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Letter to the Editor

Multiple fixed drug eruption caused by ropinirole in a patient with Parkinson's disease

Dear Editor,

Parkinson's disease is derived from a degeneration of the dopaminergic neurons in the substantia nigra pars compacta, which leads to a marked loss of striatal dopamine concentration. Among the treatment for Parkinson's disease, the number of patients taking dopamine D2 receptor agonist is on the rise. Ropinirole, a selective dopamine D2 receptor agonist, shows a strong inhibitory effect on the pathogenesis of Parkinson's disease.¹ Although several adverse events of ropinirole are well-known, such as sleep disturbance, a drug eruption due to ropinirole has not been reported in English so far. Herein, we describe here an unusual case of a patient with Parkinson's disease who developed multiple fixed drug eruption after ropinirole treatment. We also reviewed the past literature on drug eruption caused by other dopamine D2 receptor agonists further.

A 60-year-old female with Parkinson's disease was referred to our department for evaluation of an eruption of 2 days' duration. An erythematous eruption on the extremities had developed three hours after 7th daily administration of ropinirole for her Parkinson's disease. The erythematous lesions gradually became pigmented. On physical examination, well-defined pigmentations surrounded by erythema were observed on the right arm (Fig. 1A). Laboratory and biochemical profiles were within normal ranges. At the first visit, a skin biopsy specimen taken from an erythematous lesion on the right arm revealed a lymphocytic infiltrate in the epidermis and upper dermis (Fig. 1B). From clinical course and skin biopsy findings, we guessed her skin eruption as drug eruption. Two weeks after the first visit, patch testing with the concentration of 10 and 20% ropinirole using vaseline vehicle (White Petrolatum®, Kenei Pharmaceutical, Osaka, Japan) on the pigmented macule was negative.

At the first visit, we performed lymphocyte stimulation test (LST) with ropinirole as described previously.² ³H-thymidine incorporation was significantly increased by the addition of 4.3×10^{-8} M ropinirole (corresponding to C_{max}) to the peripheral lymphocyte culture with stimulation index of 2.1 (Fig. 1C). Although she had other medications, LST and patch test were negative results. Based on the clinical course and laboratory examination, we diagnosed the rash as multiple fixed drug eruption due to ropinirole. After discontinuation of ropinirole, her eruption improved remarkably in a week, with residual pigmentation.

Although several case reports have already been published on other dopamine D2 receptor agonists, to our knowledge, this is

the first report of drug eruption, especially multiple fixed drug eruption, caused by ropinirole. We reviewed the English reported cases of drug eruption caused by pure dopamine D2 receptor agonist (Table 1).^{3–6} There have been 9 reported cases including our case. Seven cases were due to bromocriptine, and the major clinical manifestation is erythromelalgia. In the past literature, the details of identification of causative drugs remained obscure. In our patient, the apparently positive LST with ropinirole confirmed the causative drug. As shown in our previous report, patients with multiple fixed drug eruption tend to show positive results in LST.² The exact pathomechanism remains unclear, however, circulating T cells might play some roles in the pathogenesis of multiple fixed drug eruption. Because the molecular weight of ropinirole is 296.84, ropinirole can penetrate under basal layer of epidermis. However, we used vaseline vehicle in the patch test, while ropinirole is a water-soluble drug. In view of this chemical nature, vaseline vehicle might be not suitable for the patch test using ropinirole. Likewise, Wiesli P, *et al.* reported case in which, the result of patch test was also negative,⁵ even though the type of eruption was different from our case. Although they did not specify a vehicle in their case report, they might also use vaseline vehicle in patch test. Therefore, the result of patch test in our case might be false-negative due to usage of inappropriate solvent. The patient declined to undertake another patch test with ropinirole solved in aqueous material. Although, it has been known that dopamine D2 receptor agonist has an inhibitory effect of T cell activation,⁷ LST might help us to identify the causative drug of dopamine D2 receptor agonist. It is necessary to keep in mind that the incidence might be a relatively rare but ropinirole has a risk of causing cutaneous adverse events.

Conflict of interest

The authors have no conflict of interest to declare.

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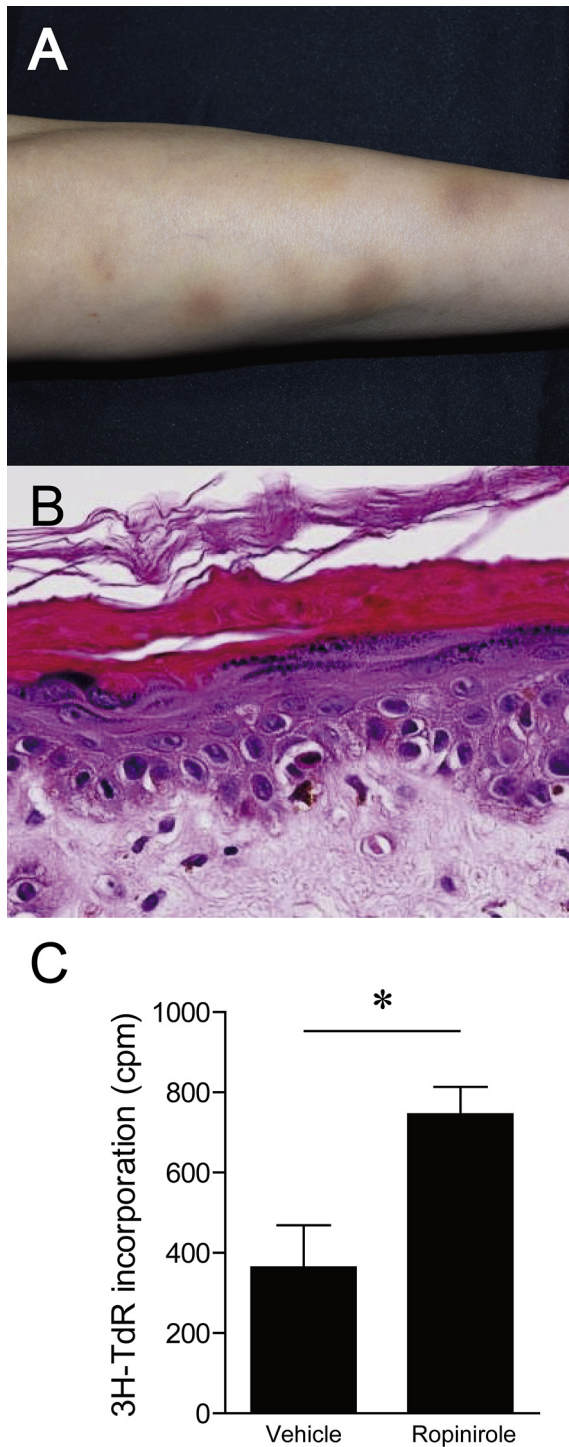


Fig. 1. (A) Physical examination revealed multiple erythematous pigmented macules of various sizes on a right arm. (B) Histological examination showing a lymphocytic infiltrate in the epidermis and upper dermis. (C) Lymphocyte stimulation index (SI). The patient's peripheral blood mononuclear cells (3×10^5 /well) taken at the initial visit were cultured for 72 h in a 96-well plate with ropinirole at 4.3×10^{-8} M (corresponding to C_{max}). Results are presented as the mean $\pm$ SEM. P -value was obtained by student's t -test. * $P < 0.05$.

Table 1

Case report of drug eruption caused by pure dopamine D2 receptor agonist.

Author	Age/Sex	Drug	Eruption type	To identify causative drug
Kaushik <i>et al.</i> ³	25/Female	Cabergoline	Erythema nodosum	Challenge test: positive
Leshin <i>et al.</i> ⁴	57/Male	Bromocriptine	Morphea	N.D
Wiesli <i>et al.</i> ⁵	28/Female	Bromocriptine	Pseudolymphoma	Patch test & scratch test: negative
Eisler <i>et al.</i> ⁶	N.D	Bromocriptine	Erythromelalgia	N.D
	N.D	Bromocriptine	Erythromelalgia	N.D
	N.D	Bromocriptine	Erythromelalgia	N.D
	N.D	Bromocriptine	Erythromelalgia	N.D
	N.D	Bromocriptine	Erythromelalgia	N.D
Our case	60/Female	Ropinirole	Fixed drug eruption	LST: positive Patch test: negative

N.D, not described.

References

- Kleedorfer B, Stern GM, Lees AJ, Bottomley JM, Sree-Haran N. Ropinirole (SK and F 101468) in the treatment of Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1991;**54**:938.
- Sawada Y, Nakamura M, Tokura Y. Generalized fixed drug eruption caused by pazufloxacin. *Acta Derm Venereol* 2011;**91**:600–1.
- Kaushik P, Soule MR, Ellison WA, Ahmed B, Kaushik R. Cabergoline-associated erythema nodosum. *Ann Pharmacother* 2008;**42**:284–7.
- Leshin B, Piette WW, Caplan RM. Morphea after bromocriptine therapy. *Int J Dermatol* 1989;**28**:177–9.
- Wiesli P, Joos L, Galeazzi RL, Dummer R. Cutaneous pseudolymphoma associated with bromocriptine therapy. *Clin Endocrinol* 2000;**53**:656–7.
- Eisler T, Hall RP, Kalavar KA, Calne DB. Erythromelalgia-like eruption in parkinsonian patients treated with bromocriptine. *Neurology* 1981;**31**:1368–70.
- Huang Y, Qiu AW, Peng YP, Liu Y, Huang HW, Qiu YH. Roles of dopamine receptor subtypes in mediating modulation of T lymphocyte function. *Neuro Endocrinol Lett* 2010;**31**:782–91.

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