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CASE REPORT

Activation syndrome caused by paroxetine in a cancer patient

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ABSTRACT

Individuals with cancer have two to four times an increased risk of depressive disorders compared to the general population. Depressive symptoms are related to impaired daily life functioning and a rise in health care utilization. Pharmacological treatments for depression are usually effective to reduce depressive symptoms, but sometimes lead to serious adverse reactions. We describe a cancer patient who developed sudden psychological and behavioral abnormalities after administration of the antidepressant paroxetine. Impulsive and aggressive symptoms are a so-called activation syndrome that can cause violent or suicidal tendencies. Palliative care staff should pay close attention to these potentially lethal reactions and make an immediate and correct diagnosis.

KEYWORDS: Activation syndrome, Selective serotonin reuptake inhibitors (SSRIs), Paroxetine, Cancer, Akathisia

INTRODUCTION

Recent reports have confirmed that selective serotonin reuptake inhibitors (SSRIs) cause adverse mental and behavioral reactions, so-called activation syndrome (Teicher et al., 1990; Breggin, 2003/2004). We describe a cancer patient who developed activation syndrome soon after receiving an SSRI, paroxetine.

CASE REPORT

A 60-year-old man was admitted to our cancer center for treatment of abdominal pain. The patient had been diagnosed with pancreas cancer 18 months previously and had received three courses of chemotherapy without success. The primal lesion in the pancreas had invaded the para-aortic lymph nodes, causing severe abdominal pain. He had been taking acetaminophen, morphine sulfate, and H2-blocker before and after admission without any adverse side effects. His hepatic and renal functions were well preserved. There was no clinical evidence of brain metastasis or neurological abnormality. He had never experienced a psychotic episode, although he had previously been quite sensitive and anxious about his physical condition. Other symptoms included hopelessness and passive suicidal thoughts due to unbearable pain without any suicidal attempts. The next day after admission, these complaints abated as he realized that his pain could be well controlled with intravenous administration of morphine chloride. His pain was finally well controlled with oral morphine sulfate on day 18 after admission. Nevertheless, he complained of several other symptoms, including depressive mood, anhedonia (he had no interest in investments although he used to be an ambitious shareholder), general fatigue, psychomotor retardation and insomnia.

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Based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR), he was diagnosed with major depressive disorder by a psycho-oncologist. He was started on paroxetine 10 mg/day. The day after beginning paroxetine treatment (day 19 after admission), he became talkative and laughed frequently in conversation with his family. On day 2 after beginning administration, he appeared more outgoing and hyperactive (he went home, cooked, and did household chores, and came back to the hospital late at night). On day 3, he insisted on going to a hot spring instead of receiving cancer treatment. He had never showed such behavior before. In the morning on day 4, he abruptly complained of inner restlessness and inability to keep his feet still. He screamed incoherent bizarre ideas and expressed a strong urge to harm himself ("I want to stab my limbs or jump out of the window"). He appeared extremely agitated and showed akathisia-like movements of rocking his feet and head.

Paroxetine treatment was discontinued and levomepromazine (LPZ) was administered for 2 days (25 mg on that day and 15 mg the next day). His subjective complaints of mental and physical restlessness improved several hours after LPZ administration, but he still made inappropriate jokes and aggressive statements the next day. On day 3 after stopping paroxetine, he was quite calm but had a short episode of hyperventilation. His objective stimulated mental symptoms were alleviated 4 days after paroxetine was stopped. Over 1 month after the discontinuation of paroxetine, the patient made a full recovery from the stimulated state and was also free from the major depressive disorder.

DISCUSSION

Although abnormal psychomotor and behavioral conditions have been observed with SSRIs, to our knowledge, this is the first report of so-called activation syndrome in a cancer patient. In the issued advisory by the U.S. Food and Drug Administration, "activation" includes the following symptoms: irritability, anxiety, agitation, insomnia, panic attacks, hostility, impulsiveness, akathisia (severe restlessness occasionally leading to suicidal thoughts and attempts), hypomania, and mania. We would like to draw attention to this potentially lethal drug reaction. Depression is quite common during cancer treatment (Rodin et al., 2007) and SSRIs are more likely to be prescribed to cancer patients because of their fewer cardiovascular side effects compared to classic tricyclic antidepressants (MacGillivray et al., 2003).

On the other hand, several adverse reactions related to SSRIs have been reported, ranging from gastrointestinal symptoms, serotonin syndrome, and activation syndrome to suicidal thoughts and violent behavior (Wagstaff et al., 2002). Unfortunately, abnormal psychotic conditions are often under- and misdiagnosed in cancer treatment settings due to the difficulty of arranging psychiatric consultations (Culpepper et al., 2004); however, it is crucial for clinicians to be aware of the clinical features of activation syndrome because of easier opportunities for self-harm in general hospitals compared to psychiatric wards. In fact, our case would have jumped out of the hospital window if his family had not been with him.

It is also important to make a correct diagnosis of activation and to distinguish it from worsening depression, which could lead to an increased dose of the inappropriate medication and worsen the condition. In previous reports, beta-adrenergic blockers and/or benzodiazepines are usually recommended for the management of SSRI-induced akathisia (Leo, 1996). Our patient required a major tranquilizer to control the intense impulse to self-harm. Although the underlying mechanisms of SSRI-induced akathisia remain uncertain, previous studies have suggested their possible pathophysiology (Lipinski et al., 1989). Our case showed immediate alleviation of the inner restlessness and characteristic leg movement after oral LPZ administration, which implies a different pathomechanism of akathisia between neuroleptics and SSRIs.

In summary, we experienced a cancer patient with paroxetine-induced activation syndrome. Not only oncologists but also staff who participate in palliative care medicine should be attentive to possible adverse mental and behavioral reactions during antidepressant treatment. These symptoms sometimes persist after discontinuation of SSRI and need additional treatment. The effects of neuroleptics on SSRI-induced akathisia may have some implications for their pathophysiological assessment.

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