

## Case Report



# Emerging of Explosive Speech after Olanzapine in Multiple System Atrophy Patient

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### Conflict of Interest

The authors have no potential conflicts of interest.

### Author Contributions

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## ABSTRACT

**Background:** Cerebellum has an important role in sensorimotor control including speech. Multiple system atrophy (MSA) is a sporadic and rapidly progressive neurodegenerative disorder that presents with autonomic failure in combination with Parkinsonism or cerebellar ataxia.

**Case Report:** We report a case of MSA-cerebellum subtype associated with emergence of irreversible explosive speech following olanzapine therapy.

**Conclusions:** Further investigation into speech problems in MSA according to subtype and disease severity is needed, and side effects of olanzapine therapy should also be considered.

**Keywords:** Antipsychotic Agents; Multiple System Atrophy; Speech

## INTRODUCTION

The role of cerebellum has overshadowed sensorimotor control including diadochokinesia, tonus, coordination, and motor aspects of speech production.<sup>1,2</sup> Multiple system atrophy (MSA) is a sporadic, adult-onset disease characterized by progressive degeneration of the nervous system.<sup>3</sup> It comprises 2 subtypes based on the clinical spectrum: parkinsonian (MSA-P) and cerebellar (MSA-C) variants.<sup>3</sup> Here, we report the case of an MSA patient manifesting irreversible explosive speech following olanzapine therapy.

## CASE REPORT

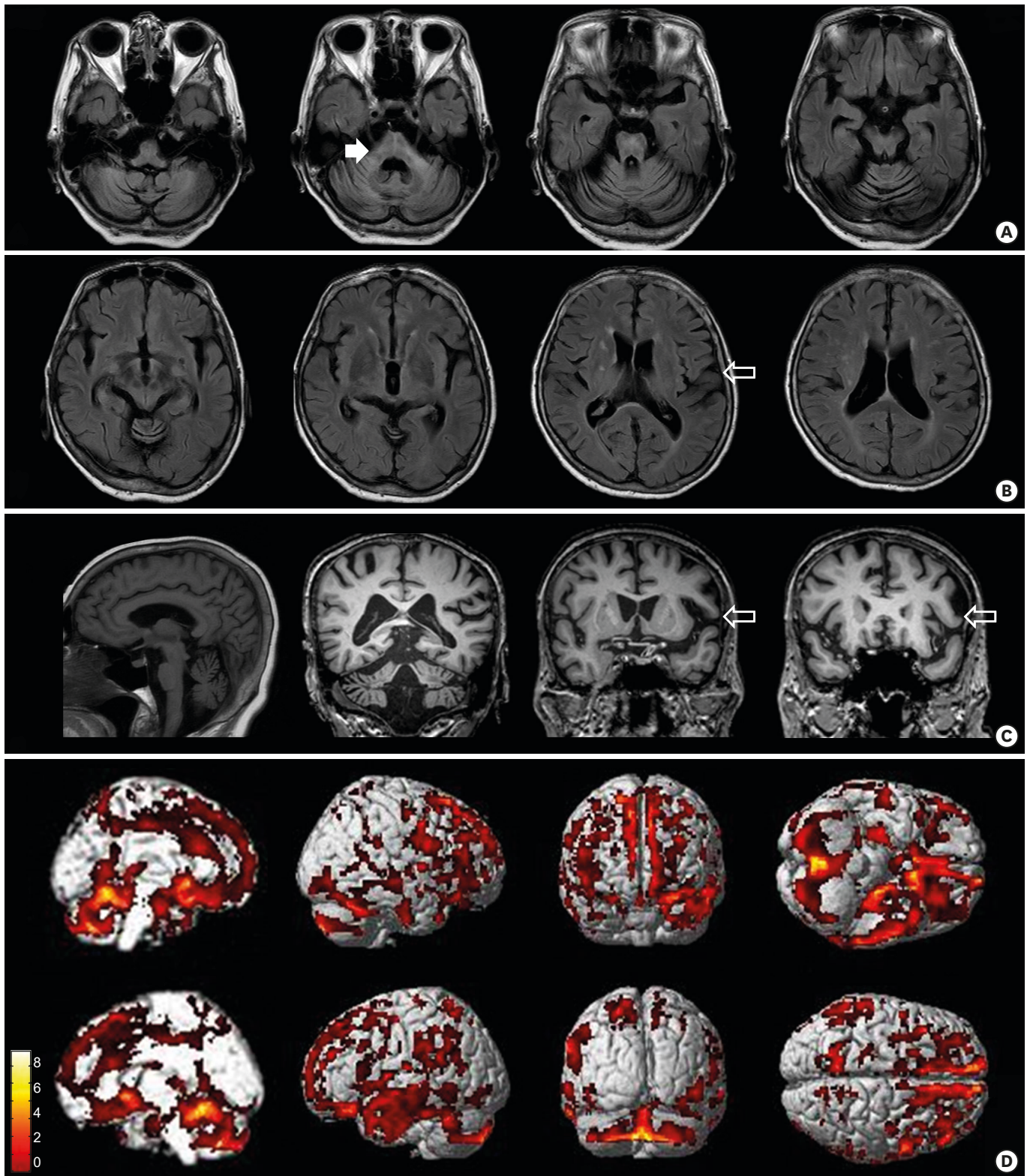
A 74-year-old female patient visited the neurology clinic. Her chief complaints were difficulties associated with decreased activities of daily living, slow responsiveness, and easy forgetfulness. She lost her interest, motivation for activities and social relationships. Patients participated less in conversation and manifested passive behavior. She also reported verbal difficulties involving complex sentences. She was also awkward with handling chopsticks and hand writing. She showed lower levels of performance in terms of time orientation and language assessments, scoring 20 on the Mini-Mental Status Examination and a Clinical Dementia Rating score of 1. A detailed neuropsychological assessment showed severe impairment in verbal memory for immediate and delayed recall. The patient exhibited notably

significant deficits in executive function with contrasting programs and other tests, indicating frontal lobe dysfunction. Her abnormal results were compatible with frontotemporal dementia according to the Neary Criteria.<sup>4</sup> Her first neurological examination revealed no abnormal findings excluding hyperactive deep tendon reflexes and mild dysdiadochokinesia in her right side. Her initial speed was slightly slow. However, other components including phonation, articulation, intonation and structure of sentences were within normal range. Magnetic resonance imaging (MRI) revealed severe atrophy of the entire cerebellum, brain stem with 'hot cross bun sign' (Fig. 1A, arrow), and frontal operculum predominantly on the left side (Fig. 1B and C), including bilateral subcortical white matter ischemic areas. These atrophic changes were observed in voxel-based morphometry analysis with the Statistical Parametric Mapping 5 software package (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, and Institute of Neurology at University College London, London, UK) (Fig. 1D). The patient showed abnormal behavioral symptoms such as repeatedly touching other people without cause or wandering during night after 6 months following initial examination. Olanzapine 2.5 mg was administered to her every night to control her behavior. Two months later, the patient presented with staccato and scanning speech. Especially, the utterance was remarkably irregular and jerky, and many syllables were explosive suggesting hyperkinetic dysarthria. Phonation was characterized by slurring and unequal utterance rather than articulation (Supplementary Video 1). Laboratory findings were normal. The frequency of the symptoms decreased but did not disappear after discontinuation of neuroleptics.

## DISCUSSION

MRI showed atrophy of the cerebellum, insular cortex, fusiform gyrus, inferior orbito-frontal gyrus, superior temporal gyrus, and caudate nucleus in the MSA patient with cognitive impairment.<sup>5</sup> Impairment of frontal lobe-related functions was reported in 41% of MSA-C type.<sup>6</sup> Patient's initial manifestation appeared to be normal, however, explosive speech started after olanzapine therapy. There are two neural networks in the synthesis of human speech.<sup>7</sup> The first network is a motor pathway for primitive vocalizations, which passes through the anterior cingulate gyrus and the adjacent mesiofrontal regions and projects via midbrain, basal ganglia, and pons to cranial nerve motor nuclei in the lower brainstem responsible for the innervation of vocal tract musculature.<sup>8</sup> The second extensive network contributes to complex forms such as linguistically meaningful sounds. At the cortical level, this second pathway encompasses the lateral and medial premotor regions and the supplementary motor area (SMA) involving the anterior insula.<sup>8</sup> At the subcortical level, the basal ganglia and the cerebellum are critically involved in this network.<sup>1,8</sup> Drug-induced speech defects have been reported following treatment with neuroleptics including clozapine and phenothiazines, theophylline, tricyclic antidepressants, selective serotonin reuptake inhibitors and benzodiazepine.<sup>9</sup> The patient's explosive speech might be attributed to not only atrophy of the frontal operculum, especially dysfunctional left side affecting cerebellar-cortical circuit in the secondary pathway of premotor area and SMA but also by olanzapine therapy resulting in MSA-C. A few case reports suggested a possible relationship between olanzapine and speech defects including dysarthria, decreased speech speed, verbal output, and voice volume.<sup>10,11</sup>

The limitations of this study related to determination of the onset time of abnormal symptoms based on the patient's subjective reports and not based on the physician's close observations. In addition, due to ethical constraints, olanzapine re-administration to confirm the causal relationship was not carried out. Although it depends on the subtype of MSA,



**Fig. 1.** T2-weighted FLAIR MRI. (A) Severe atrophy of the pontocerebellar region with hot-cross bun sign (arrow). (B, C) Axial and coronal sections showing atrophic changes in the bilateral frontal area predominantly on the left side (open arrow). (D) Midline sagittal section showed prominent pontocerebellar atrophy. These atrophic changes were observed via voxel-based morphometry (false discovery rate,  $p < 0.05$ ). FLAIR: fluid attenuated inversion recovery, MRI: magnetic resonance imaging, RT: right side, LT: left side.

speech defect in MSA-C was characterized by progressive scanning dysarthria with gait ataxia and limb kinetic ataxia.<sup>12,13</sup> This patient was clinically diagnosed based on olanzapine-related symptoms due to the speech defects occurring in the immediate aftermath of olanzapine treatment. We reported this MSA patient manifesting irreversible explosive speech following olanzapine therapy as an unusual finding.

## SUPPLEMENTARY MATERIAL

### Supplementary Video 1

Patient's speech

[Click here to view](#)

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