all patients with developmental delays, epilepsy (especially drug-resistant epilepsy) and autism, whether or not they present dysmorphic features, in order to rule out chromosomal alterations.

This case report was written for academic and pedagogical purposes in light of the low incidence rate of this disease (1:30 000 live births) and the importance of the complementary study performed on this patient. That study enabled doctors to assign a final diagnosis and thus offer appropriate genetic counselling to the patients' parents.

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Phenytoin-induced acute orofacial dyskinesia☆

Discinesia orofacial aguda inducida por fenitoína

Dear Editor,

In 1962, Peters published the first case report of a patient with dyskinesia induced by phenytoin (DPH).[1] Although dyskinesia as a side effect of antiepileptic drugs is very uncommon, it has been described in patients treated with lamotrigine, ethosuximide, carbamazepine, valproic acid,[2] gabapentin,[3] felbamate,[4] and phenobarbital.[5,6] DPH may cause different movement disorders, including orofacial and limb dyskinesias, trembling, asterixis, hemiballismus, dystonia, and myoclonias.[7] Of these disorders, orofacial dyskinesia is the most commonly described. We present the case of a patient with orofacial dyskinesia secondary to treatment with phenytoin monotherapy.

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Right-handed male aged 80 years with a personal history of hypertension and atrial fibrillation. He was being treated with acenocoumarol and had been fitted with a pacemaker; there was no family history of epilepsy or movement disorders. The patient came to the emergency department with a subacute headache resistant to conventional analgesics. Neurological examination was normal. Brain CT revealed a left hemispheric subdural haematoma with a slight midline shift. A craniectomy was performed to evacuate the haematoma. One week after surgery, the patient suffered a generalised tonic—clonic seizure. He was treated with a 750 mg intravenous bolus of phenytoin to be followed by maintenance doses of 300 mg/day administered orally. A few hours after receiving the loading dose, the patient exhibited choreic and dystonic movements of the mouth and tongue which caused mild dysarthria. All other results from the neurological examination completed at that moment were normal. The patient was taking no other medications at the time except paracetamol for pain. A complete blood count and biochemistry scan also delivered normal results. A brain CT performed as part of the same examination showed only evidence of the recent frontal craniectomy with no traces of blood. Blood levels of phenytoin were 16 μg/dL (normal range: 10—20 μg/dL). Twelve hours after the onset of symptoms, phenytoin was replaced with oral valproic

acid dosed at 500 mg/8 hours due to the persistence of the orofacial dyskinesia and the absence of other agents that could potentially be responsible for movement disorders. Discontinuing DPH treatment caused the orofacial dyskinesia to subside; 3 days later, it had resolved completely.

Acute orofacial dyskinesia secondary to phenytoin treatment is very uncommon.[8] These cases may occur at any age but they are more frequent in younger patients (80%). The correlation with plasma phenytoin is unclear because the entity has been described in patients with levels within the therapeutic range as well as in patients with higher levels. Symptoms appear after the first dose of phenytoin in 18% of all cases. In half of the cases, an underlying lesion or neurological disease is present.[9] Although some authors state that phenytoin only induces abnormal movements when there is an underlying brain lesion, current evidence contradicts that position. In the largest case series published to date,[10] 68% of patients suffering dyskinesias were treated with polytherapy, while 32% were treated with monotherapy.

The mechanism by which phenytoin induces dyskinesia is not yet understood.[11] It seems reasonable to think that an underlying condition would induce a basal ganglia dysfunction that could foster the development of hyperkinesia. On the other hand, it is well-known that phenytoin acts as a dopamine agonist since it lessens symptoms in Parkinson's disease and intensifies choreic movements in Huntington's disease.[12] Additional pathophysiological hypotheses include brain toxicity, changes in tryptophan metabolism, tryptophan accumulation caused by DPH, and alterations to basal ganglia synapses, but none of these hypotheses can be applied to all cases.[13,14] Neither can we rule out the possibility of an idiosyncratic response to phenytoin.[15] Phenytoin may also have multiple mechanisms that cause different abnormal movements, but available data does not allow us to distinguish between different mechanisms. Therefore, the most widely accepted hypothesis is that phenytoin induces dyskinesias by increasing dopaminergic and serotonergic activity in the striatum, and that patients with underlying brain lesions or subclinical functional changes may be especially likely to suffer this adverse effect.

In conclusion, phenytoin-induced orofacial dyskinesia is a very unusual adverse effect that usually occurs at normal plasma levels of phenytoin and is not correlated with treatment duration. This type of dyskinesia may occur with no underlying striatal lesion and resolve when phenytoin is discontinued; its pathophysiological mechanism is unknown.

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