Letter to the Editor

Akathisia Causing Secondary Severe Depression in a Cancer Patient

To the Editor: Akathisia is a common side effect of neuroleptics or dopamine D_2 receptor antagonists in the treatment of schizophrenia. Dopamine D_2 receptor antagonists are also used as antiemetic agents in cancer patients and can induce akathisia. However, akathisia in palliative care is often unrecognized by general physicians or oncologists.[1,2] Akathisia may cause patients severe distress, but a major depressive–like episode secondarily induced by antiemetics in a cancer patient has not been reported. We report a case of a breast cancer patient who suffered from a severe major depressive–like episode induced by akathisia.

Case report. In September 2009, Ms A, a 37-year-old woman, was referred to us by a surgeon for investigation of anxiety. She had undergone surgery for left breast cancer at 32 years of age. Since 2007, she has received radiation and chemotherapy for the treatment of metastases to the lungs and parasternal lymph nodes. To relieve pain, oxycodone tablets (5 mg/d) had been prescribed with prochlorperazine (5 mg/d) as an antiemetic agent for 6 months, and 5 weeks previously the dose of oxycodone had been increased to 10 mg/d due to increased breast pain in conjunction with the increased dose of prochlorperazine (10 mg/d). Despite her pain, her activities of daily living were maintained well and she was able to enjoy her life, in activities such as travel with her family. Two weeks before her presentation, she suddenly experienced restlessness of her limbs and anxiety, and she began to walk all day long. Insomnia and loss of appetite appeared. Her restlessness was quite burdensome, and she became severely depressed with suicidal ideation. She was unable to do anything other than walking and moving her limbs. She had no past history of psychiatric disorders, including depression and mania.

On our psychiatric examination, all 9 symptoms listed as diagnostic criteria for a major depressive episode in *DSM-IV-TR*[3] were present. Her score on the 17-item Hamilton Depression Rating Scale (HDRS)[4] was 36. However, typical symptoms of akathisia such as restlessness, fidgety movement of the legs, and inability to sit or stand still were also observed. Neurologic examination revealed slight Parkinson's syndrome, with disturbance of the gait including lack of arm swing and brachybasia, but without tremor or muscle rigidity. On the basis of the symptoms and their time course, we strongly suspected prochlorperazine-induced akathisia and substance-induced mood disorder (severe depression). We recommended that she discontinue prochlorperazine and gave her supportive psychotherapy without prescribing antidepressants since her severe depression was strongly suspected to have been triggered by neuroleptic-induced akathisia. Following discontinuation of prochlorperazine, her akathisia improved dramatically. One week later, her akathisia was only episodic and of short duration, rather than continuous. Her depression disappeared with recovery from akathisia (HDRS score = 5).

Akathisia usually develops as an acute extrapyramidal sign within a few weeks of starting or raising the dose of a neuroleptic medication (*DSM-IV-TR*).[3] Although she had taken prochlorperazine for 6 months, an increase in the dose of prochlorperazine triggered akathisia. Akathisia is commonly observed in the treatment of schizophrenia with neuroleptics, but it is not well known that it can develop during palliative care of patients with antiemetic agents, such as prochlorperazine and metoclopramide, which block central D_2 receptors. Prochlorperazine has a very high affinity for D_2 receptors comparable to that of haloperidol[5] and is likely to induce akathisia and other extrapyramidal side effects.

Akathisia induced by D_2-blocking antiemetic agents is frequently unrecognized in cancer patients.[1,2] Half of 24 cancer patients receiving metoclopramide and prochlorperazine developed akathisia.[1] Twenty of 483 patients referred to a department of psychiatry developed akathisia from an antiemetic drug (80% of such patients took prochlorperazine).[2] Major depression is also highly prevalent in cancer patients.[6] However, most oncologists and general physicians may be unaware that antiemetic-induced akathisia can cause severe depression with suicidality resembling major depressive disorder. Although prochlorperazine is one of the first-line drugs for the treatment of emesis induced by chemotherapy and opioids and is useful in caring for cancer patients, physicians should recognize that it, as well as D_2-blocking antiemetic agents other than domperidone, may have pronounced side effects. Long-term use of prochlorperazine should be avoided, or domperidone, a peripherally acting D_2 antagonist, should be substituted for it if possible.

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