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## *Lesson of the week*

### Akathisia: overlooked at a cost

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**Akathisia is an important side effect to consider in patients prescribed antipsychotics, antiemetics, or antidepressants**

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Akathisia (Greek "not to sit") is an extrapyramidal movement disorder consisting of difficulty in staying still and a subjective sense of restlessness. It is a recognised side effect of antipsychotic and antiemetic drugs but may also be caused by other widely prescribed drugs such as antidepressants. It is a difficult condition to detect reliably and may present unexpectedly in a variety of clinical settings. The patient's behaviour may be disturbed, treatment may be refused, or the patient may be suicidal and be mistaken for a psychiatric problem. We report three cases seen in the psycho-oncology service which improved when the offending drug was discontinued.

#### Case reports

##### Case 1

A 54 year old female patient on a surgical ward was referred as an urgent ward consultation for depression and anxiety. For the preceding few days she had become progressively agitated and weepy and had felt like smashing things on the ward. She seemed angry and had shouted at staff on the ward.

At the time of referral, she was awaiting surgery for a colonic stricture resulting from a recurrence of carcinoma of the colon. She had started taking haloperidol and metoclopramide for nausea and vomiting just before the onset of the agitation. At her insistence the previous day, these drugs had been stopped and she had begun to feel better. At assessment she gave a history of previous depression and overdoses, but there was no evidence of a current depressive illness or excessive anxiety. She reported a "bad reaction to tablets for nerves" in the past and had suspected that haloperidol and metoclopramide had been causing the agitation but was aggrieved that she had not been listened to until the previous day. Akathisia was diagnosed as the cause of her behavioural disturbance. Further review of her notes indicated that she had pre-

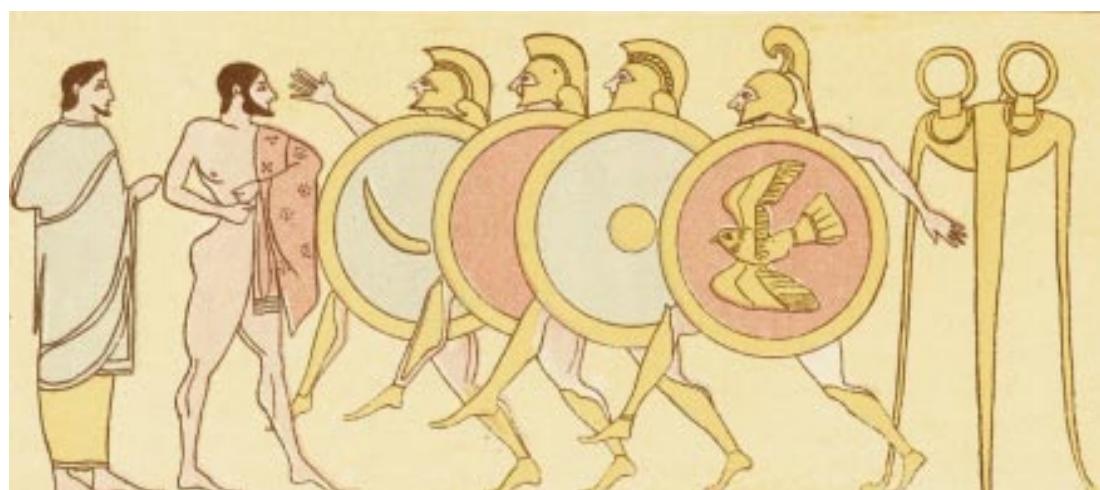
viously been given low dose trifluoperazine on the surgical ward, resulting in premature self discharge. On another occasion she had been given haloperidol and metoclopramide; her course of chemotherapy was interrupted and she was referred to psychiatrists for "bizzare behaviour," which had settled by the time she was seen.

##### Case 2

A 62 year old woman was referred to the psycho-oncology clinic from the radiotherapy department for anger and distress. Depression was diagnosed, and she responded well to antidepressants. She had had chemotherapy for breast cancer, which she described as "an ordeal," and went on to have a further course. After the first session, she became agitated, anxious, and unable to sleep and had been pacing the house. Her next chemotherapy session had to be cancelled owing to her distress and she was reviewed by her oncologist, who diagnosed akathisia due to metoclopramide. She reported similar reactions during the previous course of chemotherapy, when she had metoclopramide intravenously and orally. She settled after the antiemetic was changed to domperidone. Further psychiatric review confirmed that this episode was not a recurrence of her depressive illness. In view of the degree of distress with previous chemotherapy, she was given a dose of lorazepam for anticipatory anxiety before each chemotherapy session and completed further treatment without problems.

##### Case 3

A 62 year old man was referred urgently to the psycho-oncology clinic by the community mental health team after his general practitioner requested an urgent assessment for suicidal ideation. He had received chemotherapy and cranial irradiation for lung cancer and had been doing well except for a general



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The Greeks had a word for that restless feeling

### Non-neuroleptic drugs reported to cause akathisia<sup>3 4 10-12</sup>

**Antiemetics:** Metoclopramide, prochlorperazine, [domperidone]

**Antidepressants:** Tricyclics, selective serotonin reuptake inhibitors (fluoxetine, paroxetine, sertraline), venlafaxine, [nefazodone]

**Calcium channel blockers:** Cinnarizine, flunarizine (also H<sub>1</sub> antagonists), [diltiazem]

**Others:** Methyldopa, levodopa and dopamine agonists, [lithium carbonate], [buspirone], [anticonvulsants], [pethidine], [interferon alfa], [sumatriptan]

[ ]= anecdotal or not well established

neuroleptic drugs, which will exacerbate the condition rather than ameliorate it. Compliance with treatment may be affected, as in cases 1 and 2. Refusal of surgery after use of preoperative antiemetics has been reported,<sup>6</sup> and akathisia is thought to contribute appreciably to drug non-compliance in psychiatric settings. Suicidal ideation or suicide attempts have been reported with fluoxetine, droperidol, and metoclopramide,<sup>5 7 8</sup> attributed to the distress and unpleasantness of severe akathisia. Therefore, prompt diagnosis and management are crucial in minimising patients' distress and disruption of medical or surgical treatments.

Patients often find it difficult to explain the inner restlessness or mental unease, and the condition may easily be interpreted as acute anxiety or depression. Therefore diagnosis relies on a high index of suspicion on the part of the clinician. Thus when patients present with acute symptoms of agitation and restlessness, their medication should first be checked for a recent introduction or increase in the dose of drugs associated with akathisia. There may be a history of previous similar episodes, as in all our cases, which will help in the diagnosis. Such individual susceptibility may indicate a genetic predisposition.<sup>9</sup> The diagnosis can be confirmed retrospectively when the symptoms abate rapidly with the withdrawal of the offending drug.

On diagnosis, the offending or suspected drug should be withdrawn or the dose reduced if possible. Where this is not possible, propranolol or other lipophilic β blockers are considered to be the most effective. Benzodiazepines can be considered as additional treatment. Patients should be made aware of the diagnosis so that they can report the symptoms early if they experience similar problems in the future.

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slowing of cognition. He was taking fluoxetine, and the dose had been increased to 40 mg four weeks previously. He reported increasing agitation, restlessness, and a sense of dread triggered by minor events and had felt frightened of being on his own because of suicidal urges. Nausea had caused him to lose his appetite, and he had lost weight. He reported that the symptoms were very similar to the time he had taken metoclopramide (10 mg four times a day) during his chemotherapy. He had not reported this to his oncologist at the time.

Akathisia due to the higher dose of fluoxetine was diagnosed. Fluoxetine was stopped and he was given diazepam 2 mg twice a day for a week. He was monitored by his community psychiatric nurse, who reported rapid improvement in his mental state, and when seen in clinic five weeks later he was well with no anxiety, agitation, or suicidal ideas and without evidence of depression. The psychiatrist advised the patient and general practitioner about caution in the future use of antiemetics, selective serotonin reuptake inhibitors, and neuroleptics.

## Discussion

Akathisia has been well documented as a common and distressing side effect of antipsychotic drugs and an important cause of poor drug compliance. However, even in psychiatric settings, it is not recognised readily. In one study of movement disorders induced by neuroleptics, akathisia was diagnosed in only 26% of patients who had it.<sup>1</sup>

Akathisia is common in general medical settings, especially when patients are taking antiemetics. In cancer patients undergoing chemotherapy, 50% of patients met the diagnostic threshold of akathisia,<sup>2</sup> yet 75% stated they would not have reported the symptoms of akathisia. Therefore, diagnosis can easily be missed if it relies on patients' reports.

Antidepressants are another group of drugs known to cause akathisia<sup>3-5</sup> but are not as well recognised. The list of drugs reported to cause akathisia has been growing (box) and the disturbance of the serotonin or dopamine system has been postulated in the aetiology of the disorder.

As our cases illustrate, akathisia may manifest in various ways and is not necessarily easily recognisable as restlessness. The distress associated with the unpleasant symptoms of akathisia may lead to behavioural disturbance on the ward and to the use of