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ADULT CEREBRAL HYPOXIA: The Many Faces of the Monster

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THE FACES OF THE MONSTER

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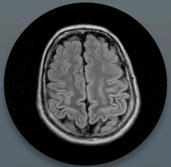
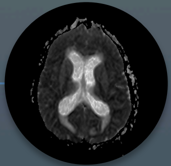
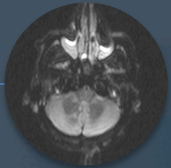


CORTICAL NECROSIS

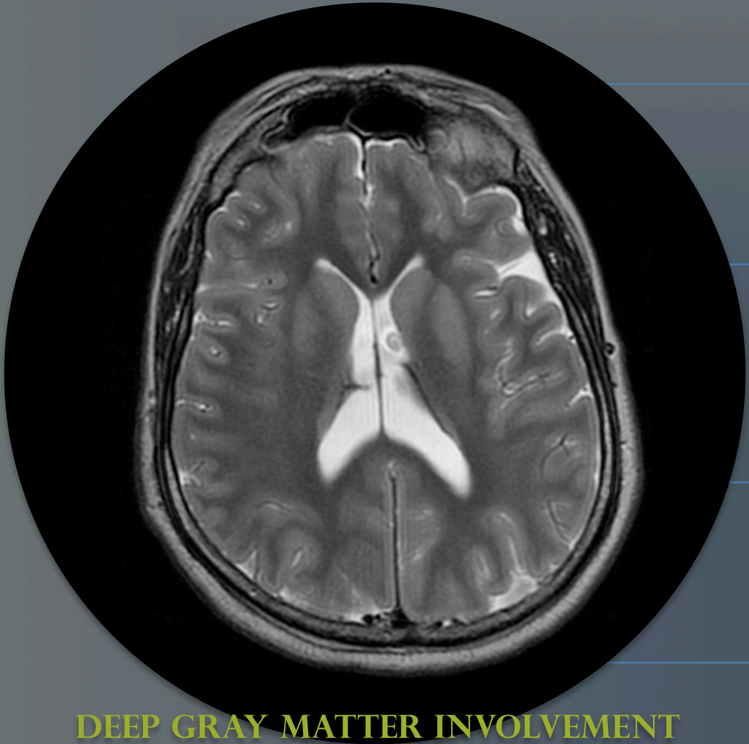


BILATERAL, SYMMETRICAL RESTRICTED DIFFUSION



BRAINSTEM OEDEMA

LUXURY PERFUSION



DEEP GRAY MATTER INVOLVEMENT

An hypoxic-isquemic insult (HII) is a potentially catastrophic event that may present itself with many faces. We aim to review when, where and how it harms our patients, and to portray it's different presentations in the hope of being better prepared to recognize this monster when we have to face it.

OVERVIEW

HYPOXIC-ISQUEMIC INSULT:

An hypoxic-isquemic insult is a lack of blood flow to the central nervous system (CNS) or a lack of oxygen in the bloodstream, for a period of time long enough that permanent damage to the neurons is inflicted.

The severity and duration of the insult determine specific structures that will be involved, depending on their metabolic requirements and nervous activation pathways.

Stage in brain development at the time of the event is the primary factor that determines the structures involved in the perinatal period and early childhood, whereas deep gray matter involvement and cortical necrosis are the main findings in older children and adults.

Imaging features can be key to the early diagnosis of these events, and lead to a more accurate prognosis and swift therapeutic action, including recently developed neuroprotective strategies to which time is of the essence.

TRIGGERING EVENTS

In the perinatal period and early childhood, the most common triggering event is asphyxia, leading to low oxygen blood levels, and therefore to cardiovascular malfunction and isquemia.

In adults, a primary cardiovascular event is most frequent, with decreased blood flow leading to poor blood oxygenation and therefore insufficient supply to the CNS.

Other type of events can trigger damage pathways and therefore show similar patterns of damage and acute symptoms, including: carbon monoxide poisoning, methanol, cyanide, sever hyper or hypoglukemia, hypovolemia or osmotic myelinolisis. A good history and contributing clinical and analytical data are essential to the differential.

TRIGGERING EVENTS

CHILDREN

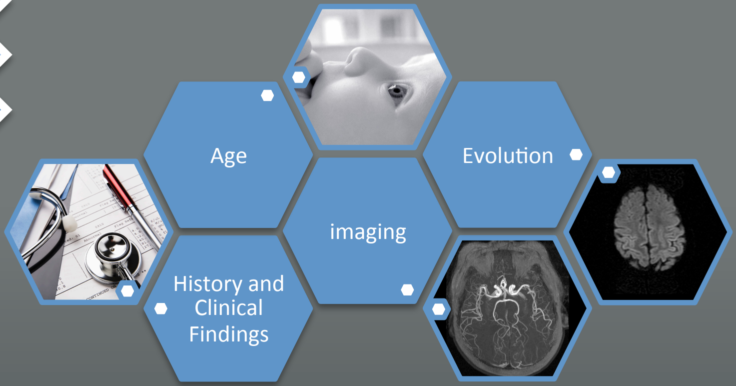
- Perinatal Complications
- Asphyxia

ADULTS

- Cardiac Arrest

OTHERS

- carbon monoxide poisoning
- methanol
- cyanide
- hyper or hypoglukemia
- hypovolemia
- osmotic myelinolisis.



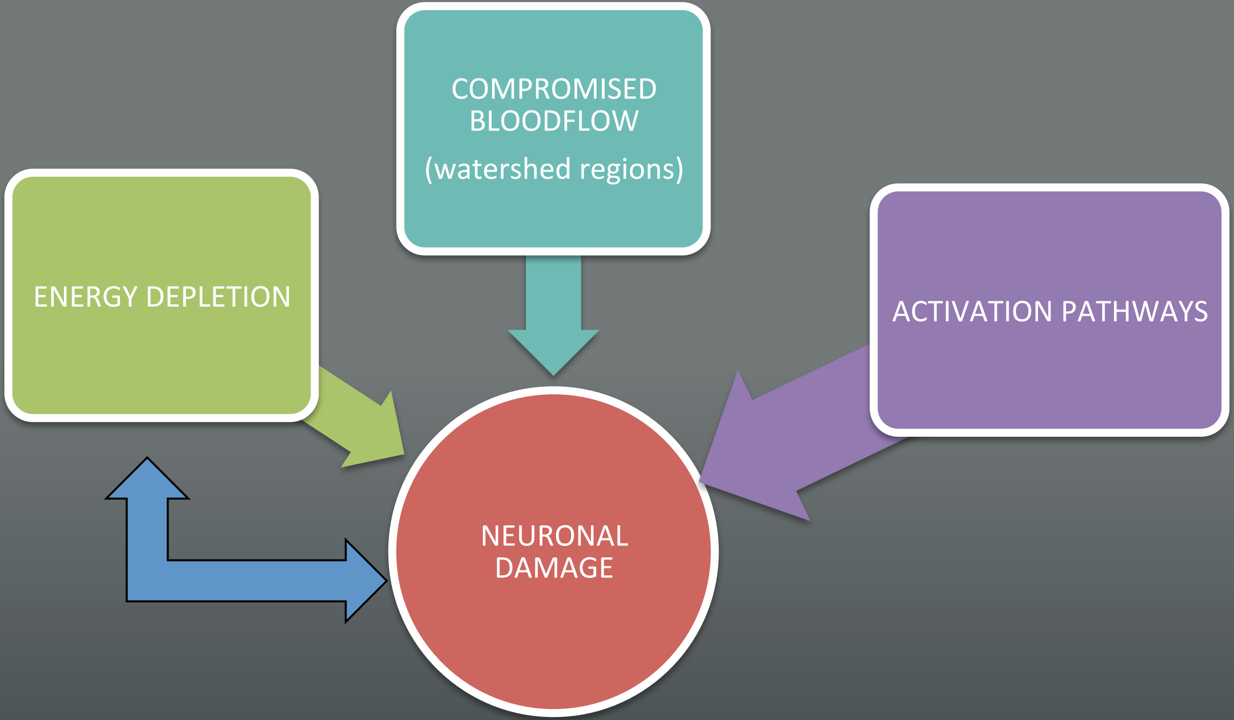
SENSIBLE TISSUE

Energy depletion is fastest in the brain due to both the lack of significative energy storage and the high and steady requirements.

Watershed regions with compromised blood flow, and highly active grey matter structures that are also rich in dendrites are the first to sustain permanent damage.

Extracellular glutamate levels leading to membrane depolarization are followed by downstream synaptic transmission of these changes and therefore determine some specific patterns of damage that we may find in this condition.

SENSIBLE TISSUE



SENSIBLE TISSUE

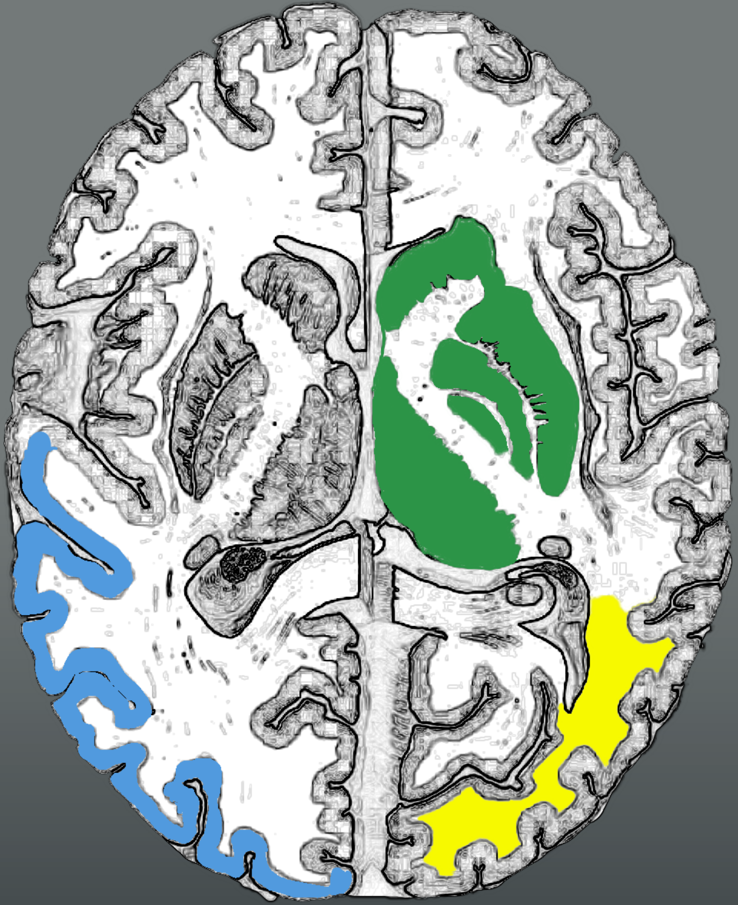
An hypoxic noxa damages first and foremost:

The Deep Gray Matter:

- Nucleus caudatus (caput)
- Putamen
- Pallidum
- Thalamus

Cortex (laminar cortical necrosis)

White Matter (delayed laeukoencephalopaty may appear)



POSTANOXIC LEUKOENCEPHALOPATY

Postanoxic Laeukoencephalopathy is a rare condition that occurs in less than 3% of cases but it must be known and suspected when after a relative improvement or stability of the neurological condition is followed by an acute decline. Radiologists must be aware of this condition and vigilant of it's apparition.

Adding to the usual findings in the deep gray matter and cortex, when and if it occurs, white matter hyperintensity can be seen it T2-weighed images in the subacute period and be predictive of this condition, therefore adding significative information to the care of the patient and helping the clinician to be prepared for the necessary support measures.

Findings can be seen even within the first week, whether a lucid period is present or not, and they tend to disappear as clinical improvement is achieved, but can last as long as 18 months or become irreversible.

DAMAGE PATHWAYS

Anaerobic metabolism caused by the lack of oxygen to the CNS cells leads to membrane depolarization, which activates glutamate release and Ca2+ channels.

Together with the inhibition of glutamate reuptake due to energy depletion in the cell, these conditions provoke a pathway of damage related to the glutamate dependent activation pathways in the brain, which explains the specificity of the damage patterns observed.

The severity of the damage to the cell can either lead to immediate cell death, or to delayed apoptosis, which explains why it may take days for some injuries to be fully instated. This can be the reason why white matter signal abnormalities may be observed in the subacute and chronic period.

DAMAGE PATHWAYS

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ANAEROBIOSIS

- CA2+ Channels
- Depolarization

GLUTAMATE

- Synaptic Release
- Reuptake inhibition

DELAYED APOPTOSIS

- White Matter involvement

CELL DAMAGE & OEDEMA

WHEN & WHAT TO STUDY

These chain of events can be subdivided in at least three periods. The findings that should be expected for each of these change over time, and the radiologist must know what to look for and how.

Acute period: the first 24h.

Standard MR may be considered normal or the findings very subtle. Diffusion-weighted images are the first to show abnormalities, even in the first six hours.

Subacute period: 24h to 20 days.

Standard MR features to be expected include increased signal intensity in the basal ganglia, thalami, hippocampi and cortical structures. Diffusion-weighted images make this findings more evident and may reveal signal abnormalities in the white matter that, if present, have an important role in determining the prognosis.

Chronic period: after 21 days.

Images may show residual increases in signal intensity in the basal ganglia or linear hyperintensities in the cortex that account for irreversible cortical necrosis. Diffusion-weighted images may be normalized by now, or show abnormalities in the white matter due to Postanoxic Laeukoencephalopathy. (Delayed white matter injury, it's exact pathogenesis is still a matter of discussion).

WHEN & WHAT TO STUDY

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ACUTE

- 0 – 24H
- Look for changes in Diffusion

SUBACUTE

- 24h – 20 Days
- Repeated studies
- Look at the deep gray matter and cortex

CHRONIC

- 21 days and over.
- Evaluate permanent damage.
- Watch for white matter abnormalities

HOW TO STUDY

MRI is the modality of choice; imaging should included diffusion sequences and ADC mapping, while spectroscopy can be very valuable specially in the newborn, but increasingly so in the adult as well.

CT can be reported as normal specially in the first hours or days, and should not hinder the realization of an MRI if an HII is suspected. It remains useful for the evaluation of the patients evolution due to it's speed and replicability.

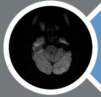
Imaging features can be subtle and they vary over time; in some cases repeated studies are advisable to determine the extent of damage and prognosis.

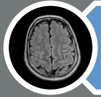
Diffusion images typically change over time, and can be the basis for controlling patients evolution, as it is the first to change, and it usually normalizes in a period of weeks.

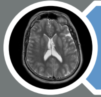
These patients are often unstable and may not allow for long studies and require ICU support and transportation. Therefore, sequences must be carefully chosen and placed in order of their foreseeable diagnostic performance.

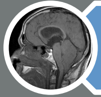
We present our general imaging strategy in this cases; this is one of many possibilities: an active approach on the side of the radiologist in programming the study will be of the essence for a swift and accurate diagnosis and to avoid possible pitfalls.

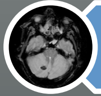
HOW TO STUDY

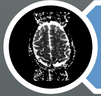

Diffusion weighted sequence (B1000)

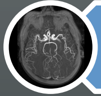

T2 Fluid-Attenuated Inversion Recovery (FLAIR) weighted sequence in the axial plane.

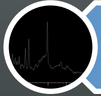

T2 Fast Spin Echo (FSE) weighted sequence in the axial plane.


T1 Fluid-Attenuated Inversion Recovery (FLAIR) weighted sequence in the sagittal plane.


T2* weighted sequence


Apparent Diffusion Coefficient (ADC) Mapping


3D Time of Flight (TOF) sequence if available and considered clinically relevant

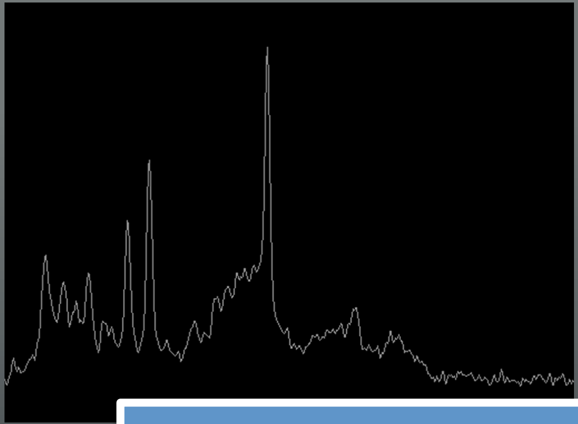

MR Spectroscopy when necessary and possible

MR SPECTROSCOPY

MR Spectroscopy may be used if necessary when in doubt, but has a limited role to play in the adult.

In children, it is of foremost importance to determine the extent of the insult and confirm the diagnosis, due in part to the smaller role played by history and clinical context.

When performed, an increase in lactate and lipids will be the most common finding, expressing anaerobiosis within the neuron.



Normal Spectroscopy in the Adult

Newborn. High peaks in the lactate and lipids regions, expressing an HII

IMAGING FINDINGS

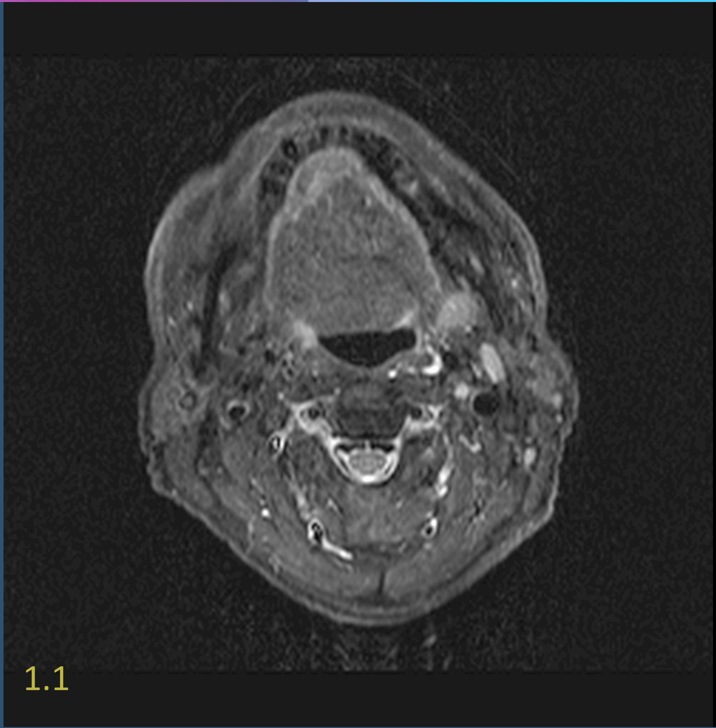
1.1 SHORT T1 Inversion Recovery sequence (STIR):

Increased signal intensity in the right anterior edge of the tongue reveals a mouth floor neoformation that will undergo surgery.

1.2 HEAD CT:

Poor grey/white matter differentiation.

No abnormalities present in the ventricular system.



1.1

1.2

65y old patient underwent surgery for mouth floor cancer and needed CPR after a surgical complication. CT was performed immediately after surgery.

IMAGING FINDINGS

1.3 T2 Fluid-Attenuated Inversion Recovery sequence (FLAIR) after HII:

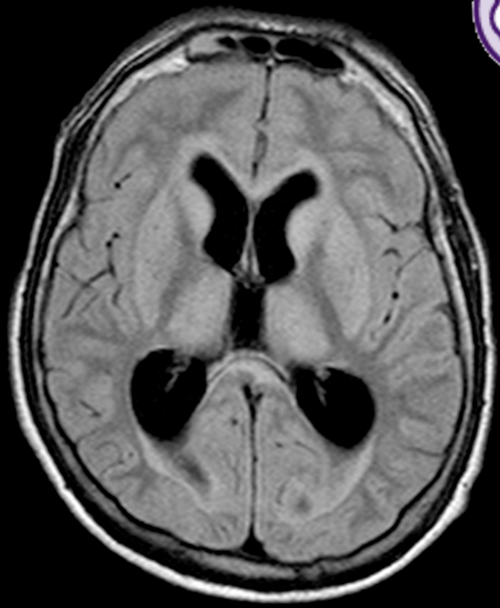
Extensive basal ganglia hyperintensity

1.4 T2 Fast Spin Echo (FSE) sequence 5 days after HII:

Cerebellar oedema

Cerebellar bleeding

Collapsed 4th ventricle



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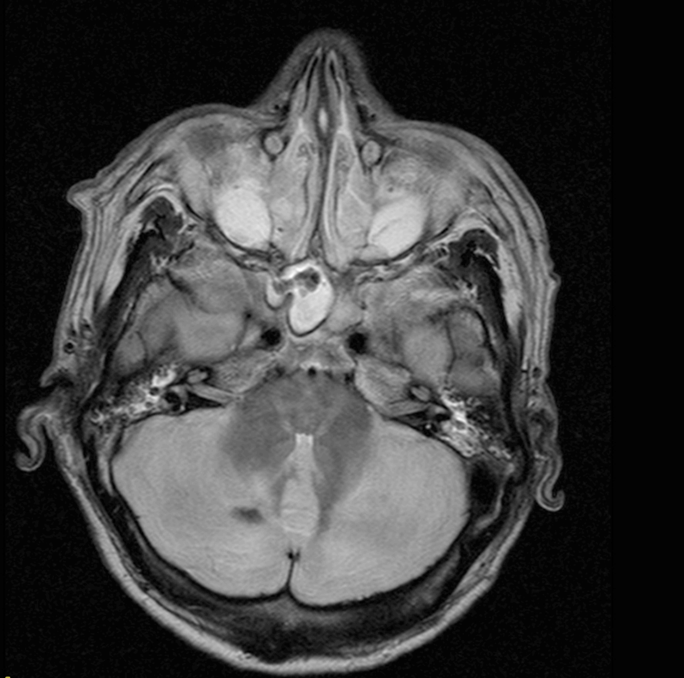

1.4

Five days after the event MRI showed increased signal in the basal ganglia and supratentorial hydrocefalia which was not previously present. Cerebellar oedema and 4th ventricle collapse are evident in the T2 FSE sequence. A cerebellar bleeding is shown where a temporary catheter had been placed.

IMAGING FINDINGS

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1.5 Short T1 weighted Inversion Recovery sequence (STIR) prior to surgery:

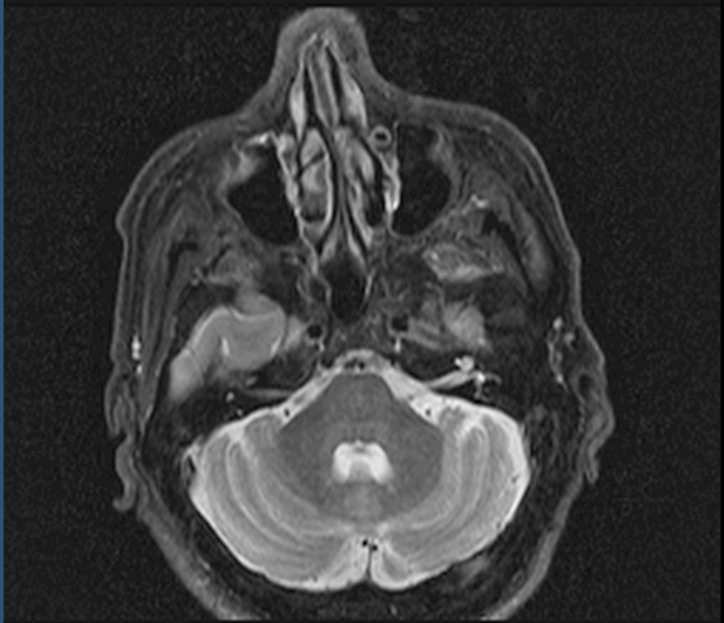
4th ventricle shows no abnormalities

1.6 T2 weighted Turbo Spin Echo sequence (TSE) 5 days after HII:

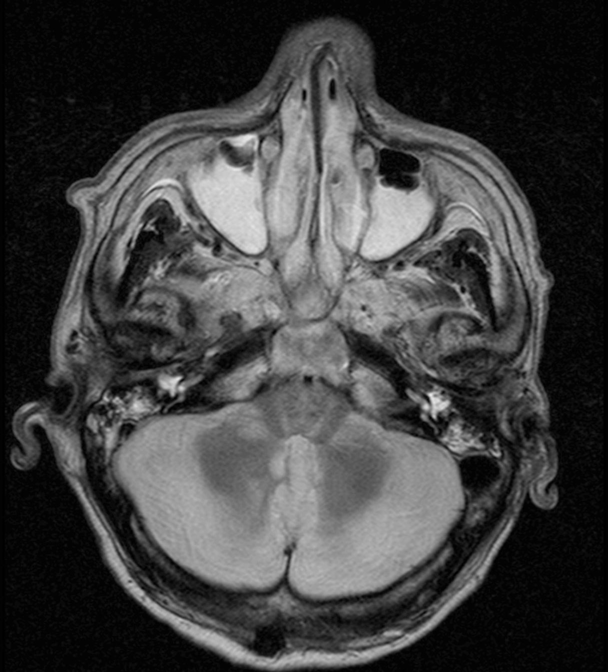
collapsed 4th ventricle

cerebellar oedema

loss of normal foliae structure



1.5



1.6

These two studies prior and after the HII shows changes in size of the fourth ventricle. The patient went from a normal ventricular caliber to a ventricular collapse due to the oedema caused by the hypoxic event. Both studies are only 30 days apart.

IMAGING FINDINGS

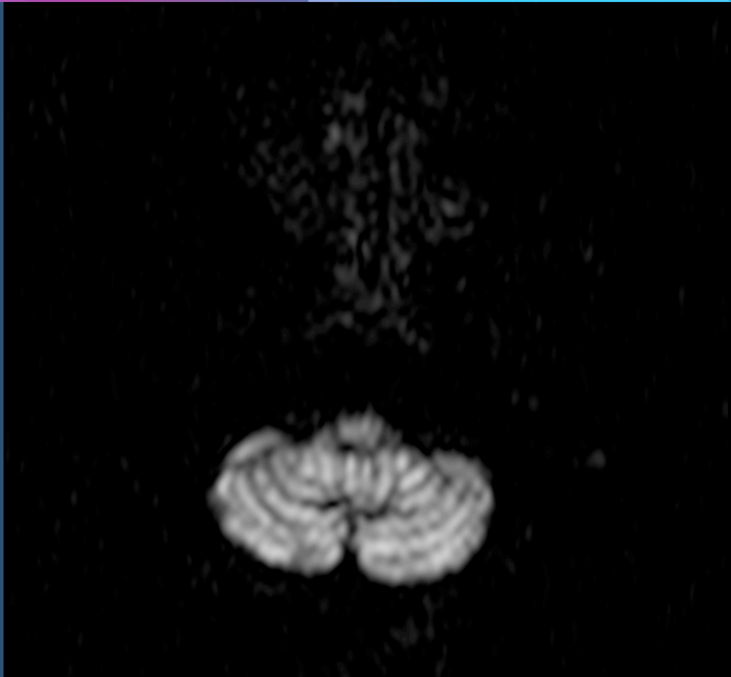
1.7 Diffusion weighted imaging:

Restricted diffusion can be seen in the cerebellum on both hemispheres.

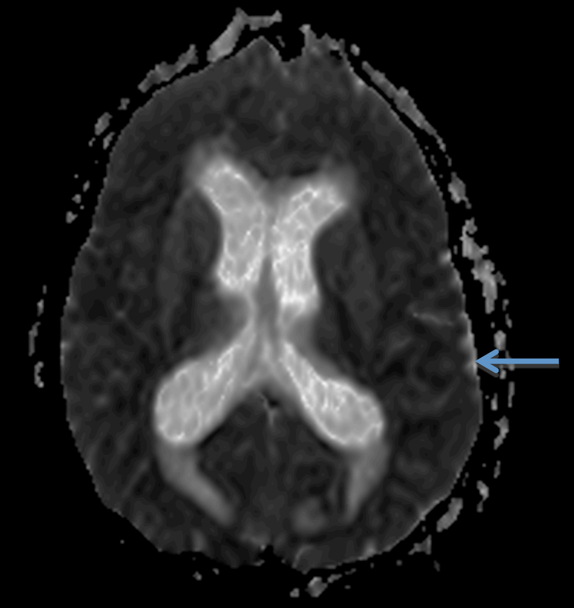
1.8 ADC Mapping:

A subtle area of restricted diffusion can be seen on the left temporal lobe. (Arrow)

Images were acquired five days after the event.



1.7



1.8

Diffusion weighted imaging was performed. It is mandatory to use it as a part of our imaging strategy to correctly assess the real extent of the damage and contribute to a more accurate prognosis. In this case, restricted cerebellar and left temporal lobe diffusion were visible, confirming the prior findings and anticipating a harsh prognosis. The patient was clinically in coma. Outcome was fatal.

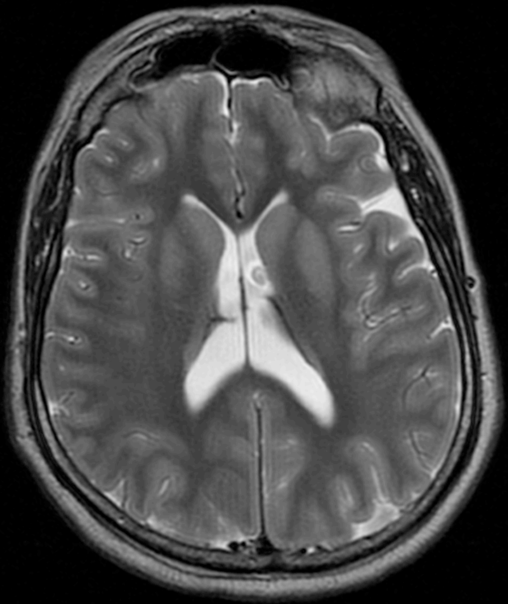
IMAGING FINDINGS

2.1 T2-Weighted sequence:

Intensity of signal is increased in the basal ganglia and cortex.

2.2 T2 weighted Fluid – Attenuation Inversion Recovery (FLAIR) sequence:

Increased signal is visible in the cortex, specially in the left occipital lobe.



2.1

2.2

65 years old patient suffered a cardiac arrest and is brought to the ICU in our hospital after a lengthy CPR. MRI is performed two days after the event when the patient is stable. Increased signal in the basal ganglia and cortical necrosis are the two most common findings associated with an HII in an adult.

IMAGING FINDINGS

2.2. Diffusion weighted imaging:

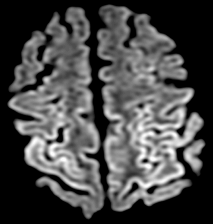
Restricted diffusion is visible throughout the cortex, specially in the occipital region.

(B1000)

2.3 ADC Mapping:

ADC confirms the findings.

In this case ADC shows that diffusion is not restricted in the basal ganglia.



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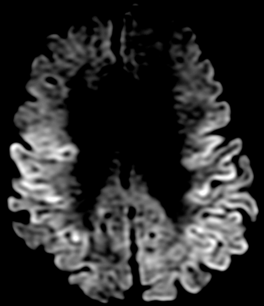

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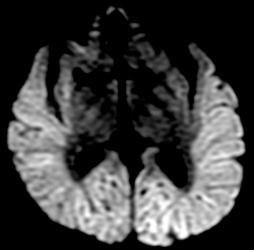

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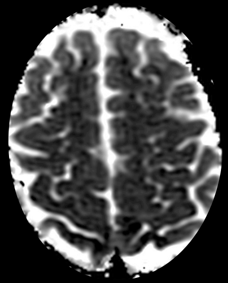

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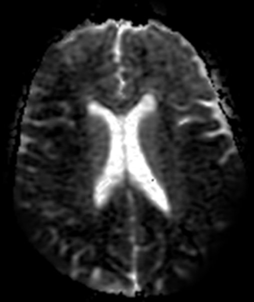

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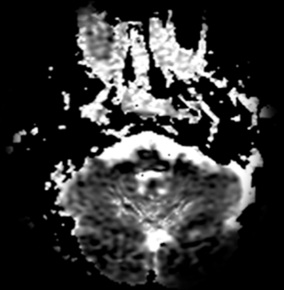


2.4

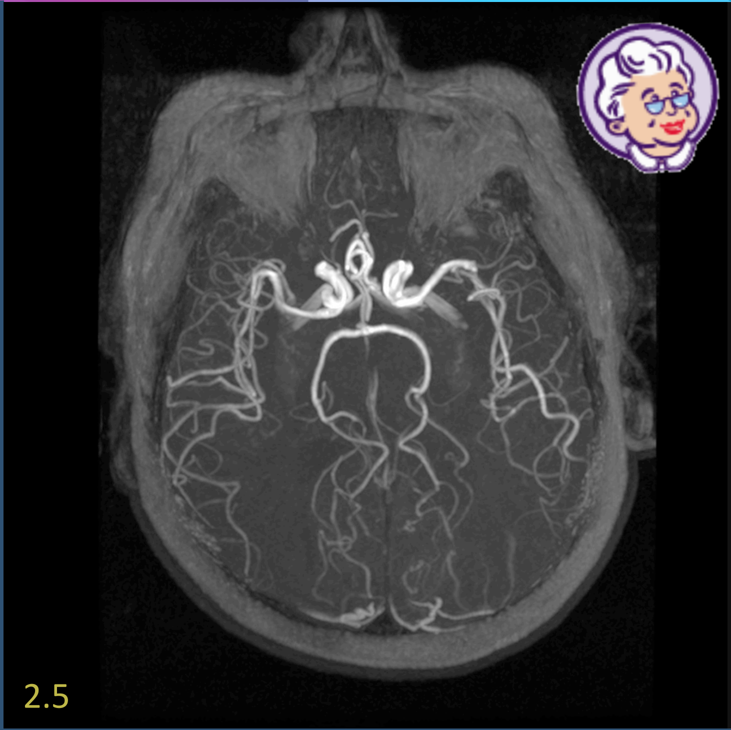
IMAGING FINDINGS

2.5 3D Time Of Flight Sequence:

Generalized luxury perfusion can be seen in this 3D TOF image composition.

2.6 3D Time Of Flight Sequence:

A normal 3D TOF performed in the same machine and in a patient with the same age.



2.5

2.6

We performed a 3DTOF at the same time to complete the patients evaluation. Luxury perfusion can be seen in all territories, expressing the compensation mechanisms the brain uses after hypoxia. Also, we show a normal study on the right to facilitate the comparison and make the finding even more evident.

IMAGING FINDINGS

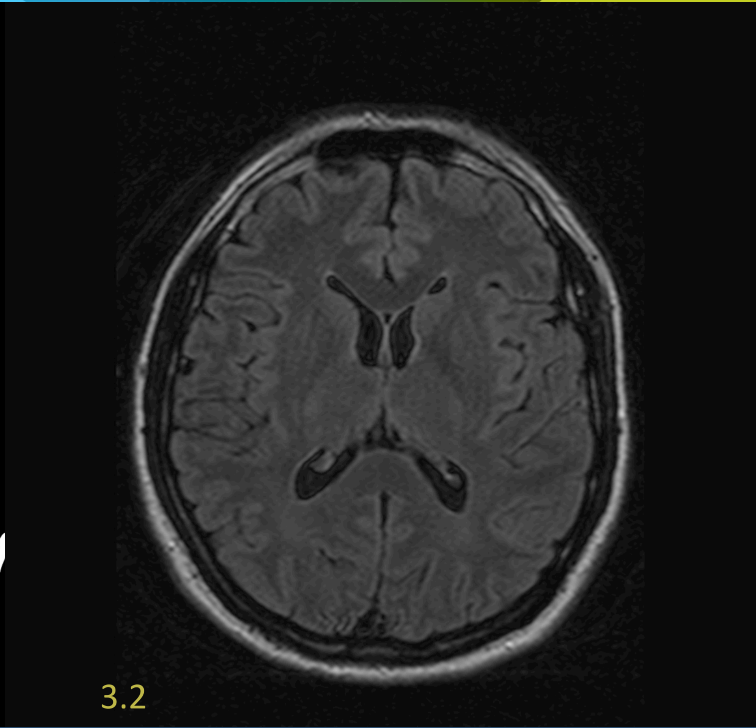
3.1 Head CT:

Normal head CT at admission.

3.2 T2 weighted Fluid-Attenuation Inversion Recovery sequence (FLAIR):

MRI was normal at the time of the admission.

3.1



3.2

40 years old patient is diagnosed with lymphoma (with no known CNS involvement) and admitted to our hospital. Patient suffers frequent headaches and a 3rd and 6th cranial pairs paresia is discovered. We perform a head CT and brain and neck MRI for evaluation, with no significant findings. These images are shown in order to compare them to the salient findings after the patient suffers an hypoxic event.

IMAGING FINDINGS

3.3 T2 weighted Fluid – Attenuation Inversion Recovery (FLAIR) sequence:

Increased signal can be seen throughout the cortex, specially on the parietooccipital region on the left hemisphere and in the basal ganglia.

3.4 T2 weighted Fast Spin Echo (FSE) sequence in the coronal plane:

Increased signal in the deep gray matter is visible.

3.3

3.4

Patient suffered a rapid decline in his condition two weeks after admission. It was first attributed to either his systemic disease or the treatment drugs he was receiving. The radiological findings where the first to hint a possible hypoxic event that had not previously been considered, illustrating the importance of swift action on the part of the radiologist.

IMAGING FINDINGS

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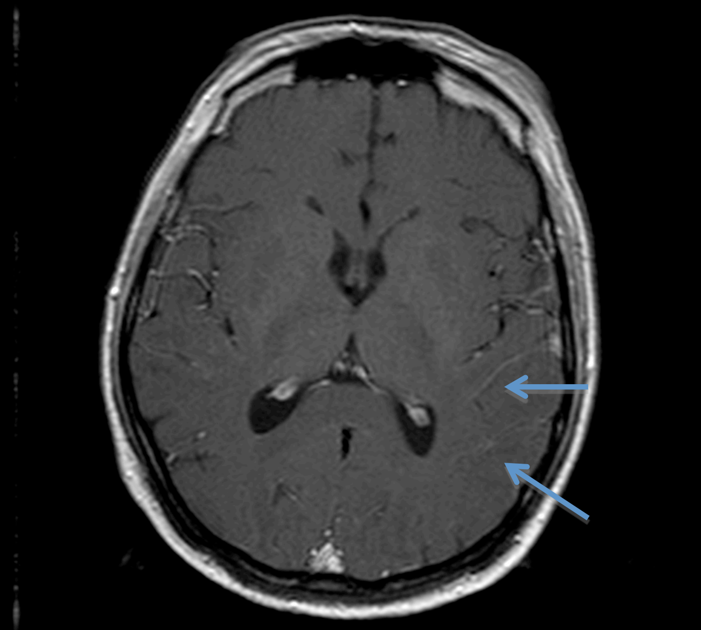
3.5 T1 weighted sequence after the administration of Gadolinium:

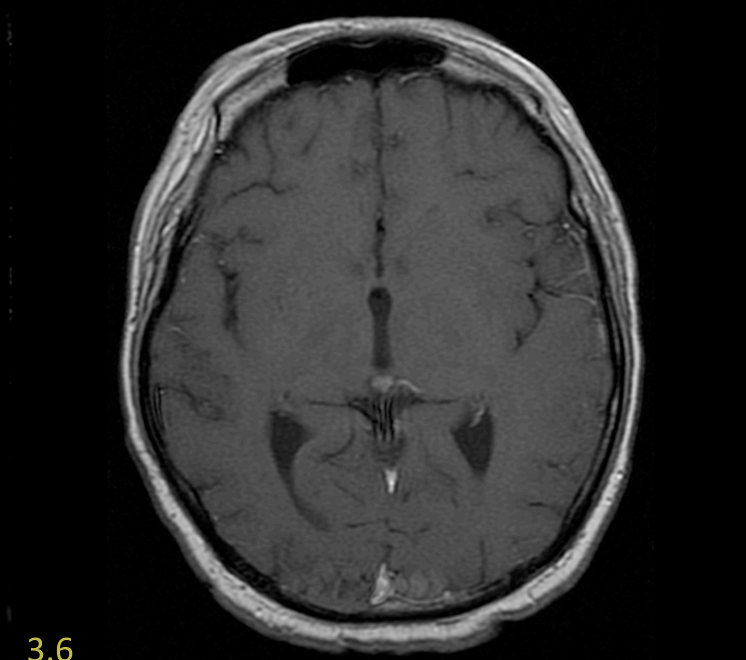
Image was acquired days after the event, and shows some increased cortical blood flow, and expresses luxury perfusion.

3.6 T1 weighted sequence after the administration of Gadolinium:

two weeks later, luxury perfusion and deep gray matter signal decrease are no longer visible, as the compensating mechanisms have been exhausted.



3.5



3.6

Image findings in the following studies and clinical evolution confirmed that the patient had suffered an hypoxic-isquemic event, leading to changes in the therapeutical strategies available. Methotrexate toxicity was first suspected, but discarded in the face of the radiological findings displayed.

HYPOXIA LIKE

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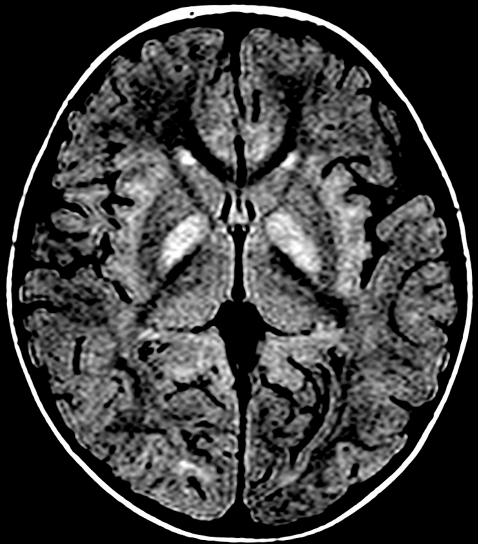
4.1 T2 weighted Fluid – Attenuation Inversion Recovery (FLAIR) sequence:

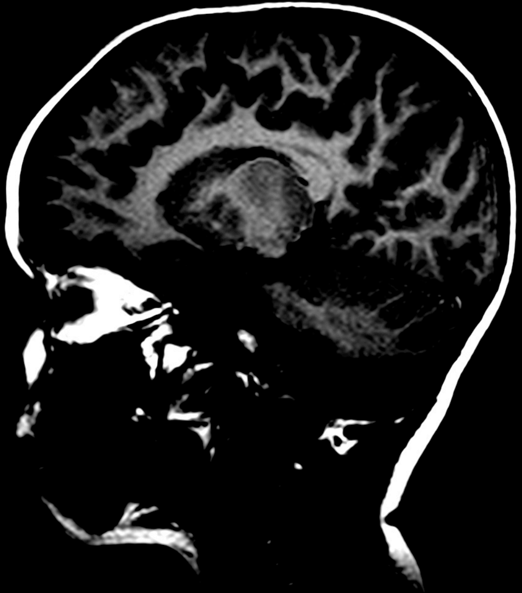
Increased signal in the pallidum, bilaterally.

4.2 T1 weighted sequence in the sagittal plane:

Hipointensity in the pallidum.



4.1



4.2

Three years old patient with a chronic history of several episodes of neurological status with motor symptoms. Hiperintensity can be seen in the basal ganglia, though no history of hypoxia can be established and no other abnormalities can be found.

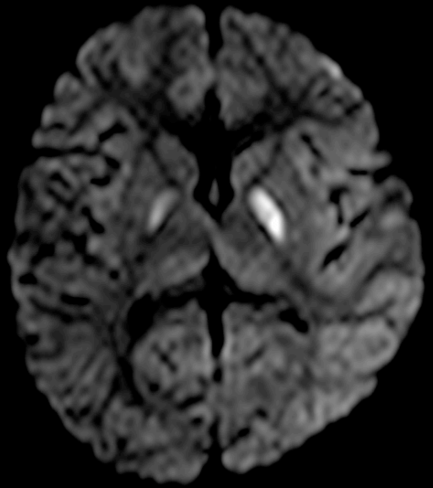
HYPOXIA LIKE

4.3 Diffusion weighted sequence:

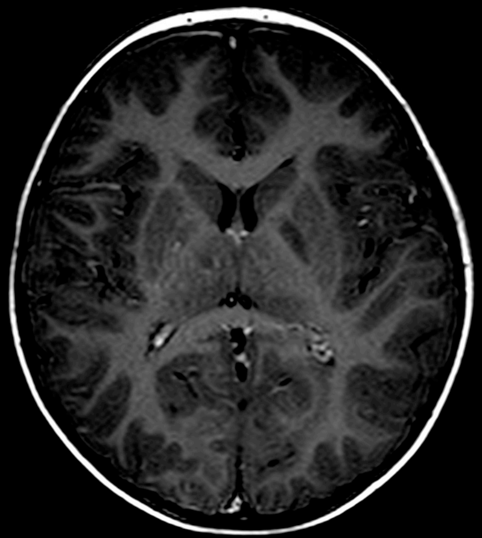
Restricted Diffusion in both pallidae only, specially on the left.

4.4 T1 weighted sequence after the administration of Gadolinium:

Hipointensity in the left pallidum. No T1 shortening can be seen after the administration of Gd



4.3



4.4

This patient showed bilateral hyperintensities in the basal ganglia with restricted diffusion, but no cortical damage and no compatible history. In this case we see a metabolic disorder (no exact diagnosis has been achieved) that presents itself in a similar fashion to an HII.

HYPOXIA LIKE

5.1 T2 weighted Fast Spin Echo (FSE) sequence:

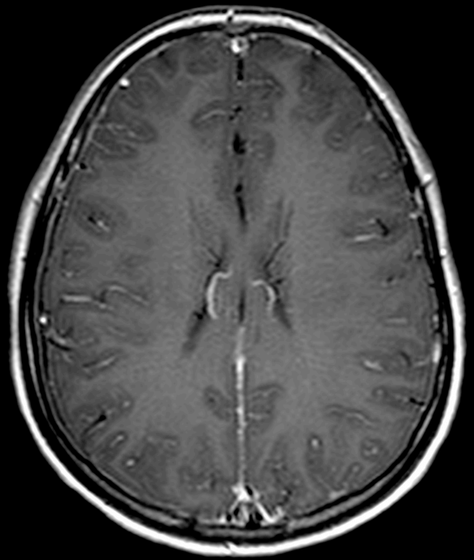
Increased signal intensity is visible in the cortex, particularly in the frontal region.

Right subdural effusion.

5.2 T1 weighted sequence after the administration of Gadolinium:

Increased cortical blood flow.

5.1



5.2

19 years old patient presents at the ER with acute neurological decline with sensory and motor symptoms. No relevant history in the weeks prior. No underlining conditions

HYPOXIA LIKE

5.3 T2 weighted Fast Spin Echo (FSE) sequence:

No signal hyperintensities are visible in the deep gray matter.

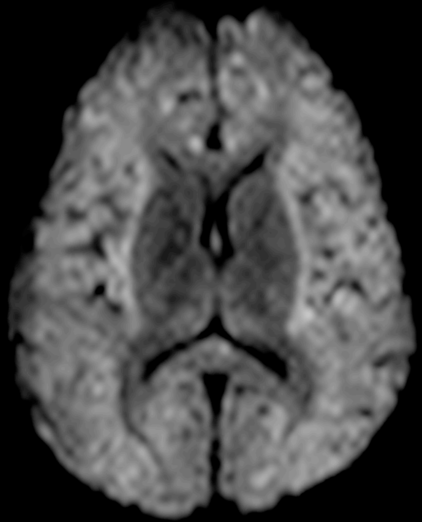
Increased signal in the cortex

Right subdural effusion

5.4 Diffusion Weighted sequence:

No restricted diffusion is apparent in the basal ganglia.

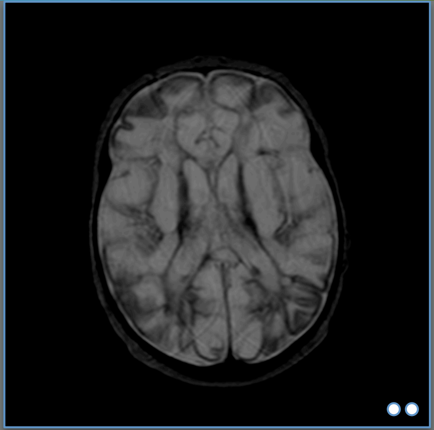
5.3

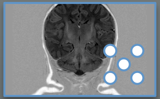


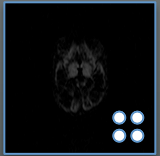
5.4

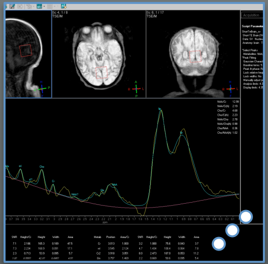
Evolution and concurrent analytical and clinical data led to the diagnosis of acute meningoencephalitis, probably of viral origin. In this case, we see no abnormalities in the basal ganglia which is uncommon in an hypoxic-isquemic insult (HII). This condition can sometimes present itself in a fashion similar to an HII, and must be considered in the differential diagnosis.

HYPOXIA IN CHILDREN









Imaging is a key aspect of the management of hypoxic-isquemic events in the perinatal period and the newborn, specially useful since patient's history and clinical exploration are not as clarifying. Findings will again depend on the severity and duration of the insult, and in this case, also on brain maturity, developmental stage, and the specific etiology. Here we present just a visual overview of the findings associated with hypoxia in children.

SUMMARY

When an hypoxic-isquemic insult is suspected due to clinical findings and history, imaging studies should consider the severity and duration of insult, it's hours of evolution, and include diffusion-weighted sequences and ADC mapping.

Imaging findings alone even in the absence of prior indications can be enough for the radiologist to consider this diagnosis, and raise these concerns to the clinician in case this possibility hasn't been ruled out.

The metabolic requirements and nervous activation pathways of the structures sustaining damage lead to a cascade of physiopatological events that cause both immediate and delayed tissue damage, and explain the very specific patterns of signal abnormalities that can be present.

SUMMARY II

Deep gray matter signal hyperintensities, cortical necrosis, and restricted diffusion are the most common of the findings in this cases.

Also, brainstem involvement, or cerebellar oedema and signal abnormalities may be present.

Postanoxic Laeukoencephalopathy is a rare entity but it should be suspected when after a relative improvement or stability of the neurological condition is followed by an acute decline. It's swift diagnosis can predate the neurological decline and significantly improve patient care.

Other entities can mimic this condition and induce the same damage pathways; it is often the case that only clinical information and history can help determine the actual cause of the changes observed.

REFERENCE

For reference and further reading:

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② **Diffusion-Weighted MR Imaging of Global Cerebral Anoxia.** Andres Arbelaez, Mauricio Castillo, and Suresh K. Mukherji. *AJNR Am J Neuroradiol* 20:999–1007

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④ **Hypoxic brain damage. Cortical laminar necrosis and delayed changes in white matter at sequential MR imaging.** Takahoshi S, Higano S, Ishii K. *Radiology* 1993;189:449–456.

⑤ **Glutamate and the pathophysiology of hypoxic/ischemic brain damage.** Rothman SM, Olney JW. *Ann Neurol* 1986;19: 105–111.

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Thank you for your attention and have a great week at the RSNA 2011!