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Case Report
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Brain Tissue Selectively Attacked by Adult T-Cell Leukemia/Lymphoma Cells: A Case Report

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Abstract

We encountered an Adult T-cell Leukemia/Lymphoma (ATLL) patient with brain lesion without the involvement of any other organ. The patient exhibited amnesia, short-temper, and gait disturbance due to left hemiplegia. Brain Magnetic Resonance Imaging (MRI) revealed a broad edematous lesion in the right frontal lobe. Whole body examination by Computed Tomography (CT) demonstrated no other lesion except for the brain lesion. ATLL cells were not detected in peripheral blood. A tumor biopsy was conducted via craniotomy, and based on biopsy results; the patient was diagnosed with peripheral T-cell lymphoma positive for CD3 and negative for CD20 and EBV-encoded RNA. Human T-Lymphotropic Virus type 1 (HTLV-1) antibody was positive, and qualitative analysis of HTLV-1 proviral DNA, using DNA extracted from paraffin-embedded specimens, showed HTLV-1 positivity. Therefore, the patient was finally diagnosed with ATLL.

Keywords: Adult T-cell leukemia/lymphoma; Brain invasion; DNA; CD3; CT

Introduction

Adult T-cell leukemia/lymphoma is a refractory peripheral T-cell lymphoma with four clinical subtypes: acute, lymphoma, chronic, and smoldering type [1,2]. Human T-Lymphotropic Virus type 1 (HTLV-1) is a causative agent of ATLL [3]. In most cases, ATLL cells are detected in peripheral blood and/or multiple lymph nodes, and ATLL cells are generally positive for CD4 and CCR4 and negative for CD8 [4]. Cases in which patients present only with non-hematological organ lesions without ATLL cell proliferation the peripheral blood and lymph nodes are quite rare. However, brain invasion of ATLL cells is occasionally observed during chemotherapy in patients with acute and lymphoma type ATLL [5]. In such cases, cure becomes extremely difficult. Here, we report a rare case of ATLL with the brain as the primary target organ without the involvement of any other organ.

Case Presentation

A 74-year-old man was hospitalized due to amnesia, short-temper, and left hemiplegia. Brain Magnetic Resonance Imaging (MRI) revealed a broad edematous lesion with enhancement in the right frontal lobe (Figure 1). The tumor oppressed the anterior horn of the right lateral ventricle. Metastatic brain cancer was suspected, but no primary tumor was detected on systemic Computed Tomography (CT). Blood tests results showed no elevation of tumor markers or presence of

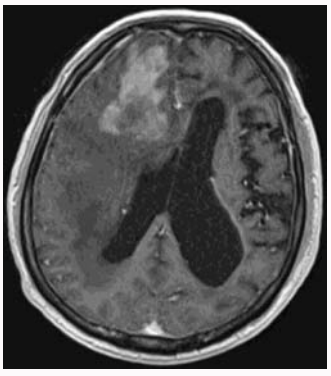

Figure 1: Brain magnetic resonance imaging showing.

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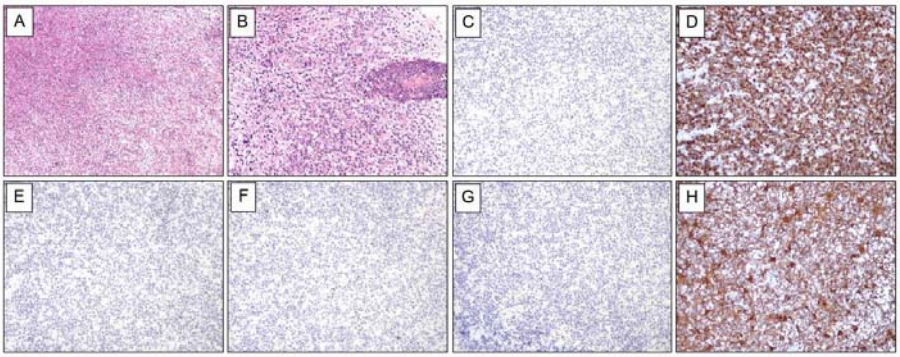

Figure 2: Hematoxylin-Eosin (HE) and immunohistochemical staining of the brain tumor specimen.
A: HE (x40); B: HE (x100); C: CD20 (x100); D: CD3 (x100); E: CD4 (x100); F: CD8 (x100); G: CCR4 (x100); H: GFAP (x100).

abnormal cells in the peripheral blood. A brain tumor biopsy was performed *via* craniotomy, leading to the diagnosis of peripheral T-cell lymphoma. He was transferred to our hospital for further examination and treatment. The lactate dehydrogenase and serum interleukin-2 receptor values on admission were 194 U/L and 744 U/mL, respectively. The biopsy samples were re-analyzed in our hospital; the lymphoma cells exhibited positivity for CD2 and CD3 but negativity for CD4, CD8, CD20, CD25, and CCR4 (Figure 2). Glial Fibrillary Acidic Protein (GFAP) staining was used for detecting astrocytes. Serological analysis revealed HTLV-1 antibody positivity. Polymerase chain reaction analysis using DNA extracted from formalin-embedded tumor biopsy samples was conducted by SRL Corporation (Tokyo, Japan) and revealed positive results for HTLV-1 proviral DNA. Based on the data of collecting from the previous hospital and our hospitals, he was diagnosed with ATLL involving a brain lesion as the primary target lesion without any other lesions.

One cycle of high-dose methotrexate and high-dose cytosine arabinoside therapy was administered with no effect. Mogamulizumab, an anti-CCR4 monoclonal antibody drug, was not used because the ATLL cells were negative for CCR4 (Figure 2). The patient and his family refused further treatment, including whole brain irradiation. He was transferred to another hospital for treatment with best supportive care.

Discussion

ATLL is a peripheral T-cell lymphoma; therefore, lymph nodes are the main sites for the proliferation of ATLL cells. However, ATLL is an aggressive lymphoma, and multiple invasions into other organs, such as the skin, liver, spleen, and lung, are often observed at diagnosis and during chemotherapy in acute and lymphoma type ATLL patients [6]. Brain invasion is observed occasionally after the initiation of chemotherapy. ATLL patients presenting with lesions in non-hematologic organs without ATLL cell proliferation in the peripheral blood and lymph nodes are rare. We previously reported a rare case of extensive and destructive invasion of ATLL cells into systemic muscular tissues [7]; this patient showed no ATLL cell proliferation in the peripheral blood and lymph nodes, as in the current case. The reason why ATLL cells only invaded non-hematologic organs in both patients is unclear. In the present case, pathological examination revealed positivity for CD2 and CD3 but negativity for CD4, CD8, CD25, and CCR4. Basically, ATLL cells are CD4-positive and CD8-netaive T-cells. Positive CCR4 and CD25 expression is observed in most ATLL patients. Therefore, our patient showed a different pattern of cell surface antigens compared to the majority of ATLL patients. This might be associated with the rare clinical target lesion in this patient. The patient's lactate dehydrogenase and serum interleukin-2 receptor levels on admission were 194 U/L and 744 U/mL, respectively, suggesting that the disease burden was not very high and that the proliferation speed was not so aggressive. This may be the reason for the lack of ATLL cell proliferation in the peripheral blood and lymph nodes. In our patient, it is possible that ATLL cells invaded the brain and proliferated slowly, evading the immune surveillance due to the blood-brain-barrier; finally, the cells formed a broad range lesion, leading to a lethal state. The blood-brain-barrier may also have contributed to chemotherapy resistance.

In summary, a rare ATLL case with only in brain involvement was reported. Although the ATLL cell characteristics were not very aggressive, the unfavorable lesion site assisted the ATLL cells in evading immune surveillance and contributed to chemotherapy resistance.

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