LETTER TO THE EDITOR

Response to Cueto-González et al

To the Editor:

We read with interest the contribution of Cueto-González et al (Cueto-González AM, Fernández-Álvarez P, Valenzuela Palafoll I, Lasa-Aranzasti A, Vendrell-Bayona T, Tizzano E. Genetics in medicine. Genet Med. 2021) who described an additional patient with NSD2 deficiency caused by the de novo p.D455Efs*19 truncating variant. The phenotype of the affected individual, characterized by stature below the familial target-height, occipitofrontal circumference in the lower-normal range, and mild to moderate intellectual disability without epilepsy, is in line with that of the patients described in our series.1

As shown in our publication (see Figure 3B in Zanoni et al1) and further emphasized by Cueto-González et al (Cueto-González AM, Fernández-Álvarez P, Valenzuela Palafoll I, Lasa-Aranzasti A, Vendrell-Bayona T, Tizzano E. Genetics in medicine. Genet Med. 2021), epilepsy occurs rarely in patients with NSD2 deficiency and may thus represent either a rare manifestation of the disorder or a chance finding. In our NSD2 deficient cohort, only 1 of 28 (3.6%) affected individuals (patient 10-I) presented with epilepsy in the form of multiple fever-related convulsions since age 1 year as well as myoclonic absences till age 5 years. In another affected individual (patient 15-I), an electroencephalogram at age 4 years and 4 months showed epileptic activity in the absence of clinical seizures.

The aforementioned low prevalence of epilepsy in our cohort is in line with previous data suggesting that other genes such as LETM1 may be responsible for the high prevalence of epilepsy in patients with Wolf-Hirschhorn syndrome.2,3

We thank Cueto-González et al (Cueto-González AM, Fernández-Álvarez P, Valenzuela Palafoll I, Lasa-Aranzasti A, Vendrell-Bayona T, Tizzano E. Genetics in medicine. Genet Med. 2021) for further stressing this point and thus reinforcing the concept that NSD2 deficiency is associated with a distinct rather mild phenotype more akin to disorders such as Silver-Russell and similar syndromes than to Wolf-Hirschhorn syndrome.

Conflict of Interest

The authors declare no conflict of interest.

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References