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Reversible dementia due to vitamin B12 deficiency in a lung cancer patient: Relevance of preoperative evaluation

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Case Report

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Abstract

Objective. Cognitive dysfunction has a negative effect on cancer treatment; however, in a cancer setting, specific treatments can restore cognitive function. Such conditions are known as reversible dementia, with one of these being vitamin B12 (VB12) deficiency. However, there have been no reports of VB12 deficiency identified by preoperative evaluation in cancer patients.

Method. We studied a patient who was referred to the Department of Psycho-oncology on suspicion of cognitive decline prior to lung cancer surgery. Preoperative evaluation revealed VB12 deficiency.

Results. The patient was an 82-year-old woman diagnosed with lung cancer. She also presented with cognitive decline and, therefore, was referred to the Department of Psycho-oncology for preoperative evaluation. The patient scored 19 points on a Mini-Mental State Examination (MMSE), which is indicative of cognitive decline. As the onset of symptoms occurred several months previously and they were subacute, the possibility of reversible dementia was considered. Extensive examination revealed VB12 deficiency, and VB12 replacement therapy normalized the MMSE score to 25 points before surgery.

Significance of the results. When cognitive decline is observed in cancer patients, it is necessary to actively evaluate the serum levels of some B vitamins, including VB12.

Introduction

Cognitive decline and dementia represent problems in cancer treatment.

Patients with dementia are characterized as older, requiring longer periods of nursing care and longer hospital stays, and experiencing more physical dysfunction during hospitalization (Mukadam and Sampson, 2011). Patients with dementia experience many problems including shorter survival and higher mortality from non-cancer causes compared to patients without dementia (Raji et al., 2008), and 24.0% of patients with severe cognitive impairment die during hospitalization (Sampson et al., 2009).

However, there are some pathological conditions in which cognitive function can be expected to be restored by treatment. Such conditions are known as reversible dementia, one of these is vitamin B12 (VB12) deficiency (Ross and Bowen, 2002).

VB12 is a water-soluble vitamin required to maintain the blood and nervous systems (Green et al., 2017). Neurological impairment due to VB12 deficiency is wide-ranging, including motor sensory impairment, postural instability, and cognitive decline. In cases in which neurological impairment becomes severe, subacute combined degeneration of the spinal cord, dementia-like illnesses, and so on can occur (Grober et al., 2013; Hunt et al., 2014; Sechi et al., 2016). Treatment involves VB12 replacement (Devalia et al., 2014).

VB12 deficiency is by no means a rare condition in patients with gastrectomy (Hu et al., 2013). However, as far as we know, there have been no cases reported in which the cause of cognitive decline was investigated before cancer treatment, allowing the diagnosis and treatment of VB12 deficiency.

We studied a patient who was referred to the Department of Psycho-oncology on suspicion of cognitive decline prior to lung cancer surgery, and VB12 deficiency was identified. As a result of VB12 replacement therapy, cognitive dysfunction improved by the time of surgery.

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Case report

An 82-year-old woman was diagnosed with lung cancer and was briefed by a respiratory surgeon on her condition and surgery, but her understanding of the situation appeared to be inadequate. Therefore, the respiratory surgeon referred her to the outpatient clinic of the Department of Psycho-oncology for preoperative cognitive evaluation and surgical indication evaluation.

At the initial visit, the patient entered the consultation room with her family.

When the psychiatrist asked the patient why she came to the hospital and the name of the surgeon, she could not answer. Her confusion was recognized, as was her inability to answer the questions. A neuropsychological examination performed by a psychologist produced a Mini-Mental State Examination (MMSE) (Folstein et al., 1975) score of 19.

According to her family, the patient had suddenly become more forgetful and her appetite had begun to decline about 2 months previously.

Physical findings showed that she was 145 cm in height, 36.6 kg in weight with the BMI of 17.3, and no weight loss had been observed during 6 months before the initial visit.

Laboratory findings at the first visit to our center showed Hb 13.0 g/dL (reference range: 11.10–14.80 g/dL), Ht 39.4% (reference range: 35.10–44.40%), and high values for mean corpuscular volume (MCV) 110.4 fL (reference range: 83.60–98.20 fL) and mean corpuscular hemoglobin (MCH) 36.4 pg (reference range: 27.50–33.20 pg). No abnormalities were found in her liver or renal function, and no brain metastases were found on head MRI images.

As for the medical history, she had been diagnosed with rheumatoid arthritis 15 years previously and had continued to take salazosulfapyridine 1,000 mg. She was not receiving any H2 blockers or proton-pump inhibitors. No history of psychiatric disorders, or alcohol or drug abuse was noted. Further, she did not show any problems with interpersonal relationships prior to the cognitive decline.

As cognitive function had declined sharply in 2 months, it was judged important to identify the cause of the cognitive decline. Also, as her appetite was decreased and the store of vitamin B1 (VB1) in the body can be depleted in about three weeks (MacLean et al., 1983), and serum VB1 measurement was performed. In addition, based on the high MCV and MCH values, VB12 and folic acid were also measured. After the measurement, VB1 (100 mg) and VB12 (1,000 μg) were administered intravenously five times.

Three days after her initial visit to the Department of Psycho-oncology, her VB12 was found to be significantly reduced to 101 pg/mL (reference range: 180–914 pg/mL). Therefore, oral administration of cyanocobalamin at 750 μg/day was started. Her VB1 level was 24 ng/mL (reference range: 24–66 ng/mL) and folic acid was 4.1 ng/mL (reference range: 4.0 ng/mL or over), with both being within the normal range. The patient was negative for anti-gastric parietal cell antibodies.

Five days later, when the patient returned to the Department of Psycho-oncology, she understood that the reason for her visit was to receive treatment for a lung disease, and she was able to inform the medical staff about it. Her MMSE score was 22 points, which showed improved cognitive function from the previous test. According to her family, she was more talkative and was able to remember things from the day before that she used to forget.

Fifteen days after her initial visit, at her next examination at the Department of Psycho-oncology, she was able to talk about recent events in detail, and her facial expressions became richer. In addition, her MMSE score further improved to 25 points, which was within the normal range. Blood data also showed an improved hemogram, with MCV (101.0) and MCH (33.2) values falling to within the normal range.

At the subsequent psycho-oncological examination 23 days after her initial visit, she responded calmly to the questions from the psycho-oncologist with a smile, and there were no vague answers, with her remarking that "I can do things for myself," and her family reported an improvement in her daily life, such as help with her family's requests.

Her blood test at 26 days after the initial visit showed further improvement on hemogram with MCV (98.7) and MCH (32.6).

Twenty-nine days after the initial visit to the Department of Psycho-oncology, a thoracoscopic left lung partial resection was performed. No particular complications were observed after the operation, and no delirium was developed.

Oral administration of cyanocobalamin at 750 μg/day was continued after the operation.

A blood sample taken on the 15th day post-surgery showed normalized MCV (92.4) and MCH (30.6) values.

Three months post-surgery, her VB12 level was 878, MCV was 89.6, and MCH was 30.2, all within the normal range. No deterioration in cognitive function or change in mental status was observed. No notable gastroscopic findings were observed.

Discussion

VB12 deficiency was found as the cause of cognitive decline in a lung cancer patient referred to the Department of Psycho-oncology.

At her first visit to the Department of Psycho-oncology, the patient was unaware of the purpose of the visit, but VB12 replacement therapy allowed recovery to the point where the purpose of the treatment could be understood prior to surgery. Given the risks of perioperative management associated with cognitive dysfunction, there was a possibility of complications and inoperability during surgery without a diagnosis of VB12 deficiency. Therefore, in this case, the accurate diagnosis and treatment of VB12 deficiency was important for the efficient treatment of cancer.

The discovery of VB12 deficiency was triggered by abnormally high levels of MCV and MCH in addition to cognitive decline over a relatively short period of 2 months. However, Hb was within the normal range. Twenty-eight percent of patients with VB12 deficiency have been reported to have no anemia or macrocytosis (Lindenbaum et al., 1988) and a completely normal hemogram (Strachan and Henderson, 1965). As in the present case, VB12 should be measured and treatment should be started promptly for patients with high MCH and MCV levels or sudden cognitive decline of unknown cause, even if anemia is not observed.

In the present case, cognitive function recovered to a normal level by the administration of VB12.

In cognitive decline caused by VB12 deficiency (Ross and Bowen, 2002), MCV and MCH were found to return to the almost the normal range in conjunction with improvement in cognitive function, and VB12 was confirmed to be deficient at 150 pg/mL or less (Stabler, 2013). Therefore, it is considered that VB12 had an effect on the cognitive decline in this case.

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This case had never shown a similar cognitive decline. The patient was negative for anti-gastric parietal cell antibodies, and no administration of drugs such as H2 blockers or proton-pump inhibitors was observed. In addition, no notable endoscopic findings were observed. However, given the age of the patient, it cannot be ruled out that age-related decline in gastric acid secretion may have an effect (Krasinski et al., 1986).

Regarding vitamin deficiency in cancer patients, cases of VB1 deficiency are more common than those of VB12 deficiency (Isenberg-Grzeda et al., 2017). However, in this case, we only observed VB12 deficiency, with VB1 level at the lower limit of the normal range. We believe that the reason for this is that the VB12 deficiency of unknown cause led to cognitive decline and a decline in appetite, resulting in a decrease in her VB1 level.

The treatment for VB12 deficiency is the intramuscular injection of cobalamin (Devalia et al., 2014). In this case, VB1 deficiency was also suspected at the same time, so VB1 and VB12 were administered intravenously. However, as a decrease in VB12 was found 3 days after the initial diagnosis, an oral preparation having the same effect as the intramuscular injection was added (Wang et al., 2018). It is also reported that the intravenous administration of VB12 improved cognitive function (Kimoto et al., 2020).

In conclusion, if oncologists observe a cognitive decline in cancer patients, careful differential diagnosis, such as nutritional evaluation including some B vitamins, is required.

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