Case report
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# Paraneoplastic limbic encephalitis in a patient with non-Hodgkin's lymphoma

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*Paraneoplastic limbic encephalitis is uncommon neurological side effect of cancer in the absence of direct effect of primary tumor or metastasis, side effects of treatment or metabolic dysfunctions (6). Non-Hodgkin's lymphoma triggers such side effect very rarely. We present a case of a young adult with complete clinical course of non-Hodgkin's lymphoma with an episode of behavioral disturbances and MRI features which were pathognomonic for paraneoplastic limbic encephalitis.*

**KEY WORDS:** *Limbic Encephalitis; Lymphoma, Non-Hodgkin*

## INTRODUCTION

Paraneoplastic neurological syndromes (PNSs) present as remote neurological effects of cancer in which nervous system dysfunction develops without evidence of direct invasion of tumor into neural tissue or of infectious or vascular complications. PNSs occur in about 1% to 6% of all cancer patients. Almost all tumor types may be associates with PNSs, but small cell lung cancer (SCLC), thymoma, ovary and breast cancer are by far the most common. Testicular carcinoma, melanoma, and lymphoma are less likely to trigger the PNSs.

Paraneoplastic limbic encephalitis (PLE) is a rare disorder characterized by psychiatric symptoms, seizures, and short-term memory loss. Symptoms may precede the tumor diagnosis by some months. At least half of the patients harbor paraneoplastic antibodies.

## CASE REPORT

Twenty-two years old male patient (B.A.) was admitted to the hospital due to fatigue, night sweating, and enlargement of the neck and axillar lymph nodes. Biopsy of the left axillar lymph nodes revealed diffuse B cell lymphocytic non-Hodgkin's lymphoma (NHL) (REAL classification), and clinically disease was staged as IIIB. Induction chemotherapy with VI CHOP (doxorubicin hydrochloride [Adriamycin], vincristine sulfate, methylprednisolone, cyclophosphamide) followed by Mantle field irradiation resulted in complete remission of disease. One year later, the patient had an episode of Jacksonian seizure. Magnetic resonance imaging of the brain revealed meningeal infiltration at the interhemispheric and parasagittal frontal region on he left side (Figure 1a,b).

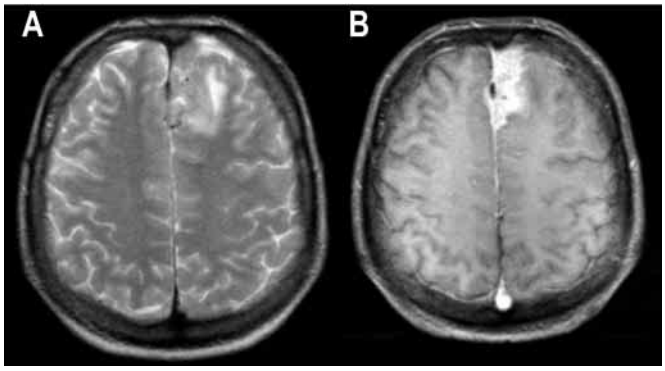


**Figure 1.** a) T2-w axial and b) correspondent T1 postcontrast axial image. NHL dural infiltration in the frontal parasagital region on the left side

Biopsy of the bilateral infiltration of the subcutaneous soft tissue of the thoracic wall at the level of ribs XI bilaterally revealed transformation of NHL in large B cell type. Therefore proMACEcytaBOM (prednisone, doxorubicin hydrochloride, etoposide, cytarabine, bleomycin sulfate, vincristine sulfate, methotrexate) chemotherapeutic regimen was introduced. During next few months the patient showed improvement with MRI proven complete disappearance of the abovementioned infiltration (Figure 2).

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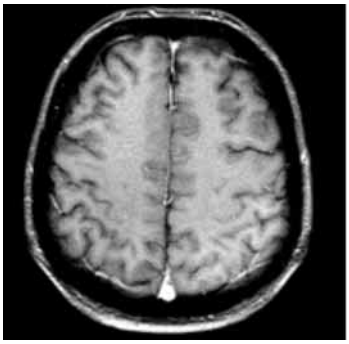

**Figure 2.** T1 postcontrast axial image. Complete remission of dural infiltration two months later

Three months later, the patient had an episode of spatial, temporal disorientation and disorientation towards the accompanying persons, and psychomotor agitation. Neurological examination revealed nuclear and peripheral facial paresis bilaterally, bilateral exophthalmus and mydriasis with poor reaction to light and with left pyramidal deficit. Due to signs of stasis of the optic nerve papilla, lumbar puncture was not performed. On the MRI of the brain, bilateral enlargement and T2-weighted high signal intensity of both hippocampi more pronounced on the right side, which were absent on previous MRI, were noticed (Figure 3A, B). In spite of antiedematous therapy symmetrical mild dilatation of the lateral ventricles was obvious.

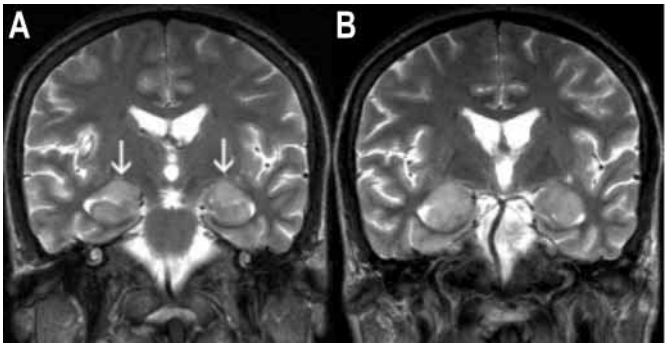


**Figure 3.** T2-w coronal images of hyppocampal gyri. Bilateral enlargement and diffuse high signal intensity of the head of both hyppocampal gyri and fimbria (arrows, A). Slight mass effect on lateral ventricles is evident. Mild dilatation of the lateral ventricles

Few months later, non-Hodgkin's lymphoma progressed with unconsciousness and deep central coma followed by death.

## DISCUSSION

The PNSs group is highly heterogeneous and includes the following syndromes: paraneoplastic limbic encephalitis, encephalomyelitis/sensory neuropathy, cerebellar degeneration, cancer-associated retinopathy, opsoclonus-myoclonus, stiff-man syndrome, syndromes affecting the neuromuscular junction, and paraneoplastic neuropathies. Etiology is most probably autoimmune mechanism while several antibodies against nervous system tissue in blood and cerebrospinal fluid (CSF) occur in many of the PNSs. They are highly specific for a paraneoplastic syndrome (if not always for a specific tumor) and important diagnostic tools. These antibodies also suggest the site of the underlying cancer (1). However, paraneoplastic disease may also occur in patients without antibodies, and in most of the syndromes the functional importance of the antibodies is unknown (2). It is not known whether the "absence" of antibodies is the result of a technical fault in detection or some paraneoplastic neurological disorders are not immune-mediates. Paraneoplastic antibodies are present in 50% of the patients with PLE (anti-Tr antibodies associated with Hodgkin's disease, anti-Hu with small cell lung carcinoma [SCLC], anti-TA with testicular carcinoma) (3). Pathologically, lymphocytic collections and degeneration of amygdaloid nuclei, hippocampi, and cingulate gyri were found.
Patients with PLE present personality changes, changes of emotional behavior, agitation, anxiety, and amnestic dementia (4). Amnesia has also been reported in association with Hodgkin's disease (1). MRI examination may be unremarkable during mild course of disease. T2-w high signal intensity may be present in the hippocampi and amygdala symmetrically (5,6). Involvement of the insular cortex and cingular gyri (also limbic structures) can be found in addition. Contrast enhancement of the affected regions is uncommon. The diagnosis is one of exclusion, and should not be accepted until metastatic and non-metastatic causes (direct effect of primary tumor or metastasis, side effects of treatment, infection, metabolic dysfunction, nutritional deficiency, coagulopathy) are ruled out. As the neurological symptoms herald the cancer in the majority of cases, a correct diagnosis may lead to earlier oncological treatment. Immunomodulatory therapy should, nevertheless, be initiated as early as possible and seems especially helpful for peripheral syndromes and limbic encephalitis (7,8). The recent fundamental advances in understanding of the autoimmune pathology of these disorders, especially the role of cytotoxic T cells, should eventually lead to more effective treatment options. Some patients may have effect of immunosuppressive therapy, particularly if there is a functional rather than irreversible neuronal damage. Plasmapheresis reduces the autoantibody titre, but does not lead to lasting clinical improvement. Symptomatic treatment may alleviate some of the patient's symptoms.

## CONCLUSION

Paraneoplastic limbic encephalitis is a very rare remote effect of cancer and far more uncommon in patients with non-Hodgkin's lymphoma. Emotional disturbances, agitation and short term amnesia along with typical MRI feature of bilateral hippocampal infiltrative enlargement, strongly support the diagnosis of PLE although the finding of paraneoplastic antibodies in blood or CSF is still mandatory.

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