Clinical commentary

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De novo 8p23.1 deletion in a patient with absence epilepsy

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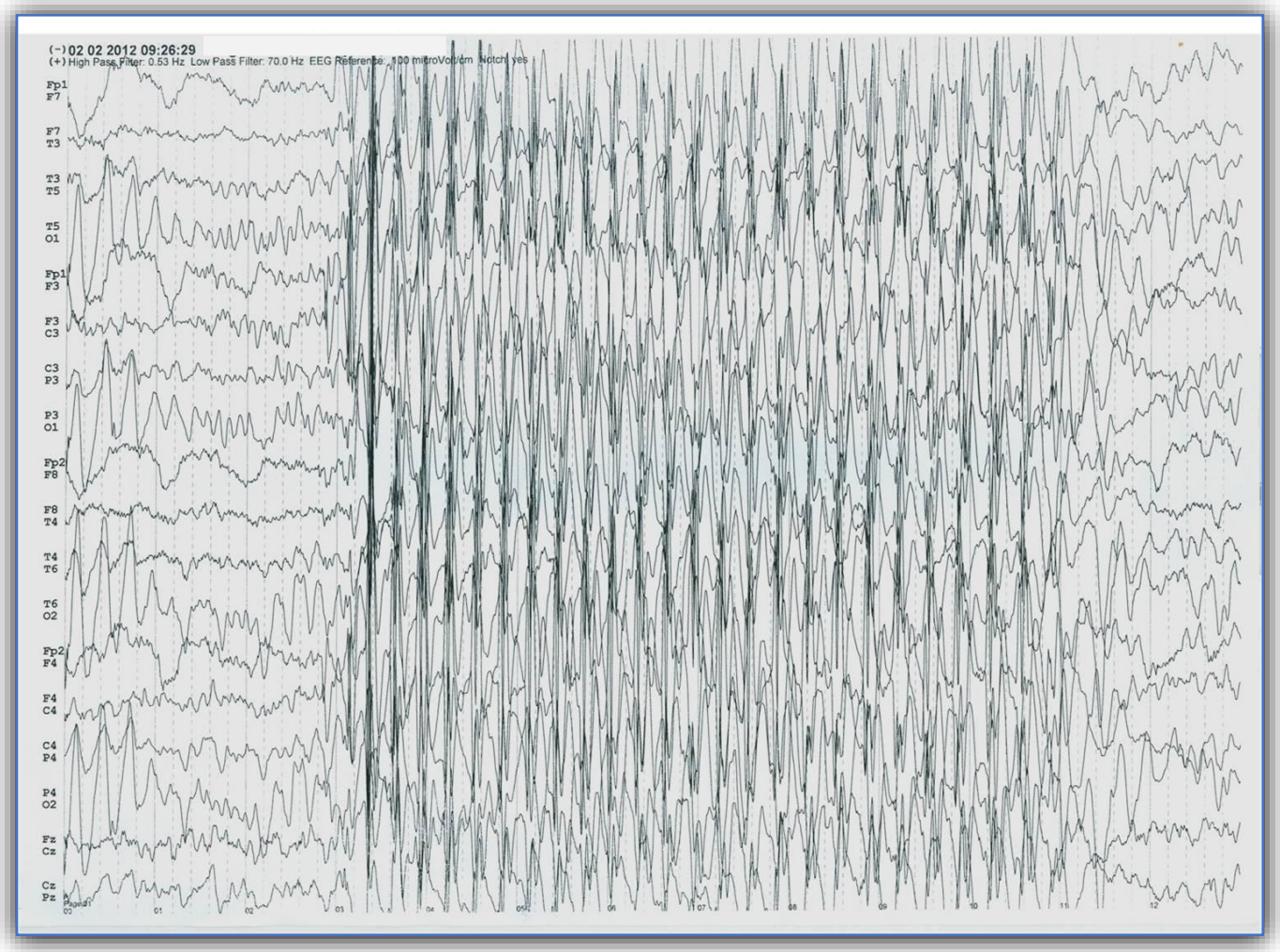
About absence seizures

- Typical absence seizures involve sudden, brief impairment of consciousness, lasting only 3-25 seconds, without a concomitant postictal phase and occur multiple times per day.
- Seizures are aggravated by hyperventilation.
- EEG shows a typical generalized, synchronous, bilateral 3-4-Hz spike and slow-wave discharges.



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About absence seizures

- Absence seizures are a type of idiopathic generalized epilepsy and are mostly seen in childhood absence epilepsy (CAE).
- CAE is the most common childhood generalized epilepsy that generally begins between three and nine years of age (Loiseau *et al.*, 1995; Shinnar *et al.*, 2015).
- Children with CAE have a normal neurological examination and normal intelligence level; however, frequent seizures may affect mental performance (Loiseau *et al.*, 1995; Glauser & Loddenkemper, 2013).

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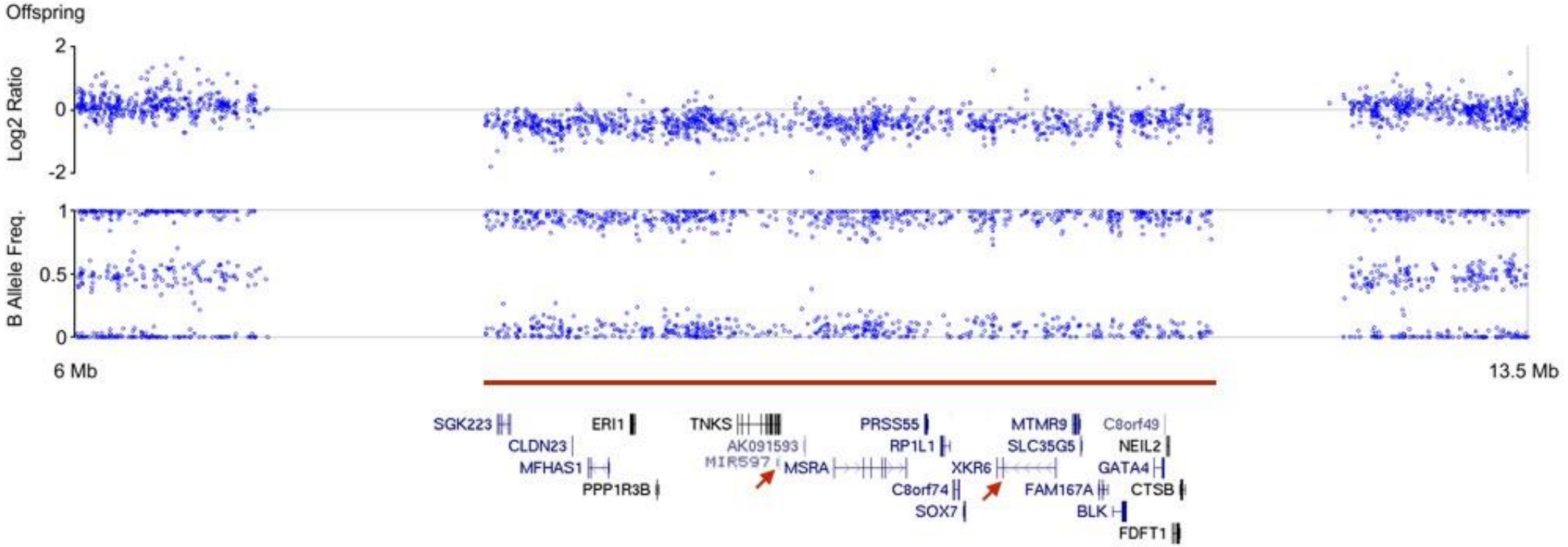
molecular pathology

- The consequence of unbalanced expression of Ca++ channel, chloride, and $GABA_A$ receptor genes can cause absence epilepsies.
- Genomic copy number variations (CNVs) constitute important genetic risk factors for common genetic generalised epilepsy syndromes (Lal *et al.*, 2015) and absence epilepsies (Addis *et al.*, 2016).
- The recurrent hotspot microdeletions disrupt genes associated with neuronal development and function, suggesting that fundamental neurodevelopmental pathways may be important in epileptogenesis of absence seizures.

In the case presented:
A 4-Mb *de novo* deletion of the chromosomal region 8p23.1 (8,109,255–12,166,733 bp (GRCh37/hg19)) in the offspring



MicroRNA genes are small non-coding RNA molecules that are responsible for regulating gene expression. MIR597 (microRNA-597) targets GABRB3, which is known to be involved in epileptogenesis of absence epilepsies.

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The 8p23.1 deletion syndrome

A rare multisystem disorder :

with high penetrance and variable phenotypic spectrum

includes:

- congenital heart disease (CHD),
- intellectual disability,
- behavioural problems,
- microcephalia,
- and sometimes epilepsy.

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Conclusions:

- *MIR597* targets *GABRB3*, which is known to be involved in epileptogenesis of absence epilepsies (Kan *et al.*, 2012).
- It is of interest that the deletion of this microRNA gene may be involved in the pathogenesis of absence seizures in our patient as well as in other patients with the 8p23.1 microdeletion syndrome with epilepsy phenotype.
- Epilepsy may be part of the phenotypic spectrum of the 8p23.1 deletion syndrome, and/or haploinsufficiency of several genes with functional diversity.
- CNV and/or Whole Exome Sequencing (WES) screenings on GGE plus patients, since it may have important implications in clinical practice with regard to diagnostic classification, clinical management of the syndromic multisystem disorders and potentially genetic counseling.

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