DOI:10.4274/tnd.81542
Turk J Neurol 2015;21:127-30



# Rasmussen's Encephalitis: A Case Report and Literature Review

## *Rasmussen Ensefaliti: Olgu Sunumu ve Literatürün Gözden Geçirilmesi*

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**Summary**

Here we present a case of a woman aged 23 years with a 10-year history of uncontrolled partial epilepsy with right-sided motor seizures, accompanied by a progressive weakness of the right side of the body of one-year duration. Magnetic resonance imaging revealed marked atrophy of the left cerebral cortex with ex-vacuo dilatation of the ipsilateral lateral ventricle. In view of the prolonged history of refractory right-sided partial motor seizures, right hemiparesis, and left-sided brain atrophy on imaging, a possibility of 'adult-onset Rasmussen's encephalitis (RE) was considered. RE is characterized by intractable focal onset seizures, namely epilepsia partialis continua, and deterioration of functions associated with the affected hemisphere, such as hemiplegia and progressive cognitive deterioration, in the majority of cases. It is common in children aged under 10 years with average age of disease onset at around 6 years, but it is uncommon in adults; the adult variant accounts for only about 10% of cases.

**Keywords:** Rasmussen's encephalitis, seizures, hemiparesis, cognitive deterioration

**Öz**

Bu sunumda bir yıldır kontrol altına alınamayan parsiyel nöbetler ve progresif sağ hemiparezi nedeni ile başvuran 23 yaşında bir kadın hasta sunulmaktadır. Hastanın beyin manyetik rezonans incelemesinde sol serebral kortikal atrofiye eşlik eden ipsilateral lateral ventrikülde ex-vacuo dilatasyon izlenmiştir. Sağ hemiparezi, beyin atrofisi ve refrakter parsiyel motor nöbetleri nedeni ile hastada erişkin başlangıçlı Rasmussen ensefaliti (RE) tanısına ulaşılmıştır. RE, hastaların çoğunda epilepsia parsiyalis kontinua, etkilenen hemisfere ait işlevlerde bozulma ve bilişsel yıkım ile seyretmektedir. Her ne kadar ortalama 6 yaşta ve daha çok on yaşın altındaki çocuklarda izlense de nadiren erişkinlerde de ortaya çıkabilmektedir. Erişkin başlangıçlı olgular tüm olguların %10'unu oluşturmaktadır.

**Anahtar kelimeler:** Rasmussen ensefaliti, epileptik nöbet, hemiparezi, bilişsel yıkım

## Introduction

Rasmussen's encephalitis (RE) is characterized by intractable focal onset seizures, namely epilepsia partialis continua (EPC), and deterioration of functions associated with the affected hemisphere, such as hemiplegia and progressive cognitive deterioration, in the majority of cases.

## Case Report

A woman aged 23 years who was right-handed and illiterate presented to our clinic with a 10-year history of uncontrolled partial epilepsy with right-sided motor seizures accompanied by a progressive weakness of the right side of the body, which began 1 year ago. At presentation, she reported that she had repeated

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**Received/Geliş Tarihi:** 12.07.2014 **Accepted/Kabul Tarihi:** 12.02.2015

episodes of abnormal movement of the right side of her body that involved both her upper and lower limb and face for 2 days. There was no associated loss of consciousness, or bowel or bladder incontinence.

She first became symptomatic with seizures when she was aged 13 years. The seizures started with a focal jerking of her right upper limb, which spread to the right lower limb and face. These episodes were sometimes associated with loss of consciousness and jerking movement of all 4 limbs (20-30% of the time). The seizure frequency increased from the initial one or two episodes per month to almost daily over the last one and a half years. During this period the patient had been treated with multiple antiepileptic drugs (phenytoin, carbamazepine, clobazam, sodium valproate, and phenobarbitone) with good compliance. In the last year she had also developed a mild, persistent motor weakness of the right half of her body. Motor weakness was further aggravated for several minutes to hours following each seizure episode.

On examination at the time of presentation, the patient's vitals were maintained and general physical and systemic examination was unremarkable. She was conscious and oriented to time, place, and person. Higher mental functions and language were normal and there were no frontal cortical release signs. The cranial nerve examination was normal. She had a right side hemiparesis with increased tone and grade 4+ limb power. Deep tendon reflexes were brisker on the right side and planters were bilaterally extensor. There were no cerebellar or extrapyramidal signs.

The clinical investigation, which included routine parameters such as hemogram, blood sugar, electrolytes, liver, kidney function tests and lipid profile were normal. Special investigations including anti-nuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) were performed to rule out cerebral vasculitis and these were also negative. Chest X-ray and electrocardiogram (ECG) were normal. On reviewing her imaging, the first computerized tomography (CT) scan performed on the patient 10 years ago at the onset of seizures was normal. A CT scan was undertaken on this admission and this was also essentially normal. Magnetic resonance imaging (MRI) taken at the time of admission revealed marked atrophy of the left cerebral cortex with ex-vacuo dilatation of the ipsilateral lateral ventricle. There was no evidence of contrast enhancement or calcification. The posterior fossa structures were normal (Figure 1). The electroencephalograph (EEG) that was performed on this admission showed diffuse slowing in the range of 8-9 hertz, with left temporal spike discharges.

In view of the prolonged history of refractory right-sided partial motor seizures, right hemiparesis, and left-sided brain atrophy on imaging, a possibility of 'adult-onset RE was considered. After admission, midazolam infusion was required for seizure control. Levetiracetam and carbamazepine was used to control seizures. Intravenous Ig could not be given because the patient could not afford the treatment. On discharge, the patient was referred for neurosurgical consultation and intervention.

## Discussion

RE is a chronic brain disease of unknown etiology that causes drug-resistant focal epilepsy, EPC and progressive neurologic deficits.

RE is a disease of childhood. Rasmussen et al. (1) first described this entity in 1958 in three patients with intractable focal seizure activity caused by a chronic, progressive encephalitis. The etiology of RE has been the subject of debate ever since it was first described. Humoral auto-antibodies like anti-GluR3 and a viral etiology have been proposed but with a lack of conclusive evidence (2). A cytotoxic T cell-mediated immune reaction against neurons with astrogliosis has recently been proposed as the cause (3).

The onset of disease is insidious, which makes it a difficult entity to diagnose. The mean age of presentation is between 6 and 8 years, and these children have typically had a normal course of development. They present with focal motor seizures, although generalized seizures have also been noted. After varying time intervals, patients develop progressive loss of motor function, which may culminate into frank hemiplegia. Cognitive deterioration, visual field deficits, buccofacial apraxia, and aphasia are seen when the dominant lobe is affected and neglect can be observed when the non-dominant hemisphere affected (4).

In our patient, the age of disease onset was 13 years and hence it falls into the category of adult-onset RE, which has been described, but is seen in only about 10% of cases. The adult form of Rasmussen's is less malignant with slower progression and has less severe neurologic deficit hemiparesis; hemispheric atrophy is also less pronounced in patients with the adult form. Patients may develop visual field defects, neglect or aphasia because the lesions

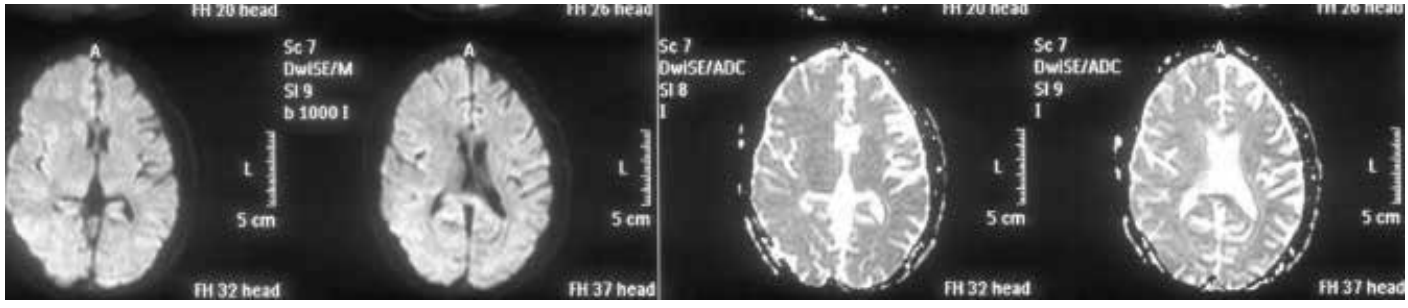


**Figure 1.** Magnetic resonance imaging showing atrophy of the left ventricle with ipsilateral ventricular dilation and atrophy of the caudate nucleus. Calcification and gliosis were absent

**Table 1. Diagnostic criteria for Rasmussen's encephalitis. Rasmussen's encephalitis can be diagnosed if either of the three criteria in part A or two out of three criteria of part B are present. Check first for the features of part A. In addition, if no biopsy is performed, magnetic resonance imaging with administration of gadolinium and cranial computerized tomography need to be performed to document the absence of gadolinium enhancement and calcifications to exclude the differential diagnosis of a unihemispheric vasculitis**

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|---|---|
| Part A | 1. Clinical focal seizures (with or without epilepsia partialis continua) and unilateral cortical deficits<br>2. EEG: Unihemispheric slowing with or without epileptiform activity and unilateral seizure onset<br>3. MRI: Unihemispheric focal cortical atrophy and at least one of the following:<br>Grey or white matter T2/FLAIR hyperintense signal<br>Hyperintense signal or atrophy of the ipsilateral caudate head |
| Part B | 1. Clinical epilepsia partialis continua or progressive* unilateral cortical deficit(s)<br>2. MRI progressive* unihemispheric focal cortical atrophy<br>3. Histopathology T cell dominated encephalitis with activated microglial cells (typically, but not necessarily forming nodules) and reactive astrogliosis.<br>Numerous parenchymal macrophages, B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE |

MRI: Magnetic resonance imaging, RE: Rasmussen's encephalitis, EEG: Electroencephalograph

occur more frequently in posterior areas (5,6). In our patient, the disease progressed over a 10-year period culminating in hemiatrophy with hemiplegia, but no visual field defect, neglect or aphasia.

The clinical diagnostic criteria for RE were proposed by Derry et al. (Table 1). In our patient, all the three criteria were present from part A, which comprises focal seizures with EPC and unilateral cortical deficits in the form of hemiplegia, unihemispheric EEG slowing, and focal cortical atrophy with atrophy of ipsilateral caudate nucleus in brain MRI (7,8). Hence, the diagnosis of RE was suspected. The differential diagnosis of stroke, cerebral vasculitis, multiple sclerosis, Creutzfeldt-Jakob disease and subacute sclerosing panencephalitis were considered, but were ruled out on the basis of history, laboratory investigations, and the absence of associated characteristics in MRI and EEG findings.

Clinically, the evolution of the disease progresses through three stages. There is an initial non-specific prodromal stage, during which patients have rare seizures and minimal neurologic deterioration. This is followed by an acute stage, which corresponds to a period of severe seizure occurrence. The neurologic deterioration becomes manifest by progressive hemiparesis, hemianopia, cognitive deterioration, and if the language dominant hemisphere is affected, aphasia occurs. Finally, a residual stage, during which the seizure frequency decreases significantly and patients develop permanent neurologic deficits such as hemiparesis (6,9). Our patient had had hemiparesis for one year with occasional seizures, consequently she appeared to be in the residual stage.

The proposed MRI diagnostic criteria for RE include unihemispheric focal cortical atrophy and at least one of the following: grey or white matter T2/FLAIR hyperintense signal; hyperintense signal or atrophy of the ipsilateral caudate head; and progressive unihemispheric focal cortical atrophy on serial MRI studies (7). Our patient's initial radiologic investigation, which was performed at the time of seizure onset, was normal but a recent MRI revealed marked atrophy of the left cerebral cortex with ex-vacuo dilatation of the ipsilateral lateral ventricle. Absence of gadolinium enhancement on MRI and a largely normal CT scan excluded the possibility of any calcification and unihemispheric vasculitis. Although a brain biopsy is needed for absolute diagnosis, our patient was not willing to undergo the procedure.

Treatment of RE remains a challenge. The aim of therapy should be to control seizures and arrest disease progression. Seizures in these patients are usually refractory to antiepileptic drug treatment. Though many combinations have been tried, none have been approved as standard. Seizures were controlled in our patient with levetiracetam and carbamazepine. Immunotherapy with corticosteroids, IVIG, and plasma exchange have all been tried in adult-onset RE in different studies but none have shown consistent results to allow approval (10,11,12). Our patient could not afford IVIG or plasma exchange.

Surgery has played a major role in the management of seizure therapy since 1950. Anatomic and functional hemispherectomy are highly effective in achieving seizure freedom and at present, it offers the only means to prevent disease progression. The post-surgical seizure freedom rates range between 62.5% to 85%, but hemiparesis and language dysfunction are complications (13). Our patient was recommended neurosurgical treatment and was referred for the same to a larger centre.

## Conclusion

RE is rare disease entity and should be suspected in any patient with refractory seizures and progressive unihemispheric cortical atrophy with motor deficit. Its recognition is important because early and timely intervention with surgery can improve patient outcomes.

**Informed Consent:** Consent form was filled out by all participants, **Concept:** Deepak Jain, **Design:** Deepak Jain, H. K. Aggarwal, **Data Collection or Processing:** Anshul Mittal, Sunil Pawar, Rajpal Verma, **Analysis or Interpretation:** Deepak Jain, H. K. Aggarwal, **Literature Search:** Anshul Mittal, Sunil Pawar, **Writing:** Deepak Jain, Anshul Mittal, Sunil Pawar, **Peer-review:** Externally peer-reviewed, **Conflict of Interest:** No conflict of interest was declared by the authors, **Financial Disclosure:** The authors declared that this study has received no financial support.

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