Primarily neurological involvement with a range of presentations The severity and combination of symptoms vary depending on the patient and the nature of the deficiency

Early neurological decompensationOccasional antenatal symptoms

Neonatal lactic acidosis with vomiting, feeding difficulties, **generalised hypotonia**, possible seizures and risk of early death

The diagnostic confirmation strategy should be discussed with a specialist laboratory.

Sometimes associated with intrauterine growth restriction (IUGR)

Brain abnormalities, most commonly agenesis of the corpus callosum, Periventricular cysts

Progressive encephalopathy with episodes of deterioration (Leigh syndrome)

Often within the first 5 years of life, mainly in boys

Moderate to severe psychomotor developmental delay

Episodes of acute or subacute psychomotor regression, often triggered by intercurrent infections, associated with hypotonia, dystonia, ataxia and sometimes feeding and respiratory difficulties, which may progress to apnoea, impaired consciousness and sometimes death, with basal ganglia abnormalities on MRI

Encephalopathy of varying severity with fixed, non-progressive disability

More common in girls

Neonatal or acquired microcephaly

Neurodevelopmental disorder (beginning in the first months of life) with axial hypotonia and spastic hemiplegia or quadriplegia Epilepsy is common

Paroxysmal episodes

With milder or even absent neurodevelopmental disorder

Intermittent ataxia triggered by carbohydrate-rich meals

Episodes of **dyskinesia**, choreoathetotic movements

Hemiplegia or episodic paralysis of a limb

Acute peripheral neuropathy-like involvement

Other manifestations

Dysmorphia²

Peripheral neuropathy

Rare ophthalmological involvement: optic atrophy, nystagmus, ptosis, ophthalmoplegia, strabismus IUGR

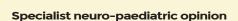
Possible growth delay

Lá C

Laboratory tests (abnormalities may be intermittent): Blood: Lactic acidosis, **Hyperpyruvicaemia and hyperlactataemia**, with normal or low **lactate-to-pyruvate ratio** (L/P around 10 and < 20) CSF: **hyperpyruvorrhachia and hyperlactatorrhachia**, with normal or low **L/P ratio**

Brain MRI with spectroscopy: **Dysgenesis or agenesis of the corpus callosum**, periventricular or subependymal **cysts** (especially in early presentations), cerebral atrophy, ventriculomegaly, **Leigh syndrome**: T2 hyperintensity in the basal ganglia and sometimes in the brainstem and cerebellum; lactate peak on spectroscopy

Pyruvate dehydrogenase deficiency?



Specialist assessment

in parallel with the investigation of other possible differential diagnoses

Lactate and pyruvate measurement in blood and CSF if not previously performed:

Hyperpyruvicaemia and hyperlactataemia, with normal or low L/P ratio (around 10 and < 20)

CSF: hyperpyruvorrhachia and hyperlactatorrhachia, with normal or low L/P ratio

Chromatography of plasma amino acids and urinary organic acids: abnormalities that are sometimes suggestive and more or less specific

Confirmation by genetic testing +/- measurement of enzyme activity (lymphocytes, fibroblasts)⁴

Referral to an Expert Centre:

Reference and Expert Centre for rare diseases: https://www.filiere-g2m.fr/annuaire/

Specialist management coordinated by an Expert Centre

Genetic counselling and family screening at a specialist centre

Further information:

emergency protocols by symptom and/or disease: https://www.filiere-g2m.fr/urgences



Specialist medical opinion and reference laboratory





