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CASE REPORT

A case of respiratory akathisia in a cancer patient: A case report

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ABSTRACT

Objective: It has been reported that akathisia is a neurological side effect induced by antiemetic drugs and/or antipsychotics. Akathisia can occur in any area of the body, but respiratory akathisia is an unusual type of akathisia. Cases of respiratory akathisia in cancer patients taking antiemetic drugs have not previously been reported.

Methods: We report on a case of a cancer patient taking prochlorperazine as an antiemetic drug who experienced dyspnea accompanied by severe restlessness associated with respiration. By administration of biperiden, his restlessness in respiration and dyspnea promptly disappeared.

Results: This finding led us to conclude that this cancer patient was experiencing respiratory akathisia.

Significance of results: Respiratory akathisia is uncommon. It is important for cancer patients that dyspnea induced by disease progression be ruled out as a cause of the respiratory restlessness. It is necessary to consider the possibility of akathisia in patients that complain of vague anxiety, chest discomfort, or dyspnea following antipsychotic medication.

KEYWORDS: Respiratory akathisia, Cancer, Antiemetic drug

INTRODUCTION

Akathisia is a neurological side effect produced by antipsychotic or antiemetic drug therapy (Blaisdell, 1994). The clinical picture of akathisia is a feeling of inner restlessness in the limbs, especially in the legs (Gibb & Lee, 1986). However, reports have indicated that akathisia can occur in any area of the body, such as the arms or abdomen (Raskin, 1972; Ratey & Salzman, 1984; Walters et al., 1989). A rare manifestation of akathisia reported by patients receiving antipsychotic treatment is an inner restlessness in respiration as dyspnea.

Prochlorperazine is an antiemetic agent frequently used by cancer patients taking opioids (e.g., morphine, oxycodone) for cancer pain. In oncological settings, prochlorperazine is used as an antiemetic drug for nausea, a side effect of opioid. It is a phenothiazine antiemetic that has central dopamine antagonist properties and that has been reported to cause acute extrapyramidal side effects,

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parkinsonism, dystonia, and akathisia (Bateman et al., 1989). It is well known that neuroleptic-induced akathisia may be difficult to recognize and can occur in the absence of other extrapyramidal signs. Furthermore, cases of akathisia due to antiemetic drugs used by cancer patients have been little reported.

CASE REPORT

The patient was an 66-year-old man with squamous cell carcinoma of the esophagus, stage II(T2N0M0). Due to his renal impairment and the presence of emphysema, surgical resection was not performed; furthermore, chemotherapy was not indicated. Therefore, he attempted radiation therapy and received a total dose of 70.2 Gy. He used opioid, 20 mg/day of morphine hydrochloride, for pain of esophagitis by irradiation, with taking prochlorperazine as an antiemetic drug. He complained of chest discomfort after receiving 5 mg/day of prochlorperazine p.o. for 3 weeks and was admitted to the hospital. When he arrived in the hospital, he acknowledged dyspnea with vague anxiety and a subjective restlessness in respiration, with a temperature of 36.8°C, blood pressure of 118/72 mm Hg, pulse 79 beats/min, respiratory rate 18 breaths/min. Resting room-air oxygen saturation was 98%. First, radiation pneumonitis was suspected, but chest X-ray was normal. He felt that he could not respire leisurely nor stop breathing at any time because of this restlessness in respiration. He denied restlessness in the limbs or other body areas except for the chest. He showed no signs or symptoms of parkinsonism. He was administered 5 mg of biperiden d.i.v.; his restlessness in respiration and dyspnea simultaneously disappeared approximately 1 h later (Hirose & Ashby, 2000). Subsequently, 6 mg of oral biperiden was added to the treatment regimen. The next day, the dyspnea with vague anxiety and other restless movements completely ceased. No signs or symptoms of akathisia have appeared in this patient since that time.

DISCUSSION

We reported respiratory akathisia in cancer patients taking prochlorperazine as antiemetics. This is the first report of respiratory akathisia recognized in cancer patients.

It was necessary that other medical problems known to produce dyspnea, such as panic attacks and dyskinesia and dystonia or pulmonary diseases, could be ruled out as a cause of the respiratory restlessness (Hirose, 2000). In this case, the patient did not have anxiety about dying or a history of panic disorder before. Respiratory dyskinesia presents as involuntary movements of respiratory muscles, but not as a restless feeling in respiration, and is not improved on treatment with biperiden (Kruk et al., 1995; Esmail et al, 1999; Heard et al., 1999). Furthermore, in this case, dystonia was ruled out by the absence of tonic contractions of respiratory muscles (Dressler & Benecke, 2005).

Respiratory akathisia is uncommon, so one needs to ask specific questions about restlessness in breathing to recognize this type of akathisia. Therefore, if physicians is not aware of inner restlessness in respiration, it is possible that dyspnea in akathisia may be overlooked or misdiagnosed as a symptom of anxiety disorders, agitation, or respiratory symptoms of cancer itself (Hirose, 2000).

Antiemetics possessing a central antidopaminergic effect are suspected to have caused the akathisia (Seeman, 2002; Matsui-Sakata et al., 2005). Antiemetic-induced akathisia has been reported in cancer patients receiving metoclopramide or prochlorperazine to help control chemotherapy-related nausea and vomiting (Fleishman et al., 1994; Tsuji et al., 2006). In this case, prochlorperazine was used as an antiemetic drug for nausea and vomiting, a side effect of opioid.

Prochlorperazine is a phenothiazine antiemetic that has central dopamine antagonistic properties. It has been reported that the presumed community standard of prescribing prochlorperazine, dexamethasone, or a 5HT3 receptor antagonist after moderately high to highly emetogenic chemotherapy results in equivalent outcomes in terms of control of vomiting and measures of satisfaction and quality of life (Burris et al., 1996; Crucitt et al., 1996).

In Japan, many cancer patients taking opioids for cancer pain clinically use prochlorperazine as an antiemetic drug. Therefore, it should be noted that akathisia is considered a possible side effect during the management of cancer pain.

The clinicians' attitude toward akathisia is important to recognize. It is also important to consider the possibility of akathisia in patients that complain of vague anxiety, chest discomfort, or dyspnea following antipsychotic medication.

REFERENCES

Bateman, D.N., Darling, W.M., Boys, R., et al. (1989). Extrapyramidal reactions to metoclopramide and prochlorperazine. *Quarterly Journal of Medicine*, *71*, 307–311.

Blaisdell, G.D. (1994). Akathisia: A comprehensive review and treatment summary. *Pharmacopsychiatry*, *27*, 139–146.

Burris, H., Hesketh, P., Cohn, J., et al. (1996). Efficacy and safety of oral granisetron versus oral prochlorperazine in preventing nausea and emesis in patients receiving

moderately emetogenic chemotherapy. *The Cancer Journal from Scientific American*, *2*, 85–90.
Crucitt, M.A., Hyman, W., Grote, T., et al. (1996). Efficacy and tolerability of oral ondansetron versus prochlorperazine in the prevention of emesis associated with cyclophosphamide-based chemotherapy and maintenance of health-related quality of life. *Clinical Therapeutics*, *18*, 778–788.
Dressler, D. & Benecke, R. (2005). Diagnosis and management of acute movement disorders. *Journal of Neurology*, *252*, 1299–1306.
Esmail, Z., Montgomery, C., Courtrn, C., et al. (1999). Efficacy and complications of morphine infusions in postoperative paediatric patients. *Paediatric Anaesthesia*, *9*, 321–327.
Fleishman, S.B., Lavin, M.R., Sattler, M., et al. (1994). Antiemetic-induced akathisia in cancer patients receiving chemotherapy. *American Journal of Psychiatry*, *151*, 763–765.
Gibb, W.R.G. & Lee, A. (1986). The clinical phenomenon of akathisia. *Journal of Neurology, Neurosurgery, and Psychiatry*, *49*, 861–866.
Heard, K., Daly, F.F., O'Malley, G., et al. (1999). Respiratory distress after use of droperidol for agitation. *Annals of Emergency Medicine*, *34*, 410–411.
Hirose, S. (2000). Restlessness of respiration as a manifestation of akathisia: Five case reports of respiratory akathisia. *Journal of Clinical Psychiatry*, *61*, 737–741.
Hirose, S. & Ashby, C.R. (2000). Intravenous biperiden in akathisia: An open pilot study. *International Journal of Psychiatry in Medicine*, *30*, 185–194.
Kruk, J., Sachdev, P., Singh, S. (1995). Neuroleptic-induced respiratory dyskinesia. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *7*, 223–229.
Matsui-Sakata, A., Ohtani, H., & Sawada, Y. (2005). Pharmacokinetic-pharmacodynamic analysis of antipsychotics-induced extrapyramidal symptoms based on receptor occupancy theory incorporating endogenous dopamine release. *Drug Metabolism and Pharmacokinetics*, *20*, 187–199.
Raskin, D.E. (1972). Akathisia: A side effect to be remembered. *American Journal of Psychiatry*, *129*, 345–347.
Ratey, J.J. & Salzman, C. (1984). Recognizing and managing akathisia. *Hospital and Community Psychiatry*, *35*, 975–977.
Seeman, P. (2002). Atypical antipsychotics: Mechanism of action. *Canadian Journal of Psychiatry*, *47*, 27–38.
Tsuji, Y., Miyama, S., Uemura, Y., et al. (2006). Three cases of drug-induced akathisia due to antiemetics during cancer palliative care. *Gan To Kagaku Ryoho*, *33*, 267–269.
Walters, A.S., Hening, W., Chokroverty, S., et al. (1989). Restlessness of the arms as the principal manifestation of neuroleptic-induced akathisia [letter]. *Journal of Neurology*, *236*, 435.