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LETTER

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Sotos syndrome and the added value of genetic workup in epilepsy surgery

To the editors,

We read with great interest the study by Fortin et al[1] describing the phenotypic spectrum of seizures and epilepsy in 49 patients with Sotos syndrome based on a structured clinical interview and chart review. The authors report patients' seizure semiologies, with more than two-thirds showing "staring spells," half showing afebrile generalized tonic-clonic seizures and half having a history of febrile convulsions. In line with previous reports,[2] seizures in these patients usually respond to antiseizure drug treatment, with only a small fraction of patients having a drug-resistant epilepsy. The high prevalence of "staring spells" by Fortin et al[1] suggests a high incidence of focal seizures with impaired awareness. Yet, no potentially epileptogenic focal lesions were noted on neuroimaging. Focal seizures, often with temporal lobe semiology and ictal EEG patterns, have previously been noted in patients with Sotos syndrome by Nicita et al,[2] similarly without associated structural brain lesions. However, Sotos syndrome is associated with a 2%–3% risk of malignancy.[3] Most commonly, these comprise lympho-hematological tumors, but can very rarely include potential epileptogenic low-grade brain tumors.[4,5]

We have recently reported a challenging case[6] of drug-resistant epilepsy with temporal lobe seizures evolving into bilateral tonic-clonic seizures in the presence of a mesiotemporal brain tumor in a boy with developmental delay and overgrowth. Because of the focal-onset epilepsy associated with a low-grade neuroepithelial tumor, our patient underwent presurgical evaluation and subsequent epilepsy surgery. Histopathology confirmed a diffuse astrocytoma, but its gross-total resection failed to control the seizures. Genetic testing performed during the reevaluation of this case of unsuccessful epilepsy surgery identified an *NSD1* pathogenic variant, thus establishing the diagnosis of Sotos syndrome.

Our case turns the spotlight on this rare, potentially misleading presentation of Sotos syndrome. Here, a focal epileptogenic brain lesion did not fully explain the clinical picture of focal seizures associated with dysmorphic features and medical comorbidities and an unsuccessful epilepsy surgery ultimately led to the unifying diagnosis of Sotos syndrome.

In the context of the case series presented by Fortin et al,[1] which indicates that patients with seizures and Sotos syndrome have favorable outcomes in terms of seizure control, our case clearly represents a rare exception in terms of poor seizure control. Yet, the rarer cases of drug-resistant epilepsy in Sotos syndrome can pose important diagnostic challenges that should be taken into account. Our case thus highlights Sotos syndrome as an important differential for drug-resistant epilepsy in the context of an overgrowth syndrome. Most importantly, our case underlines the importance of genetic testing as part of presurgical workup in drug-resistant focal epilepsy, even in apparently straightforward cases of lesional epilepsy, to rule out an underlying genetic substrate that may preclude surgical success.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to disclose. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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