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Research article

# Autoimmune neurological syndromes associated limbic encephalitis and paraneoplastic cerebellar degeneration

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## HIGHLIGHTS

- This study conducted that 7 patients (5 limbic encephalitis, 2 paraneoplastic cerebellar degeneration) diagnosed with autoimmune neurological syndrome were retrospectively examined.
- All patients had abnormal brain imaging. Five patients had typical involvement of the bilateral mesiotemporal region on FLAIR and T2 sequences. Two patients had cerebellar degeneration.
- One of patientshad anti-GABAR B1 positivity. Tumors were detected in 2 patients while investigation for paraneoplasia screening. Early diagnosis and treatment are of paramount importance.
- We some results very different in literature. One of patients with LE presented first attack neuro-Behçet's syndrome. One of patients with LE first presented parotid adenoma. One of patients first presented nasopharenx adenocarcinoma.

## ARTICLE INFO

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## ABSTRACT

*Introduction:* Autoimmune neurological syndrome is a group of disorders caused by cancer affecting nervous system by different immunological mechanisms. In this study, we aim to study the clinical symptoms, cerebrospinal fluid (CSF) findings, autoantibody tests, computed tomography (CT), magnetic resonance imaging (MRI) signs and treatment outcome of patients with autoimmune syndromes.
*Methods:* In this study, 7 patients (4 male, 3 female) diagnosed with autoimmune neurological syndrome were retrospectively examined.
*Results:* Five of patients were diagnosed with limbic encephalitis, two of them were paraneoplastic cerebellar degeneration. Confusion and seizure were the most seen symptoms. Two patients had psychiatric disturbances (28,5%) followed by seizure. Headache was seen in 2 patients (% 28,5), disartria in 1 patient (% 14,2), and gait disorder in 2 patients (28,5%). The duration of symptoms was 46 (3–150) days on average. CSF abnormalities were detected in 2 patients. CT and MRI of the brain was available in all patients. Five patients had involvement of mesiotemporal region, two patients had diffuse cerebellar atrophy. One of patients had anti-GABAR B1 positivity. Tumors were detected in 2 patients while investigation for paraneoplasia screening.
*Conclusion:* Remission is only possible with the detection and treatment of the malignancy. Early diagnosis and treatment are of paramount importance.



## 1. Introduction

Autoimmune neurological disorders of central nerve system (CNS) can be paraneoplastic and non-paraneoplastic. Paraneoplastic autoimmune neurological syndrome is a group of disorders caused by cancer affecting nervous system by different immunological mechanisms which are independent of metastatic process, metabolic or drug side effects. Limbic encephalitis (LE) is among the common autoimmune neurological disorders. Limbic system is a center that comprises hippocampal formation, septal region, cingulate gyrus, parahippocampal gyrus, indusium griseum, amygdaloid complex, and mammillary body; it regulates memory, emotional responses, self-protection, sleep, appetite, anger, fear, sexual behavior and motivation functions. LE is a dysfunc-

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tion of this system's due to inflammation, and characterized by antegrade amnesia, psychiatric symptoms such as, anxiety, depression, personality disorder and hallucinations, as well as seizures [1]. Mostly characterized by subacute symptoms, LE particularly locates mesiotemporal region and is most commonly secondary to small cell carcinoma of lung. Paraneoplastic cerebellar degeneration (PCD) is characterized by rapid cerebellar Purkinje cell death. It is a rapidly progressive disease with acute or subacute onset.

The diseases diagnosed with clinical signs and symptoms, cerebrospinal fluid (CSF) examination, computed tomography (CT), magnetic resonance imaging (MRI), and autoimmune antibody screening; early diagnosis and treatment may control the disease. In this study the clinical, laboratory, and radiological examinations of 7 patients diagnosed with autoimmune neurological syndrome (5LE, 2 PCD) were evaluted and reviewed literature.

## 2. Methods

The medical records of 7 patients diagnosed with autoimmune neurological syndrome at Sakarya University Training and Research Hospital between 2011 and 2015 were retrospectively examined. We investigated all patients with encephalitis, infectious causes were excluded. The study did not include patients who were suspected diagnosed autoimmune neurological syndrome but no certain results and observation following the alteration of events. Age, sex, premorbid disorders, symptoms, tumour markers (CEA, CA-125, Ca19-9, AFP, PSA, fPSA), results of laboratory CSF examinations (glucose/simultaneous blood glucose, protein, sodium, chloride, culture, herpes simplex virus polymerase chain reation (HSV PCR), autoantibodies (anti-Hu, Anti-Yo, anti-Ri, anti-CV2, anti-Ma, anti-amphiphysin, anti-NMDA-R, anti-AMPA-1, anti-AMPA-2, anti-CASPR-2, anti-LGI-1, anti-GABAR B1), CT, MRI results, and treatment protocols were analyzed. All patients were performed tumour screening (pap smear samples for women, abdominal and urinary ultrasonography, thorax CT, bone sintigraphy and body fluorodeoxyglucose positron emission tomography (FDG-PET).

## 3. Results

Our study involved a total of 7 patients, of whom 4 were male and 3 were female. The mean age of the study population was 40,8 (range 27–60 years) years. Table 1 presents the main characteristics of the patients (Table 1).

Three patients had seizure as the admission symptom. Of these, 2 had post-ictal confusion. One patient had psychiatric symptoms that started 5 months prior to seizure. The other 2 patients had agitation and restlessness following seizure. Apart from these, 2 patients had headache, in one of whom speech disorder accompanied headache. One patient had apathy, disorientation, and gait disturbance, another patient had gait disorder and speech difficulty.

Two patients had no history of systemic disease. One of these patients was 39-week pregnant. One patient had a history of Behçet's disease and smoking; one patient was a smoker and alcoholic, two patients had only a history of smoking. One patient had hypertension.

The duration of symptoms was 46 (3–150) days on average.

All patients had normal tumor marker levels that were studied as part of the investigation process for a paraneoplastic condition. One patient had positive Anti-GABAR B1 antibody as autoantibody.

CSF examination revealed normal biochemical and cellular findings in 5 patients. Two patients had pleocytosis, one of them having also elevated protein level. All patients had negative CSF culture and HSV PCR.

**Table 1**
Main characteristics of patients.

| | Sex | Age | Duration of symptom (day) | Symptom | Premorbid Disease | CSF | Autoantibody | CT/MRI | Treatment |
|---|---|---|---|---|---|---|---|---|---|
| I | M | 36 | 3 | disorientantion, gait disorder | Behçet, smoke | N | – | Bilateral mesiotemporal | IVMP + IVIg + cyclophosphamide |
| II | F | 37 | 35 | headache, disatria | – | N | – | Cerebellar atrophy | Excision of mass |
| III | F | 34 | 3 | seizure, pyschiatric symptom | Smoke | N | – | Bilateral R > L mesiotemporal, amigdala, frontal | IVMP + IVIg |
| IV | F | 27 | 150 | headache, confusion, pyschiatric symptom | – | Pleocytosis +elevated protein | – | Bilateral R > L temporal insula, frontal, parietal | IVMP + IVIg |
| V | M | 36 | 4 | seizure, confusion | Smoke | N | NA | Bilateral mesiotemporal | IVMP |
| VI | M | 56 | 7 | seizure, confusion, psychiatric symptom | HT | Pleocytosis | Anti-GABAR B1(+) | Bilateral Limbic region | IVMP + IVIg |
| VII | M | 60 | 120 | Speech difficulty, gait disorder | Smoke, alcohol | N | – | Cerebellar atrophy | IVIg |

M: Male, F: Female, HT: Hypertension, DM: Diabetes, Mellitus, N: Normal, NA: Not avaliable.