Rasmussen's Encephalitis in Children: A Case Report

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Abstract:
Rasmussen's Encephalitis (RE) is one form of chronic and progressive focal encephalitis of children presented with intractable epilepsy and progressive neurologic deficits. The cause of the disease is still unknown but thought to be an immunological disorder following a viral infection. Brain imaging is one of the best tools for diagnosis. We presented a case of Rasmussen's encephalitis.

Key words: *Rasmussen's Encephalitis (RE)*

Introduction:
Rasmussen's Encephalitis (RE) was first described by Theodore Rasmussen in 1958 about its clinical and pathological characteristics[1]. RE is one of the rare chronic progressive focal inflammatory lesions in the brain of unknown etiology clinically manifested as refractory epilepsy, progressive motor and cognitive deterioration. Epileptic activity of RE is thought to be responsible for the neurocognitive decline of the patients.[2] Exact incidence of this disease is yet not clearly calculated however it is estimated 2.4 per 10^7 people d" 18 year.[3] Brain imaging plays an important role for the diagnosis of RE, MRI of the brain will also help to assess the prognosis. Proper antiepileptic drugs, immunotherapy and surgery are the current treatment strategy for the patients of RE. Clinical diagnosis of RE depends on European consensus criteria proposed on 2005 described in two parts, all three conditions in part A or two conditions in part B need to be satisfied for a diagnosis of RE.[4]

Part A:
1. Clinical : Focal epilepsy (with or without EPC) and unilateral cortical deficit
2. EEG: Unilateral hemispheric slowing with or without epileptic activity and unilateral seizure onset
3. MRI: Unihemispheric focal cortical atrophy and at least one of the following grey or white matter T2/Flair hyperintense signal or atrophy of the ipsilateral caudate head

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Part B:
1. Clinical: EPC or progressive unilateral cortical deficits
2. MRI: Progressive unihemispheric focal cortical atrophy
3. Histopathology: T cell dominated encephalitis with activated microglial cells and reactive astrogliosis. Numerous parenchymal macrophages. B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE.

Here we reported a pediatric case of RE with typical clinical, electroencephalographic and MRI findings.

Case study:
A 3 year 6 month old boy only son (Figure-1) of non-consanguineous parents was reasonably well up to 18 months of age, then he had a attack of fever, convulsion and unconsciousness and was diagnosed as a case of meningoencephalitis and treated accordingly in a tertiary care hospital. His neuroimaging was normal during this illness (figure-2) after recovery he developed recurrent episodes of focal seizure in the form of myoclonic jerks and occasional staring, for this illness he was treated with antiepileptic drugs phenobarbital without any improvement of symptoms. At the age of 25 months of age he was hospitalized again with symptoms of encephalitis and was treated for 15 days, during that period his neuroimaging showed hyperintensity on right hemisphere in T2WI, FLAIR and DWI with normal ventricles (figure 3,4). MRA of brain, cardiac evaluation, metabolic screening, coagulation profile, EEG findings all were normal. At the age of 40 months he came to us with a history of recurrent fall, weakness of left side of body and recurrent seizure in the form of myoclonic jerks. His antenatal and perinatal history was uneventful. His developmental age was age

appropriate up to 18 months of age before the attack of meningoencephalitis then there is stagnation of motor, cognitive and speech development. He is anthropometrically well thrived and vaccinated as per EPI schedule. On examination there is no facial dysmorphism, OFC 48 cm which lies above 10th centile on centile chart. On neurological examination he was conscious, cooperative, no sign of meningeal irritation, no cranial nerve palsies, and motor examination reveals hypertonicity present in left upper and lower limb with brisk deep tendon reflexes, plantar extensor on left. His motor developmental age was around 18 months, speech and cognitive age corresponded to the age of 18 months. Interictal EEG showed right fronto-temporo-parietal discharge with generalized slowing of background activity (figure-7). Brain MRI showed hyperintensity on T2WI and FLAIR images on the whole right cerebral hemispheres with leptomeningeal enhancement. Right lateral ventricles are effaced (figure-5,6). Magnetic resonance spectroscopy (MRS) of the brain showed decreased NAA peak and normal choline peak. His routine blood and CSF investigations all were within normal limits. On the basis of clinical criteria based on European consensus criteria proposed in 2005 we diagnosed the case as Rasmussen's Encephalitis and started Inj. Methylprednisolone at a dose of 30mg/kg for 5 days followed by oral prednisolone 2 mg/ kg for one month and tapering for next one month along with antiepileptics, levetiracetam and clobazam. With this treatment his clinical improvement was obtained and he was seizure free for 3 months. Now he can run and is able to speak two word sentences. Parents were advised to come for follow up visits regularly; they were also counseled about the nature and treatment plan of the disease and also instructed to continue his physiotherapy, speech therapy and cognitive behavior therapy.

Fig.-1: the case

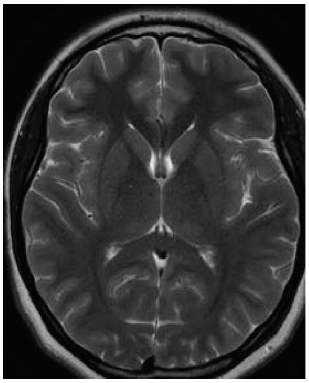

Fig.-2: MRI of brain at 25 months of age, Slight symmetrical cortical atrophy

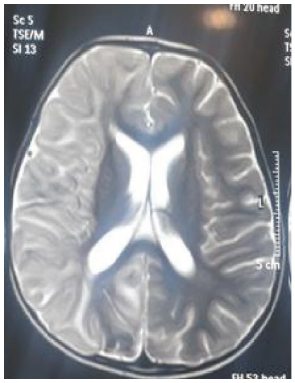

Fig.-3: *MRI of brain at 25 months of age shown T2 hyperintensity of right hemisphere*

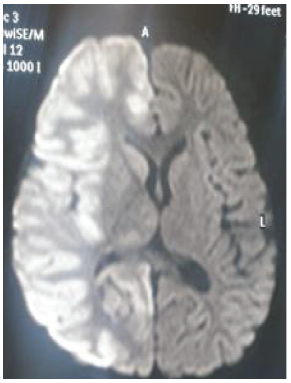

Fig.-4: *Hyperintensity in DWI involving right hemisphere at 25 month of age*

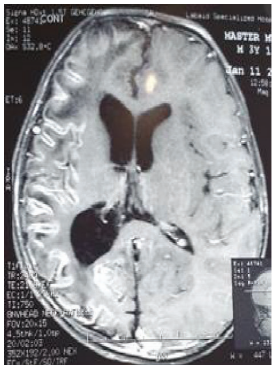

Fig.-5: *Hyperintense right cerebral hemisphere with leptomeningeal enhancement in FLAIR at 40 th month of age*

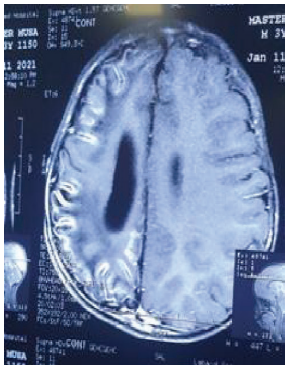

Fig.-6: *Atrophied right hemisphere at 40 th month of age*

Fig.-7: *EEG: Epileptiform discharge from right frontotemporoparietal region with slow background*

Discussion:

Here we reported a case of a three year six month old boy presented with recurrent focal seizure, weakness of one side of body after 18 months of normal development. Diagnosis of RE was based on clinical and neuro-radiological criteria based on European consensus criteria proposed on 2005.[4] Progressive neuroimaging deterioration indicates the chronic inflammatory nature of the disease.

This rare disorder usually affects children with a median age of onset 6 years, but our patient presents at an early age. Delayed presentation was also reported by Klaa H et al.[5] RE almost in every patients involved one hemisphere of brain which progressively atrophied in the course of time, typical disease course usually follow the pattern of variable prodromal period which usually contains minor sign and symptoms of viral fever then the patients enters in to the acute stage which is characterized by progressive deterioration of functions of the affected hemispheres like hemiparesis, hemianopia, cognitive deterioration, aphasia and predominantly intractable unilateral focal motor seizure with or without secondary generalization.[6-8] Epilepsia partialis continua (EPC) in the form of focal myoclonic twitching of facial muscles or muscles of distal extremities persisted for more than one hour with seizure free interval less than ten seconds is one of the characteristics features of RE. Acute stage of the disease usually persists around 8 to 10 months thereafter a phase of residual stage comes which has a stable neurological deficit but seizure activity remains high but low compared to acute stage.[8-10] Several studies have been carried out to search the etiology of RE but exact etiology is still unknown.[11] Antibody mediated pathogenetic hypothesis originated in 1994, antibodies to subunit 3 of the AMPA receptor (GluR3 antibodies) had been suggested to dominate pathogenesis. Other anti-neuronal antibodies such as Munc-18, and the alpha7-acetylcholine receptor were identified in some patients with RE.[12-14] Function of cytotoxic T cells is now considered in the pathogenesis of RE, where affected hemispheres found to be infiltrated with cytotoxic CD8+ T cell, astrocytic degeneration caused by cytotoxic T lymphocyte attack give rise to neuronal cell death and seizure induction.[15] Abnormal EEG as a slow background with slow focal and epileptic abnormalities in the lesion hemisphere present in the acute stage later on interictal abnormal discharge may appear on unaffected hemispheres.[16] Brain MRI is one of the best tools for diagnostic evaluation and to assess the prognosis of the disease, at the early stage of unilateral hyperintensity in T2, FLAIR image is usually noticed in the cortical, subcortical region, then unihemispheric atrophy sets in. Our case typically followed those changes. Most of the tissue loss happens from the 12 months onset of symptoms. Usually post contrast enhancement is less commonly present in RE. Functional imaging like fluorodeoxyglucose-positron emission tomography (FDG-PET) shows diffuse hypometabolism of affected segment.[17,18] Magnetic resonance spectroscopy (MRS) studies showed decresed N-acetyl-aspartate (NAA) levels and increased or normal choline peaks resulting in a decreased NAA/Cho-ratio suggestive of neuronal loss or dysfunction.[7,19] As the etiology is still clearly not known so the treatment is aimed to reduce symptoms and inflammation, to control seizure and to prevent further deterioration of neurological deficit, effective AEDs, immunotherapy and surgery are the main modalities of treatment. IVIG and IVIG plus steroids along with other modalities of immunotherapy were also found effective by some reports.[20] Tacrolimus was also found as a superior outcome regarding neurological function but not found as effective in seizure control.[21] Other immunotherapies targeting T –cells like cyclophosphamide, natalizumab and alemtuzumab help to reduce the inflammatory reaction of RE patients.[22] Epilepsy surgery may be considered in case of refractory epilepsy for seizure control but neurological deficit could not be avoided. Functional hemispherectomy and hemispherotomy are associated with lower complications compared to anatomical hemispherectomy.[12]

As the etiology of the disease is still controversial so specific management approach is directed at pathogenic factors. Most work is now directed to the activation of infiltrating CD8+ T cells and microglia to ensure the alternative of surgical management. Early suspicion at an early stage with proper management to halt the inflammatory process will help to prevent neurological deficits.

Conclusion:

Rasmussen encephalitis (RE) is a rare chronic progressive unihemispheric inflammatory disease manifested with recurrent focal seizure, hemiparesis and neurocognitive deterioration. Neuroimaging, EEG findings, early suspicion with exclusion of possible differential diagnoses may help to diagnose the patients earlier and will add better prognosis.

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