Rasmussen’s Encephalitis

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Introduction
Rasmussen’s Encephalitis (RE; also called Rasmussen’s syndrome) is a progressive inflammation of the part of the brain called the cerebral cortex, which is made up of a right and left hemisphere and spreads to adjoining areas on the same side. Curiously, it does not spread to the other hemisphere. The inflammation leads to loss of nerve cells and scar formation and usually results in severe disability. Although RE is most often diagnosed in children under the age of 10 years, it can also start in adolescence and adulthood. It is a rare disorder and probably affects one person in every 500 000 to 1 000 000.

Clinical Features
The clinical problems in RE are determined by which areas of the affected hemisphere are inflamed: each area has different functions. As the disease spreads, more areas are damaged and the greater the severity and range of disabilities. Typically, the disease progresses relentlessly until most of one hemisphere is affected. The inflammation burns out by itself only rarely before severe disability has occurred. However, the speed of the spread varies between patients. At one end of the spectrum, the disease advances rapidly over a few weeks or months. As the other end, progression occurs slowly over several years. This slower clinical variant seems to be more common in adolescents and adults than in children. It is possible that there are milder forms of RE that we fail to recognize.

The typical clinical features are

- **Epilepsy**
  Usually, the first sign of the disease is focal epilepsy. If the motor cortex (the area that controls movement) is affected, the patients have motor seizures with jerking to one side of the body. Sometimes the motor seizures become continuous, and this state is called continuous partial epilepsy. Similarly, if the temporal cortex is affected, patients have temporal lobe seizures (complex partial seizures) with altered
awareness of their surroundings. Although seizures start at one site, they can spread to the rest of the brain and cause generalized epilepsy with loss of consciousness. As the disease progresses, the seizures become more frequent, more severe, and more difficult to treat with anti-epileptic drugs.

- Neurological deficits
  - Hemiparesis. The wiring of the nervous system determines that a lesion of one side of the brain causes problems on the opposite side of the body. Thus, involvement of the motor cortex in one hemisphere causes weakness on the other side of the body. If the sensory cortex is affected the patient has numbness of the other side of the body (hemianaesthesia).
  - Visual loss. Damage to the visual areas in one hemisphere causes loss of vision in the opposite direction (hemianopia).
  - Speech problems. If the speech areas are affected, patients may be unable to translate their thoughts into words (expressive dysphasia) and have difficulty understanding what others say to them (receptive dysphasia).

- Electroencephalogram (EEG). This records the electrical activity of the brain and is useful in characterising the type of seizures the patient has.

Treatment
Because in RE the seizures often do not improve with anti-epilepsy drugs and the disease only ends with destruction of the affected cerebral hemisphere, surgical removal of large areas, sometimes all, of the hemisphere became a standard treatment. However, the research evidence of autoimmune abnormalities in many patients, and the clear need for effective medical therapy early in the disease to prevent progression, helped prompt trials of immune therapy.

- Immune therapy
  Trials of various combinations of powerful drugs that suppress the immune system (prednisolone, azathioprine, methotrexate, and
cyclophosphamide) and therapies that modulate the function of the immune system (plasma exchange and intravenous Rasmussen’s Encephalitis cont. immunoglobulin) have been tried. However, these trials have usually been performed in individual patients and there are no good data on the optimum combination, dosing, or duration of immune treatments. It seems likely that to modify or arrest the progression of a chronic, destructive disease such as RE, most patients will need a combination of therapies at high dose for prolonged periods – perhaps indefinitely.

The combination of daily oral prednisolone (a steroid) and monthly pulses of intravenous immunoglobulin appears promising. All eight patients, mostly with adult-onset RE, that we have treated in this way for up to five years have had useful improvement in their epilepsy control and, so far, have not developed any new disabilities.

- **Cognitive deficits**
  Patients can develop memory problems, intellectual impairment, and other neuropsychological deficits.

**Causes**
There is convincing evidence that in most patients RE is an autoimmune disorder. Many patients have antibodies in their blood that bind to nerve cells and which are capable of damaging the brain. Of particular interest is an antibody that binds to an important nerve protein called the type-3 glutamate receptor (GluR3). In addition, activated immune cells called T cells that are toxic to nerve cells are found in inflammatory brain tissue in biopsies from RE patients. In most patients, it is not clear what triggers the abnormal immune response, although sometimes RE has followed an otherwise minor bacterial or viral infection, or head injury.

**Diagnosis**
A serious disease needs intensive investigation. The tests are designed to confirm RE and to exclude other conditions. Diseases that can mimic RE...
include viral and toxoplasma encephalitis, autoimmune disorders such as vasculoitis, and tumours. The most useful investigations are

- **Brain scans.** MR, SPECT, and if available PET scans are useful. Figure 1 shows an MR brain scan of severe RE.
- **Blood tests.** These include assays for a range of antibodies and tests to exclude infection.
- **Lumbar puncture.** Spinal fluid is examined for evidence of inflammation and infection.
- **Brain biopsy.** This is needed to confirm the diagnosis.

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