

## Pelizaeus disease Merzbacher like: About an observation

F. ETIENE IRINEU <sup>1,\*</sup>, H. LACHRAF <sup>1</sup>, H. RHOUDA <sup>1</sup>, G. ZOUIRI <sup>1</sup>, S. MOUSSAOUI <sup>1</sup>, H. LAJI <sup>1</sup>, H. TALBAOUI <sup>2</sup>, S. DAHRI <sup>2</sup>, L. CHABRAOUI <sup>2</sup> and Y. KRIOUILE <sup>1</sup>

<sup>1</sup> *Neuropaediatrics and Neurometabolic Disease Unit, Paediatric II Department, Faculty of Medicine and pharmacy of Rabat, Rabat Children's Hospital, Ibn Sina University Hospital, Mohamed V University, Rabat, Morocco.*

<sup>2</sup> *Department of Metabolic Biochemistry and Disease. CHU Ibn Sina Rabat, Morocco.*

World Journal of Advanced Research and Reviews, 2024, 22(01), 206–209

Publication history: Received on 11 February 2024; revised on 01 April 2024; accepted on 03 April 2024

Article DOI: <https://doi.org/10.30574/wjarr.2024.22.1.1024>

### Abstract

Pelizaeus-Merzbacher disease (PM) is an X-linked leukodystrophy causing developmental delay, nystagmus, hypotonia, spasticity and variable intellectual deficit. Three forms are described according to age of onset and severity: neonatal forms (+ severe), classical form (moderate, first 2 months of life) and transient form (the least serious 2-3 years). Prevalence is estimated at 1/400,000.

We report the sighting of a 12-year-old and 8-month-old girl, with no significant history, from a non-indigenous marriage. Presents since the age of 5 months a bilateral horizontal nystagmus, myoclonia and a psychomotor retardation and whose examination revealed a pyramidal syndrome and a discreet hepatomegaly. The biological balance objectivéhyperlactatémie, hyperammoniémieet Chromatography of *Amino Acids* in urine showed an *increase in glycine, alanine and tyrosine with Amino Acid chromatography* in the blood and chromatography of Organic Acids normal. *MRI brain objectified a demyelinating aspect of the white substance and atrophy of the corpus callosum.* PEV *pathological retina-cortical conduction, PEA altered left, Muscle biopsy absence of shredded red fibers and genetic study confirms PelizaeusMerzbacher disease like.*

Given the difficulty in diagnosing PD and the risk of rapid worsening of symptoms depending on the age of onset, multidisciplinary management and regular follow-up is required.

**Keywords:** Pelizaeus-Merzbacher; Leukodystrophy; Demyelination; Genetic Study

### 1. Introduction

Pelizaeus-Merzbacher disease (PM) is an X-linked leukodystrophy causing developmental delay, nystagmus, hypotonia, spasticity and variable intellectual deficit. Three forms are described according to age of onset and severity: neonatal forms (+ severe), classical form (moderate, first 2 months of life) and transient form (less serious 2-3 years).

Prevalence is estimated at 1/400,000. PM is related to X and due to mutations or assay alterations of the PLP1 gene (Xq22) resulting in hypomyelination of the central nervous system. Patients without mutations of the PLP1 *gene* but with a similar clinical picture and neuro-radiological characteristics almost identical to those of MPM are classified in Pelizaeus-Merzbacher-like disease (PMLD).

Diagnosis is based on clinical, electro-physiological and neuro-radiological examinations. The treatment is multidisciplinary, involving neurologists, physiotherapists, orthopedists, pulmonologists and gastroenterologists. The evolution is progressive and varies according to the phenotype.

\*Corresponding author: F.ETIENE IRINEU

## 2. Observation


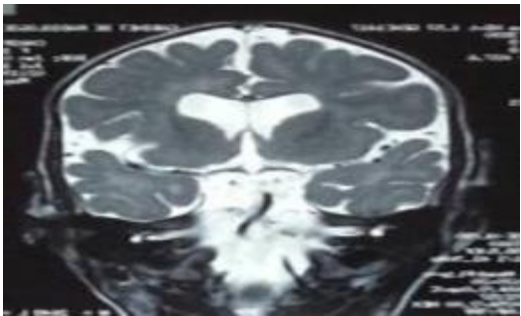
We report the sighting of a 12-year-old and 8-month-old girl, with no significant history, from a non-indigenous marriage. Presents since the age of 5 months a bilateral horizontal nystagmus, myoclonia and psychomotor retardation and whose examination revealed a pyramidal syndrome and a discrete hepatomegaly. (Figure1)

The biological balance objective hyperlactatemia, hyperammonemia et *Chromatography of Amino Acids* in urine showed an increase in glycine, Alanine and tyrosine with *Amino Acid Chromatography in the blood and Chromatography of Normal Organ Acids*, Infection negative Balance, *Normal Hepatic Balance*, *EPP* shows decreased gammaglobulin, *immunoglobulin assay normal*, *viral serology negative*.

Objective abdominal echography a discrete homogeneous hepatomegaly. EEG tracing poorly organized sleep with generalized paroxysmal activity

MRI brain objectified a demyelinating aspect of the white substance and atrophy of the corpus callosum. (Cerebral atrophy with enlargement of the subarachnoid spaces, bulbo-pontic atrophy and corpus callosum, demyelinating aspect of the white substance reaching the U-fibers more accentuated in the occipital lobe → Demyelinating involvement of the white substance metabolic type) ( Figures 2)

*PEV* pathological retina-cortical conduction, *PEA* altered left, *Muscle biopsy* absence of shredded red fibers and genetic study confirms Pelizaeus Merzbacher disease like.

	
<p><b>Figure 1</b> Image of our patient; who suffers from PM disease</p>	<p><b>Figure 2</b> Brain MRI objectified a demyelinating aspect of the white substance and atrophy of the corpus callosum.</p>

## 3. Discussion

Pelizaeus-Merzbacher disease (or PMD) is a rare genetic disease of the X-leukodystrophised family. It is part of hypomyelinating leukodystrophies, these white matter diseases characterized by a permanent myelin deficiency in the brain. Its frequency is 1 for 400,000 births.

Pelizaeus-Merzbacher disease is characterized by a pendulum nystagmus, that is, involuntary oscillatory movement of the eyes, trembling of the head and hypotonia, but also developmental delay, spasticity (contraction of the muscles) and a variable intellectual deficit.

Pelizaeus-Merzbacher disease comes in different forms depending on the age of onset and severity of symptoms:

- The neonatal + severe form: Hypotonia, nystagmus, neonatal respiratory distress and stridor, then motor and cognitive delay and quadriplegia spastic.
- The classical moderate form 2 first months of life: Nystagmus, hypotonia gradually replaced by spasticity and ataxia, impaired motor development and intellectual deficit.
- The least serious form 2-3 years: Slight delay in development and motor, later paraplegia spastic, ataxia and/or slight intellectual deficit. No rapid degradation, sir.

The gene whose mutation is responsible for Pelizaeus-Merzbacher disease is the PLP1 gene which is actually located on the sex chromosome X (in Xq22.2). For this reason, men and women do not report the disease in the same way, and the disease typically affects boys or men. This gene encodes proteolytic protein 1 (PLP1)

There are different types of gene mutations, the main ones being: duplications, point mutations and null mutations.

No biochemical marker, normal brain CT

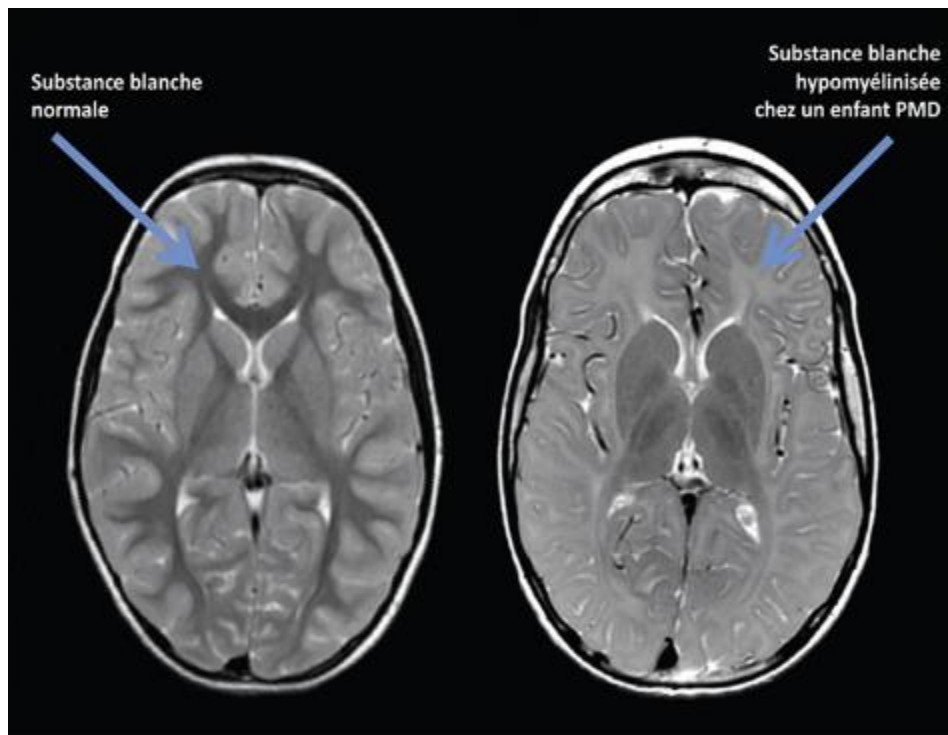
The diagnosis of Pelizaeus-Merzbacher disease is discussed before the clinical picture and white substance abnormalities on MRI.

MRI will show complete hypomyelination (neonatal form and some transient forms), partial (for the moderate form) or diffuse (Pelizaeus-Merzbacher disease, non-sense mutation of PLP1). (Figure 3)

The study of auditory evoked potentials of the brainstem may be useful to differentiate Pelizaeus-Merzbacher disease (absence of II to V waves) from PMD-like disease (recordable II to V waves). A genetic test confirms the diagnosis. Prenatal or preimplantation diagnosis if mutation on *PLP1* identified in the family

The management of patients with Pelizaeus-Merzbacher disease is multidisciplinary and involves many medical specialties. The role of parents and relatives is essential.

Currently, treatment is symptomatic supportive treatment. It may include drugs for stiffness and spasticity that are present in most patients. In case of seizures anti epileptics may be necessary, functional rehabilitation is useful for maintaining joint flexibility, and maximizes the patient's abilities.



**Figure 3** Representative MRIs showing normal white matter on the left and hypomyelinated white matter on the right in a child with Pelizaeus-Merzbacher disease

Crutches or walkers can help with walking. Orthopedic surgery can also help reduce contractures, joints blocked by spasticity or scoliosis of the spine. If speech or swallowing is impaired, a speech therapist can provide important advice.

When swallowing is severely affected, a feeding tube, inserted directly into the stomach, can help increase food intake. Vitamin D and calcium supplements can be helpful.

Hope is now focused on cell therapy and cells induced pluripotent strains (iPSC) as a source of neural progenitors.

---

#### 4. Conclusion

Given the difficulty in diagnosing PD and the risk of rapid worsening of symptoms depending on the age of onset, multidisciplinary management and regular follow-up is required.

---

#### Compliance with ethical standards

##### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

##### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

---

#### References

- [1] Vanderver A, Prust M, Tonduti D, Mochel F, Hussey HM, Helman G et coll. Case definition and classification of leukodystrophies and leukoencephalopathies. *Mol Genet Metab* 2015 Apr;114(4):494–500.
- [2] Kevelam S, Steenweg M, Srivastava S, Helman G, Naidu S, Schiffmann R et coll. Update on Leukodystrophies: A Historical Perspective and Adapted Definition. *Neuropediatrics* 2016 Aug 26;47(6):349–54.
- [3] Vanderver A, Simons C, Helman G, Crawford J, Wolf NI, Bernard G et coll. Whole exome sequencing in patients with white matter abnormalities. *Ann Neurol* 2016;79(6):1031–7.
- [4] Biancheri R, Rosano C, Denegri L, Lamantea E, Pinto F, Lanza F, Severino M, and Filocamo M. (2013). Expanded spectrum of Pelizaeus-Merzbacher-like disease: literature revision and description of a novel GJC2 mutation in an unusually severe form. *Eur J Hum Genet* 21, 34–39.
- [5] Boespflug-Tanguy O, Mimault C, Melki J, Cavagna A, Giraud G, Pham-Dinh D, Dastugue B, and Dautigny A. (1994). Genetic homogeneity of Pelizaeus-Merzbacher disease: tight linkage to the proteolipoprotein locus in 16 affected families. PMD Clinical Group. *Am J Hum Genet* 55, 461–467.
- [6] Bouloche J, and Aicardi J. (1986). Pelizaeus-Merzbacher Disease: Clinical and Nosological Study. *Journal of Child Neurology* 1, 233–239
- [7] Miller WP, Rothman SM, Nascene D, Kivisto T, Defor TE, Ziegler RS et coll. Outcomes after allogeneic hematopoietic cell transplantation for childhood cerebral adrenoleukodystrophy: The largest single-institution cohort report. *Blood* 2011;118(7):1971–8.
- [8] Helman G, Van Haren K, Bonkowsky JL, Bernard G, Pizzino A, Braverman N et coll. Disease specific therapies in leukodystrophies and leukoencephalopathies. *Mol Genet Metab* 2015 Apr;114(4):527–36.
- [9] Van Haren K, Bonkowsky JL, Bernard G, Murphy JL, Pizzino A, Helman G et coll. Consensus statement on preventive and symptomatic care of leukodystrophy patients. *Mol Genet Metab* 2015 Apr;114(4):516–26.