

**LETTER TO THE EDITOR**

# Levodopa-Associated Barking Vocalizations

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Involuntary vocalizations include a wide spectrum of sounds associated with physiological responses such as coughing or sneezing, emotional responses such as laughing or crying, and even the utterance of words that have a specific intended meaning.<sup>1</sup> These are often associated with Tourette's syndrome and other tic disorders. However, they can be observed in a plethora of conditions and may be part of the disease complex or secondary to medication. Drug-induced vocalizations have been frequently reported in association with antipsychotics and rarely in association with other drugs, such as metoclopramide, lenalidomide, etc.<sup>2</sup> Involuntary vocalizations associated with levodopa consumption are rare, and thus far, there is only a single report of peak dose levodopa-induced dyskinesia presenting as palilalia.<sup>3</sup> This report describes involuntary vocalizations akin to barking that were probably induced by levodopa in a child with dystonia and parkinsonism.

A nine-year-old boy with a 2nd degree consanguineous parentage, normal birth, and delayed motor and speech milestones presented with a seven-year history of posturing of the right leg and a two-month history of tremor of the right upper limb (UL) and lower limb (LL). The posturing was described as internal rotation of the foot that worsened while walking. Tremor was continuous and present at rest and during activity, and the leg tremor worsened upon standing. There was no history suggestive of left UL or LL involvement. He had no other relevant medical history, and there was no family history of tremor, dystonia or parkinsonism.

At the first visit, the child was drug-naïve, and examination (segment 1, Supplementary Video 1 in the online-only Data Supplement) revealed asymmetric dystonia and parkinsonism with symptoms that were more pronounced on the right side. He had

normal speech, mild upgaze restriction, resting and postural tremor of both ULs, and a proximal, adduction-abduction-type of tremor of the LL that worsened significantly in the right leg upon standing. There was dystonic posturing of both LLs, with inversion and plantar flexion of the right foot, mild bradykinesia in both ULs, and bilateral LL rigidity that was more severe on the right than on the left. While walking, truncal dystonia was observed, and the arm swing was reduced bilaterally, with dystonic posturing of the right UL and both LLs (segment 1, Supplementary Video 1 in the online-only Data Supplement). The rest of his neurological and systemic examination was normal. There was no Kayser-Fleischer ring on slit-lamp examination. Routine blood investigations to assess serum copper and ceruloplasmin were normal. The work-up for inborn errors of metabolism was normal, and MRI revealed an incidental septum cavum pellucidum (Supplementary Figure 1 in the online-only Data Supplement) with no other abnormality. Unfortunately, genetic testing could not be performed, and the patient was lost to follow-up. Videos of the patient were recorded after written informed consent was obtained.

In view of the dystonia and parkinsonism, a trial of levodopa was planned. Slight improvements in the UL tremor and gait were observed one hour after administration of one tablet of levodopa/carbidopa (100 mg/25 mg). However, the patient continued to have tremulousness of the right leg and dystonic posturing of both LLs (segment 2, Supplementary Video 1 in the online-only Data Supplement). Considering the mild response, a prolonged trial with gradual dose escalation was planned.

Two days after the dose escalation to 1-½-1-½, the tremor and dystonia were significantly reduced. However, the child developed involuntary vocalizations that resembled barking and were

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associated with repeated protrusion of the tongue, lip smacking, choreiform movements of the hands, and pelvic thrusts (segment 3, Supplementary Video 1 in the online-only Data Supplement). These vocalizations were not suppressible or distractible; he had no associated respiratory distress and had normal speech during the episode. In view of these new onset symptoms and the possibility of their being associated with levodopa, the medication was withheld. Subsequently, the above symptoms completely subsided over the next 48 hours with the reappearance of dystonia and parkinsonism. He was discharged on ropinirole and reported improvement of symptoms on follow-up.

Barking or animalistic vocalizations have often been described in association with temporal lobe epilepsies.<sup>4</sup> To the best of our knowledge, involuntary vocalizations associated with levodopa are restricted to palilalia,<sup>3</sup> and the phenomenology in the current report has not been previously described. Movement disorders associated with levodopa have been reported long before the actual use of levodopa as a therapeutic agent. For instance, it was used to induce chorea and aided in the detection of presymptomatic Huntington's disease.<sup>5</sup> Typically, levodopa-induced dyskinesias usually manifest as truncal, cervical and limb-predominant chorea. Though less prevalent, myoclonus, ballism, and stereotypic movements, especially of the legs, have also been reported. Although the respiratory musculature may be involved, this usually presents as respiratory distress rather than vocalization.<sup>6</sup> In the present case, the child developed these abnormal vocalizations at a relatively low dose of levodopa, which may be attributable to the increased risk in young patients of the development of side effects after administration of levodopa. In addition to vocalizations, the child also showed tongue protrusion and lip smacking, which is usually associated with tardive dyskinesia, reflecting the prominent oro-buccal-lingual distribution of dyskinesia.<sup>7</sup>

Unfortunately, the exact etiology of dystonia and parkinsonism in this child could not be ascertained, as genetic testing could not be performed. Furthermore, the exact phenomenology of the vocalizations was also difficult to ascertain. It is uncertain whether the vocalizations were a characteristic feature of an unknown primary illness or a feature that was induced or aggravated by levodopa.

In conclusion, even though it is rare, levodopa may induce atypical vocalizations. This etiology should be considered in patients with a similar phenomenology.

### Supplementary Video Legends

Video 1. Segment 1: There was bilateral foot dystonia that was more severe

on the right than on the left, with internal rotation of the right foot. Continuous proximal tremors involving both lower limbs that were more severe on the right than on the left were observed. The patient exhibited both resting tremor and postural tremors of the bilateral upper limbs, and the right leg tremor worsened upon standing. There was bilateral upper limb bradykinesia that was more severe on the right than on the left. The arm swing was reduced bilaterally, with dystonic posturing of the feet while walking. Segment 2: While seated, the child showed dystonic posturing of both feet with a continuous tremor of the right leg and postural tremor of both upper limbs. The gait was better in comparison with the gait in the drug-naïve state (Segment 1). Segment 3: There were vocalizations resembling barking, with repeated tongue protrusion, choreiform movements of hands, and pelvic thrusting. Tremor and dystonia had significantly subsided.

### Supplementary Materials

The online-only Data Supplement is available with this article at <https://doi.org/10.14802/jmd.20086>.

### Conflicts of Interest

The authors have no financial conflicts of interest.

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None.

### Author Contributions

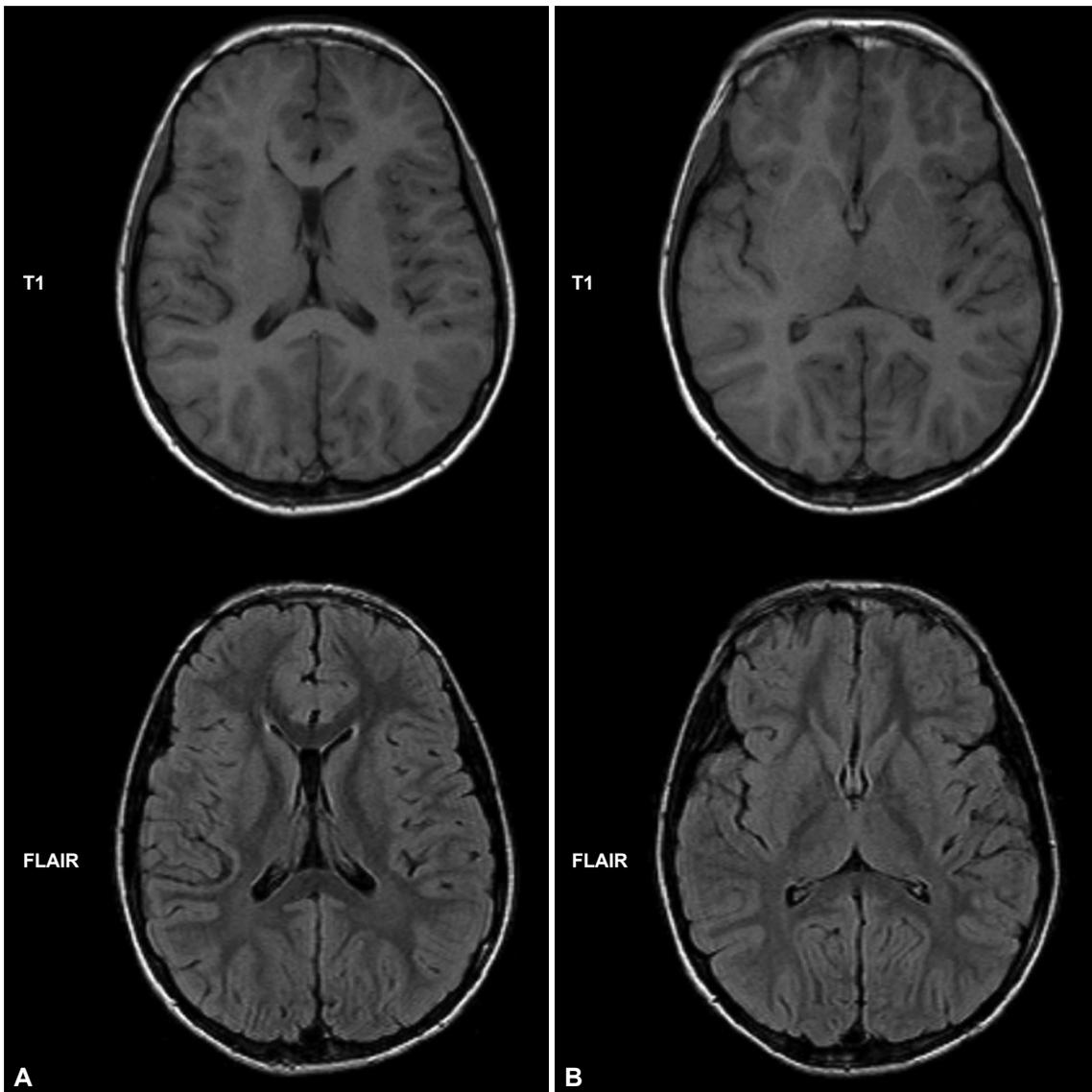
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**Supplementary Figure 1.** T1 and fluid attenuated inversion recovery (FLAIR) images showing incidental septum cavum pellucidum (A) and normal basal ganglia (B).