A DIFFERENT CLINICAL PERSPECTIVE FOR THE DIAGNOSIS OF WHITE MATTER DISORDERS

MYELINATION DEFECTS
–
LEUKODYSTROPHIES
-
LEUKOENCEPHALOPA-THIES

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A case report

- Mais was referred at the age of three months, due to "Inability to control the movements of her head"
- maybe early to decide if it is abnormal?

case report cont..

Her physical examination at 5 months age showed:

A head was hanging down, and moved by gravity.

Rapid eye oscillating movements -(nystagmus).

Her percentile showed that her head circumference had declined.

case report cont..

The Neuro-ophthalmologist wrote at sixteen months of age :

There is no cherry red spot,
No Dysmorfism,
No social smile,
Eyes did not follow an object,
Head circumference was 41 cm.,

Head-lag & axial hypotonia,
no bulbar signs.
Spastic paraplegia of limbs.

Deep tendon reflexes were alert".

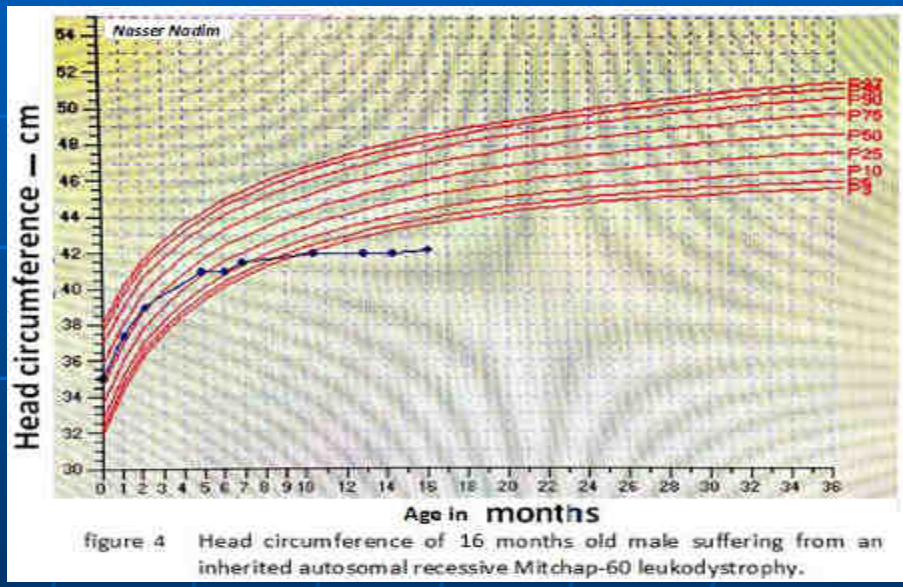


figure 4 Head circumference of 16 months old male suffering from an inherited autosomal recessive Mitchap-60 leukodystrophy.

case report cont..

- **Genetic consultation:**

No specific diagnosis. metabolic disease is suspected.

case report cont..

three major clinical markers are at our hands:

- ❖ The uncontrolled head movements and head lag
- ❖ nystagmus
- ❖BERA test revealed a sensori-neural deafness

case report cont..

In the coming months , the physical examination revealed:

Loss of sight,

failing to swallow and to thrive- PEG feeding

Chronic bronchitis dominated her coming visits.

To be continued

Conclusions from the case report

Primary infantile motor developmental delay or hypotonia is a serious sign,

A chaos of non-systematic, non-directive symptoms and signs

Goals

1- A NEW PERSPECTIVE for easy access to children with developmental retardation

2- The logic behind the chronology of clinical symptoms of leukodystrophies.

MRI when and why

Quick diagnosis

Chips of DNA, CMA ?

The logic behind myelin disorders

LDs have gradual clinical course

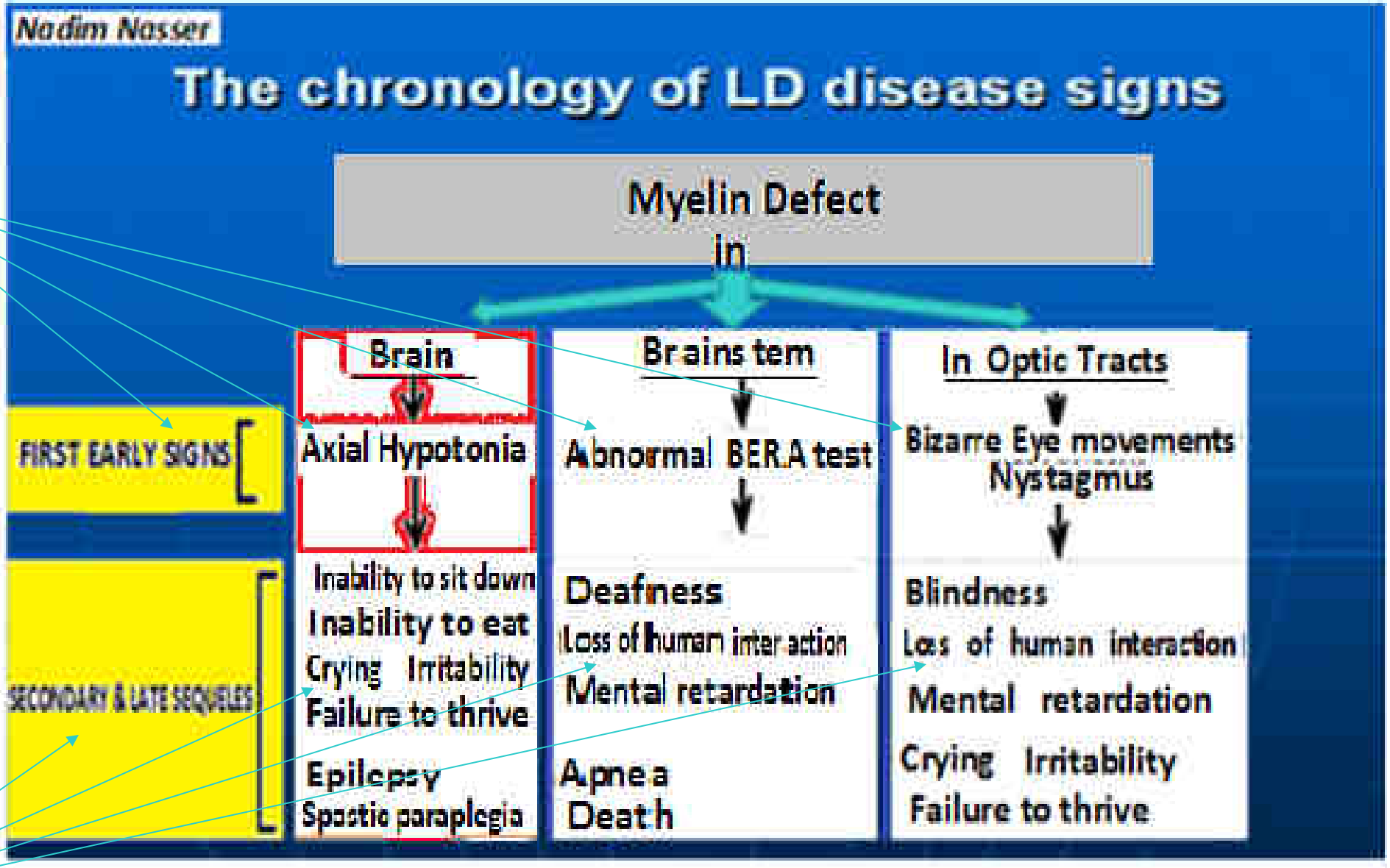


Figure 3 The chronology of leukodystrophies primary and secondary signs

Signs and symptoms are divided into: first early signs (the major signs), and to secondary or late sequels, at the bottom.

THE WIDE DISTRIBUTION OF WHITE MATTER IN THE CENTRAL NERVOUS SYSTEM

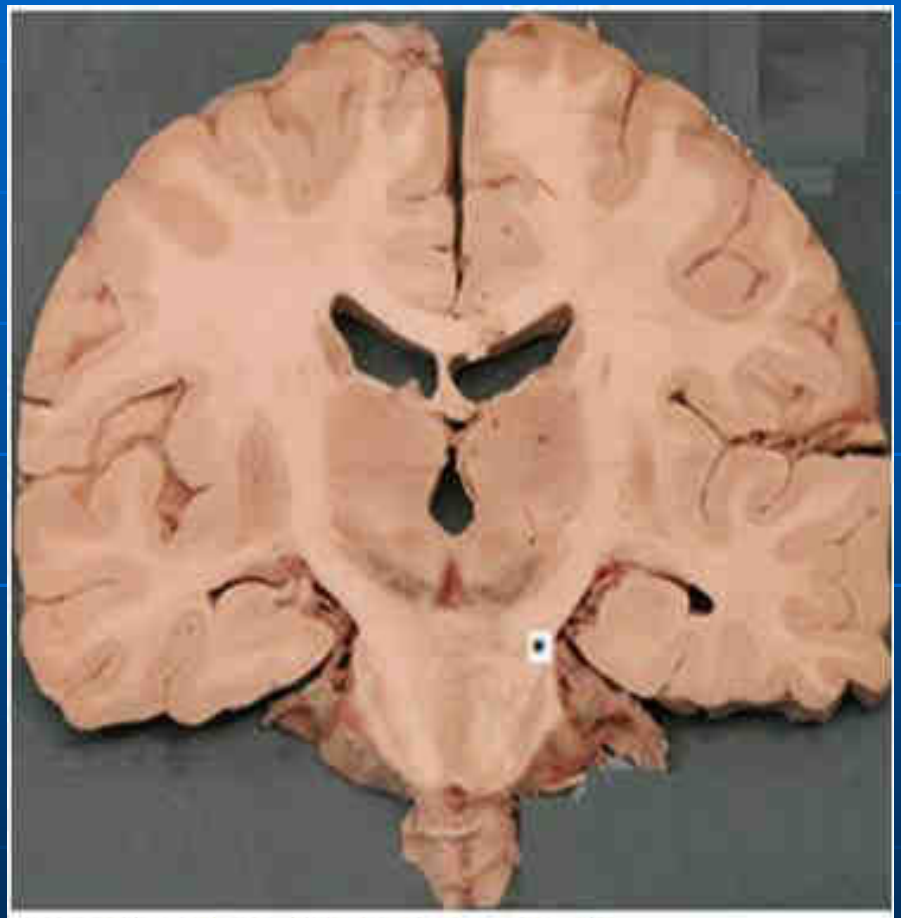


Figure 1 *Brain- brainstem continuity
[edited from Google images]

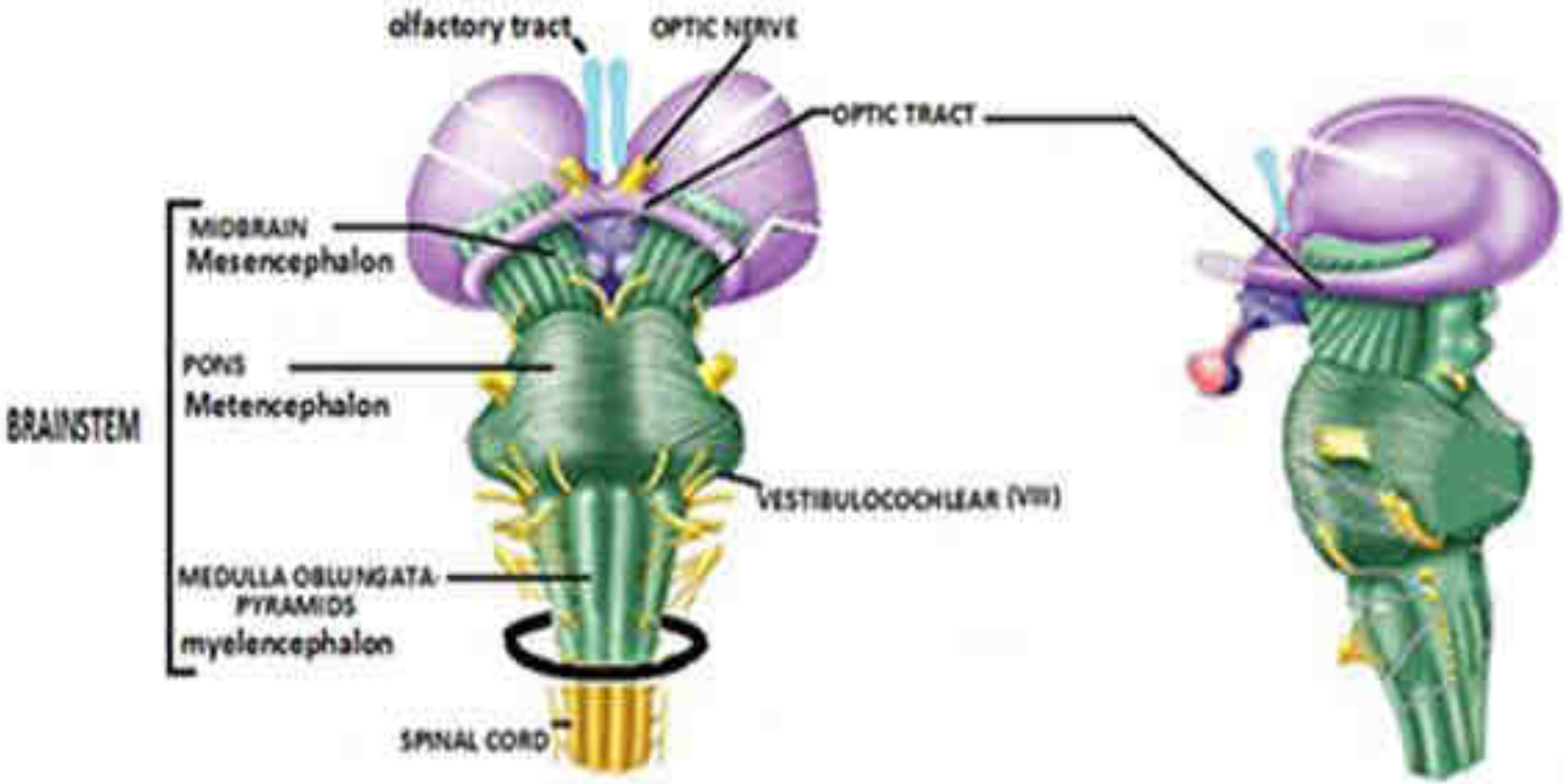
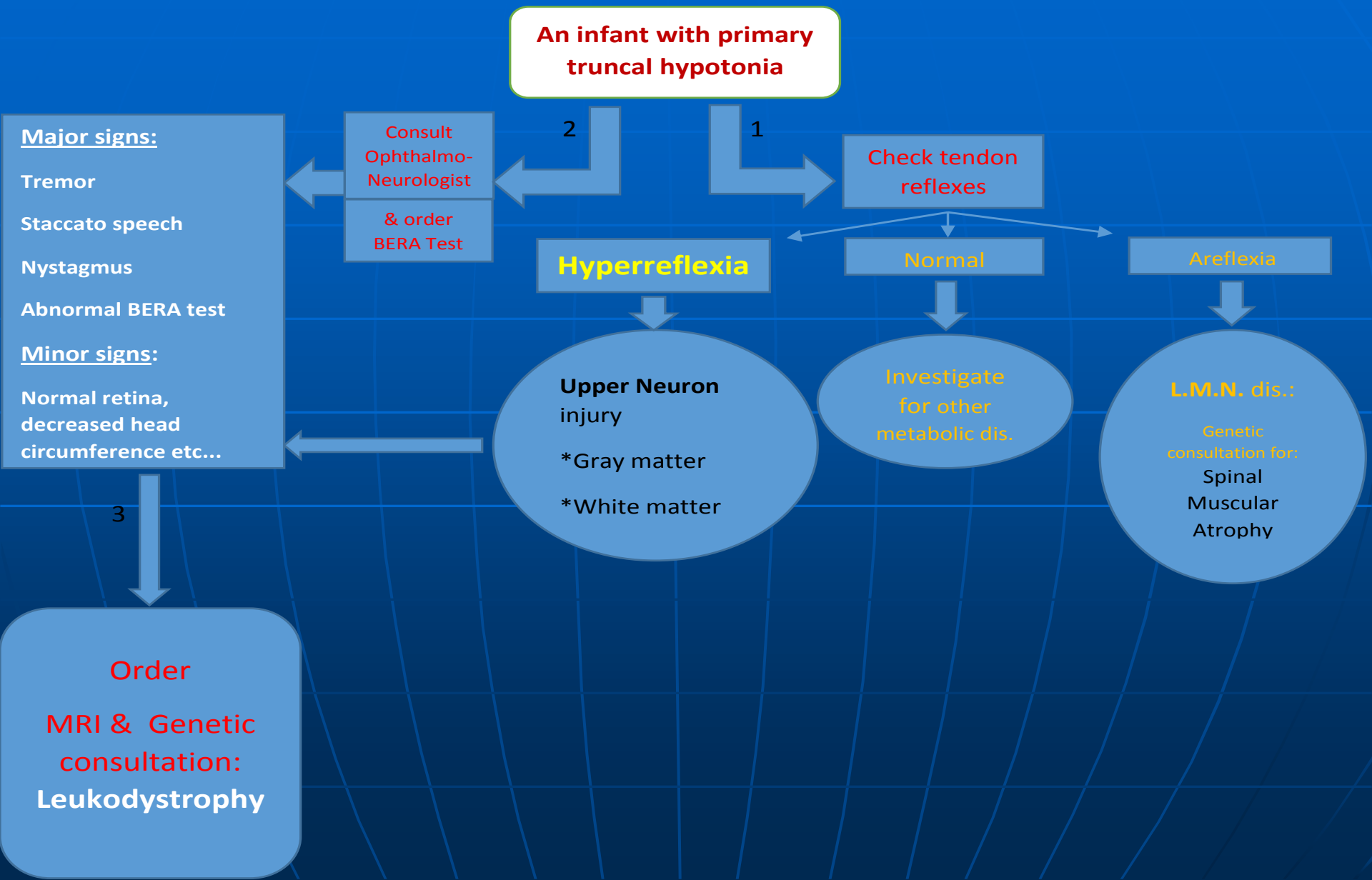


Figure 2 - BRAINSTEM – OPTIC TRACTS ANATOMICAL RELATIONSHIP

Note that almost all the cranial nerves originate from the Brainstem, except the Olfactory (1st nerve) and the optic (2nd nerve) that originate from the brain itself. [edited from Google images]

Has the infant a white matter disorder?

Figure1: A flowchart for the differential diagnosis of primary truncal hypotonia



case report cont..

MAIS PRESENTED

MAJOR SIGNS:

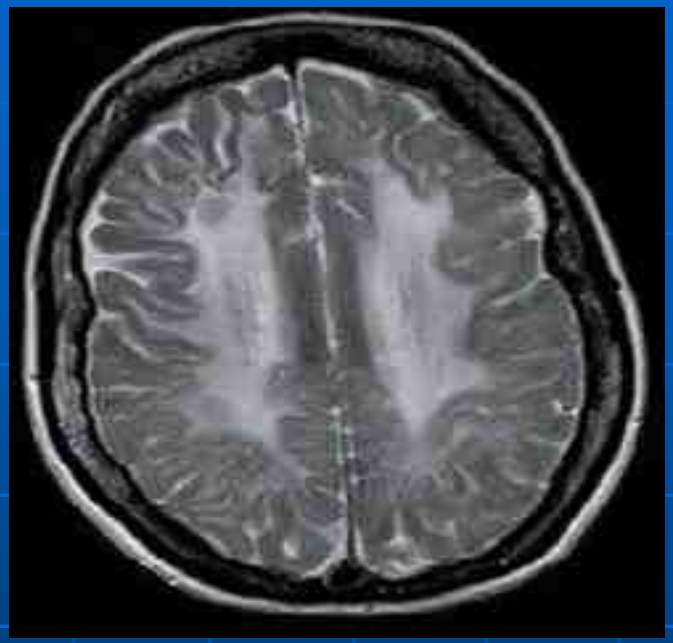
TRUNCAL (AXIAL) HYPOTONIA,
NYSTAGMUS
ABNORMAL BRAINSTEM AUDIOMETRY

LATER:

SOCIAL DEPRIVATION
IRRITABILITY, FTT…

case report cont.. MRI results

the brain MRI was
done at 13 months old



Case report cont..

Mais has a leuko-dystrophy:

The mutation is D29G (*by Magen Daniella group*).

Name of disease: "Mitchap-60" leukodystrophy

All the patients who had this disease presented the three major signs!


HEAG-LAG
NYSTAGMUS
ABNORMAL BERA TEST

The new perspective - THE TRIAD

- ✓ Those three apples actually are the three major signs of the MAIS-NADIM NASSER TRIAD.
- ✓ They originate from three different brain structures:

  sub-cortex | Optic tracts | & Brainstem

- ✓ They are the most frequent features in all our group of patients.

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Research Article Open Access

"Mais-Nadim-Nasser Triad", A Useful Marker for Leukodystrophies Diagnosis

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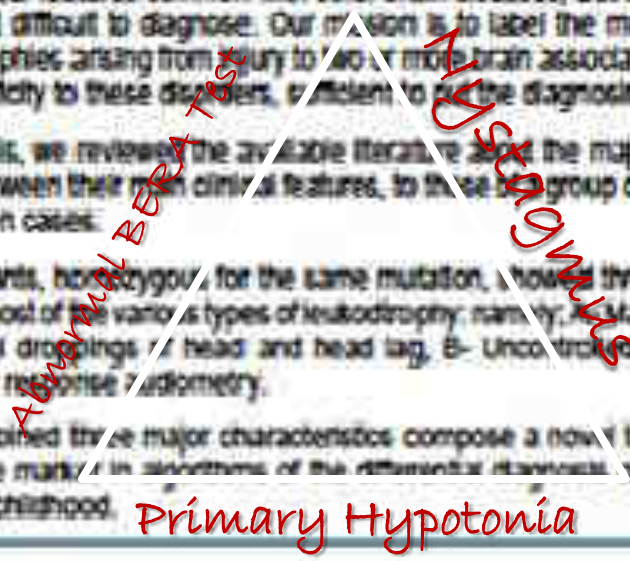
Abstract

Background: Primary Hypotonia is a challenging diagnostic issue for pediatricians. Gray and white matter disorders are its main causes; the former, the neuronal storage diseases, have specific characteristics which make them relatively easy to diagnose. The latter, subject of this article, also called leukoencephalopathy, or leukodystrophy, has a wide spectrum of clinical features common with other brain diseases, but does not have any pathognomonic clinical sign, which makes it difficult to diagnose. Our mission is to label the most frequent combination of major characteristics of leukodystrophies arising from injury to white matter brain associated organs, and have, at the same time, a high degree of specificity to these disorders, sufficient to make the diagnosis within our reach.

Methods: To achieve this, we reviewed the available literature about the majority of white matter disorders and examined the correlation between their main clinical features, to these in a group of leukodystrophic infants, of whom we report three out of thirteen cases.

Results: All thirteen infants, homozygous for the same mutation, showed three identical clinical and laboratory features which prevailed in most of the various types of leukodystrophy: namely; A- Marked truncal hypotonia, expressed by uncontrolled gravitational droppings of head and head lag, B- Uncontrolled eye movements; nystagmus, C- Abnormal brainstem evoked response audiometry.

Conclusions: The conjoined three major characteristics compose a novel triad that we named "Mais-Nadim-Nasser Triad", an applicable marker in algorithms of the differential diagnosis of truncal hypotonia, nystagmus or sensory-neural deafness in childhood.



Buddha (500 B.C.)

I never see what has been done;

I only see what remains to be done.