# Rasmussen's Encephalitis: Literature Review and Case Study

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**Abstract.** Rasmussen's encephalitis is a rare and debilitating neurological disease that affects mainly children and young adults. It is characterized by chronic inflammation of the brain, which results in frequent seizures, loss of brain function and permanent damage. Symptoms of Rasmussen syndrome usually begin with simple partial seizures, which can progress to more severe and frequent seizures. This article will address the main aspects of RE, including its causes, symptoms, diagnosis, treatment and possible clinical case.

**Keywords.** Autoimmune disease; Seizure; Encephalitis; Hemispherectomy; Child.

## Introduction

Rasmussen's Encephalitis - ER -, is a rare disease of the central nervous system that affects mainly children between 6 years old, and may also arise in adulthood. It is characterized by chronic inflammation in the brain, leads to continuous seizures, muscle weakness and loss of motor skills. ER triggers the response of T cells to more than one epitope, contributing to the autoimmune response. Rasmussen encephalitis was described by *Theodore Rasmussen* in 1958, having a 7-year-old boy as a patient and presenting focal epilepsy associated with chronic encephalitis, accompanied by progressive hemiparesis and intellectual deterioration.

The exact cause of Rasmussen's encephalitis is unknown, but it is believed to be an autoimmune disorder, where the body's immune system attacks brain tissue. The disease may progress slowly, with symptoms that gradually worsen over time. The treatment causes debates because the most effective option would be to undergo a surgical cerebral disconnection from the affected hemiphery, where it brings the high probability of decreased seizures but there may be irreversible loss of functions that depend on the hemisphere removed. Bibliographic reviews and case study will be used to make an analysis of literature review about the etiology of the disease, diagnosis and treatment

## Objective

This article aims to review the most recent studies on Rasmussen's encephalitis in order to understand its etiology, clinical cause and analyze possible cases of RE. The expected results are to comprehensively show the theme and bring scientific knowledge to the case.

## Etiology

Its etiology is still unknown. Some studies show cytomegalovirus or herpes simplex virus as possible causative agents of encephalitis. Chronic encephalitis is shown with microglial nodules, neuronophagia, neuronal decrease and gliosis, perivascular lymphocytic infiltrate and leptomenid

inflammatory infiltrate. The morphological appearance has suggested the involvement of viral pathogen.

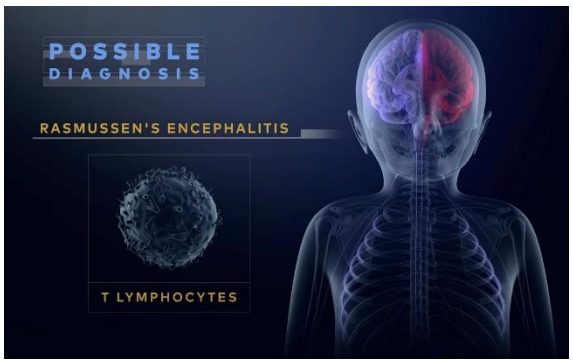
Autoimmune mechanisms, via GluR3 antibodies (glutamate receptor), is shown as a determining factor of Rasmussen syndrome. There is a theory that talks about the formation of GluR3 antibodies as a consequence of cortical dysgenesis, which could cause injury to the blood-brain barrier[8].

[3] Additional immunohistochemical studies in the brain of patients with Rasmussen encephalitis show evidence of an attack against neurons caused by Granzim B.

## Clinical Presentation

Rasmussen's encephalitis manifests mainly in childhood, at the age between 6 years [4]. Its clinical presentation is described by 2 important aspects: epilepsy and deterioration of neurological functions (will depend on the affected hemisphere) [1]. The onset of encephalitis is due to seizures and may present different semiologies due to the progression of the epileptogenic zone in the affected hemisphere. Just as the type of crisis will also be variable, the most common will be motor, then complex and somatosensory. There are also two subtypes of Rsmussen's encephalitis.

Fig. 1 Rasmussen's Encephalitis




Source: Netflix Series Diagnosis

The most common will affect the cerebral cortex of one of the hemispheres, its clinical manifestation happens with motor seizures that can be generalized by the body, and myclonic crises (brief spasms and similar to shocks of a muscle or a group of muscles). Atrophy of brain tissue and neurological deficits are more severe in this type.

The second subtype is the least common, with frequent manifestations of base gloglia (they are a group of subcortical nuclear clusters involved in movement, located deep to the cerebral hemispheres), thus presenting spasms or convulsions (paroxysmal movements) and hemidystonia (involuntary contractions by the body).

According to the Institute of Neurology of Montreal, Canada, Rasmussen's encephalitis occurs in three stages [5]:

1- **Prodromal Phase**: comprises the period in which the first epileptic cirsis occurs, where it can last for months or years (longer in adolescents/adults than in children). During this phase crises occur less frequently [5];

2- **Acute Phase**: There is an increase in seizures (but 10 attacks per day) with worsening of hemiparesis (muscle weakness or partial paralysis of one side of the body that can affect the arms, legs and facial muscles), which leads to neurological detoriation. It has an average duration of 8 months, where the largest loss of volume of the affected hemisphere occurs [2].

3- **Residual Phase**: stable state of the disease [2]. With severe and already permanent cognitive and motor deficits. There is the paersitencia of epilepsy, and treatment with drugs is not controlling the crises anymore.

The neurological deficit is the marked one that is used to monitor the progress of the

disease [5]. The change in behavior precedes the first signs of mental decline.

## Diagnosis

Particularly, Rasmussen's Encephalitis is difficult, mainly in the acute phase of the disease [4]. But early diagnosis is essential to delay the disease. Rasmussen encephalitis has 3 criteria to be diagnosed:First it should be checked if the patient presents the features of part A, which will include characteristics of the early phase.

Second, if the patient does not present the characteristics of part A, it should be checked if it presents part B, which has progressive disease.

**PART A:**

**Clinical**: Focal epileptic seizures and unilateral deficits

**Electroencephalogram:** Progressive focal cortical hemispheric atrophy

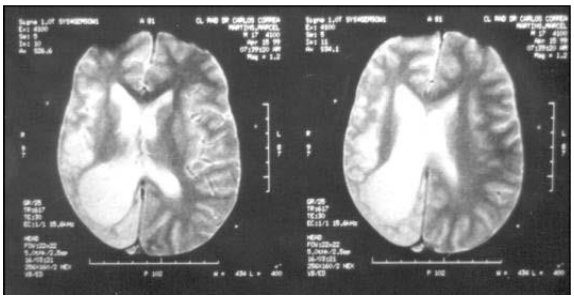
**MR:** White/grey substance in T2/FLAIR (antibody-mediated inflammation that typically surrounds the limbic system). Head of the caudate nucleus with atrophy.

**PART B:**

**Clinical:** Progressive unilateral cortical deficit

**RM:** Progressive focal cortial unihemispheric atrophy

Fig. 2 MRI of the brain, axial section, demonstrating cerebral hemiatrophy D



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## Treatment

Treatment of Rasmussen's encephalitis should cover symptoms to reduce the severity and frequency of attacks. There are types of treatment:

1- **Antiepileptic therapeutic treatment**: It will be the control of seizures, especially when encephalitis manifests itself in the form of EPC (Epilepsy partialis continua) [7]. Even if it won't end crises, the goal is suppression.

2- **Immunomodulatory Therapeutic Treatment**: high intensity short-term treatment that should control seizures and prevent brain damage. It should be initiated even at the earliest stage since in the residual phase brain lesions are already established. In most patients, treatment results are partial or brief. Corticosteroids are the most used and most effective drugs (both in the control of crises and in the delay of disease progression) [5].

3- **Immunosuppressive therapeutic treatment:** Tacrolimus is a T cell inhibitor, has a moderate effect for the reduction of seizures and with atrazo in hemiatrophy (brain atrophy). is recommended to use the

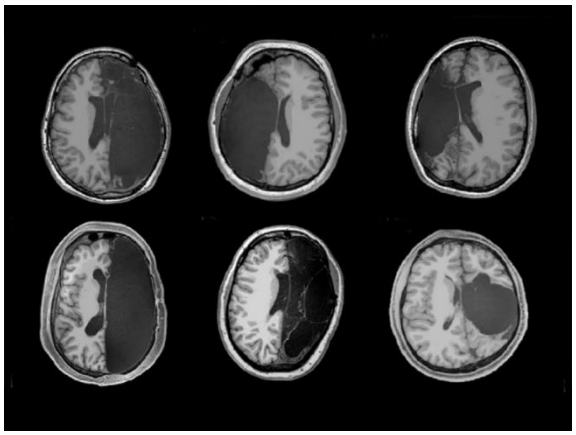
remedy after 12 months of cortidoterapia use if it has eased the crises.

4- **Surgical Therapeutic Treatment**: In most cases, surgical intervention is inevitable, mainly in children [4]. Hemisferectomy is the only cirugia that can prove its speed and effectiveness. The goal is to completely control crises and promote the neurodevelopment of the other hemisphere [9].

## Hemispherectomy

Hemisferectomy is a surgical procedure in which the total or partial removal of one of the hemispheres of the brain occurs. For an adult, it is impossible for him to survive with only one side of the hemispheres, but for a child, the remaining hemisphere can replace what was removed.

Fig. 3 Hemispherectomy



Source: https://hypescience.com/pessoas-com-metade-do-cerebro-removido-sao-tao-normais-quanto-nos-estudo/

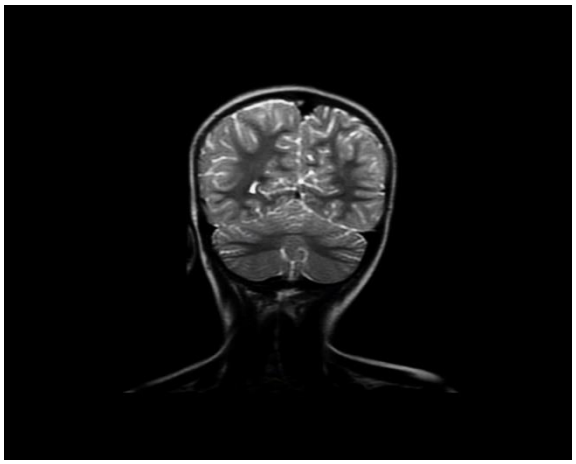
Their approach may be atanomic: traditional hemispherectomy (resection of the affected hemisphere) or functional (disconnective and less recessive) [1]. In functional hemisferectomy, there are two techniques: vertical-parasagital of Delalande and the peri/transsilvania hemisferectomy of Schramm. Functional is an approach with fewer intraoperative complications, lower incidence of hydrocephalus (accumulation of excess fluid in normal spaces within the brain and between layers of internal tissue) and mortality. The effectiveness of surgery is 65-85% and prevents cognitive deterioration in 80% of cases [6]. The earlier the surgery is performed, the better the result of cognitive and intellectual performance of the child [5].

There are discussions about Hemispherectomy, such as the time to be done: It should be done at the early stage of the disease or when neurological deficits have already established. Still, there are discussions about whether or not surgery causes a significant improvement in the patient [2]. It is known that if the affected hemisphere is disconnected before 4-6 years, the probability of recovery is much higher, but most often the diagnosis happens after 6 years which increases the probability of risks.

## Clinical Case

A 7-year-old female patient presents with focal motor convulsions in the minute by several parts of the body (mainly in the mouth, leg and left arm) even disperta. It began at age 6 after a family trip to the mountains, as soon as they returned, he began to have seizures. The patient was taken to the hospital and submitted to an electroencephalogram, which showed that subclinical seizures were occurring at all times. She was hospitalized for 24 hours without a seizure. Even with steroids and Keppra, the seizures did not react to the drugs.

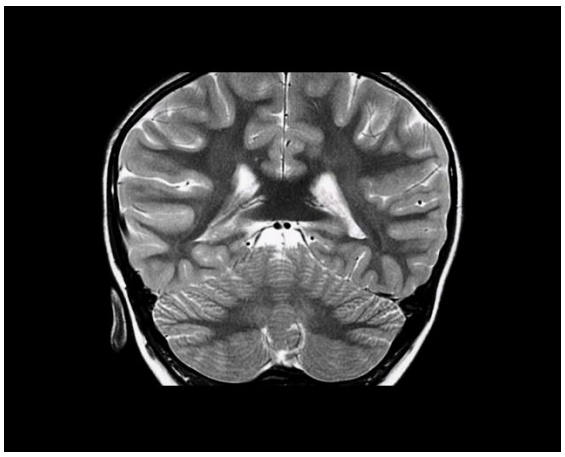
Fig. 4 Resonance of the Patient



Source: Netflix Series Diagnosis

The patient underwent magnetic resonance but no tumor or stroke was seen. As was the lumbar pulse, which did not present infection or antibodies that demonstrated autoimmune disease. Doctors will give the possible diagnosis of Rasmussen's Encephalitis after the biopsy, and recommended hemispherectomy, in which, the consequences for the patient would be: loss of vision of one eye, loss of movements of half the body and possible loss of speech. Even though the behaviour is ER, the resonances showed that the brain without reduction of the affected hemisphere (possibly because the symptoms were recent).

Fig. 5 Resonance of the Patient



Source: Netflix Series Diagnosis

The final suggested treatment was the implantation of a neurostimulator system, which functions as a pacemaker, which will short-circuit the brain to react to the seizure. When the device senses the onset of seizures, it sends a stimulus to abort the seizure. By preventing the crisis, the deterioration of the brain is prevented. Once implanted, the neurostimulator is tested to see if it is reading the correct area of the brain. The patient made the implementation of the neurostimulator, where a month later she presented positive results. Doctors gave a period of 6 months to 1 year to really know if it gave positive results.

## Conclusion

Through this article it was possible to analyse that Rasmussen's encephalitis is a rare disease that affects mainly children and young adults. It is a chronic inflammatory condition that affects only one side of the brain, leading to seizures, loss of motor and cognitive abilities, and brain atrophy. The exact cause of Rasmussen's encephalitis is still unknown, but it is known that the immune system plays an important role.

The goal of treatment for Rasmussen encephalitis is to control seizures and decrease brain inflammation. This usually involves a combination of anticonvulsant and immunosuppressive drugs. However, in severe cases, surgery may be needed to remove the affected part of the brain.

The present article was of paramount importance for the researcher, as it provided a greater knowledge about the reported problem, as well as an opening to search more information about the problem and understand the subject discussed with the contribution to the scientific environment and society.

It is urgent, therefore, that the subject of Rasmussen's Encephalitis be more addressed in our scientific environment today, studies that question the factors that lead to this problem and seek to promote

campaigns that promote general knowledge in the population on the subject discussed in this article.

## Bibliography


[1] Bien CG et al., The natural history of Rasmussen's encephalitis. Brain, 2002. 125(Pt 8): p. 1751-9.

[2] Bien CG, Schramm J, Treatment of Rasmussen encephalitis half a century after its initial description: Promising prospects and a dilemma. Elsevier: Epilepsy Research, 2009. 86, 101- 112.

[3] Bien C G et al. **Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement.** Estados Unidos, Oxford Academic, 2005

[4] Granata T and F. Andermann, Rasmussen encephalitis. Handb Clin Neurol, 2013. 111: p. 511-9.

[5] Granata T et al, Hemispherotomy in Rasmussen encephalitis: Long-term outcome in an Italian series of 16 patients. Epilepsy Research, 2014. 108, 1106-1119.

[6] Takahashi Y et al, Immunomodulatory therapy versus surgery for Rasmussen syndrome in early childhood. Brain & Development, 2013. 35, 778-785.

[7] Varadkar S et al., Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol, 2014. 13(2): p. 195-205.

[8] Wang D et al, Clinico-pathological investigations of Rasmussen encephalitis suggest multifocal disease progression and associated focal cortical dysplasia. Epileptic Disord, 2013. 15 (1): 32-43.

[9] Yacubian EM, Rosemberg S, Marie SKN, Valerio RMF, Jorge CL, Cukiert A. Double pathology in Rasmussen's encephalitis: etiologic considerations. Epilepsia 1996;37:495-500.