www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i3.145

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Case Report

Rasmussen's Encephalitis - Chronic Focal Encephalitis (CFE) - A Rare Entity

Authors
Dr Surender Kumar[1], Dr Hitender Kumar[2]
[1]MD Medicine, Senior Resident, Department of Cardiology at IGMC Shimla, Himachal Pradesh, India
[2]MD Radio-diagnosis, Consultant, Radiologist at Sri Ram Hospital, New Shimla, Himachal Pradesh, India

ABSTRACT
Rasmussen's encephalitis, also known as chronic focal encephalitis (CFE), is a rare inflammatory neurological disease, characterized by frequent and severe seizures, loss of motorskills and speech, hemiparesis (paralysis on one side of the body), encephalitis (inflammation of the brain), and dementia. The illness affects a single cerebral hemisphere and generally occurs in children under the age of 10.
Advances in neuroimaging suggest that progression of the inflammatory process is seen and MRI might be a good biomarker in Rasmussen's encephalitis.
Cerebral hemi-spherectomy remains the only cure for seizures, but there are inevitable functional compromises. Decisions of whether or when surgery should be undertaken are challenging in the absence of a dense neurological deficit, and vary by institutional experience. Further, the optimum time for surgery, to give the best language and cognitive outcome, is not yet well understood. Immuno-modulatory treatments seem to slow rather than halt disease progression in Rasmussen's encephalitis, without changing the eventual outcome.
Keywords: *Encephalitis, seizures, hemiparesis, dementia.*

CASE REPORT

A 12 year old male child presented with history of focal seizures in the form of jerky movements of left upper limb and left lower limb associated with history of up-rolling of eyeball, frothing from mouth and deviation of angel of mouth to right side. There was no associated history of tongue bite, loss of consciousness, altered sensorium, post-ictal confusion, involuntary urination or defecation during episode. These complains were slowly progressive with increasing weakness on left half of body.

There was no significant past history and family history related to patients complains.

On Examination: Patient was conscious, cooperative, well oriented to time, place and person. Patient was obeying commands and was not able to open eyes. Vitals were normal. No other abnormal finding was found on general physical examination.

Nervous system examination suggestive of UMN hemiparesis left side, hemianopia and conitive impairment.

Investigations: Hb-12.1 g/dl, RBCs-4.82 million/microlitres, Hematocrit-43.6%, MCV-90.8 fl, MCH-32.6pg, MCHC-32.8g/dl, Platelet count-1,60,000/microlitres, WBCs-9,300, DLC (N-68%, L-26%, M-04%, E-02%, B-00%), ESR-18mm at

1st hour (westergren method), RBS-90mg/dl, Sodium-141.7mmol/L, Potassium- 4.58mmol/L, Chloride-106.9mmol/L, BUN-9mg/dl, Creatinine-0.8mg/dl, Bilirubin (Total-0.7mg/dl, Conjugated-0.13mg/dl), AST (SGOT)- 45U/L, ALT (SGPT)-36U/L, ALP-88U/L, Protein (Total-5.9g/dl, Albumin-3.3g/dl).

MRI Brain suggestive of Rasmussen' encephalitis

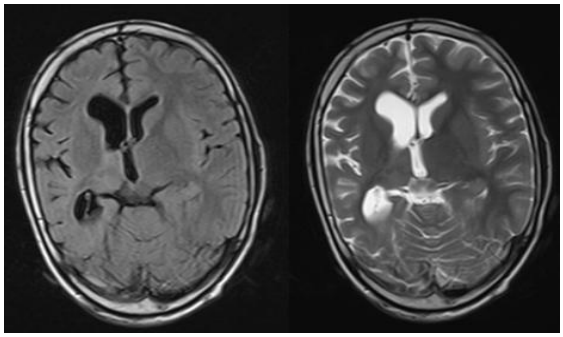

Figure 1A: MRI Brain – T2WI and FLAIR axial images showing unilateral cortical atrophy in right cerebral hemisphere with ex-vacuo dilatation of right lateral ventricle.

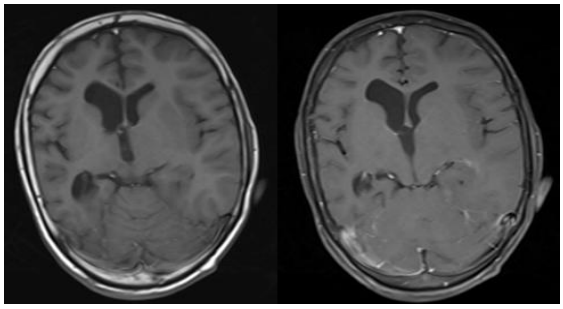

Figure 1B: MRI Brain – T1WI and T1WI post contrast axial images showing unilateral cortical atrophy in right cerebral hemisphere with ex-vacuo dilatation of right lateral ventricle. No significant post contrast enhancement is seen.

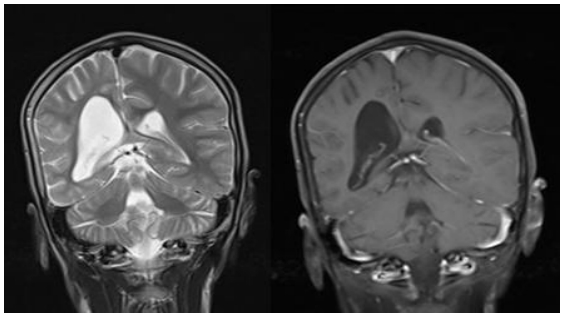

Figure 1C: MRI Brain T2WI and T1WI post contrast coronal images showing unilateral cortical atrophy in right cerebral hemisphere with ex-vacuo dilatation of right lateral ventricle. No significant post contrast enhancement is seen.

INTRODUCTION

Rasmussen's encephalitis, also known as chronic focal encephalitis (CFE), is a rare inflammatory neurological disease, characterized by frequent and severe seizures, loss of motor skills and speech, hemiparesis (paralysis on one side of the body), encephalitis (inflammation of the brain), and dementia. The illness affects a single cerebral hemisphere and generally occurs in children under the age of 10.

Epidemiology

Most cases (85% cases) occur in children under the age of 10 years [1]. However, detection in adults is increasing with routine MRI investigations for intractable seizures [2]

It was first described by American neurosurgeon Theodore Brown Rasmussen (1910-2002) in 1958[3]

Since then, the variable clinical features and lack of understanding of cause have created dilemmas in clinical decision making. The 2005 European consensus on pathogenesis, diagnosis, and treatment of Rasmussen's encephalitis remains the accepted guideline for evaluative criteria (panel 1).[4,5]

Investigators in a German studyestimated the countrywide incidence at 2·4 cases per 10 million people aged 18 years and younger per year.[6] Similarly, researchers in a recent UK surveillance study estimated an incidence of 1·7 per 10 million people aged 16 years and younger per year (a prevalence of 0·18 per 100 000 people).[7]

CLINICAL FEATURES

The typical clinical course has been characterised during the past century.[8]The median age of onset is 6 years, with a range from infancy to adulthood.[8,9,10] In some patients, a prodromal period of mild hemiparesis or infrequent seizures might precede the onset of the acute stage by up to several years. The acute stage is marked by

frequent seizures arising from one cerebral hemisphere. About 50% of patients with Rasmussen's encephalitis have epilepsiapartialis continua.[11,12,13] As the disease progresses, different focal seizure semiologies emerge, suggesting newly affected areas of inflammation in the hemisphere.[9] Untreated, children will develop hemiparesis, hemianopia, and cognitive decline within a year of epilepsy onset,[14] and if the language-dominant hemisphere is affected, dysphasia. Finally, there is a relatively stable residual stage with a severe fixed neurological deficit, motor and cognitive problems, and with persisting difficult-to-treat relapsing epilepsy.[15]

ETIO-PATHOGENESIS

The exact cause of the disease is unknown. RE is a rare disease that should be envisaged as sporadic, since there is no evidence for a genetic component.[16]There is, at present, no conclusive evidence why and how RE starts. A viral aetiology was already suggested by Rasmussen based on the constituents of the immune reaction in the brains such as lymphocyte infiltration and microglial nodules.[17]

Also, various viral (SSPE-like, EBV or CMV), or inflammatory episodes have been implicated by different authors [18]

However, so far all attempts to identify a pathogenic viral agent have been contradictory and inconclusive. [19]

An autoimmune mechanism has also been proposed describing antibodies against GluR3 subunit of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor in a few patients [20]

IMAGING

CT

CT may not show any specific feature in early imaging; however, patchy hypodense attenuation areas (similar to viral encephalitis) may be seen. Late stage disease may show unilateral cortical atrophy. CT perfusion may show decreased cerebral blood flow (CBF) [1].

MRI

MRI of the brain has become a mainstay for diagnostic assessment and follow-up in Rasmussen's encephalitis.[21,22] Usually, within months of onset of the acute stage, most patients show unilateral enlargement of the ventricular system. A T2/FLAIR hyperintense signal is often present in cortical or subcortical regions, or both, the distribution is heterogeneous, and temporal fluctuation might be related to seizure frequency in patients without epilepsiapartialis continua.[23]

The perisylvian region is a predilection site for signal change and volume loss. Ipsilateral atrophy of the head of the caudate nucleus is a typical but not an invariable accompanying feature of hemispheric atrophy, and can be an early sign.[24]

Serial MRIs typically show progression of signal change and atrophy. Recent radiological volumetric approaches describe the highest rate of volume loss in the first 8 months of disease, the acute clinical phase, and putamen predominance, rather than caudate predominance, in the basal ganglia.[25]

Some atrophy is always evident, even of the unaffected hemisphere, probably as a result of degeneration of commissural fibres. Functional studies using F-FDG PET show diffuse unilateral cerebral hypometabolism that might manifest when MRI atrophy is still at a minimum.[26]

DIAGNOSIS

The diagnosis may be made on the clinical features alone, along with tests to rule out other possible causes. An EEG will usually show the electrical features of epilepsy and slowing of brain activity in the affected hemisphere, and MRI brain scans will show gradual shrinkage of the affected hemisphere with signs of inflammation or scarring.

Brain biopsy can provide very strong confirmation of the diagnosis, but this is not always necessary.[27]

TREATMENT

Surgery still remains the only cure for the seizures caused by Rasmussen's encephalitis. Hemisphe-rectomy offers one of the best chances of making patients with Rasmussen's encephalitis seizure free (>70–80% long-term seizure-free outcome).[28] Moreover, findings of studies of children undergoing hemispherectomy for pathologies including Rasmussen's encephalitis show short seizure duration is associated with better cognitive outcome,[29,30] suggesting that earlier surgery should be considered to improve these outcomes. Most results show cognitive stabilisation after hemispherectomy,[31] with better cognitive outcome in non-dominant-hemisphere surgery and poorer outcome in dominant-hemisphere surgery and in individuals with refractory seizures after surgery.[32]

Timing of surgery; there is a controversy as to whether HE should be proposed early in the disease course[33]or only when the neurological deficits, which inevitably induced by the operation (loss of fine finger movements, hemianopia and, if the dominant hemisphere is affected, aphasia), have been brought about by the natural course of the disease. [34]

DISCUSSION

In 1958, Rasmussen et al. described three patients who suffered from seizures due to chronic localized encephalitis.[35] Subsequently, Rasmu-ssen's name has become associated with this generally unilateral, hemispheric condition. Pathologically, the salient features include chronic meningeal and parenchymal inflammation, consisting primarily of benign appearing T lymphocytes, both diffuse and nodular microglial cell proliferation, gliosis, and neuronal cell death.[36] The underlying pathogenesis of the disorder is still of some debate. Evidence supporting GluR3 autoantibody-induced injury is conflicting and there are cases in which such autoantibodies do not appear to exist; however, there is evidence to support a T-cell-mediated cytotoxicity targeting neurons in the disorder.[37] Treatment strategies have employed various combinations of surgery and immunotherapy, with the goals of decreasing seizure frequency and slowing or preventing further neurologic deficits from developing; treatment results have been mixed.

CONCLUSION

Since the causes of Rasmussen's encephalitis are known, it is difficult to anticipate how the treatment will improve. Various attempts using immunotherapy have been tried in the past decade. Some slow down the progress of the disease, but none has successfully cured or even halted the progression of disease.

A therapeutic dilemma; hemispherectomy causes inevitable postoperative functional deficits, but a real risk exists that treatment which is used to delay progression of the disease will delay definitive surgical treatment beyond the time, when an optimum post-hemispherectomy outcome could be expected.

Use of immunotherapies in patients with acute encephalitis and the relevant viral or antibody biomarkers has changed clinical practice and outcomes of the patients. We should hope that combined descriptive clinical studies, genetic analyses, and early histopathological examination of Rasmussen's encephalitis tissue specimens, looking for both viral and autoimmune pathology, will accelerate research efforts to identify the main causes of this disease.

Further clinical studies / trials are needed to know the efficacy of new non-surgical treatment options that might be used to control seizures and preserve / reverse neurological function.

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