

significant negative correlation ($r = -0.87$). Increase of Cu, Fe levels in the patients with PA were identificate in the prevalence cases.

Conclusions Microelement status of patients with pneumonia is characterized by synergistic correlation between Fe and Cu ($r = 0.64$), and reverse dependence between Ca and Fe/Cu ($r = -0.87$)., increase of Cu, Fe levels. Our dates show the dynamics of development of inflammatory process in Lung and possible role of violations of microelement status of child in pathogeny of diseases of breathing organs.

1028 RESPIRATORY CHAIN DISORDERS: REVIEW OF 16 CASES

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Introduction Respiratory chain disorders (RCD) are a heterogeneous group of diseases associated with multisystemic disorders. The diagnosis should be considered if there are 2 major criteria or 1 major and 2 minor criteria (Modified Walker Criteria).

Purpose Medical records of 16 cases of RCD diagnosed in Metabolic Unit of our hospital, between 2005 and 2010 were analyzed.

Results The results showed that all the patients have psychomotor delay and more than half cases hypotonia, strabism and acquired microcephaly at presentation. Other symptoms were multisystem such as: neurosensory deafness (1/16), mioclonic epilepsy (3/16), intestinal duplication (1/16), ductus arteriosus persistent (1/16), renal hypoplasia (2/16). We found important association with endocrinological changes (9/16), hypothyroidism in most situations, but also hypoparathyroidism, insipidus diabetes, growth hormone defect and hyperinsulinemia. Complex 2 deficiency was the most common cause of RCD (8/16). In one case we found depletion in mitochondrial DNA. No histopathology abnormalities were found in the muscle biopsy. Only (8/16) exhibited elevated plasma lactate. The treatment with Coenzyme Q10, carnitine and ketogenic diet seemed to improve their clinical course (less epileptic crisis after ketogenic diet – 6/6, better concentration after coenzyme Q10 – 6/16, less hypotonia after carnitine – 5/11).

Discussion and Conclusion Mitochondrial cytopathies should be considered in patients with an unexplained combination of neuromuscular and/or nonneuromuscular symptoms, with a progressive course, even if oxphos studies are normal.

Endocrinological changes are an important association of respiratory chain disorder and hormone screening must be included in all the patients with this metabolic disease.

1029 GLYCINE SUPPLEMENTATION IMPROVES THE CONCENTRATION, SOCIALIZATION, PERCEPTION AND AUTONOMY OF PATIENT WITH CREATINE TRANSPORT DEFECT

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Introduction Creatine transport defect (CTD) is a x-linked disorder with neurological symptoms. Glycine can help inhibit the neurotransmitters and supply the body with glucose needed for energy. Also act as a creatine precursor.

Purpose Treat with oral glycine in the period of 12 months, a patient with CTD and compare the clinical, analytic and brain magnetic resonance spectroscopy results, before and after therapy.

Material A fourteen year-old boy with CTD diagnosed at the age of five years, treated unsuccessfully with daily 20 mg of oral methylphenidate for is behaviors disturbances.

Method Oral glycine in a dose of 250 mg/kg/day, divided in two doses.

Results After 12 months, we found some improvement in concentration, socialization, perception and autonomy. No evolution of speech. The creatine peak was slightly better than before (5 to 8 mm). Urine creatine level reduces from 24427 to 10994 $\mu\text{mol}/\text{mmol}$ creatinine.

Discussion We believe that the clinical and analytic evolutions are associated with increase creatine peak level secondary to oral glycine. Glycine, because of its inhibitory action over the neurotransmitters, in research studies has shown that helps improve memory retrieval loss in those patients that suffer from a wide variety of sleep-depriving conditions, including schizophrenia, Parkinson and Huntington diseases. He also has a sedative effect and is used in attention-deficit, by reducing the excitability of nerves cells. Glycine is useful in patients with CTD and should be encouraged to use because has no side effect and can improve some behaviours disturbances that is common in this disease.

1030 A CASE OF RHIZOMELIC CHONDRODYSPLASIA PUNCTATA IN NEWBORN

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Rhizomelic chondrodysplasia punctata is a rare autosomal recessive peroxisomal disease. The main features of the disease are shortening of the proximal long bones, punctate calcifications in the metaphysis and epiphysis of long bones and the thoracic and lumbar vertebrae, dysmorphic face, and severe growth retardation, whereas cervical spinal stenosis may also rarely be present. Imaging of the brain and spinal cord in patients with this disorder may aid prognosis and guide management decisions. We report the newborn diagnosed as rhizomelic chondrodysplasia punctata with cervical stenosis. As far as we know, our case is the first case of autosomal recessive form with a cervical spinal stenosis detected in the neonatal period.

1031 AMINOACIDOPATHIES: REVIEW AND DATA OF 12 YEARS EXPERIENCE FROM A SPANISH TERTIARY CARE CENTER

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Background/Aims Range and severity of symptoms hugely variable in aminoacidopathies, mainly diagnosed during acute episodes. Tandem Mass spectrometry (Ms/Ms) used in our unit since 2010 for diagnosing asymptomatic infants (very important for prognosis).

Methods Retrospective, descriptive study in which field data were collected from clinical histories of patients diagnosed of aminoacidopathies (excluding phenylketonuria) since 2000 till 2012.

Results 30 children detected. 22/30 male; 24/30 caucasians.

10/30 diagnosed by newborn screening, all of them asymptomatic: 1 methylmalonic acidemia (MMA), 3 glutaric aciduria type 1, 2 homocystinuria, 2 methylcrotonylglycinuria, 1 hipermetioninemia and 1 maple syrup urine disease.

20/30 diagnosed because of clinical symptoms, 2/20 since MS/MS newborn screening was performed. Mean age of clinical debut in intoxication type aminoacidopathies was 64.5 days (median 8 days). Most frequent symptoms were clouding of consciousness (9/20), convulsions (2/20) and apnoea (2/20). Laboratory results showed metabolic acidosis (6/20), hyperammonemia (8/20), coagulation defects (4/20) and hipoglycemia. Main complications were: shock (9/20), multiple organ failure (5/20), coagulopathy (4/20), brain injury (1/20), liver failure (1/20) and seizures (2/20). The final diagnosis was: 5 OTC-deficiency, 2 citrullinemia, 3 methylmalonic

acidemia, 1 3-OH-metilglutaric aciduria, 1 glutaric aciduria type 1, 1 metilglutaconic acidemia, 1 trimethylaminuria, 1 propionic acidemia, 2 tyrosinemia and 3 homocystinuria. Ventilatory support needed in 13/20, vasoactive agents 11/20, peritoneal dialysis 8/20, continuous veno-venous haemofiltration 4/20. 8 patients died; among survivors, 2/12 maturative failure, 3/12 serious neurological sequelae, 1/12 liver failure, needing transplantation.

Conclusions Aminoacidopathies diagnosed by Ms/Ms start early with treatment. Wide range of presentation symptoms and findings.

1032

THE NIEMANN-PICK TYPE C SUSPICION INDEX TOOL: EXAMINATION OF ITS DISCRIMINATORY POWER BY AGE AND ASSOCIATIONS BY LEADING SYMPTOMS

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Background and Aims The Suspicion Index (SI) screening tool was developed to identify suspected patients with Niemann-Pick disease type C (NP-C, Neurology, 2012). The SI provides Risk Prediction Score (RPS) based on NP-C symptoms within and across domains (visceral, neurological, and psychiatric). To further examine a) discriminatory power of the SI by age and b) symptom-associations by NP-C suspicion-level and leading symptoms.

Methods The original retrospective data were split into three age groups, where NP-C positive cases were: >16 years (n=30), 4–16 years (n=18), and < 4 years (n=23), and patients' RPS was analysed by logistic regression. Co-occurrence of symptoms within groups of suspicion-level (low, medium, and high) and leading symptoms (presence/absence of ataxia, cognitive decline, psychosis, and splenomegaly) were analysed descriptively.

Results NP-C positive cases vs. controls showed strong discriminatory power of RPS. Area under the Receiver Operating Characteristic curve was 0.964 (>16 years) and 0.981 (4–16 years) but a weaker 0.562 for infants (< 4 years). Patients with RPS < 70 were characterised by a lack of psychiatric symptoms and low levels of neurological involvement, suggestive of a more visceral phenotype. In patients >4 years, prominent leading symptoms' associations were: ataxia with "dystonia, dysarthria/dysphagia and cognitive decline"; psychosis with "dysarthria/dysphagia"; and psychotic symptoms with "cognitive decline and treatment-resistant psychiatric symptoms".

Conclusions The SI tool maintains strong discriminatory power in patients >4 years but is not as useful for infants < 4 years. The SI is informative regarding the association and co-occurrence of symptoms in patients with NP-C.

1033

CENTRAL NEUROGENIC HYPERVENTILATION MAY CAUSE METABOLIC ALKALOSIS IN MITOCHONDRIAL ENCEPHALOPATHY

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Background The differential diagnosis of respiratory alkalosis (RA) includes a state called central neurogenic hyperventilation (CNH). In the few reported cases of CNH the etiology was a stimulation of the respiratory center by an infiltrative tumor in the cerebral pons. In some cases, a shift in the cerebral pH to acidic range was also hypothesized.

Case Report We report the case of a six year-old boy with a known Pearson syndrome, a mitochondrial disorder affecting bone marrow, pancreas and renal tubules. He was admitted to our PICU with deteriorating mental status and compensated metabolic acidosis (lactic, hyperchloremic and tubular). On admission, blood gas analysis showed a pH of 7.30 with a disproportionately low compensating pCO₂ of 10 mmHg (HCO₃ 4.9 mmol/L). Serum HCO₃ normalized by substitution (21.0 mmol/L), when he developed a RA (pH 7.51, pCO₂ 24 mmHg) persisting over 48 hours, even during sleeping periods. After reviewing his previous blood gas results, this phenomenon was present for years. After excluding known etiologies of RA, we suspected CNH caused by intra-cerebral acidosis. The pH and HCO₃ were lower, while lactate was higher in cerebro-spinal fluid than in serum. An MR spectroscopy confirmed cerebral lactate accumulation, showing a peak in the posterior cerebrum. Encephalopathy is not among the classic manifestations of Pearson syndrome.

Conclusion We were able to demonstrate elevated local lactate level leading to intra-cerebral acidosis, stimulation of the respiratory center and causing long-standing hyperventilation. This phenomenon adds a new aspect to the complex clinical picture of mitochondrial disorders.

1034

A HYPOTONIC INFANT WITH METHYLENE TETRAHYDROFOLATE REDUCTASE (MTHFR) DEFICIENCY; HOMOZYGOUS MUTATION OF C.1015T>G IN MTHFR GENE

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Background Methylene tetrahydrofolate reductase (MTHFR) deficiency is a rare autosomal recessive disorder, caused by mutated alleles of the MTHFR gene. Since this enzyme catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, its deficiency results in hyperhomocysteinemia, homocystinuria and hypomethionemia. The clinical manifestations vary from asymptomatic to fatal disease with severe neurodevelopmental delay and epileptic encephalopathy.

Case Our patient was a two-month old female born from consanguineous parents presenting with infantile spasms, hypotonia and microcephalus. She was transferred to our pediatric intensive care unit for respiratory failure. The biochemical work-up revealed low vitamin B12 level: 152.6 pg/ml (197–866 pg/ml), close to lower limit of folate: 4.62 ng/ml (3.1–17.5 ng/ml), increased homocysteine level: 9.85 nmol/ml (0–1 nmol/ml), and very low methionine level: 7.32 nmol/ml (19–51 nmol/ml). Magnetic resonance imaging of the brain showed white matter changes of the frontal lobes, posterior legs of capsula interna, pons and nucleus dentatus consistent with demyelination. MTHFR deficiency was suspected, and treatment with folic acid, vitamin B12, methionine and betaine was initiated. The peripheral blood DNA analysis of the patient demonstrated a homozygous mutation of c.1015T>G in MTHFR gene. Both parents were confirmed to be asymptomatic heterozygote carriers. Despite treatment, the prognosis was fatal.

Conclusions As related reports suggest better prognosis with early treatment, pediatricians need to consider MTHFR deficiency in similar cases. Prenatal diagnosis is available and should be encouraged for the future pregnancies.