

# Isolated Dysphagia Due to the Drug-Induced Parkinsonism in Subacute Stroke Patient

## Subakut İnmeli Hastada İlaça Bağlı Parkinsonizm Nedenli İzole Disfaji

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Geliş Tarihi/Received: 26.11.2016  
Kabul Tarihi/Accepted: 19.06.2017

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**ABSTRACT** Dysphagia can be due to many reasons both neurologically and non-neurologically. Although neurological causes, especially stroke are the most common cause of dysphagia, additional comorbidities present in patients and medications used for them may also cause a secondary dysphagia. Although drug-induced parkinsonism is affected whole body muscles by the formed akinesia, bradykinesia and dyskinesia, it can cause swallowing disorder especially in oral phase due to swallowing and chewing difficulties. It is frequently associated with the use of antipsychotic medication. Herein as the first case in the literature, we present a drug-induced dysphagia case in a 57-year-old male with stroke, which can easily be misdiagnosed as a stroke-induced dysphagia.

**Keywords:** Stroke; dysphagia; antipsychotic drug; adverse effect; parkinsonism

**ÖZET** Disfaji hem nörolojik hem de non-nörolojik olarak pek çok sebebe bağlı olabilir. Nörolojik sebepler özellikle inme en sık disfaji sebebi olarak bilinmesine rağmen, hastalarda mevcut ek komorbiditeler ve bunlar için kullanılan ilaçlar da sekonder bir disfajiye sebep olabilmektedir. İlaça bağlı parkinsonizmde tüm vücuttaki kaslarda oluşan akinezi, bradikinezi ve diskinezi nedeni ile etkilenim olmakla birlikte, yutma ve çiğneme zorluğu ile özellikle oral fazda yutma bozukluğuna sebep olabilmektedir. Sıklıkla antipsikotik ilaç kullanımı ile ilişkilendirilmiştir. Bu yazıda literatürde ilk vaka olarak, inmeli 57 yaşındaki erkek hastada, inmeye bağlı disfaji ile kolayca karışabilmesi nedeni ile ilaca bağlı bir disfaji olgusu sunulmuştur.

**Anahtar Kelimeler:** İnme; disfaji; antipsikotik ilaç; yan etki; parkinsonizm

Dysphagia is defined as difficulty in delivering the food to the stomach and it can result from functional or structural deficits of the oral cavity, pharynx or esophagus. Although dysphagia has many causes, both neurological and non-neurological, but neurogenic events, particularly stroke is the most common cause of neurogenic dysphagia.<sup>1</sup> Its incidence increases in large middle cerebral artery involvement and in hemorrhagic stroke. It occurs especially within first 2 weeks of stroke, and 19-81% of stroke patients present with dysphagia and 10% of patients still have dysphagia 4-6 months after stroke.<sup>1-3</sup>

Drug treatment can also lead to dysphagia; as a normal drug side effect, as a complication of the drug action, or medication-induced injury to swallowing structures.<sup>4</sup> Antipsychotics are the major cause of drug-induced

Parkinsonism (DIP). Particularly, long-term use of antipsychotics can lead to dysphagia due to oral phase disorder caused by chewing and swallowing difficulty as a result of orofacial and tongue muscles weakness in 10-20% of patients.<sup>5-7</sup>

In the literature, there has been no reported case of DIP except two neurologic disorder patients with Alzheimer and mental retardation.<sup>8,9</sup> Also, there was not coexistence with DIP and stroke in the literature.

Here, as the first case in literature, we describe a rare case of drug-induced dysphagia following stroke, which can easily be misdiagnosed as a stroke-induced dysphagia.

## CASE REPORT

In December 2014, a 57-year-old man was admitted to our Physical Medicine and Rehabilitation Clinic with the diagnosis of hemorrhagic stroke and left hemiplegia. In the history of patients; he had been admitted to the emergency department with weakness in the left upper and lower extremities and aphasia before 3 weeks. In cranial computerized tomography showed hematoma 46x32 mm in centrum semiovale, right lentiform nucleus and temporal lobe with surrounding edema. Doppler ultrasound of extracranial internal carotid artery and vertebral artery were normal. The patient diagnosed with hemorrhagic stroke had been transferred to neuro-intensive care unit (ICU). He was unconscious for three days but had started recovering slowly in neuro-ICU and transferred to rehabilitation clinic at 22<sup>th</sup> day.

Physical examination in our clinic admission; he was conscious, cooperated and oriented. Brunnstrom stages of hand, upper and lower limb were 5/6, 5/6 and 3/6 on the left side respectively. Deep tendon reflexes were exaggerated and Babinski's reflex was positive along with the hypoesthesia on the left side.

Previous medical history revealed hypertension and hyperlipidemia for the last 5 years and schizophrenia for the last 25 years and was taking 5 mg/day amlodipine, 20 mg/day atorvastatin, and

25 mg/month fluphenazine decanoate which was stopped following stroke. His family history was not remarkable.

On neurological examination for swallowing, facial asymmetry, difficulty in closing the lips, weakness and incoordination in tongue movements were detected. There were no palatal asymmetry, gag reflex and cough reflex disorder. Endoscopic evaluation during swallowing of solid, semi-solid, semi-liquid and liquid food revealed no residue, penetration and aspiration. He was given general motor, sensorial, respiratuar and cognitive rehabilitation as well as 15 sessions of thermal-tactile stimulation and traditional swallowing exercises including lip, tongue and jaw exercises as he had mild difficulty in chewing.

During inpatient rehabilitation, he was consulted to psychiatry for suspected hallucinations and intramuscular injection of 25 mg fluphenazine decanoate has been restarted once every month.

After 15 sessions of inpatient rehabilitation, patient achieved independent ambulation with a forearm crutch and was discharged to home following establishment of safe and efficient oral feeding.

Three months after hospital discharge, the patient was readmitted to our clinic with complaints of excessive salivary flow, inability to close the lips, difficulty in chewing and swallowing, and coughing during or after meals.

On neurological examination he was conscious, cooperated and oriented. Systemic examination was not remarkable. Sensory examination was normal, Brunnstrom stages of hand, upper and lower limb were all 6/6 on the left side and he was ambulating independently.

On clinical swallowing evaluation, patient had the dysphagia symptoms including the difficulty in closing the lips, weakness and incoordination in tongue movements and chewing, difficulty to control and accumulation of food and saliva in the mouth, and coughing during feeding with solid, semi-solid, semi-liquid and liquid foods. Endoscopic evaluation during swallowing of solid, semi-

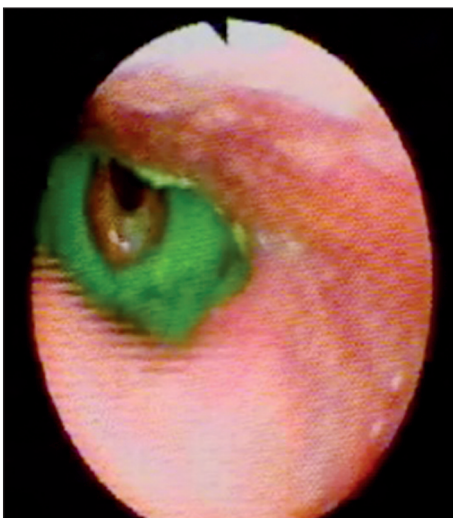
solid, semi-liquid and liquid food revealed a residue in valleculae and pyriform sinus, laryngeal penetration and reduced laryngeal elevation, but aspiration was not detected possibly due to sufficient cough reflex (Figure 1).

The patient was reevaluated. His blood chemistry was within normal limits. When he consulted with a neurology clinic, magnetic resonance imaging of the brain revealed no evidence of acute infarction (Figure 2).

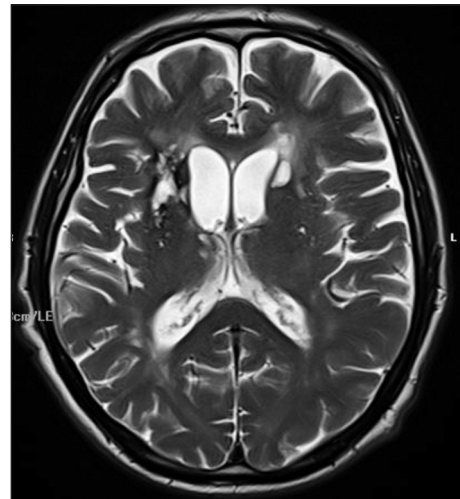
More detailed history elucidated that the dysphagia was associated with DIP due to used antipsychotic. Thus, fluphenazine treatment shifted to atypical antipsychotic clozapine after stopping the fluphenazine, the patient experienced distinct improvement of oral control of drooling and swallowing, and was able to eat both liquid and solid foods again. Endoscopic control revealed an absence of residue and penetration.

## DISCUSSION

Drug-induced parkinsonism (DIP) is the second most common cause of parkinsonism after Parkinson's disease.<sup>6,7,10</sup> Drug-induced parkinsonism is related to drug-induced changes in the basal ganglia motor circuit secondary to dopaminergic receptor blockade that are widely distributed in the brain.<sup>11</sup>



**FIGURE 1:** View of the residue in right and left pyriform sinus as well as vallecula, and laryngeal penetration with semi-solid food by using endoscopy. Arrow: laryngeal penetration; Asterisk: residue.



**FIGURE 2:** View of the chronic infarct including a portion of the right caudate nucleus in transverse T2-weighted sequence.

Although there is a long list of other drugs reported to cause Parkinsonism, DIP is most commonly attributed to antipsychotic.<sup>6,7,10,11</sup> All antipsychotic drugs may act on dopamine receptors in the striatum and they have potent dopamine-2 receptor blocking capacity. The therapeutic effects of these drugs on psychosis are related to their action on this limbic system, where they reduce dopamine transmission.<sup>11,12</sup>

In studies reported that the Parkinsonism estimated that up to 50% of antipsychotic-users will eventually develop DIP.<sup>13-15</sup> Typical antipsychotics exhibit high affinity dopamine-2 receptor antagonism which can eventually lead to neurotoxicity because of the accumulation of iron in the basal ganglia.<sup>5,11,12</sup> Although the our patient had short-term interruption in his fluphenazine therapy, he had been on antipsychotic therapy for 25 years which might be associated with a higher risk of DIP.

In addition, the patient had a lesion affecting the lentiform nucleus which might increase the sensitivity to antipsychotic drug. In a study evaluating the association of tardive dyskinesia and neuronal damage in the lentiform nucleus, Ando et al. reported that the all patients with or without tardive dyskinesia who had been using antipsychotics, had neural damage at the cellular level in the basal ganglia including lenticular nucleus, which may support our way of thinking about etiology.<sup>16</sup>

Oropharyngeal dysphagia that similar to our case can be seen in tardive dyskinesia and idiopathic Parkinson's disease, but our case did not meet the clinical diagnostic criteria of tardive dyskinesia or Parkinson's disease.

Tardive dyskinesia is characterized by oral-facial-lingual-buccal dyskinesias and manifests itself with involuntary movements in mouth and jaw muscles causing dysphagia and difficulty in chewing.<sup>12</sup> Tardive dyskinesia may occur due to postsynaptic dopamine receptor hypersensitivity and long-term blockade of dopaminergic receptors induced by chronic antipsychotic therapy.<sup>10-13</sup>

Unlike in our case, there were no involuntary movements on examination, also he had weakness in mouth and jaw muscle.

Both DIP and idiopathic Parkinson's disease can cause weakness in mouth and jaw muscles, difficulty in chewing, reduced lip closure and excessive drooling.<sup>6,10,11,15</sup> Unlike in idiopathic Parkinson's disease, DIP has acute and bilateral onset symptoms including difficulty in chewing related to oral-buccal muscle weakness after antipsychotic drug intake, mild or absent rest tremor, freezing and postural problems and recovery after stopping antipsychotic drugs. Similar to other reports in the literature, our case also presented with dysphagia without motor features of Parkinsonism 3 months after antipsychotic therapy had been restarted.

The most difference between DIP and both tardive dyskinesia and idiopathic Parkinson's disease is treatment of disease. While levodopa remains the gold standard treatment for Parkinson's disease, the most effective therapy for drug-induced Parkinsonism is discontinuation of the offending drug. Discontinuation of the drug can cause adverse effects via dopamine hypersensitivity in tardive dyskinesia.<sup>5,12</sup>

Dysphagia symptoms in the present case showed improvement after termination of antipsychotic treatment. Additionally, our patient was treated with atypical antipsychotic to ensure treatment continuity of schizophrenia.

Atypical antipsychotics have been reported to cause a lower incidence of extrapyramidal side effects than conventional agents.<sup>10,11,13,17</sup> The literature consistently reports that the use of atypical antipsychotics, particularly clozapine display transient and faster dissociation rates and are only loosely bound to the dopamine-2 receptor which is associated with a lower risk of extrapyramidal symptoms and tardive dyskinesia than the conventional antipsychotics.<sup>5,17</sup> They are also more strongly antagonistic toward serotonin-2A receptors than toward dopamine receptor. Serotonin inhibits the release of dopamine in the striatum. Thus, the atypical antipsychotic blocking the serotonin will promote dopamine release and prevent extrapyramidal symptoms.<sup>5,17</sup>

The present case showed improvement of dysphagia symptoms after discontinuation of antipsychotic treatment. After fluphenazine treatment shifted to clozapine the patient's dysphagia symptoms showed rapid improvement. Besides these, psychotic symptoms were not observed.

## CONCLUSION

Dysphagia can be seen in DIP, however, it is most often associated with another symptom of the EPS, but can also be isolated, making its diagnosis more difficult. Drug-induced Parkinsonism should be considered in the differential diagnosis of dysphagia in patients with stroke receiving any antipsychotic drug.

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