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Editorial

Endocrinological Changes in Respiratory Chain Disorders

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Abstract

Respiratory chain disorders (RCD) are a heterogeneous group of diseases associated with genetic alterations of nuclear or mitochondrial encoded genes involved in the synthesis of subunits of the electron transport chain.

The diagnosis of this disorder should be considered if there are 2 major criteria or 1 major and 2 minor criteria. (Modified Walker Criteria).

Endocrinological changes are described in RCD, such as mellitus diabetes (hyperinsulinemia), insipidus diabetes (low urine density), hypoparathyroidism (low parathormone), hypothyroidism (low Ft4) and short stature (growth hormone deficiency). They are associated with RCD and hormone screening must be included in all patients with this metabolic disease.

Keywords: *Respiratory Chain Disorders; Endocrinological Changes*

Respiratory chain disorders (RCD) are a heterogeneous group of diseases associated with genetic alterations of nuclear or mitochondrial encoded genes involved in the synthesis of subunits of the electron transport chain. RCD should be considered in patients with an unexplained combination of neuromuscular and/or non-neuromuscular symptoms, with a progressive course, even if oxphos studies are normal.

They are multisystemic disorders which can appear since infancy to adulthood and occur with an incidence of 1/10000 live births.

The diagnosis of this disorder should be considered if there are 2 major criteria or 1 major and 2 minor criteria. (Modified Walker Criteria) (Table 1).

Major criteria • Clinically complete RCD encephalopathy* or a mitochondrial cytopathy defined as fulfilling all 3 of the following**. • > 2% ragged red fibers (RRF) in skeletal muscle. • Cytochrome c oxidase negative fibers or residual activity of a RCD complex < 20% in a tissue; < 30% in a cell line, or < 30% in 2 or more tissues. • Fibroblast ATP synthesis rates > 3SD below mean. • Nuclear or mtDNA mutation of undisputed pathogenicity.
Minor criteria • Symptoms compatible with RCD defects***. • Smaller numbers of RRF, SSAM, or widespread electron microscopy abnormalities of mitochondria. • Antibody-based demonstration of RCD defect or residual activity of RCD complex 20 - 30% in a tissue, 30 - 40% in a cell line, or 30 - 40% in 2 or more tissues. • Fibroblast ATP synthesis rates 2 - 3SD below mean, or fibroblasts unable to grow in galactose media. • Nuclear or mtDNA mutation of probable pathogenicity. • One or more metabolic indicators of impaired metabolic function. • *Leigh Disease, Alpers Disease, Pearson Syndrome, Kearns-Sayre Syndrome, MELAS, MERRF, NARP, MNGIE and LHON. • **1) Unexplained combination of multisystemic symptoms that is essentially pathognomonic of RCD disorder; 2) a progressive clinical course with episodes of exacerbation or a family history strongly indicative of a mtDNA mutation; 3) other possible metabolic or non-metabolic disorders have been excluded. • ***Stillbirth associated with a paucity of intrauterine movement, neonatal death or collapse, movement disorder, severe failure to thrive, neonatal hypotonia and hypertonia as minor clinical criteria. • SSAM - subsarcolemmal accumulation of mitochondria.

Table 1: *Modified walker criteria.*

The main symptoms are hypotonia, strabismus, microcephaly, facial dysmorphy, mental retardation but a variability of clinical features was found in this group of disorders.

Thin corpus callosum is one of the important signs in brain MRI but the normal appearance does not rule out RCD.

Biochemical results showed complex 1 and 2 in most cases. There is no correlation between the type of RCD and the clinical presentation.

The treatment, mainly supportive, does not influence the course of the disease and the prognostic is unfavourable. We can use carnitine, coenzyme Q10 and ketogenic diet with different respond in each affected patient. Less hypotonia, concentration and seizures can be found in some cases.

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