



Pramipexole-induced antecollis in patients with Parkinson's disease: Two cases and literature review



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ABSTRACT

Antecollis is considered to be relatively rare in Parkinson's disease (PD). Few cases of dopamine agonist-induced antecollis in PD have been reported. We described literature review of 12 PD patients including our 2 cases with pramipexole (PPX)-induced antecollis. The patients were predominantly Japanese, women and above 3 of Hoehn and Yahr stage. PPX-induced antecollis in PD was considered a type of dystonia of flexor neck muscle, and was improved soon after cessation or reduction of PPX. Our two cases improved their antecollis by overnight changing from PPX to ropinirole without deteriorating motor functions. Overnight switching of DA was considered useful as one option in the treatment of antecollis.

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1. Introduction

Patients with Parkinson's disease (PD) often present with abnormal posture, such as camptocormia, antecollis, Pisa syndrome, and scoliosis [1]. Antecollis refers to forward flexion of the head and neck [2,3]. It was first reported in patients with multiple system atrophy (MSA), and has been suggested as a useful clue for the diagnosis of multiple MSA [3]. Antecollis is considered to be relatively rare in PD, and its prevalence is as 5–6% in PD [1,2,4–6]. Reports of antecollis in PD have originated from Japan more frequently than from elsewhere [1,4–12]. The pathophysiology of antecollis in PD is unclear, but various different central mechanisms (dystonia, rigidity, proprioceptive disintegration) and peripheral processes (myopathy, skeletal and soft-tissue changes) have been proposed [1]. Dopamine agonists (DA) are known to induce or aggravate antecollis in PD [1,4–11,13], and it was found in 0.8% [4]. In addition, there were rare reports that amantadine and donepezil hydrochloride caused antecollis in Japanese patients with PD [12,14]. Here, we describe the literature review of 12 PD patients including our 2 cases with pramipexole (PPX)-induced antecollis.

2. Present the two cases

Case 1 involved a 64-year-old woman with PD who had developed resting tremor and mild postural tremor of the right hand at 57 years

old. At that time, marked orthostatic hypotension and dysuria were not observed, and her brain MRI was normal without abnormal signals of the putamen and the pons. The patient had started to take immediate-release pramipexole (PPX-IR) at 1.5 mg/day. After 2 years, resting tremors had expanded to all extremities, postural tremor appeared on both upper hands, and daily medication was PPX-IR 3 mg and levodopa/carbidopa 300 mg. At 62 years old, entacapone 300 mg and zonisamide 2.5 mg had been added because of wearing-off phenomenon. Antecollis appeared at 63 years old, and gradually worsened. Although PPX-IR had been decreased to 1.5 mg, no improvement in antecollis was seen. The patient complained of neck pain at 64 years old. Laboratory tests, including muscle enzymes, were normal. Needle electromyogram did not show myopathic pattern in the neck extensor muscles, but tonic muscle discharges during passive head up in the sternocleidomastoid muscles (SCM). We injected a total of 40 units botulinum A toxin to bilateral SCM. Injections relieved neck pain, but antecollis remained unchanged. We then changed her medication overnight from 1.5 mg PPX-IR to 6 mg of immediate-release ropinirole (ROP-IR). After 1 month, she was able to lift her head smoothly without deterioration of motor function (Fig. 1A, Video A and B).

Case 2 involved a 71-year-old woman with PD who had developed mild resting tremor and postural tremor, cogwheel rigidity of the right hand, and mild orthostatic hypotension at 68 years old. There was not any abnormal signal in her brain MRI. Her motor symptoms were improved by taking PPX-IR 1.5 mg. Two years later, at Hoehn and Yahr stage II, levodopa/carbidopa had been added at 300 mg. The patient experienced neck pain during exercise, and antecollis appeared shortly thereafter, at 71 years old. Muscle tonus of the bilateral SCM increased.

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(A) Case 1



(B) Case 2



Fig. 1. A) Case 1 shows marked antecollis during PRX-IR 1.5 mg, levodopa/carbidopa 300 mg, entacapone 300 mg and zonisamide 2.5 mg (left). One month after overnight switching from 1.5 mg PPX-IR to 6 mg ROP-IR (right). B) Case 2 shows antecollis while taking PRX-IR 1.5 mg and levodopa/carbidopa 300 mg (left). Two weeks after overnight switching from 1.5 mg PPX-IR to 6 mg ROP-IR, antecollis has improved (right).

Laboratory tests including serum creatine kinase were normal. She was switched overnight from 1.5 mg PPX-IR to 6 mg ROP-IR. By 2 weeks later, she was able to lift her head smoothly (Fig. 1B). The improvements of their drop head were continuing after one year. Both patients did not undergo physiotherapy during one month after changing DA.

3. Literature review

Twelve PD patients with PPX-induced antecollis including two our patients were summarized in Table 1 [6–10,12]. All patients were reported from Asia (11 patients were Japanese and 1 was Korean). Ten patients (2 patients of gender has not been described) were women. Hoehn and Yahr stage was above 3 in 7 patients of the described 8 patients. The disease durations were 3 to 17 years. Daily doses of PPX were from 1 to 3 mg. There were two types of intervals starting from PPX to the appearance of antecollis; the short interval of few weeks in 9 patients and the long interval of 2 to 4 years in 3 patients. To the treatment of the antecollis, PPX were stopped in 10 patients or reduced in 2 patients. Our cases were switched from pramipexole to ropinirole. The antecollis in all patients were improved in 1 to 4 weeks after cessation or reduction of PPX.

4. Discussion

We describe the literature review of 12 PD patients with PPX-induced antecollis. The patients were predominantly Japanese, women and above 3 of Hoehn and Yahr stage. PPX-induced antecollis was considered dystonia, rather than myopathy, based on their disproportionate tonus of the neck muscles, laboratory data, and EMG findings. Kashiwara et al. [6] reported that the frequency of antecollis in PD was 0% at Hoehn and Yahr 1, 1.4% at 2, 4.7% at 3, and 9.1% at 4. Thus the incidence of antecollis increases as the disease progress. Regarding to the gender differences of deformities in PD, female are predominant in antecollis [6,7,9,11] and in anterior flexion of the trunk [6], however male are predominant or gender difference was not shown in camptocormia [6,15,16].

Ergot DAs, cabergoline and perldolide, also induced antecollis [5,9,11, 18]. It is not statistically different in the appearance of antecollis between ergot DAs and non-ergot DAs [6]. Deformity developing after DA treatment usually resolves after discontinuing the offending drug [1,5–11,13]. However, we sometimes have experienced patients with DA induced antecollis whom motor symptoms were worsened after stopping DA. In our cases, overnight switching from PPX-IR to ROP-IR successfully resolved antecollis without deterioration of motor

Table 1

Antecollis induced by pramipexole in patients with Parkinson's disease.

Authors	Age (year)/sex	HY stage	Duration (year)	PPX dosed (mg/d)	Interval from starting PPX to appearance of antecollis	Treatment	Combined drugs/d
Suzuki et al. ⁸⁾	80/F	4	3	3	Few weeks	Cessation of PPX	l-dopa/carbidopa 200 mg
Oyama et al. ⁹⁾	75/F	3	6	UD	8 weeks	Reduction	UD
	64/F	3	9	UD	4 weeks	Reduction of PPX	UD
	79/F	3	17	UD	4 weeks	Cessation of PPX	UD
Taguchi et al. ¹⁰⁾	80/F	UD	3	1	1.5 years	Cessation of PPX Increase dose of l-dopa	none
Uzawa et al. ¹¹⁾	64/F	4	6	2.5	Few weeks	Cessation of PPX	l-dopa/benserazid 450 mg
	47/F	4	5	1	2 weeks	Cessation of PPX	l-dopa/carbidopa 50 mg, Cabergoline 3 mg
Kashihara et al. ⁶⁾	UD	UD	UD	UD	Few weeks	Cessation of PPX	UD
	UD	UD	UD	UD	Few weeks	Cessation of PPX	UD
Kim et al. ¹³⁾	80/F	UD	3	1	6 weeks	Cessation of PPX	l-dopa/benserazid 450 mg
Our patient 1	64/F	3	7	3	4 years	Reduction of PPX 1.5 mg, and Overnight switched from PPX to ROP 6 mg	l-dopa/carbidopa 300 mg, Entacapone 300 mg, Zonisamide 2.5 mg
patient 2	71/F	2	4	1.5	3 years	Overnight switched from PPX to ROP 6 mg	l-dopa/carbidopa 300 mg,

HY stage; Hoehn and Yahr stage, UD; undescribed, PPX; pramipexole, ROP; ropinirole.

symptoms. The cause in this response was unclear. One proposed mechanism for antecollis is an imbalance between dopamine and norepinephrine, serotonin, acetylcholine, or glutamine levels, and the ways in which these neurotransmitters regulate axial muscle tone [1]. The binding profile at multiple classes of dopaminergic and serotonergic receptors differs somewhat between PPX and ROP, and affinity at the 5HT_{2B} receptor was much stronger for ROP than for PPX [19]. In our patients, a dopaminergic-serotonergic imbalance in the striatum by PPX might be improved by changing ROP.

In conclusion, PPX-induced antecollis are rare, but should be considered in female and advanced PD patients treated with PPX. Switching to DA was successful in early and advanced PD patients with antecollis, and it appears useful as one option in the treatment of antecollis.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ensci.2015.09.001>.

Disclosure

The authors declare that they have no conflicts of interest.

We obtained the permission for the publication of the video material by the patient.

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