A Case with Hodgkin Lymphoma and Fronto-temporal Lobular Degeneration (FTLD)-like Dementia Facilitated by Chemotherapy

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We report a case of a 39-year-old man with Hodgkin lymphoma who developed depressive symptoms after starting adriamycin, bleomycin, vinblastine and dacarbazine chemotherapy and later exhibited sexual disinhibition in addition to cognitive dysfunction (mainly executive dysfunction). Seven months after the start of adriamycin, bleomycin, vinblastine and dacarbazine chemotherapy, he was finally diagnosed as having fronto-temporal lobular degeneration-like dementia facilitated by adriamycin, bleomycin, vinblastine and dacarbazine chemotherapy. At the time of writing, the patient’s condition has persisted for more than 6 months after the discontinuation of adriamycin, bleomycin, vinblastine and dacarbazine chemotherapy, and the changes in brain function brought on by the adriamycin, bleomycin, vinblastine and dacarbazine chemotherapy may now be irreversible. This case points to the importance of being attentive to the appearance of neuropsychiatric symptoms and evaluating brain functions properly when performing anti-cancer chemotherapy.

Key words: malignant lymphoma – chemotherapy – dementia – cognitive dysfunction – neuropsychiatric symptoms

INTRODUCTION

Anti-cancer chemotherapy is accompanied by various adverse events, and cognitive function impairment has been reported in some cancer patients who have received chemotherapy (1–5). In general, however, changes in cognitive function associated with chemotherapy are slight and temporary. Furthermore, to our knowledge, no other previous reports have addressed the topic of whether chemotherapy aggravates dementia progression. Here, we report the case of a 39-year-old man with Hodgkin lymphoma. The patient developed cognitive dysfunction (mainly executive dysfunction) and behavior abnormalities such as sexual perversion. An inspection of brain images revealed significant brain atrophy, confirming a diagnosis of fronto-temporal lobular degeneration (FTLD)-like dementia. The present case suggests that chemotherapy may cause executive dysfunction and/or dementia.

We obtained an oral consent from the patient’s family to report this case. Several items of personal information have been modified to preserve the anonymity of the patient.

CASE REPORT

A 39-year-old male patient who was married is described. Prior to any treatment, the patient had a mild and amiable personality. He did not have a family history of dementia. At 6 months prior to the start of chemotherapy, he developed an idiopathic fever and hemolytic anemia; the causes of these conditions were not determined even though the patient was hospitalized and examined at Hospital A. At 3 months prior to the start of chemotherapy, a brain computed tomography examination was performed as part of efforts to determine the cause of the patient’s fever; the imaging findings were within the normal limits at that time. Finally, he was
diagnosed as having malignant lymphoma (classical Hodgkin lymphoma, mixed cellularity) based on the results of a lymph node biopsy and chemotherapy was initiated. A total of four courses of the ABVD protocol (adriamycin, 40 mg; bleomycin, 15 mg; vinblastine, 10 mg; and dacarbazine, 400 mg; 1-month intervals) were performed over a period of 3 months. The patient gradually lost his vigor and began to converse less after the completion of the first course of chemotherapy. Although he spent more time lying down throughout the day, his condition had a circadian variation. A physician in the Internal Medicine Department of Hospital A diagnosed the patient as having a depressive state, and antidepressant medication (paroxetine, 10 mg/day) was begun 1 month after the start of chemotherapy. Since this treatment was not effective, the patient visited the outpatient clinic of the Psychiatry Department at Hospital A 2 months after the start of chemotherapy. The psychiatrist diagnosed the patient as having depression, since he exhibited obvious fatigue, reduced motivation, had been overeating and had hypersomnia. Despite the use of a sufficient dose of another antidepressant (milnacipran, 100 mg/day), the patient’s symptoms gradually worsened and he began to perform several bizarre actions (i.e. repetitive movements such as tapping a rhythm with both hands while lying down or reaching out as if to grab a piece of sushi). Although the chemotherapy allowed him to enter remission, he became irritable at 3 months after the start of chemotherapy. From this time on, he refused to attend any hospital consultations because of overwhelming fatigue, and he spent his entire day lying down, with the exception of mealtimes and smoking at his home.

At 4 months after the start of chemotherapy, the patient was introduced to the Psychiatry Department at Hospital B. On his first visit, he rarely talked voluntarily and he was uncooperative with the medical examination, although he exhibited an almost clear consciousness. During the visit, he moved to a bed without permission and fell asleep. The psychiatrist also diagnosed the patient as suffering from a depressive state at that time, even though the patient exhibited atypical symptoms. At 5 months after the start of chemotherapy, he was hospitalized in the Internal Medicine Department of Hematology at Hospital A so as to undergo a detailed inspection. However, he was discharged on the day of hospitalization after he performed several sexually deviant acts. The patient subsequently visited the outpatient clinic of Hospital B, where a cognitive functional disorder was suggested because his Mini-mental State Examination score was 23 at 6 months after the start of chemotherapy.

At 7 months after the start of chemotherapy, the patient was hospitalized in the Psychiatry Department at Hospital B for a thorough examination because his activity level had decreased remarkably (he lay in bed all day long and rarely bathed) and his abnormal behavior and psychotic manifestations, such as overeating (he had 5–6 meals per day), had persisted. Observations of the patient while he was hospitalized revealed severe fatigue, hypersomnia, fractiousness and a cognitive function disorder. In addition, he had no insight as to his disease, exhibited an obvious decrease in spontaneity, was unable to care for himself (he did not care about his personal hygiene or appearance), and exhibited personality changes such as sexual perversion (he unabashedly attempted to touch the bodies of female nurses on several occasions). On the other hand, his neurological findings were normal, and no blood test abnormalities were found. Encephalitis, other progressive degenerative diseases and paraneoplastic syndrome were ruled out during consultation with neurologists after a spinal tap and electroencephalography examination also yielded normal results. However, atrophy of the insular and orbitofrontal cortex was detected using brain MRI (Figs 1 and 2), and a decrease in the blood flow to the frontal lobe and near temporal lobe was revealed using cerebral blood flow single photon emission computed tomography. We diagnosed the patient as having FTLD-like dementia based on these imaging findings, the decrease in his social interpersonal skills, apathy and his unawareness of his disease.

Since his discharge from hospital, the patient’s case has been followed in the outpatient clinic for 6 months, but no change or improvement in the patient’s condition has been noted despite psychiatric and psychological treatment.

**DISCUSSION**

The present patient was a 39-year-old man who was diagnosed as having FTLD-like dementia after receiving anti-cancer chemotherapy. This patient was initially diagnosed as having depression after he began to receive chemotherapy for the treatment of Hodgkin lymphoma. However, several behavioral abnormalities, such as sexual deviation and cognitive dysfunction, subsequently appeared, and atrophy of the insular and orbitofrontal cortex was eventually confirmed by brain imaging.
FTLD typically causes dementia in the elderly. FTLD induces social conduct abnormalities and unique personality changes as well as executive dysfunction as a result of decreased function and atrophy of the frontal and frontotemporal lobes (6–8). In the present case, sexual disinhibition, significant apathy, lazy thinking, unawareness of his disease, a remarkable decrease in volition and amimia, a lack of concern for cleanliness and appearance, abnormal eating behavior and stereotypic behavior were observed. These symptoms are consistent with those caused by FTLD. Additionally, cognitive dysfunction (mainly executive dysfunction) was also observed in this case. The symptoms of FTLD usually progress gradually and unobtrusively. In the present case, however, the symptoms of dementia became apparent within several months after the start of chemotherapy, suggesting that the chemotherapy itself might have induced brain dysfunction, causing the symptoms of FTLD to become apparent.

RELATION OF CHEMOTHERAPY AND FTLD

Cognitive dysfunction after chemotherapy has been reported in some patients (2,4,5). Some evidence suggests that brain atrophy after chemotherapy is not necessarily rare. However, most cognitive dysfunction symptoms are transient (9). In one previous case report, however, obvious diffuse atrophy of the brain and a cognitive disorder appeared 2 years after the end of chemotherapy and persisted for at least 18 months (10). As far as we know, however, no previous reports have suggested that chemotherapy might advance brain atrophy of the insular and orbitofrontal cortex within a period of several months or that chemotherapy and FTLD might be related.

Some postulations regarding the mechanism of chemotherapy-induced cognitive dysfunction can be made, with a disturbance in the blood brain barrier, the failure of DNA repair and the dysregulation of immunoreactivity all being possible contributing factors (1). In addition, some reports have suggested the presence of a specific genotype that is susceptible to the influence of chemotherapy on cognitive function (11,12). However, much remains unknown, such as the incidence, risk factors and pathophysiology; furthermore, the optimal treatment also remains uncertain, and future research in this area is needed.

The present case suggests that chemotherapy may cause or accelerate atrophy in specific brain regions, leading to corresponding behavioral disorders and cognitive dysfunction.

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Conflict of interest statement

None declared.

References


Figure 2. Coronal and Axial T1-enhanced MR images. Significant atrophy of the insular cortex is visible.


