Rare Neurological Disorders – Diagnostic and Clinical Challenges

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Rare disorders – definition and burden

A disease is considered rare when it affects one person out of 2000 or less.

Rare diseases are serious chronic diseases, most of them are genetic and are often life-threatening.

For many rare diseases basic knowledge, like cause of the disease, pathophysiology, semiology, natural course of the disease and epidemiological data is limited;

This significantly hampers the ability to both diagnose and treat these diseases.

Case presentation

Clinical history:

Male, 34 years old with normal early development.

At the age 14, patient developed acute headache and vomiting with subsequent seizures. Seizures recurred again after three days and carbamazepine was initiated.

At the age of nineteen, seizures recurred with numbness of fingers of the right hand with upward propagation, and bilateral tonic-clonic seizures.

Clinical history

Sometimes the patient would develop episodes of mental status change, fixed gaze with occasional progress into eyes and head adversion to the left with bilateral tonic-clonic seizures;

In 2011, the patient underwent bilateral parietal cysts biopsy and afterwards radiotherapy at another hospital for unknown reasons.

Clinical history

During last two years emotional lability and memory problems have become prominent;

Patient has developed walking difficulties with ataxia and episodes of confusion with difficulties of writing.

Investigations

Neurological exam:

Patient is hipocritic. Speech with elements of sensory-motor aphasia, Gerstman syndrome (***dysgraphia, acalculia, right-sided finger agnosia and left-right disorientation***), gait with slight ataxia, mild bilateral pyramidal and cerebellar symptoms, bilateral Babinski sign and diffuse muscle hypertonia.

Investigations

Neuropsychological assessment:

2006 - Slight impairment in dynamic praxis;

2013 - Emotional lability, depressed mood, impairment in long term and short term memory. Organic cerebral dysfunction with bilateral frontal localization and mild dysfunction of temporal and parietal lobes.

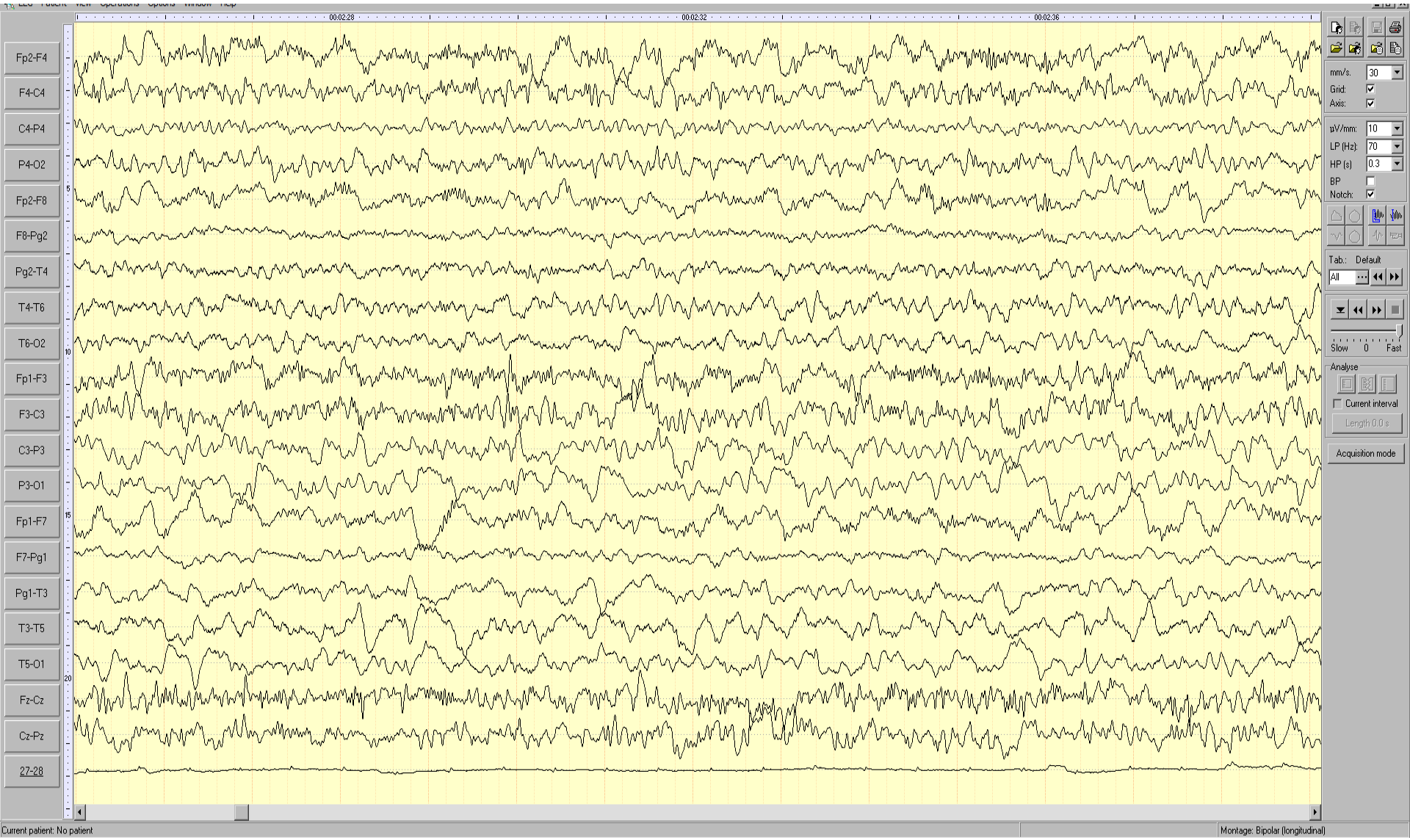
Investigations

Electroencephalogram (EEG):

2006 **–** Focal slow waves in right fronto – temporal regions. Sharp waves in left frontal and occipital regions.

2018 – Continuous delta waves in left center and left temporal regions. Single sharp waves in left temporal montages.

Electroencephalogram (2018)



Investigations

Laboratory investigations - no significant findings in routine tests.

Serology parasitic infections:

- ✓**Echinococcus IgG 0.3 (negative);**
- ✓**Taenia solium IgG 0.6 (negative)**

Investigations

Magnetic Resonance Imaging (MRI) – Multifocal intraaxial supra - infratentorial cysts with fragments of granulomatous transformation. Diffuse chronic leucoencephalopathy.

CT - scan revealed marked calcifications at semioval center, thalamus and basal ganglia.

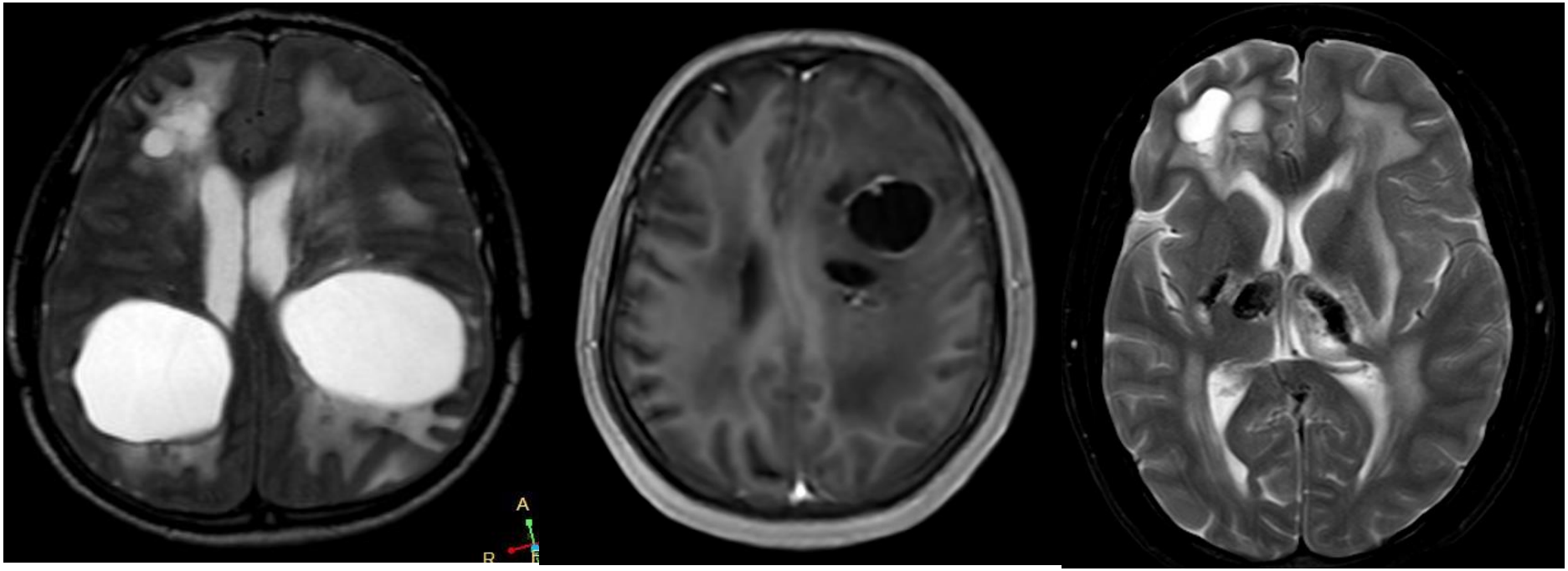
Neuroimaging

MRI- 2014

T1W axial image

T1W C+ axial image

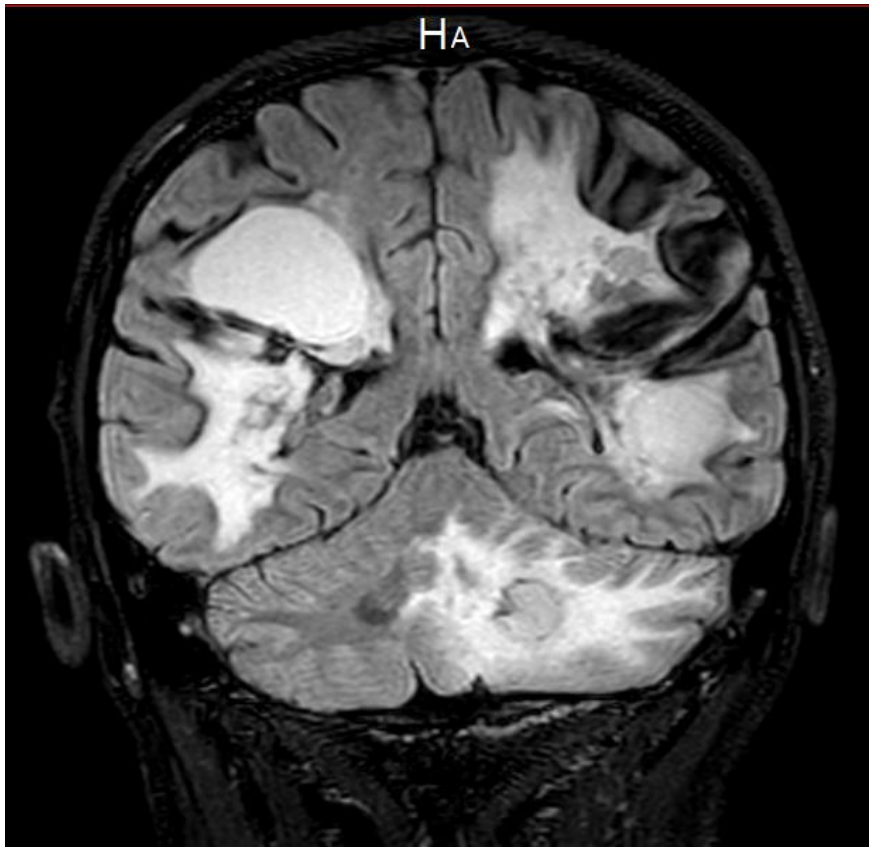
T2W axial image



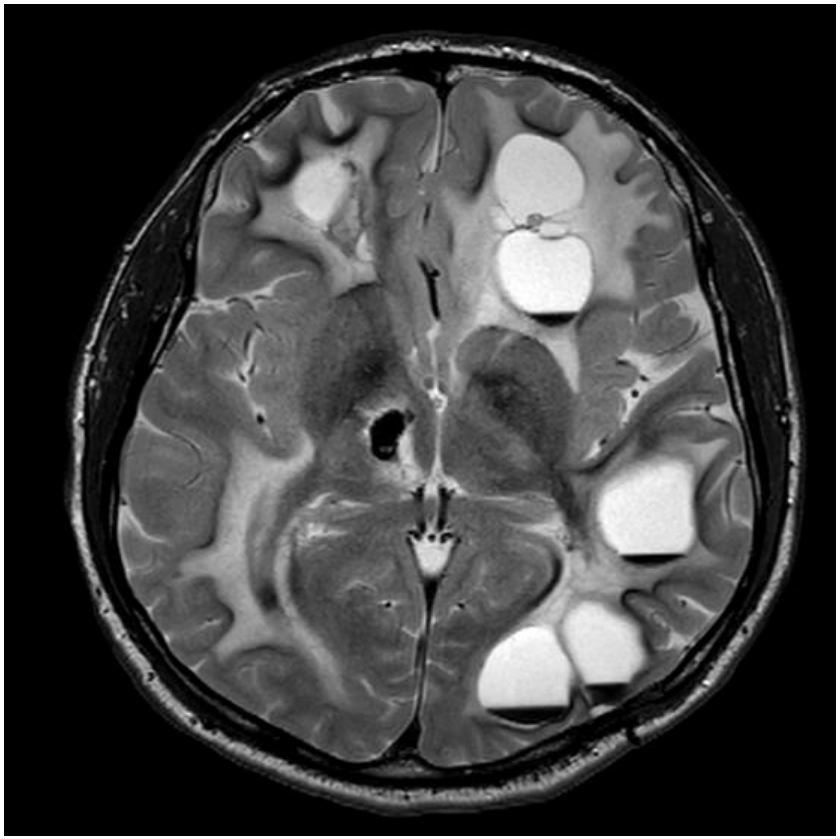
Neuroimaging

MRI- 2018

Coronal FLAIR image



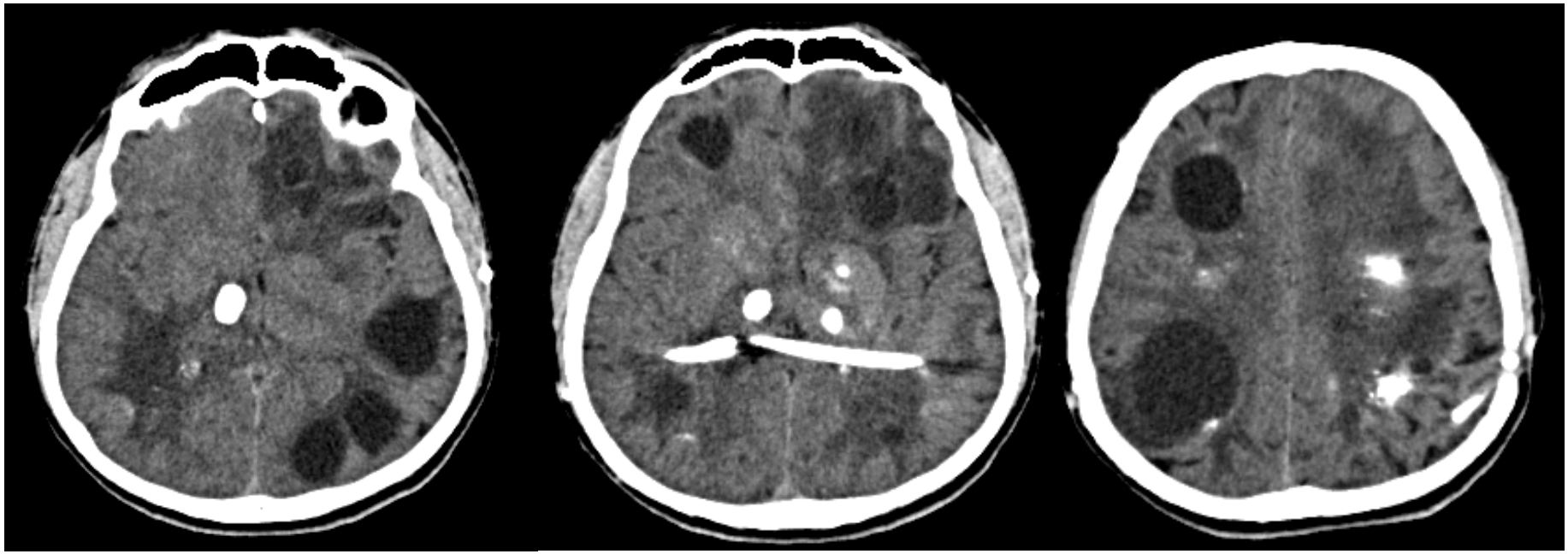
Axial T2W image



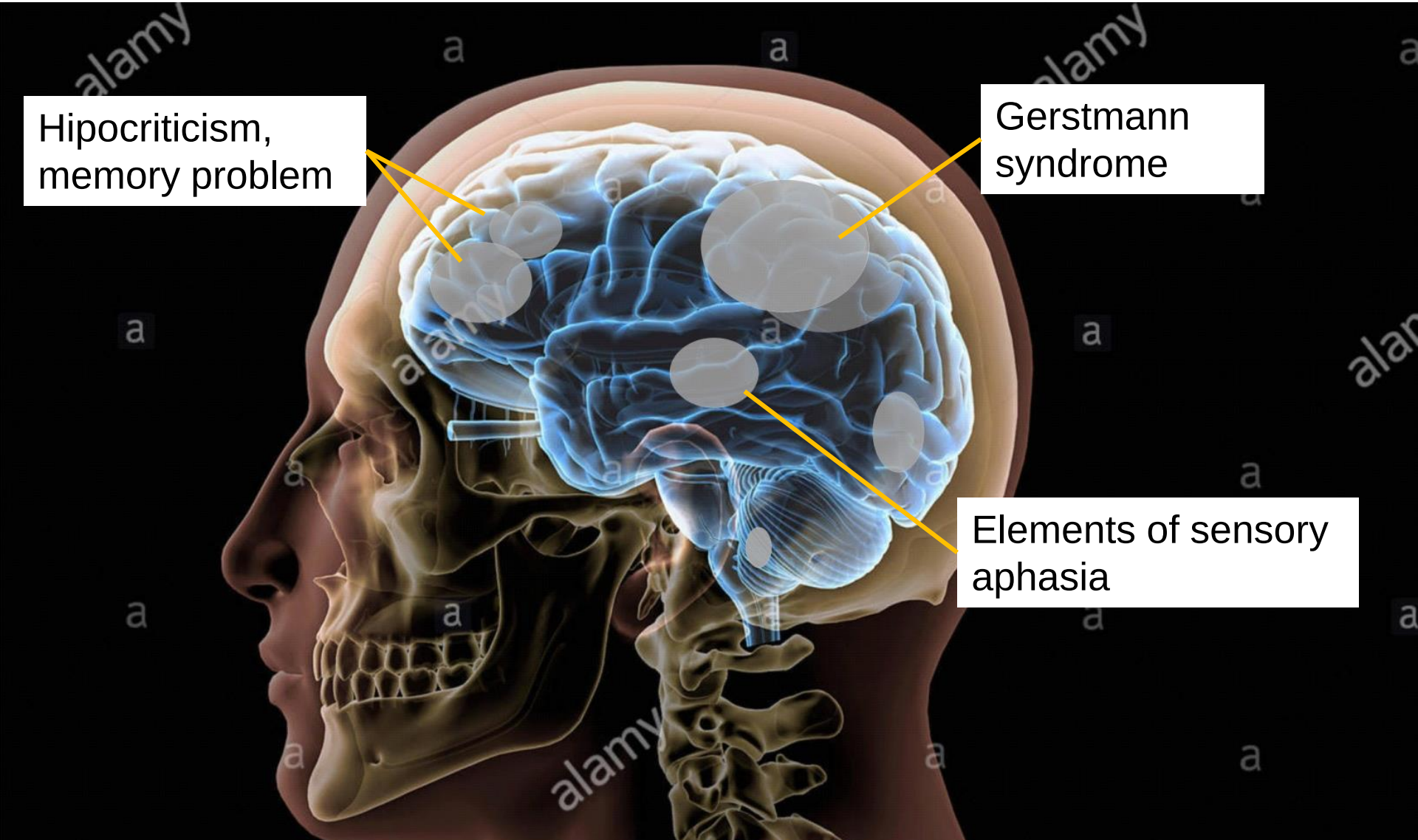
Neuroimaging

Computed Tomography - 2018

Multiple cysts and calcifications (hyperdence spots)



Neuroimaging findings linked with neurological syndromes



Treatment

Various **AED** therapies were applied with intermittent effectiveness;

Anthelmintic therapy: Albendazol + corticosteroids (without effect)

During the disease progression some cysts became clinically significant and **surgical intervention** became necessary;

Neurosurgical treatment

24.09.2014 - Bilateral parietal cysts was drained. Postoperatively, the dramatic improvement was remarkable. However, after three months the symptoms recurred. Brain MRI showed that drained cysts had been refilled.

25.12.2014 - Ventriculo-cysto-peritoneal shunting was conducted for both parietal cysts. Symptoms were reduced again and remained stable for the next two years;

In **2016** the patient gradually developed sensory aphasia. MRI investigation revealed grooving cyst in **left temporal** lobe and an additional new cyst in occipital lobe. Ventriculo-cysto-peritoneal shunting was conducted to evacuate temporal cyst (21.01.2016). Symptoms were alleviated again

Neurosurgical treatment

11.03.2019 resection of right parietal and left occipital cysts;

In addition, intraoperatively block of existing shunts were detected due to viscous cystic fluid;

Shunts were cleaned and restored.

Investigations

Cytology of cyst fluid content centrifugates:

Dismorphic erythrocytes and macrophages with haemosiderine sediments in cytoplasm. Haemosiderin is visible in extracellular matrix;

No neoplastic cells were identified.

Diagnosis

The clinical and radiological picture was consistent to diagnosis: **Leukoencephalopathy with Cerebral Calcifications and Cysts (Labrune syndrome).**

Leukoencephalopathy with calcifications and cysts (Labrune syndrome)

ıkoencephalopathy with calcifications and cysts: A case report

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Longitudinal clinical and neuro-radiological findings in a patient with leukoencephalopathy with brain calcifications and cysts (Labrune syndrome)☆

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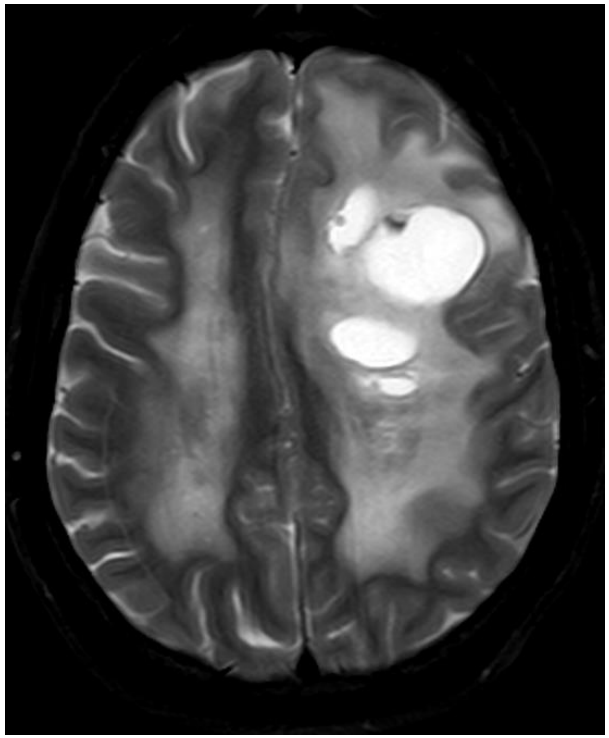
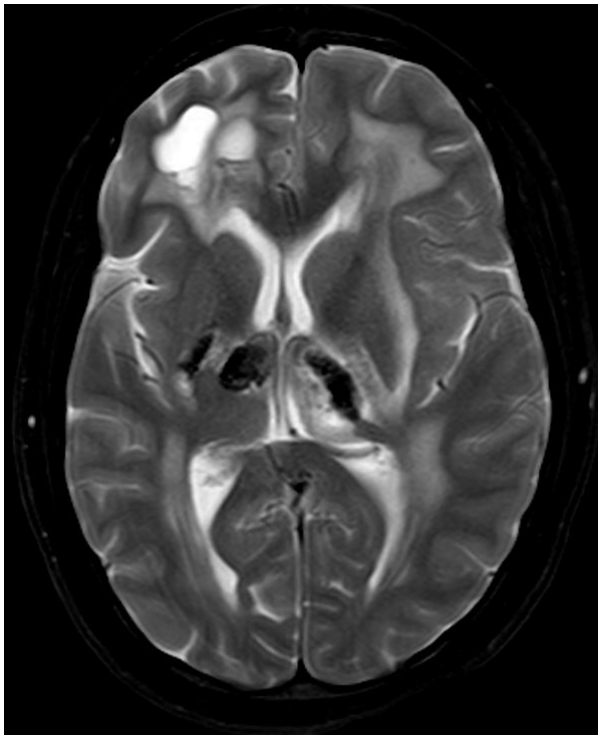
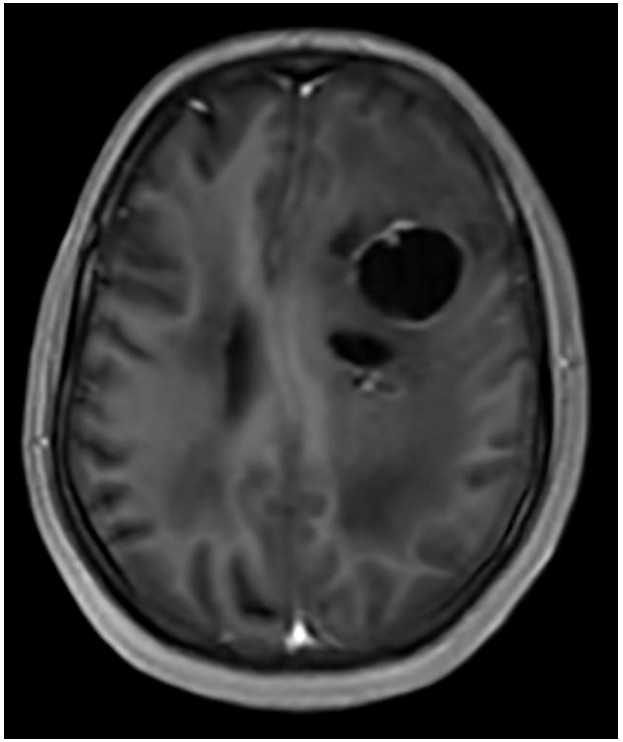
Abstract

Go to:

Since she was 4 years old, the patient had exhibited frequent convulsive seizures, and she experienced severe headaches and depression in adulthood. At the age of 37 years, cerebral calcifications were detected, with a 1-month history of headache. Brain computed tomography showed multiple asymmetric calcifications in the bilateral basal ganglia and white matter. Magnetic resonance imaging revealed a cyst in the right parietal lobe.

Labrune Syndrome In Publications

- Case courtesy of Dr Carl Prem Trevor Colaco, Radiopaedia.org, rID: 58633

Leukoencephalopathy with calcifications and cysts (**Labrune syndrome)**

Labrune syndrome is an extremely rare condition which consists of a triad of leukoencephalopathy, cerebral calcifications and edematous cysts;

The first case of the disease was recorded in 1996, and currently there are 32 cases described around the world.

Leukoencephalopathy with calcifications and cysts (Labrune syndrome)

Disease onset at age of 10 - 15 years. First manifestation in most cases is seizure

Etiologic factor:

- Disease is associated with **SNORD118 gene mutation**.

Pathogenesis:

- Diffuse cerebral microangiopathy with micro- and macrocistic evolution and parenchimal degeneration;

- Disease progression is variable and depends from localization and growth rate of the cysts

Labrune et al. Extensive brain calcifications, leukodystrophy, and formation of parenchymal cysts: A new progressive disorder due to diffuse cerebral microangiopathy. Neurology. 1996;46:1297–301

Differential Diagnosis

Coats plus syndrome

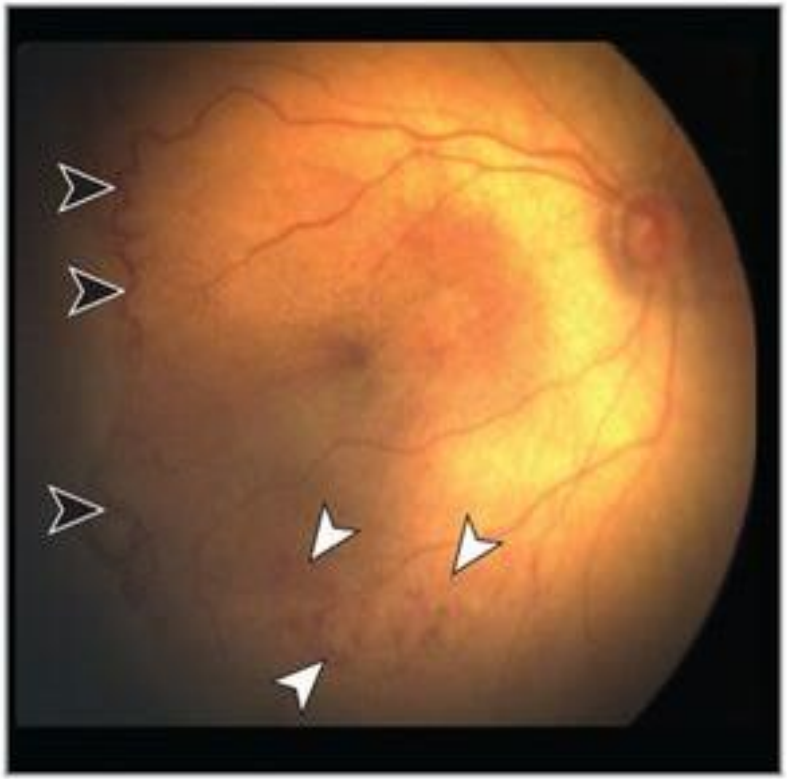
- Disease has similar neuroradiological findings, but in addition affection of bone, liver, retinal angioma is observed with disease onset at early childhood;

- **CTC1 gene mutation** is considered as underling etiology.

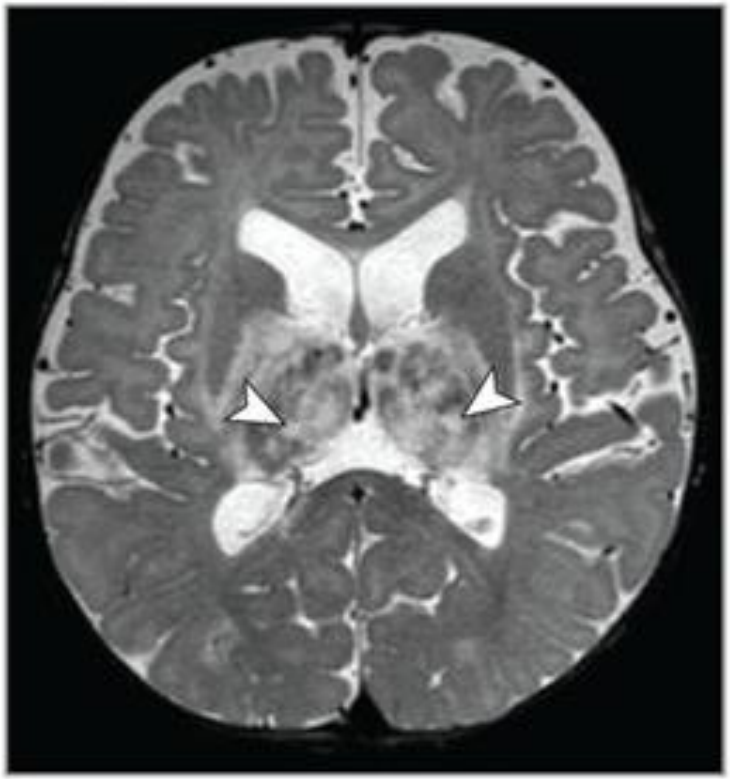
Differential Diagnosis

Coats plus syndrome

Retinal angiopathy with affected arteries and spots with petechial bleeding



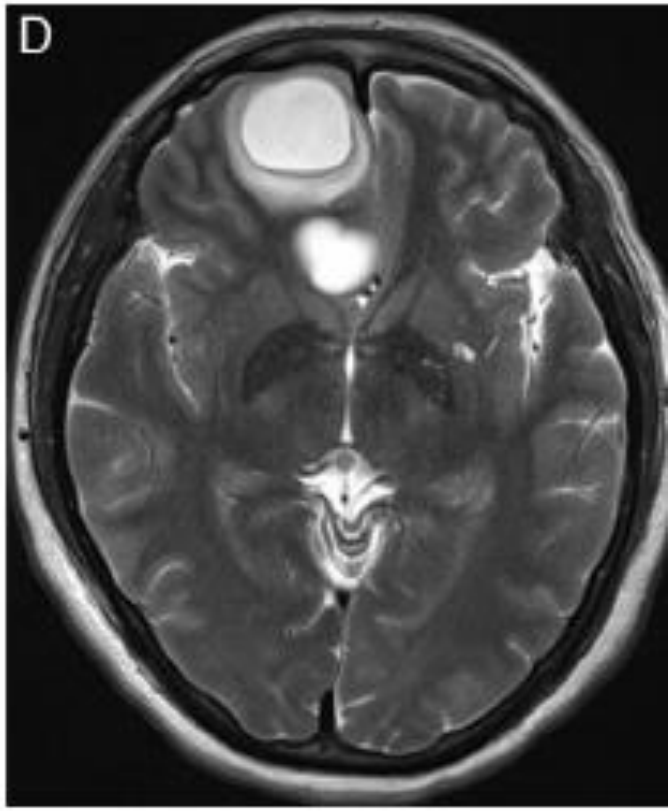
MRI shows bilateral cystic lesions in thalamus region



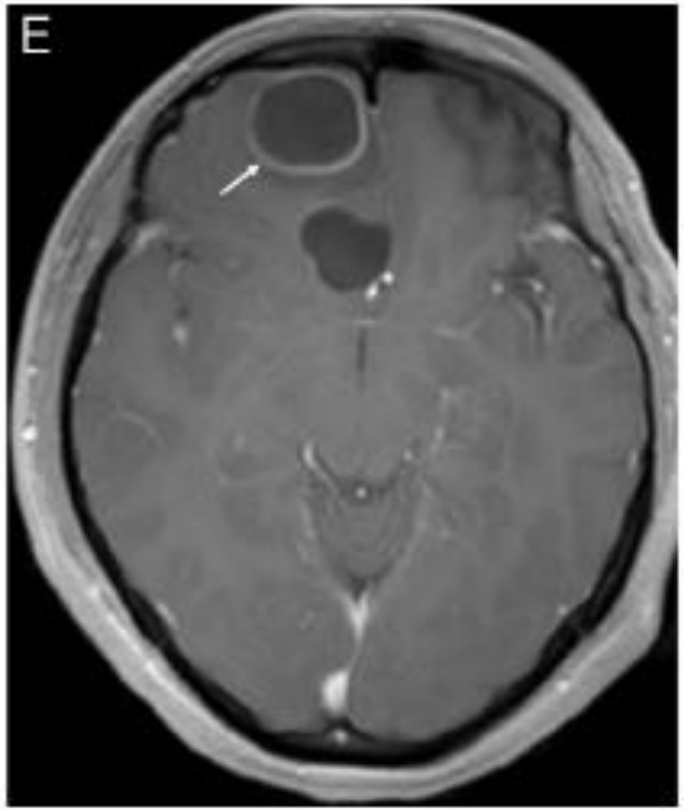
Differential Diagnosis

Neurocysticercosis - colloid-vesicular phase

T2W axial image,
right frontal cysts



T1W contrast +, right frontal
cysts with ring-like enhancement



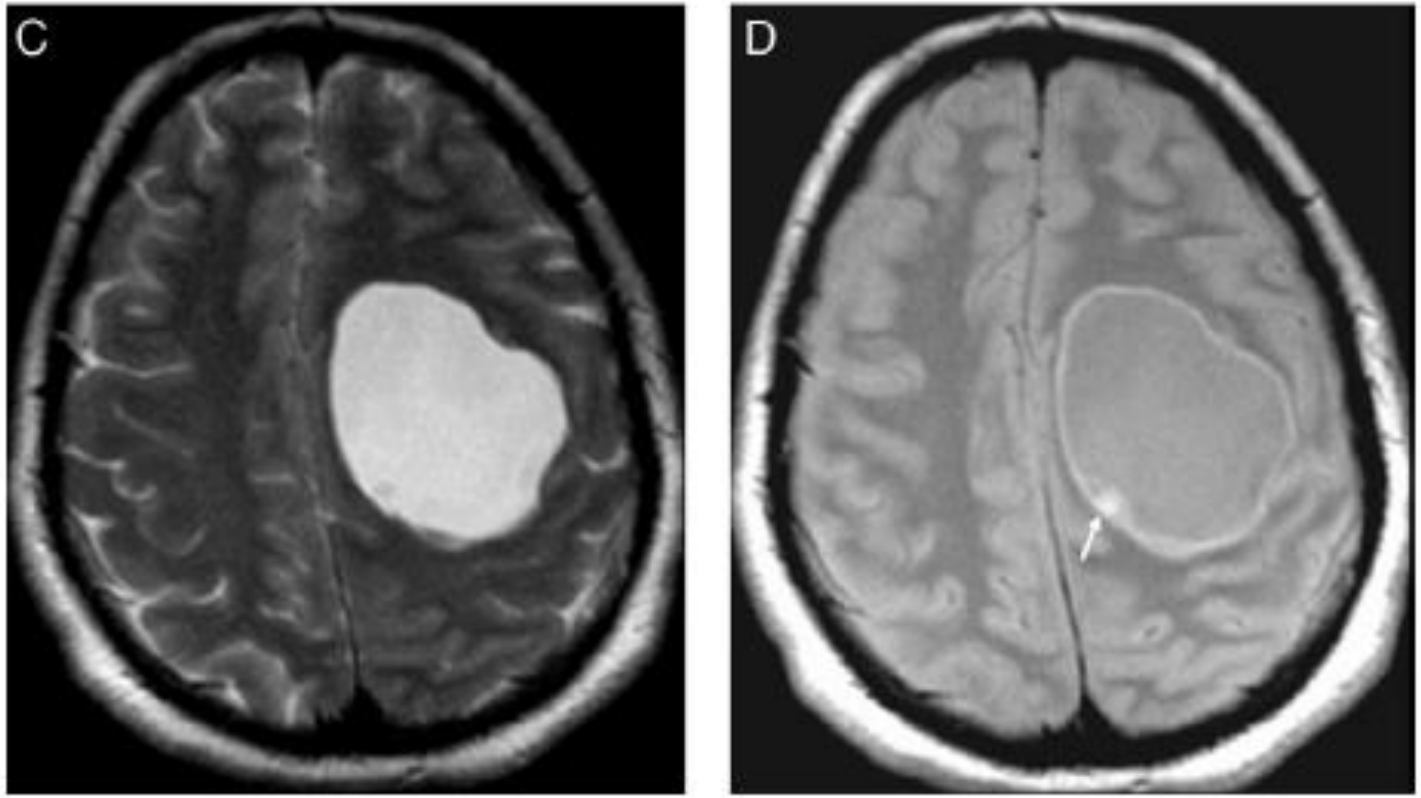
Estrada et al. Imaging findings in neurocysticercosis, Radiología. 2013;55(2):130---141

Differential Diagnosis

- **Neurocysticercosis - vesicular phase**

T2W axial image, left fronto-parietal cyst

FLAIR axial image, the same lesion

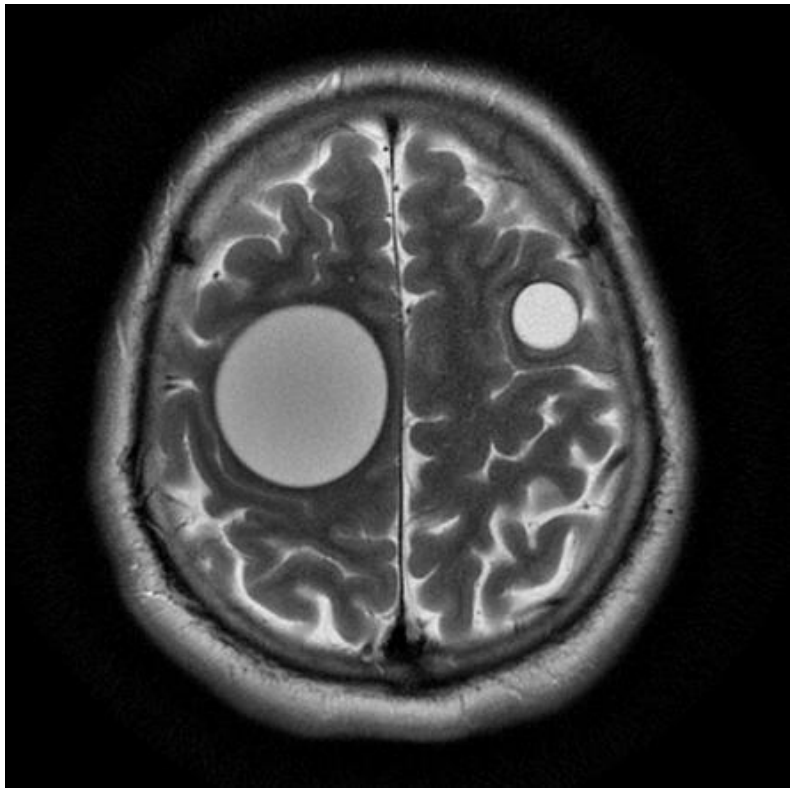


Estrada et al. Imaging findings in neurocysticercosis, Radiología. 2013;55(2):130---141

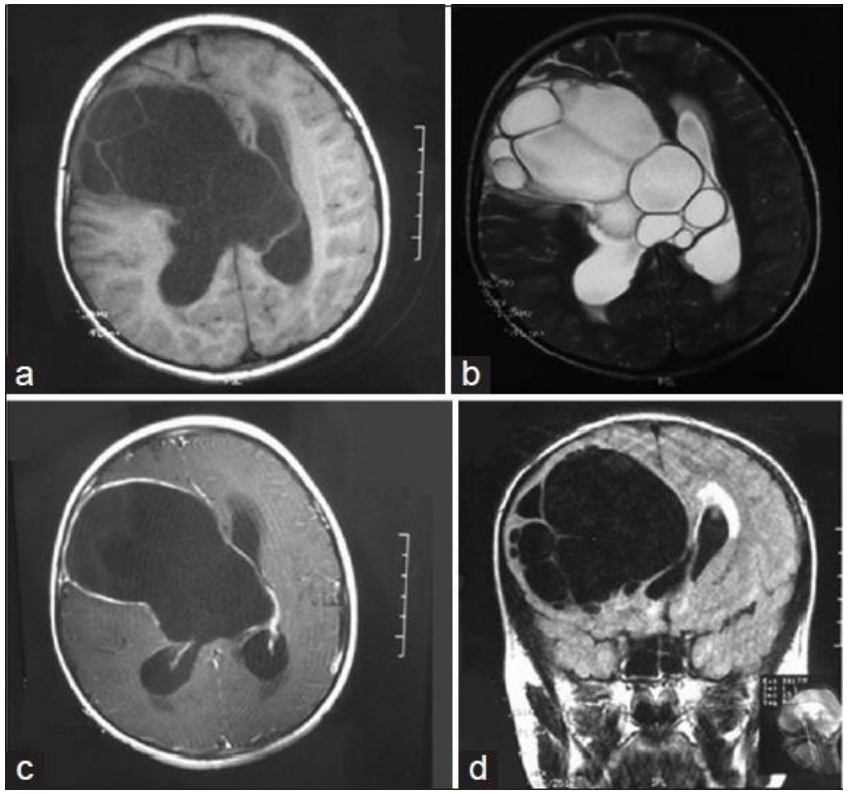
Differential Diagnosis

- Echinococcus granulosus cysts

T2W axial image, bilateral hydatid cysts



Hydatid cyst with multiple daughter cysts



Recommendations

To our knowledge, case describes a longest period of clinical observation and treatment of Labrune syndrome.

Rare disorders must be considered in patients with non-typical appearance of symptoms in order to avoid unnecessary investigations and manipulations;

In our case patient underwent radiation therapy that was definitely helpless and possibly harmful;

For neurologists/neurosurgeons:

Draining of the symptomatic cysts gives only a temporary effect and after a few months the symptoms return again;

In our case, a more stable effect was achieved with shunting;

MRI monitoring once every six months can detect clinically important growth of a particular cyst;