Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Psychiatry

Paraneoplastic Encephalopathy with Psychiatric Presentation in a Patient with Lymphoma: A Case Report

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DOI: https://doi.org/10.36347/sjmcr.2025.v13i10.061 | **Received:** 25.08.2025 | **Accepted:** 10.10.2025 | **Published:** 22.10.2025

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Abstract | **Case Report**

Background: Paraneoplastic neurological syndromes (PNS) are rare immune-mediated complications of cancer that may present with atypical cognitive or psychiatric symptoms, particularly in hematologic malignancies. Early recognition remains challenging. ***Case presentation:*** We report a 58-year-old man with Hodgkin's lymphoma who developed generalized tonic–clonic seizures followed by an acute psychiatric syndrome characterized by persecutory delusions, disorientation, and agitation. Extensive investigations ruled out infectious, metabolic, and toxic causes. The findings were consistent with a probable paraneoplastic encephalitis, despite negative neuronal antibodies. ***Conclusion:*** This case highlights the importance for psychiatrists and clinicians to consider autoimmune and paraneoplastic encephalopathies in the differential diagnosis of acute psychosis and confusional states in oncology patients.

Keywords: limbic encephalitis; paraneoplastic syndrome; lymphoma; acute psychosis; autoimmune encephalopathy; neuroimmunology.

INTRODUCTION

Paraneoplastic neurological syndromes (PNS) are rare, immune-mediated complications of malignancy that occur independently of direct tumor invasion or metastasis of the nervous system. They are most frequently associated with small-cell lung carcinoma and hematologic malignancies [1]. PNS may involve the central or peripheral nervous system and can manifest as isolated psychiatric symptoms such as mood disturbances, psychosis, or delirium [2]. Among them, paraneoplastic limbic encephalitis (PLE) represents a well-defined clinical entity characterized by inflammation of limbic structures—particularly the hippocampus and amygdala—resulting in memory impairment, seizures, and psychiatric manifestations [3,4]. Diagnosis can be difficult, especially in antibody-negative cases, which are frequent in lymphoma-associated forms [5]. We present the case of a patient with Hodgkin's lymphoma who developed an acute psychiatric syndrome in the context of a presumed autoimmune encephalopathy.

CASE PRESENTATION

A 58-year-old man, married and father of two, had been followed since 2014 for Hodgkin's lymphoma. His medical history included type 2 diabetes, well controlled on oral agents.

He was admitted to the clinical hematology department for a generalized, non-febrile rash, which was rapidly complicated by generalized tonic–clonic seizures without any identifiable trigger. Within a few days, he developed abnormal behavior with psychomotor agitation, incoherent and obscene speech, and episodes of aggressive anger.

Psychiatric assessment

- Difficult contact, marked anxiety, and mobile facial expression
- Temporal and spatial disorientation
- Impaired anterograde memory
- Incoherent speech with interpretative persecutory delusions
- No hallucinations reported, but false recognitions present
- Fluctuating level of consciousness

Investigations

- **Brain MRI and CT:** Normal; no limbic lesion or mass effect

- **EEG:** Diffuse slowing with right-predominant cerebral dysfunction
- **CSF analysis:** Clear fluid; lymphocytic pleocytosis (23 cells/mm³), normal protein and glucose levels
- **Peripheral blood immunophenotyping:** Clonal proliferation of mature T lymphocytes, no blasts
- **Viral serologies, multiplex PCR, GeneXpert, and neuronal antibodies (anti-Hu, anti-Ma2, anti-NMDAR, anti-GAD65, anti-AMPAR, etc.):** All negative
- **Liver, renal, glucose, and electrolyte panels:** Within normal limits
- **Toxicology screen:** Negative

Given these findings, the diagnosis of probable paraneoplastic encephalopathy associated with Hodgkin's lymphoma was retained.

DISCUSSION

The emergence of acute psychiatric symptoms in a cancer patient warrants careful consideration of organic etiologies, particularly when accompanied by cognitive impairment, confusion, or neurological signs. In this case, persecutory delusions, agitation, and anterograde amnesia suggested limbic system involvement, characteristic of autoimmune or paraneoplastic encephalitis.

Psychiatric presentations of paraneoplastic encephalitis

Initial psychiatric manifestations may include [6,7]:

- Mood disorders or manic symptoms
- Acute delusional states with paranoid or mystical content
- Aggressive or disinhibited behavior
- Thought disorganization or incoherent speech
- Transient auditory or visual hallucinations

In the study by Kayser and Dalmau [8], approximately 70% of patients with autoimmune encephalitis were initially managed for a primary psychiatric disorder. Differentiation from primary psychosis (e.g., brief psychotic disorder) can be difficult; warning signs include age > 40 years, subacute onset, neurological abnormalities, or unusual resistance to antipsychotics.

Diagnostic Framework

The Graus *et al.,* criteria (1) emphasize that diagnosis can rely on clinical and paraclinical evidence even without detectable antibodies, provided the following are present:

1. A known malignancy
2. Progressive neurological symptoms developing within 3 months
3. Compatible MRI, EEG, or CSF findings

In our patient, lymphocytic pleocytosis, EEG abnormalities, and rapid progression supported a paraneoplastic etiology, despite normal MRI and negative antibody assays.

Pathophysiology

The underlying mechanism involves immune cross-reactivity: antibodies or T cells generated against tumor antigens react with shared neuronal antigens, leading to autoimmune CNS damage [9]. In T-cell lymphomas, cytotoxic T-cell–mediated mechanisms may predominate, explaining the absence of detectable serum antibodies [10].

Management

Psychiatrists play a crucial role in identifying atypical psychiatric manifestations of PNS. Management is multidisciplinary and includes:

- Treatment of the underlying malignancy
- Immunotherapy (corticosteroids, intravenous immunoglobulins, rituximab, or plasmapheresis)
- Cautious psychiatric management (low-dose antipsychotics to limit neurological side effects)
- Neurocognitive monitoring during follow-up

Prognosis depends primarily on early diagnosis and effective oncologic control.

CONCLUSION

This case emphasizes the importance for psychiatrists to recognize the warning signs of paraneoplastic or autoimmune encephalopathies, especially in immunocompromised or lymphoma patients. An acute psychotic or confusional state should not be hastily attributed to a primary psychiatric disorder in oncological settings. Early multidisciplinary collaboration between psychiatry, neurology, and oncology is essential to optimize patient outcomes.

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