RASMUSSEN ENCEPHALITIS - A CASE REPORT
GANESHTHANGAMUTHUKUMAR KALYANASUNDARAM
Department of General Medicine,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract:
Rasmussen Encephalitis is a rare, immune mediated disease characterized by refractory seizures, progressive neurological dysfunction and unilateral hemispheric atrophy. This disorder typically involves a single cerebral hemisphere, affecting mainly children and adolescents. We report a case of Rasmussen Encephalitis in a young girl who was admitted with complaints of recurrent focal motor seizures involving right upper and lower limbs for the past 5 years. There was a progressive increase in the seizure frequency and severity despite adequate drug compliance. Patient also developed weakness of right upper and lower limbs for the past 2 years which is insidious in onset and gradually progressive in nature. There was history of progressive cognitive decline in the form of difficulty in memorizing events and difficulty in doing calculations for the past 2 years. In 2003, patient had the first episode of seizure at the age of 12 years, initially diagnosed as seizure disorder and was treated with antiepileptic drugs. Patient was asymptomatic for 2 years. For the past 5 years, there was a progressive increase in the seizure frequency and severity which compromised even her schooling and made her to become confined to home despite adequate drug compliance.

Keyword : Partial Seizures, Rasmussen Encephalitis

CASE REPORT:
A 19 year old girl was admitted with presenting complaints of recurrent focal seizures involving the right upper and lower limbs for the past 5 years without loss of consciousness or post ictal confusion. There was history of difficulty in speaking with decrease in fluency with relevant content for the past 2 years. Patient also developed weakness of right upper and lower limbs for the past 2 years which is insidious in onset and gradually progressive in nature. There was history of progressive cognitive decline in the form of difficulty in memorizing events and difficulty in doing calculations for the past 2 years. In 2003, patient had the first episode of seizure at the age of 12 years, initially diagnosed as seizure disorder and was treated with antiepileptic drugs. Patient was asymptomatic for 2 years. For the past 5 years, there was a progressive increase in the seizure frequency and severity which compromised even her schooling and made her to become confined to home despite adequate drug compliance.

Patient’s antenatal and birth history were uneventful. Developmental milestones were attained normal as per the age during childhood. Patient was born of non consanguineous marriage as the first child and has 2 younger sisters. No similar illness among her siblings.
Menarche was attained at the age of 13 years with regular cycles and normal flow. On Examination, there was no evidence of Neurocutaneous markers. Her vitals were stable. Central Nervous System examination showed MMSE score of 20/30, memory disturbances involving both immediate and recent memory, acalculia, expressive dysphasia and dysgraphia. Cranial nerve examination was normal.

Motor system revealed right sided hemiparesis – Upper Motor Neuron type with power of 3/5 MRC grading. Plantar was extensor on right side (Babinski’s sign). Sensory system, Cerebellum and Autonomic nervous system were normal. Palmomental reflex was present on right side. Spine and cranium were normal. Cardiovascular, respiratory and abdomen examination were normal. Complete hemogram, Renal Function Test and Liver Function Test were normal. HIV-ELISA was Negative. Rheumatologic evaluation was Normal. ECG and Chest X ray were normal. CSF Analysis was normal.

CT BRAIN - 2003
CT Brain Imaging done during the first episode in 2003 was normal. Repeat CT Brain in 2005 showed mild sulci prominence in left temporoparietal region.

MRI Brain in 2008 showed T2 hyperintensity in left frontal and perisylvian region not suppressed by FLAIR with sulci prominence in left temporoparietal region.
CT BRAIN - 2010
CT Brain in 2010 showed prominence of sulci involving the entire left cerebral hemisphere with dilatation of left lateral ventricles suggestive of left hemispherical atrophy. EEG showed bilateral epileptiform discharges with diffuse slowing of waves during the interictal period. Both the clinical presentation and Brain imaging showed the classical features of Rasmussen Encephalitis, one of the rare causes of refractory partial seizures.

Our case was diagnosed as Rasmussen Encephalitis and because of its spontaneous remission in some patients and high risk of post operative neurological deficits, definitive neurosurgical intervention like hemispherectomy or hemispherotomy which would give the patient, a permanent cure from her symptoms was deferred. Our patient was treated with a combination of 5 antiepileptic drugs (T.Phenytoin, T.Valproate, T.Carbamazepine, T.Gabapentin and T.Clobazam) as per Neurologist’s opinion and has been on regular follow up in the Neurology Department.

Discussion:
Rasmussen Encephalitis also known as Rasmussen Syndrome is a progressive immune mediated inflammatory disease of the brain affecting the cerebral cortex. It is named after the Neurosurgeon Theodore Rasmussen (1910–2002), who served as the Head of the Montreal Neurological Institute, and as Neurosurgeon-in-Chief at the Royal Victoria Hospital [6]. The disease starts at one site in one cerebral hemisphere and spreads to the adjoining areas on the same side. Typically, it spares the opposite cerebral hemisphere. Rasmussen Encephalitis is most often diagnosed in children below 10 years of age. However, it can also affect adolescents & adults.

ETIOLOGY:
Rasmussen Encephalitis is a rare disease that should be envisaged as sporadic, since there is no evidence for a genetic component [1, 4]. Rasmussen Encephalitis is an autoimmune disorder. Most patients have circulating antibodies against the nerve protein called the Type – 3 Glutamate Receptor (GLUR-3) [7]. The trigger for the abnormal immune response is still unclear, may be due to viral infection as suggested by Rasmussen or bacterial. But this is no longer thought to be the case [9]. Recently, antibodies against NMDA Type Glutamate Receptor subunit Glu receptor 2 (anti NR2A antibodies) are reported in patients with Rasmussen Encephalitis [8].

PATHOGENESIS:
Both humoral and cell mediated mechanisms play a role in the pathogenesis of Rasmussen Encephalitis. Auto – antibodies directed against GLUR- 3 Receptor cause over-excitation of the glutamate receptors resulting in excitotoxicity of the neurons. In addition, Cytotoxic CD-8 cells attack the neurons containing MHC – 1 molecule causing apoptosis of the neurons.
causing progressive cerebral atrophy. Typically, one hemisphere is affected, the exact mechanism being still unclear. Though the other cerebral hemisphere is typically unaffected, there may be mild atrophy due to Wallerian degeneration of the commissural fibers. Epileptiform discharges can be seen in the opposite hemisphere during the interictal period but not during the ictus.

CLINICAL FEATURES:
The most common presentation is focal seizures. The nature of seizures depends on the part of the hemisphere which is involved, most commonly simple partial motor seizures. At times, the seizures become continuous and hence termed as Epilepsia Partialis Continua. Secondary generalization of seizures can also occur causing loss of consciousness. As the disease progresses, the seizures become more frequent, more severe and more refractory to anti epileptic drugs.

Neurological deficits usually occur which is progressive in nature, and the type is determined by the area of the brain affected. Contralateral hemiparesis, hemisensory loss, speech disturbances, homonymous hemianopia, memory disturbances, cognitive dysfunction and other neuropsychological deficits may be present.

DIAGNOSIS:
The diagnosis of Rasmussen Encephalitis rests on clinical, electrophysiological (EEG) and morphological studies (MRI, in some cases histopathology). In most chronic patients (i.e after a disease duration of >1 year), differential diagnoses are few. The particular challenge, however, is the early recognition of the disease, i.e. before progressive hemi atrophy and progressive loss of neurological functions is evident. Early diagnosis is desirable \(^2,3\) as immunosuppressive therapy may be most effective at this time.

At present, there is no specific laboratory test to detect Rasmussen Encephalitis. Even the detection of antibodies against GLUR-3 is neither specific nor sensitive. CSF analysis is done mainly to rule out CNS infections. EEG shows multifocal ictal discharges with slowing of background activity in the affected hemisphere during the ictus. In the interictal period, bilateral epileptiform discharges with diffuse slowing occurs. CT scan done in early cases may be normal. As the disease progresses, unilateral hemispherical atrophy will be present. MRI Brain shows hyper intense T2 / FLAIR signals in acute stages in the affected area. Typically, Gadolinium enhancement is never seen in the affected area. The Gold Standard test to diagnose Rasmussen Encephalitis is Brain Biopsy which shows perivascular cuffing with inflammatory T Cells, microglial nodules, neuronal loss and gliosis in the involved hemisphere. Presence of B cells, plasma cells and viral inclusion bodies virtually excludes the diagnosis of Rasmussen Encephalitis.

DIAGNOSTIC CRITERIA FOR RASMUSSEN ENCEPHALITIS \(^2\) : PART A:
· CLINICAL: Focal seizures with or without Epilepsia Partialis Continua and unilateral cortical deficits.
· EEG: Unihemispheric slowing with or without epileptiform activity and unilateral seizure onset.
· MRI: Unihemispheric focal cortical atrophy and at least one of the following:
  1. Grey or white matter T2/FLAIR hyperintense signal.
  2. Hyperintense signal or atrophy of the ipsilateral caudate head.
PART – B: CLINICAL: Epilepsia Partialis Continua or Progressive unilateral cortical deficit(s). MRI: Progressive unihemispheric focal cortical atrophy. HISTOPATHOLOGY: T cell dominant encephalitis with activated microglial cells and reactive astrogliosis. Numerous parenchymal macrophages, B cells or plasma cells or viral inclusion bodies exclude the diagnosis of Rasmussen Encephalitis.

Rasmussen Encephalitis can be diagnosed if either all three criteria of Part A or two out of three criteria of Part B are present.

MANAGEMENT:
Treatment of Rasmussen Encephalitis pursues two goals: alleviation of the seizure disorder and cessation of the progressive neurological deficit and associated loss of brain tissue. The seizures in Rasmussen Encephalitis often do not improve with anti-epileptic drugs and the disease usually ends with the destruction of the affected cerebral hemisphere. Hence, surgery either hemispherectomy or hemispherotomy becomes the standard treatment. Epilepsy surgery has played a major role in seizure treatment of Rasmussen Encephalitis since the 1950s. It remains the only 'cure' of the disease progression, but not without neurological deficit. Examination of histopathological specimens from surgery permits the identification of the encephalitic nature of the disease. Surgical intervention carries a high risk of post operative neurological deficits and even recurrence if done incompletely.

Many trials are still ongoing regarding the use of immune modulators like corticosteroids, immunosuppressive drugs, IVIg and Plasmapheresis for the treatment of Rasmussen Encephalitis. Intravenous immunoglobulin is found to be effective both in the short term and in the long term, particularly in adults where it has been proposed as the first-line treatment. There is still no good data regarding the dosage, duration and combination of immunotherapy. Immunotherapy also carries serious side effects particularly in children and requires careful monitoring.

REFERENCES:


