University Journal of Medicine and Medical Specialities

ISSN 2455- 2852 2020, Vol. 6(2)

RASMUSSENS ENCEPHALITIS - A CASE REPORT

PRASANTHA KUMAR G GURUSARANM
Department of Paediatrics, GOVERNMENT MOHAN KUMARAMANGALAM MEDICAL COLLEGE

Abstract : CASE HISTORY A 3 year old boy presented with status epilepticus, aphasia and right hemiparesis. On evaluation he was found to have atropy of left cerebral cortex on MRI and Unilateral slowing and epileptiform activity on left side in EEG. He was diagnosed to have RE as per EUROPEAN CONSENSUS STATEMENT. INTRODUCTION RE is a chronic progressive, inflammatory disease of the brain affecting one hemisphere. The characteristic feature inclue Epilepsia Partialis Continua, hemiparesis, congnitive disturbances and speech disturbances. ETIOLOGY It is of unknown etiology. The postulated hypothesis include direct viral insult, primary autoimmune injury and immune response secondary to viral infection. DIAGNOSIS The diagnostic criteria as proposed by European consensus statement 2005 has primary and secondary criteria. The primary criteria includes Clinical (partial seizures and unilateral neurological deficits), MRI(unilateral focal cortical atropy and T2FLAIR hyperintense signal or atropy of head of caudate nucleus) and EEG (Unilateral slowing with or without epileptiform activity, unilateral ictal onset).The Secondary criteria includes Clinical (EPC or progressive unilateral neurological deficit), MRI (progressive unilateral focal cortical atrophy) and Histopathology (T-lymphocyte dominated encephalitis with activated microglial cells and reactive astrogliosis.TREATMENT The various treatment modalities include anticonvulsants, physiotherapy, immunotherapy, plasmapheresis, Monoclonal antibodies and surgical procedures like functional hemispherectomy.

Keyword : Rasmussens encephalitis(RE), Epilepsia Partialis continua(EPC), hemiparesis.

Introduction:

Rasmussens Encephalitis (RE) also called Rasmussens Syndrome is a rare progressive and inflammatory disease of the brain affecting one hemisphere. RE was originally described by Theodore Rasmussen in 1958. Rasmussen`s Encephalitis is associated with intractable focal epilepsy-leading to Epilepsia Partialis Continua, cognitive decline, speech abnormalities and hemiparesis. The age of onset is in children below 10 years of age. It can also start in adolescence and adulthood. RE is rare disorder and affects one person in every 5,00,000 to 10,00,000. We report this case of RE from our hospital.

CASE REPORT:

A 3 Year old boy was brought by his mother to paediatric c ausualty with focal tonic clonic seizures involving right side of the body which was sudden in onset and lasted for about an hour. There was no history of fever, rash, unconsciousness or vomiting. Before admission he was well and developmentally normal. Birth history was unremarkable with a developmentally normal elder sibling The child was stabilized and treated for status epilepticus. He was transferred to PICU and was started on Phenytoin infusion and seizures got controlled. Second episode of right focal tonic clonic seizures occurred on the next day and was treated with Phenobarbitone infusion.

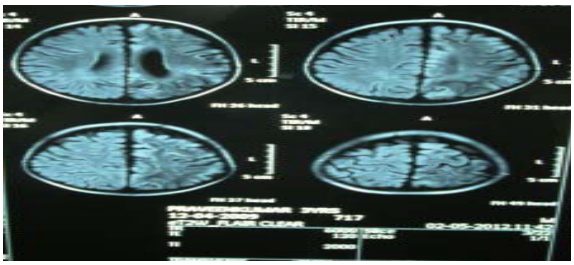
CHILD WITH RASMUSSEN`S ENCEPHALITIS SHOWNG RIGHT SIDED FACIAL WEAKNESS

Clinical examination revealed a developmentally normal conscious child with right hemiparesis and upper motor type facial weakness. Child was aphasic. Rest of cranial nerve examination was normal. Fundoscopy was also normal. The deep tendon reflexes were exaggerated on right side with extensor plantar response. Examination on left side was normal. Gait was hemiplegic. There were no extrapyramidal, meningeal or cerebellar signs. Examination of other systems were normal.

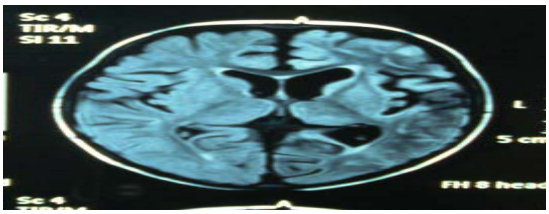
1)Investigations: Hematological and Biochemical investigations were normal.
2)CSF analysis was also normal.
3) Coagulation profile was normal.
4) X-ray chest and Mantoux test were normal.
5) Urine metabolic screening was found to be negative.
6) ECG and Echocardiogram were normal.

7)EEG was taken which showed unilateral slowing with epileptiform activity on Left hemisphere.
8) CRP and ANA were negative.
9) Serum fasting Lipid profile was normal.

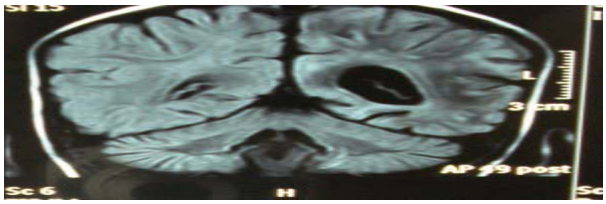
MRI STUDY OF THE BRAIN:

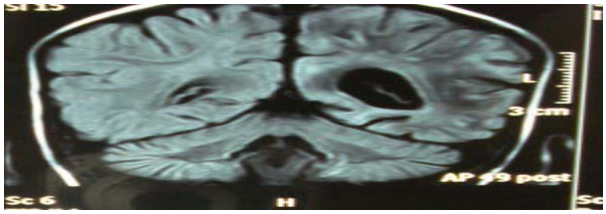


T2W/FLAIR MRI IMAGE SHOWING LEFT CEREBRAL HEMIATROPHY AND HYPERINTENSE SIGNAL IN THE LEFT CORTEX



FLAIR MRI IMAGE SHOWING LEFT CEREBRAL HEMIATROPHY AND MINIMAL ATROPHY OF CAUDATEFLAIR IMAGE SHOW-





ING PROMINENT
SULCI AND HYPERINTENSE SIGNAL IN CORTEX

This patient was diagnosed to have RE as he had all the primary criteria of European Consensus Statement (discussed later). Course in the hospital: The child was treated with oral Phenytoin and Phenobarbitone. The child was started on Physiotherapy. He was registered in Paediatric Neurology clinic and he is on regular follow-up. Counselling: The parents were counseled about the disease.

DISCUSSION:

Rasmussen`s Encephalitis (RE), a rare chronic inflammatory disease of the brain affecting one hemisphere was first described by Theodore Rasmussen in 1958. RE is associated with intractable focal epilepsy, cognitive decline and hemiparesis. The age of onset is in childhood between 6 and 8 years (1-13 years), affects healthy child. Both sexes are equally affected. The disease starts as focal seizures and sometimes as status epilepticus, Epilepsia Partialis Continua(EPS) which is a purely motor status epilepticus. Polymorphic seizures may occur in Rasmussen Encephalities which include somatosensory, motor, visual and psychomotor seizures. The disease leads to cognitive, motor and visual defects. Typically, the central cortex is affected earlier in the disease process, followed by frontal, parietal, the hippocampus and the amygdala. The disease process affecting dominant lobe causes cognitive deterioration, visual field defect, buccofacial apraxia and aphasia. Seizures may be the predominant clinical picture followed by hemiparesis.

Etiology and pathogenesis:

The etiology remains unknown. Three hypothesis have been proposed:
a) direct viral insult
b) autoimmune process triggered through a viral agent
c) a primary autoimmune process

In biopsies, there is cortical inflammation with perivascular lymphocytic cuffing, gliosis with microglial activation and microglial nodules, as well as astrocytes and neurons loss have been noticed. Research to identify autoantibodies in the etiology of Rasmussen`s encephalitis is going on . Histology showing a predominance of cytotoxic T lymphocytes supports their role as the mediator of damage and apoptotic neuronal death. Now the autoimmune hypothesis is accepted as the etiology of RE.

1) The clinical course of the disease is divided by Oguni et al (into 3 stages).

Stage-1 correlates to the development of seizures. Seizures are simple partial in nature and the frequency and intensity progressively increase.

Stage-2 is characterized by fixed hemiparesis and intellectual decline.

Stage-3 is marked by stabilization of the disease with decrease of seizure activity. 2) A similar 3-stage model by Bien et al proposes the Prodromal stage with low frequency of seizures and moderate hemiparesis, if present. The second stage, acute stage is charecterised by augumentation in frequency of seizures, often Epilepsia Partialis Continua. The final, residual stage presents with fixed but irreversible mostly severe hemiparesis and decrease in frequency of seizures.

3) Bien et al. also proposed a 5-stage model based on Magnetic Resonance Imaging (MRI). In this model the chronology is median of the minimal and maximal duration of each stage is expressed in months.

NUCLEUS FLAIR IMAGE SHOWING PROMINENT SULCI AND HYPERINTENSE SIGNAL IN CORTEX

This patient was diagnosed to have RE as he had all the primary criteria of European Consensus Statement (discussed later). Course in the hospital: The child was treated with oral Phenytoin and Phenobarbitone. The child was started on Physiotherapy. He was registered in Paediatric Neurology clinic and he is on regular follow-up. Counselling: The parents were counseled about the disease.

STAGING BASED ON MRI FINDINGS (Bien et al)

STAGES	VOLUME	T2/FLAIR SIGNAL	CHRONOLOGY
I	NORMAL(SUBCLINICAL PRESENTATION)		NOT ASSESSABLE
II	OEDEMA	INCREASED	0.3-12.3
III	NORMAL	INCREASED	2.1-22.6
IV	ATROPHY	INCREASED	4.6-103.8
V	ATROPHY	NORMAL	NOT ASSESSABLE

CLINICAL VARIANTS:

In contrast to classical RE, there are a few clinical variants.

1. Late onset of Rasmussen`s encephalitis:

In 10% of cases the encephalitis starts after the age of 12 -13 years. It has a insidious onset, with predominantly involving the occipital lobe during the initial phase. In late onset for of RE the prodromal phase is characterized by discrete hemiparesis and a longer prodromal phase. The patient may suffer from visual field defects due to involvement of posterior areas.

2. Bilateral hemispheric involvement:

In very young children (< 2 years),the blateral involvement leads to fatal outcome. This type of presentation is rare.

3. Rasmussen`s encephalitis with basal ganglia involvement:

In this subset the patients present with dystonia, choreiform movements or other hyperkinetic movements. Major MRI changes are seen in the caudate nucleus or putamen which shows progressive atrophy.

Diagnosis:

RE is diagnosed from electroencephalogram (EEG), MRI and histological features. EUROPEAN CONSENSUS STATEMENT has adapted the diagnostic criteria proposed by Bien et al.

	Primary criteria	Secondary criteria
Clinical	Partial seizures & neurological deficit	Epilepsia partialis continua or progressive unilateral neurological deficits
MRI	Unilateral focal cortical atrophy -T2/FLAIR hyperintense signal -atrophy of ipsilateral head of the caudate nucleus	Progressive unilateral focal cortical atrophy
EEG	Unilateral slowing with or without epileptifor activity, unilateral ictal onset	
Histology		T-lymphocytes dominated encephalitis with activated microglial cells and reactive astrogliosis.|

If all the primary criteria are present the diagnosis is very likely. If not then two out of three secondary criteria must be present. Among all criteria for diagnosis, the major finding is monohemispherical aspect. In beginning the EEG shows slowing and multiple epileptogenic anomalies in the same hemisphere.

In MRI, hyperintense signals in the white matter of the affected hemisphere and cortical swelling are seen, followed by cortical atrophy which most often starts in the perisylvian and central area or in the late-onset cases in the posterior cortices. Other imaging techniques are positron emission tomography or single photon emission computed tomography shows changes confined to one hemisphere. Cerebrospinal fluid analysis shows inconsistent finding of elevated cell count, protein and oligoclonal bands. Thus CSF is not diagnostic requirement.

DIFFERENTIAL DIAGNOSIS:

1) Unispheric epileptic syndromes: cortical dysplasia, stroke,Tuberous sclerosis, Struge webers syndrome, Hemiconvulsion-hemiplegia-epilepsy syndrome.

2) Epilepsia partialis continua due to metabolic disorders: Diabetes, renal or hepatic encephalopathy.

3) Metabolic and degenerative progressive neurologic disease: MELAS and mitochondriopathies

4) Inflammatory and infectious disease: cerebral vasculitis in systemic connective tissue disease, Unisphereic cerebral vasculitis mimicking rasmussens encpephalitis, subacute sclerosing pan encephalitis, multiple sclerosis.

TREATMENT:

Rasmussen`s encephalitis is highly pharmacoresistant in more than 80% of cases. AED's have little or no effect on partial seizures and EPC, but they reduced the risk of generalized seizures, so AED's are recommended throughout the disease.

1)IMMUNOMODULATORY TREATMENT:

The treatment includes steroids, immunoglobulins, plasmapheresis and immunosuppressive therapy. Studies show that high dose steroid pulse therapy produce only transient result(4,5).When started earlier in the course of the disease, they produce better response(4) Compared to steroids, 0immunoglobulins are better tolerated. Variable results were reported(5,6,7). The rationale behind this therapy is introducing natural antibodies that counteract patient antibodies. Plasmapheresis have been implicated in removing circulating antibodies or other inflammatory factors which damage the brain(8). Among immunosuppressive therapy,Cyclophosphamide was tried, with no major effect(9) Granata et al compared the efficacy of different immunomodulatory treatment(9). It was proposed that steroids have higher efficacy when they are used in early course with childhood onset and during acute aggravations. In case of late onset RE, Ig ,alone or in combination of corticosteroids may be used. Bien et al proposed Tacrolimus(10), which when used showed less cerebral hemiatrophy and less hemiparesis. Rituximab, a monoclonal antibody directed against the glycoprotein CD20 of B lymphocytes, which when used allowed the reduction of EPC. But it has no effect on hemiparesis(11).

2)SURGICAL TREATMENT:

The surgical approach for RE, is anatomical hemispherectomy carried on earlier. Currently functional hemispherectomy and its variants are preferred frequently. A recent study evaluated the outcome of children who benefited from hemispherectomy. Among Rasmussen syndrome 65% were seizure free, 26% had minor seizures and only 9% were left out without significant benefit. The studies by Pulsifier et al(12) focused on cognitive outcome in larger population of Rasmussen`s encephalitis patients. Overall, surgery preserves the cognitive abilities of the patient.

Bibliography:

1) Rasmussen`s encephalitis, created 05/2003 Last updated 07/2005.by Dr.Ian Hart,senior lecturer in neurology, Neuroimmuology group,university department of neurological science.Lower lane,LIverpool.

2)Rasmussens encephalitis: An overview- Mayowa owolabi,university of Ibadan,Nigeria.

3) Rassmussens Encephalitis: an update by Laurent sheybani,Karl schaller,Margitta seeck 2011.

4)Chinchilla D,Dulac O, Robain O, Plouin P, Ponsot G, Pinel JF, Graber D, -Reappraisal of Rasmussens`s syndrome with special emphasis on treatment with high doses of steroids.J Neurol Neurosurg Psychiarty 1994;57:1325-33.

5)Hart YM, Cortez M, Andermann F, Hwang P, Fish Dr, Dulac O, et al. Medical treatment of Rasmussen`s syndrome (chronic encephalitis and epilepsy); effect of high-dose steroids or immunoglobulins in 19 patients.Neurology 1994;44:1030-6.

6) Leach JP, Chadwick DW, Miles JB, Hart IK. Improvement in adult-onset Rasmussen's encephalitis with long-term immunomodulatory therapy. Neurology. 1999;52(4):738–42.

7)Leach JP, Chadwick DW, Miles JB, Hart IK. Improvement in adult-onset Rasmussen's encephalitis with long-term immunomodulatory therapy.Neurology. 1999;52(4):738–42.

8) Wise MS, Rutledge SL, Kuzniecky RI. Rasmussen syndrome and long-term response to gamma globulin. Pedi-atr Neurol. 1996;14:149–52.

9)Granata T, Fusco L, Gobbi G, Freri E, Ragona F, Broggi G, et al. Experience with immunomodulatory treatments in Rasmussen's encephalitis.Neurology. 2003;61(12): 1807–10.

10)Bien CG, Gleissner U, Sassen R, Widman G, Urbach H, Elger CE. An open study of tacrolimus therapy in Rasmussen encephalitis. Neurology. 2004;62(11):2106–9.

11)Thilo B, Stingele R, Knudsen K, Boor R, Bien CG, Deuschl G, Lang N.A case of Rasmussen encephalitis treated with rituximab. Nat Rev Neurol.2009;5(8):458–12) Pulsifer MB, Brandt J, Salorio CF, Vining EP, Carson BS, Freeman JM.The cognitive outcome of hemispherectomy in 71 children. Epilepsia. 2004;45:243.