

2–3 years old

By age 2, Oliver was starting to pull to stand and was still not speaking. His parents also began to suspect autistic behaviors based on poor eye contact and lack of social behavior in daycare. Oliver was referred to a developmental behavioral pediatrician and scheduled for an appointment 11 months later. His diagnostic evaluation revealed autism and abnormal eye movement. A pediatric ophthalmologist subsequently diagnosed Oliver with Duane's syndrome and mild myopia.

Based on these findings and for future family planning for Oliver's parents, the developmental behavioral pediatrician ordered *FMR1* and chromosomal microarray testing. Both tests were negative.

6 years old

Oliver's parents had another baby who was also noted to have mild motor delays by 12 months. Around the same time, Oliver was placed into a special education program for intellectual disability at school and was also identified to have mild scoliosis by his pediatrician. Based on Oliver's complex history and these new concerns in his sibling, their pediatrician requested a genetics referral for both children.

7 years old

After 9 months on the waitlist, the geneticist evaluated Oliver and ordered exome sequencing as a trio including the parental samples. Exome sequencing provided results in 6 weeks, and identified a de novo pathogenic variant in *MED13,* finally explaining the findings of:

- autism spectrum disorder
- intellectual disability and developmental delay
- hypotonia
- expressive language delay
- Duane's syndrome
- scoliosis

His journey could have been 4 years shorter.

Following society guidelines, Oliver's doctor could have ordered exome after his initial presentation of developmental delay. The exome would have delivered results in 6 weeks, enabling a specific diagnosis, informing family planning, and connecting Oliver and his family with gene-related support groups and resources when he was 3 years old.

† - Fictionalized case study for illustrative purposes only

References: 1. Khachadourian V, *et al. Transl Psychiatry.* 2023 Feb 25;13(1):71. **2.** Arteche-López A, *et al. Genes.* 2021(12):560. **3.** Ní Ghrálaigh F, *et al. J Autism Dev Disord.* 2023 Jan;53(1):484-488. **4.** Srivastava S, *et al. Genet Med.* 2019 Nov;21(11):2413–2421. **5.** Tammimies K, *et al. JAMA.* 2015 Sep 1;314(9):895-903. **6.** Lindy A, *et al.* Poster Presented at: AAN 2022 Annual Meeting; April 24-26, 2022; Seattle, WA. **7.** Manickam K, *et al. Genet Med.* 2021;23(11):2029-2037. **8.** Smith L, *et al. J Genet Couns.* 2023 Apr;32(2):266-280.