Dear Editor,

Rasmussen’s encephalitis (RE) was first described in 1958 by Rasmussen[1] and his colleagues as a very rare and chronic neurological disorder characterized by unilateral cerebral inflammation. Although diagnostic criteria have been framed [Table 1], the definite underlying pathophysiology is yet to be elucidated. Immunological mechanisms are postulated most consistently[2] but an association with other chronic epileptogenic pathologies has also been described. We present a case report of an adult-onset Rasmussen’s encephalitis with immunological pathology along with focal cortical dysplasia and hippocampal sclerosis.

A 30-year-old gentleman presented with history of right focal motor seizures without loss of consciousness since the past 8 years. He was initially treated with anti-epileptic drugs with good seizure control and occasional breakthrough seizures (once in a few months, despite treatment). Thereafter, he discontinued treatment 4 years back following which he started having daily seizures and also developed behavioral changes. He became disinhibited and started using obscene words and gestures, had episodes of violent outbursts, and occasionally had urinary incontinence without embarrassment.

He presented to us at this time with multiple seizures per day and was found to have motor aphasia with perseveration, right sided grade 1 spasticity in limbs with 4/5 power (on MRC scale) with hyperreflexia and extensor planter. Left sided examination was normal. A neuropsychological assessment was suggestive of profound intellectual impairment and social maladaptation, functionally equivalent to a 1.5-year-old child. A clinical possibility of RE was considered and magnetic resonance imaging (MRI) of the brain revealed left hemispheric atrophy with head of caudate and putamen involvement, and dilatation of frontal horn of ipsilateral lateral ventricle [Figure 1a]. Electroencephalogram (EEG) was suggestive of left frontal predominant spike and wave discharges [Figure 1b]. The patient fulfilled the diagnostic criteria of RE and therapeutic options of plasma exchange and hemispherotomy were explained to the family members. Five cycles of plasma exchange were done (surgery refused) following which his seizure frequency decreased to 1–2 per week; but his right-sided weakness and behavioral issues persisted. All three complaints started increasing again after 2 months and the patient presented with epilepsia partialis continua (EPC) 4 months later. He was treated with additional pulse steroids and intravenous immunoglobulins and repeat MRI Brain was suggestive of increased atrophy in the left perisylvian region, left caudate and putamen. EEG showed discharges localized predominantly to the left frontal lobe. Positron Emission Topography-Computed Topography (PET-CT) also localized to left frontal and opercular region. Thereafter, the patient underwent a functional left hemispherotomy with left temporal lobectomy and the histopathological examination revealed loss of neurons in the pyramidal layer and granular layer of

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**Table 1: Diagnostic Criteria for Rasmussen’s encephalitis**

| PART A (ALL THREE) | PART B (two of three) |
|-------------------|-----------------------|
| 1. Clinical: Focal seizures (with or without epilepsy partialis continua) and unilateral cortical deficits | 1. Clinical: Epilepsia partialis continua or progressive* unilateral cortical deficits |
| 2. EEG: Unihemispheric slowing with or without epileptiform discharges | 2. MRI: Progressive* unihemispheric focal cortical atrophy |
| 3. MRI: Unihemispheric focal cortical atrophy and at least one of the following: | 3. Histopathology: T cell-dominated encephalitis with activated microglial cells typically, but not necessarily, forming nodules and reactive astrogliosis; numerous parenchymal macrophages, B cells, or plasma cells or viral inclusion bodies exclude the diagnosis of Rasmussen’s encephalitis |

Grey or white matter T2/FLAIR hyperintense signal

Hyperintense signal or atrophy of the ipsilateral caudate head

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**Figure 1:** (a) MRI Brain demonstrating left hemispheric atrophy (predominantly perisylvian, caudate and putamen). (b) EEG showing 3.5–4 Hz spike and wave discharges and polyspikes localized to the left frontal lobe
temporal lobe with concomitant ischemic changes and cortical dyslamination suggestive of focal cortical dysplasia (FCD) type IIa with hippocampal sclerosis [Figure 2a-d].

There was marked reduction in the seizure frequency post-operatively but the patient had a residual right-sided weakness with a seizure frequency of 1–2 per week on antiseizure drugs. This particular combination of RE with FCD along with hippocampal sclerosis is very rare and has not been reported to our knowledge. Our case highlights a new plausible clinicopathological association of RE.

RE is characterized by drug resistant focal epilepsy and progressive neurological and cognitive deterioration. It usually affects children and young adults and is rare, with an incidence of 2.4 cases per 10 million aged 18 years or younger.[3,4] Typical symptoms consist of a prodrome of infrequent seizures (prodromal stage) followed by frequent ones, and progressive hemiparesis (active stage) and if untreated, cognitive decline and hemianopia with the spread of the pathology.[2] Refractory focal status epilepticus occurs in around 50% of patients.[3] Rare manifestations include chorea, dystonia[6] and progressive neurological deficit sans seizures.[7,9] Although, the exact pathophysiology is debatable, histopathological examination demonstrating cortical inflammatory cells (T lymphocytes), neuronal loss, gliosis and microglial nodules is the gold standard for diagnosis.[10] MRI Brain characteristically demonstrates unilateral hemispheric atrophy with atrophy of caudate.[10] However, it needs to be differentiated from other unihemispheric epileptic syndromes like cortical dysplasia, tuberous sclerosis and Sturge-Weber Syndrome. There is no definitive cure, with immunotherapy reported to halt the progression of disease temporarily and the only palliative option being surgeries like functional hemispherectomy and hemispherotomy. Their opportune timing is still under debate.[2]

Association between RE and other causes of chronic drug-resistant conditions is known but is a rare finding. The same was first reported in 1996 by Yacubian et al.[11] in a 7-year-old girl with concomitant FCD. Subsequently various other studies have reported an association with other conditions like tuberous sclerosis, tumours (Ganglioglioma, Astrocytoma) and vascular malformation.[12] The most common association has been reported with FCD (especially Type I) with a reported prevalence of around 10%.[13] Only one case of triple pathology has been reported which was in a 27-year-old male with late-onset Rasmussen’s encephalitis in association with old ischemic changes and Type II FCD.[14] Various possible explanations have been proposed for the association between RE and other structural abnormalities with one particular mechanism being that alterations in the blood–brain barrier leading to infiltration of pathogenic antibodies and subsequent development of RE.[13] Another plausible reasoning is that continuous seizure activity in RE may lead to dysplastic neurogenesis resulting in cortical dysplasia.[13] Interestingly in the study done by Takei et al.[13] involving 7 patients, there was co-occurrence of concomitant pathologies in all 7 cases, leading them to propose that the same is underappreciated and requires more careful pathological studies. Most of the cases had no previous suspicion of a dual pathology based on pre-operative neuroimaging and the same was only elucidated on biopsy, underlining the importance of the same. Nevertheless, the association between two rare chronic epilepsy pathologies appears not to be by chance and might have implications for elucidating underlying mechanisms, definitive treatment and surgical procedures.[13]

In our particular case, clinic-radiological definitive Rasmussen’s was associated with FCD type IIa and hippocampal sclerosis. Careful pathological examination of operated RE cases might lead to further identification of similar cases and might lead to better understanding of this scarcely understood rare chronically progressive debilitating entity.

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Conflicts of interest
There are no conflicts of interest.

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Figure 2: Histopathological specimen. (a) H and E stain from hippocampus, shows loss of neurons and ischemic changes in neurons at pyramidal layer. (b) Neu-N immunostain highlights the dispersion of neurons at pyramidal layer. (c) Neu-N immunostain highlights the cortical dyslamination of neurons and loss of neurons with ischemic changes. (d) GFAP immunostain highlights the supial gliosis

[1,2]
Once again, he received injections and his vision improved partially to 6/36. Seven months later, he again developed ataxia, dysarthria, and headache. Brain imaging was repeated and showed a contrast enhancing well-demarcated lesion in the brain. He was treated with intravitreal triamcinolone. Vision improved partially to 6/36 and 15 days later ataxia and diplopia developing over a week. A 46-year-old man presented at another centre with headache. A provisional diagnosis of primary CNS lymphoma with corticosteroid necrosis—a diagnosis of cytomegalovirus (CMV) retinitis was made at another centre and was treated with valacyclovir and intravitreal triamcinolone. Vision improved partially to 6/36 completely. Three months later, he developed complete vision loss in the right eye over 1 week. He had features of retinal necrosis—a diagnosis of CMV retinitis was made at another centre and was treated with valacyclovir and intravitreal triamcinolone. Vision improved partially to 6/36.

No other tests were performed as the patient recovered. A 55-year-old man presented with ataxia and dysarthria. Headache started on intravenous methylprednisolone followed by a short course of oral prednisolone with which his symptoms resolved. A 46-year-old man presented at another centre with headache. A provisional diagnosis of primary CNS lymphoma with corticosteroid necrosis—a diagnosis of CMV retinitis was made at another centre and was treated with valacyclovir and intravitreal triamcinolone. Vision improved partially to 6/36.

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