NEUROMETABOLIC DISORDERS WITH PSYCHOSIS AS PSYCHIATRIC MANIFESTATION

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Introduction: Neurometabolic disorders (NM) are a group of diseases characterized by the absence or deficit of an intracellular component that is part of a metabolic pathway, and result in alterations of the processes beyond synthesis or catabolism of that same pathway. NM disorders are rare causes of psychiatric manifestations, and in a good part of it, these are the first sign of an underlying NM disturbance and can present with psychotic symptomatology.

Neurometabolic Disorders with psychosis as manifestation

NM Diseases may present various types of psychiatric manifestations, such affective conditions, catatonia or psychotic conditions, with delusional or visual and auditory hallucinations. There are several neurometabolic diseases that can develop with psychiatric presentations isolatedly, namely with psychosis-like conditions:

Urea Cycle Disorders

- 6-enzyme deficiency group - increased plasma levels of ammonia and blood amino acid abnormalities - most common is the deficiency of the ornithine transcarbamilase enzyme.
- Manifestations: gastrointestinal, nausea and vomiting associated with severe headaches.
- The hallucinatory activity in these cases can be episodic and very intense, and of visual or auditory nature.

Homocysteine Metabolism Disorders

- Deficit of Cystathionine Synthase
 - Skeletal, vascular (thromboembolic) and ocular (lenticular ectopia) alterations and 50% with varied psychiatric manifestations.
- Deficit of methylenetetrahydrofolate reductase.
 - Young age - early neurological symptoms, apnoea, microcephaly and epileptic seizures.
 - Late age - ataxia, intellectual disability and psychotic symptoms.
 - Psychotic manifestations of auditory and visual hallucinatory type, exuberant and of insidious course, and also as form, continuity and content disorders of thought.

Acute Intermittent Porphyria

- Changes in haeme group metabolism, resulting in accumulation of porphyrin or its precursors, porphobilinogen or delta-aminolevulinic acid, in the liver or bone marrow.
- Acute hepatic presentation progresses with neurological (paresis, sensory alterations) and visceral abnormalities, namely acute abdominal pain.
 - Behaviour changes and delusions may also occur.

Wilson`s Disease

- Mutations of the ATP7B gene, which codes for copper transport protein – its deficit leads to copper accumulation preferentially at the cerebral and hepatic level.
 - Neurological changes, mostly motor, extra-pyramidal symptoms, acinesia and dysarthria.
- Delusions and recurrent hallucinations may occur.

Niemann-Pick type C Disease

- Abnormalities in cell transport of lipids resulting in accumulation of cholesterol and glycosphingolipids at the cerebral level (gangliosides GM2 and GM 3) and in soft tissues – rapidly fatal or degenerative progressive forms.
- The earlier symptoms in the evolution of the disease are the motor ones, with ataxia of the arms and gait, abnormal movements, and with a very characteristic sign that is consistently found, the supranuclear paralysis of the vertical look.
- Most common psychiatric manifestations are the psychotic, of gradual or acute installation with spontaneous remissions and frequent recurrences, namely paranoid delusions, visual and auditory hallucinations, self-referentiality.

Cerebrotendinous Xanthomatosis

- Sterol-27-hydroxylase enzyme deficiency, resulting in decreased cholesterol degradation and accumulation of cholestanol, mostly in the brain and tendons.
- Neurological manifestations of progressive spastic paraparesis, cerebellar ataxia, peripheral polyneuropathy and cognitive deficits. A very common and characteristic sign of the disease is the presence of xanthomas in the tendons.
- Psychiatric manifestations are felt in about 10% of cases in the form of psychotic conditions, hallucinations and paranoid delusions.

Atypical signs can lead to diagnosis

There are some atypical signs that can guide us, or make us suspect that we are facing a secondary psychiatric condition, namely, visual hallucinations, mental confusion, catatonia, fluctuation of symptoms, atypical or paradoxical response to treatment, cognitive decline. Aspects such as the early age of symptoms onset, the acute presentation, the observation of delay in the intellectual development and the observation of ineffective treatment are also important for a greater degree of suspicion.

Conclusion

Psychotic symptoms can be the first sign and remain isolated for years. The importance of the awareness of these disorders resides in the possibility of detection in a precocious stage of the disease and rapid referral, which can lead to stabilization of the evolution or even reversion of some of the disorders symptoms. The detection in a psychiatric stage opens the possibility of early intervention in the course of the disease and correct referral for treatment, making it crucial to raise the awareness of clinical psychiatrists for signs that may suggest a NM disorder.

Bibliografy:

1. Figueira,M.L.,Sampaio,D.,Afonso,P.(2014).ManualdePsiquiatriaClínica.(pp.214-237).Lisboa:Lidel–edições técnicas,lda.

2. Gelder, M., Gath, D., & Mayou, R. (1989). Oxford medical publications. Oxford textbook of psychiatry (2nd ed.). New York, NY, US: Oxford University Press.

3. Herrera P.M. , Vélez Van Meerbeke, A. , Bonnot, O. . Psychiatric Disorders Secondary to Neurometabolic Disorders. Rev Colomb Psiquiatr. 2018 Oct - Dec;47(4):244-251. doi: 10.1016/j.rcp.2017.05.004.

4. Bonnot, O. , Herrera, P.M. , Tordjman, S. , Walterfang, M.. Secondary psychosis induced by metabolic disorders. Front Neurosci. 2015 May 19;9:177. doi:10.3389/fnins.2015.00177.

5. Nia, S. . Psychiatric signs and symptoms in treatable inborn errors of metabolism. J Neurol. 2014 Sep;261 Suppl 2:S559-68. doi:10.1007/s00415-014-7396-6.