

[CASE REPORT]

Drug-induced Pressure Ulcers in a Middle-aged Patient with Early-stage Parkinson's Disease

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Abstract:

Drug-induced pressure ulcer (DIPU), which is a newly recognized adverse drug reaction, is associated with the administration of psychiatric drugs in geriatric patients with dementia. The notification of the causative drugs is crucial to the treatment of DIPU. We herein report the case of a 56-year-old woman with early-stage Parkinson's disease who developed DIPUs after starting olanzapine treatment for depressive symptoms. Our findings illustrate that if an akinetic patient with pressure ulcers is encountered, the patient's medication should be reviewed by a multidisciplinary team, to evaluate whether the development of the pressure ulcer is drug-related, regardless of the patient's age.

Key words: adverse drug reaction, drug-induced parkinsonism, drug-induced pressure ulcer, pressure ulcer, Parkinson's disease, psychiatric drug

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Introduction

The prevention and evaluation of pressure ulcers are important for patients who are immobile or in a bed-bound state. However, drugs are not typically considered when attempting to prevent or evaluate pressure ulcers. Drug-induced pressure ulcer (DIPU) is a new disease concept that was proposed by Mizokami et al. in 2016 (1). They reported that DIPU is a newly recognized adverse drug reaction (ADR), which is associated with the administration of psychiatric drugs to geriatric patients with dementia, including dementia with Lewy bodies (1). However, as illustrated by our case, elderly individuals are not the only population that is prone to developing DIPUs, and the identification of the causative drugs is crucial for the treatment of DIPU.

Case Report

The patient was a 56-year-old woman with a 2-year history of depression and mild Parkinsonism; she could walk

unaided and lived in her home until 2 months before admission to our hospital. Olanzapine had been used to treat her psychiatric symptoms since January 2017; however, her motor symptoms were left untreated. Thereafter, her motor symptoms showed an acute deterioration, and she became bed-ridden because of drug-induced akinesia within 1 month after the administration of olanzapine. Her medical history included total hysterectomy for cervical cancer in 1999, and adhesive obstructive ileus in 2000. There was no recurrence of cervical cancer after the surgery.

The patient was subsequently hospitalized in a psychiatric hospital due to immobility and dehydration. Laboratory tests revealed an elevated white blood cell count (9,670/ μ L), as well as elevated C-reactive protein (6.86 mg/dL) and creatine kinase [1,100 IU/L (normal range: 20-170 IU/L)] levels. The laboratory data after the correction of dehydration showed decreased serum total protein (5.6 g/dL) and albumin (2.5 g/dL) levels. The patient's fasting blood sugar (98 mg/dL) and HbA1c (5.8 %) levels were normal. At admission to the psychiatric hospital, her height was 150 cm, her body weight was 34.0 kg, and her body mass index was

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Figure. A drug-induced pressure ulcer located above the coccyx. The figure shows the ulcer located above the coccyx. The deep ulcer was covered with yellowish necrotic tissue and was associated with the loss of the overlying full-thickness skin and subcutaneous fat. The pressure ulcer healed after surgical debridement, 6 weeks of topical treatment, and the discontinuation of the causative drug (olanzapine).

15.1 kg/m². She had deep pressure ulcers above her coccyx (Figure) and left knee due to drug-induced akinesia. As the patient's consciousness was alert, a coma blister was ruled out. The ulcer above the coccyx was graded as stage IV, according to the revised National Pressure Ulcer Advisory Panel (2), and had a score of 39 points (D4-e3s9I9G6N6P6) on the DESIGN-R scale (3). Olanzapine (5 mg/day) was discontinued. She was then transferred to our hospital for the diagnosis of the underlying neurological disorder. On admission, a neurological examination revealed a small voice, truncal and limb rigidity, clumsiness, slight hand tremor, akinesia, and gait disturbances, which showed slight improvement after the cessation of olanzapine treatment (2 weeks before transfer to our hospital). We diagnosed the patient with Parkinson's disease (PD) based on dopamine-responsive parkinsonism, which overlapped with drug-induced parkinsonism based on her rapid deterioration to a bed-bound state (within a period of 1 month, which is unusually rapid progress for PD alone). Her motor symptoms improved with the administration of levodopa/carbidopa (400 mg/day), and she was able to walk unaided. Her psychiatric symptoms improved without psychiatric drugs, and she was discharged. Her deep pressure ulcers were treated with surgical debridement and 6 weeks of topical treatment. The ulcers had completely healed within 2 months after cessation of olanzapine.

Discussion

In 2016, Mizokami et al. proposed DIPU as a newly recognized ADR (1). DIPU was recognized in 4 of 148 (2.7%) elderly patients with pressure ulcers (1). DIPU is caused by acute-onset drug-induced akinesia or drug-induced gait disturbance. Clinicians, especially neurologists and psychia-

trists, often encounter patients with acute-onset drug-induced dyskinesia. However, according to a PubMed search in August 2017, no other similar cases with the exception of the first case series reported by Mizokami et al., have been reported in the English literature. Similar cases might not be recognized as being drug-induced, because drug-related items are not involved in the scales used for preventing and/or evaluating pressure ulcers. The combination of the causative drug and the underlying disease is crucial for understanding the mechanism underlying the development of DIPUs. Olanzapine, a multi-acting receptor targeted antipsychotic agent, which has an antagonistic effect on the dopamine 2 receptor, can cause akinesia, and was reported to be a DIPU-causing drug (1). Based on our own case and previously reported cases, we propose that the clinical characteristics of DIPU are as follows: 1) the patient is able to walk unaided before the administration of the causative drug, even if the patient suffers from a neuropsychiatric disease; 2) the patient has acutely impaired mobility after the administration of the causative drug, 3) the patient develops deep pressure ulcers such as stage IV ulcers, which do not receive adequate care from home care service providers and/or family members, because of the unexpected impairment of the patient's mobility, and 4) the pressure ulcers recover after both the discontinuation of the causative drug(s) and the performance of appropriate treatment, including surgical debridement (Table). In our case, the underlying disease was untreated early-stage PD. The administration of the causative drug was associated with an acute worsening of the patient's Parkinsonism, leading to a bed-bound state because her motor symptoms were not subsequently treated.

As psychiatric symptoms often accompany PD, even in patients with early-stage disease (4), they are sometimes overlooked or misdiagnosed as psychiatric disease. In our case, the use of a psychiatric drug was associated with the development of deep pressure ulcers. DIPU is iatrogenic; thus, the psychiatric symptoms of patients with early-stage PD should be treated carefully.

In conclusion, the concept of DIPU should be widely relayed to medical staff members (doctors, nurses, and pharmacists), and it should be clarified that the condition can develop in non-elderly patients. If the normal treatment for pressure ulcers is provided, the ulcers may recur, as the patient's drug-induced akinesia would remain unimproved. Thus, both the treatment of pressure ulcers and discontinuation of the causative drugs are crucial in the treatment of DIPU (Table). If an akinetic patient with a pressure ulcer is encountered, the patient's medications should be reviewed by a multidisciplinary team (5) regardless of the patient's age to evaluate whether any drugs are associated with the development of the pressure ulcers.

Table. Clinical Characteristics, Causal Drugs, and Treatment of Drug-induced Pressure Ulcers.

Reference	Age of onset/ sex	Underlying diseases	Causal drugs	Walks unaided before causal drug administration	Acutely impaired mobility after causal drug administration	Impaired mobility was recovered by ceasing causal drug administration	Drug-induced akinesia overlapping with underlying diseases	Coma blister	Serum CK elevation	Location and stage (NPUAP) of PU	Surgical debridement	Topical treatment	Duration until PU healed
1	85/F	DLB, knee OA	Olanzapine	+	+	+	+	-	-	Right heel, stage IV	-	+	6 mo.
1	78/F	AD, right knee OA	Fluvoxamine, VPA	+	+	+	+	-	+	Sacrum, stage IV	+	+	14 w
1	84/F	AD, DM, bradycardia	Clotiazepam, Triazolam	+	+	+	+	-	+	Back, stage IV, Left greater trochanter, stage II	+	+	16 w
1	80/M	AD, COPD, sarcopenia	Rimazafone	+	+	+	+	-	-	Sacrum, stage IV	-	+	11 w
Present case	56/F	Undiagnosed PD (Yahr II)	Olanzapine	+	+	+(ceased causal drug and added levodopa for underlying disease)	+	-	+	Coccyx, stage IV, Left knee, stage IV	+	+	2 mo.

AD: Alzheimer's disease, CK: creatine kinase, COPD: chronic obstructive pulmonary disease, DLB: dementia with Lewy bodies, F: female, M: male, mo.: months, NPUAP: National Pressure Ulcer Advisory Panel, OA: osteoarthritis, PD: Parkinson disease, PU: pressure ulcer, VPA: valproic acid, w: weeks, +: yes or positive result, -: no or negative result

The authors state that they have no Conflict of Interest (COI).

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