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Wernicke encephalopathy without delirium that appeared as agitation in a patient with lung cancer

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Case Report

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Abstract

Objective. Wernicke encephalopathy (WE) is a neuropsychiatric disorder caused by thiamine deficiency, and is sometimes overlooked because of the diversity of clinical symptoms.
Method. From a series of WE patients with cancer, we report a lung cancer patient who developed WE, the main symptom of which was agitation.
Result. A 50-year-old woman with lung cancer was referred to our psycho-oncology clinic because of agitation lasting for three days. No laboratory findings or drugs explaining her agitation were identified. Although the patient did not develop delirium, ophthalmoplegia, or ataxia, WE was suspected because she experienced a loss of appetite loss lasting 5 weeks. This diagnosis was supported by abnormal serum thiamine and disappearance of agitation one hour after intravenous thiamine administration.
Significance of results. This report emphasizes the clinical diversity of WE and indicates the limits of the ability to diagnose WE from typical clinical symptoms. The presence of a loss of appetite for more than two weeks may be the key to the accurate diagnosis of WE.

Introduction

Wernicke encephalopathy (WE) is a neuropsychiatric disorder caused by a deficiency of thiamine, which is necessary for oxidative metabolism (Sechi & Serra, 2007).

This disorder is reversible if properly diagnosed and treated with supplementary thiamine; however, it often goes unrecognized because of the diversity of symptoms (Isenberg-Grzeda et al., 2012; Onishi et al., 2016; Sechi et al., 2016b). If left untreated, it can cause severe and irreversible brain damage (Korsakoff syndrome), leading to death. The estimated mortality rate is about 20% (Victor et al., 1971).

The classical symptoms of WE are delirium, ataxia and ophthalmoplegia; however, these symptoms are not specific to WE and only 16% of autopsy samples and 11% of clinical cases exhibit these symptoms, whereas 19% of autopsy samples show none of these three clinical symptoms (Harper et al., 1986; Isenberg-Grzeda et al., 2016a). The best aid for the diagnosis of WE, particularly in patients with cancer, is clinical suspicion (Sechi et al., 2016a).

Recent studies have revealed that WE patients with cancer can be recognized at several points during the cancer trajectory (Isenberg-Grzeda et al., 2016a; Onishi et al., 2004, 2016, 2017b).

Most clinical cases of WE are recognized when patients develop delirium; however, little is known about the clinical features of WE in cases without delirium (Onishi et al., 2017a, 2017b).

In this communication, we have identified cancer patients with WE, the main symptom of which was agitation, whereas the typical symptoms of WE, including delirium, ophthalmoplegia, and ataxia, were not apparent. Clinical suspicion, correct diagnosis, and subsequent parenteral thiamine administration relieved the symptoms and prevented irreversible brain damage.

Case Report

A 50-year-old woman with lung cancer was referred by her oncologist to the psycho-oncology outpatient clinic because of depressed mood and restlessness.

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She had been diagnosed with lung cancer 5 years previously and had undergone surgery followed by chemotherapy.

Ten months ago, bone metastasis and pleural dissemination were recognized. She was administered gefitinib, oxycodone (20 mg), and prochlorperazine (15 mg) for back pain; however, the gefitinib was discontinued because of paronychia and skin eruption.

Five weeks ago, she was admitted to hospital for chemotherapy and pain control. She was administered erlotinib as well as oxycodone and loxoprofen for pain control. Four days ago, she was discharged from hospital; however, after her return home, she became restless and her condition worsened. Her oncologist referred her to the psycho-oncology outpatient clinic.

On her first psychiatric examination, she was agitated and stood up and sat down repeatedly. Her husband stated that while she was waiting for consultation, she walked around the hospital corridors.

Orientation to date and place appeared normal and she was able to make calculations, so no delirium was indicated. Neurological examination revealed no significant findings, including ataxia or eye symptoms. She was treated with oxycodone and loxoprofen for approximately 5 weeks. Laboratory findings revealed that her sodium and calcium values were slightly decreased; however, we could not find any drug or laboratory findings to explain her agitation.

The patient was a nursery teacher who was very kind to others and had no medical history of psychiatric illness or alcohol or drug abuse. A detailed interview with her husband revealed that her appetite had been 10% of normal for the 5 weeks since she was last admitted to our hospital. Appetite loss was also apparent from her nursing chart during her admission.

Although the patient did not develop any signs or symptoms indicative of WE, we suspected WE because her loss of appetite lasted 5 weeks and ingested thiamine is stored in the body for approximately 18 days (MacLean et al., 1983). We therefore administered 100 mg of thiamine intravenously and one hour later her agitation disappeared. No restlessness was evident on the next day when she came to the hospital.

Her serum thiamine level measured using high-performance liquid chromatography was 14 ng/mL (reference range: 24–66 ng/mL), whereas her serum vitamin B12 level was within normal range (reference range: 180–914 pg/mL). Based on these findings, she was diagnosed with WE presenting as agitation without typical clinical symptoms.

Discussion

We experienced a lung cancer patient with WE, the main symptom of which was psychomotor agitation. Agitation was reported as a feature of WE as early as Carl Wernicke's original case reports in 1881 (Thomson et al., 2008). A comparison of this case with the findings presented in a recent systematic review (Isenberg-Grzeda et al., 2016b) reveals that this case has two characteristic features: the first is that the agitation appeared as an isolated symptom, and the second is that the patient showed none of the classical symptoms of WE. These features indicate the diversity of clinical symptoms associated with WE and that the diagnosis of WE cannot be based on the typical clinical symptoms of WE alone, as we and another group have repeatedly emphasized (Isenberg-Grzeda et al., 2016b; Onishi et al., 2017a).

The diagnosis of WE in this patient was difficult because the main symptom was agitation and none of the classical symptoms of WE were recognized. In the systemic review of Wernicke-Korsakoff syndrome in patients with cancer, this disorder is described as often under-recognized (Isenberg-Grzeda et al., 2016b). The clue to the diagnosis in this patient was appetite loss and a medical history of cancer. Thiamine deficiency can occur any time when nutrition is unbalanced for 2–3 weeks (Sechi et al., 2016b) because thiamine is only stored in the body for about 18 days (MacLean et al., 1983). In our previous paper, a two-week loss of appetite was seen as the key to clinical suspicion and treatment of WE (Onishi et al., 2017b). Therefore, thiamine deficiency should be considered when appetite loss lasts more than two weeks, which also corresponds to the one of the diagnostic criteria of a depressive episode (American Psychiatric Association, 2013).

Both our and another group have published reports on WE among cancer patients (Isenberg-Grzeda et al., 2012, 2016a, 2018; Onishi et al., 2004, 2017b, 2018). WE in cancer patients might, therefore, be more common than is currently thought; further study is required to clarify this.

In conclusion, oncologists should always consider thiamine deficiency if the patient experiences appetite loss lasting more than two weeks regardless of the presence or absence of classical symptoms of WE. Careful consideration of this situation will be of help to cancer patients.

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