

CSF ANALYSIS IN METABOLIC DISORDERS: **INDICATIONS FOR LUMBAR PUNCTURE**

Many of the clinical features seen in inherited neurotransmitter disorders are non-specific, although for some specific disorders there are a characteristic set of clinical manifestations.

Investigation of some neuro-metabolic disorders requires biochemical analysis of CSF for routine biochemistry, amino acids, neurotransmitters and pteridines. Such disorders fall into the following groups:

Lactic acidoses: CSF lactate measurement. A normal CSF lactate argues strongly against, but does not exclude, a mitochondrial encephalopathy.

Glucose transporter: (GLUT-1 defect) Paired CSF and plasma glucose analyses. CSF/plasma glucose ratio < 0.4 is suggestive.

Non-ketotic hyperglycinaemia, and serine deficiency disorders: Paired CSF and plasma amino acid analysis.

GABA metabolism disorders, dopamine, serotonin and catecholamine disorders and pteridine disorders: All require CSF neurotransmitter and pteridine analyses.

PRINCIPAL INDICATIONS FOR LUMBAR PUNCTURE TO DIAGNOSE GENETIC METABOLIC ENCEPHALOPATHY

CSF neurotransmitter and pteridine studies should be performed in the following clinical settings (particularly in patients with a combination of these clinical features):

Neonatal and infantile seizures of unknown cause

Clinical features suggestive of dopamine and serotonin deficiency (hypersalivation, swallowing difficulties, abnormalities of temperature regulation, pinpoint pupils, oculogyric crises, hypokinesia, distal chorea, truncal hypotonia, peripheral hypertonia, reduced spontaneous movements [incl. mask-like face], growth retardation)

Dystonia (with or without diurnal variation, with or without a response to L-dopa)

Other movement disorders (incl. chorea, tremor, myoclonic jerks, ballistic movements)

Hyperekplexia

“Primary” postural hypotension

Also in carefully selected cases with:

cerebral palsy, especially with an athetoid component; microcephaly or macrocephaly combined with other features; psychomotor retardation; difficult to control seizures; raised urinary vanillyl-lactic acid.

CLINICAL AND BIOCHEMICAL FEATURES

Lactic acidoses: Widely variable clinical features. Elevated CSF lactate in disorders with cerebral expression.

Glucose transporter defect: Hard-to-control seizures, developmental delay, low CSF glucose and lactate, with CSF: plasma glucose ratio < 0.40

Non-ketotic hyperglycinaemia: Neonatal onset: hypotonia, seizures, apnoeic attacks, lethargy, hiccoughs. Late-onset: nonspecific neurological symptoms. Burst-suppression EEG. Elevated CSF glycine, with CSF: plasma ratio > 0.05 (lower in late-onset).

Serine deficiency disorders: Microcephaly, psychomotor retardation, and intractable seizures. Low CSF serine, and usually glycine.

Folinic acid responsive seizures: Very early seizures. Rapid response to folinic acid. Unknown compound in CSF

Disorders of GABA metabolism:

Glutamic acid decarboxylase: Some B6-responsive seizures may be due to defective Glutamic acid Decarboxylase. CSF GABA is low while CSF glutamine may be elevated in some.

GABA transaminase deficiency: Only three cases reported: Feeding problems, axial hypotonia, seizures, hyperreflexia, severe psychomotor retardation accelerated growth. CSF GABA, β -alanine, homocarnosine increased. Same profile seen with Vigabatrin therapy.

Succinic semialdehyde dehydrogenase deficiency: Variable psychomotor retardation, delayed speech, hypotonia, ataxia, seizures, aggression, oculomotor apraxia, nystagmus, choreoathetosis. Gamma-hydroxybutyrate elevated in urine, plasma and CSF

Hyperekplexia: Stiffness on handling, excessive startle response. Disorder in glycine receptor, α -1 subunit. Response to clonazepam.

Inborn errors of monoamines:

1. Affecting dopamine metabolism

Tyrosine hydroxylase deficiency 1st year presentation: extrapyramidal signs: dystonia (lower limbs), tremor, or hypokinetic-rigid Parkinsonian syndrome. Some have diurnal variation. Low CSF HVA and MHPG; normal 5-HIAA.

2. Affecting dopamine and serotonin metabolism

Aromatic l-amino acid decarboxylase deficiency: Extrapyramidal movement disorder, axial hypotonia, abnormalities of eye movement, including oculogyric crises. Autonomic features, increased startle, sleep disturbance, etc Low HVA, MHPG, and 5-HIAA in CSF. High levels of L-dopa, 5-HTP, 3-O-methyl-L-dopa, vanillylactic acid in CSF. Elevated vanillylactic acid in urine. Pteridines normal.