Case Study

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Case study on phenylketonuria: a memic autism

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Abstract

Phenylketonuria (PKU) is a phenylalanine catabolism metabolic condition characterized by a decrease in the activity of the phenylalanine hydroxylase or Dihydro pteridine reductase enzyme. This inherited condition causes a build-up of phenylalanine in the bloodstream. Elevated phenylalanine levels in the blood can cause muscle rigidity, choreoathetosis, tremors, hyperreflexia, dermatitis, pale skin, and pseudo-scleroderma. The central nervous system deficiencies in PKU are caused by phenylalanine and phenyl pyruvic acid competing for dopamine, adrenaline, norepinephrine, and serotonin in the brain. Structural changes are caused by neurotransmitter inhibition and phenylalanine and phenyl pyruvic accumulations in the white matter of the posterior periventricular, frontal, and subcortical areas of the brain1. Greater myelin turnover decreased synaptogenesis, and reduced neuronal digenesis ensues from myelin deficit, resulting in cognitive development and mental retardation1. The patient in this case study is an 8-year-old boy who has been diagnosed with phenylketonuria. The patient's parents had a history of consanguinity marriage. The patient has had seizures since he was nine months old. Speech and language delays, hearing loss, and tooth discoloration are all common symptoms. He had an MRI and a brain scan, as well as a blood amino acids test, which revealed that he has mild developmental delays. Mild to Moderate Autistic Features is Delayed.

Key Words: Phenylketonuria, phenylalanine levels, neurotransmitter inhibition, synaptogenesis.

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Introduction

Phenylketonuria: A mutation in the gene that codes for the phenylalanine hydroxylase enzyme cause this metabolic disease [1]. Phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine-to-phenylalanine

Tyrosine conversion is hindered in phenylketonuria, resulting in phenylalanine buildup in the blood and tissues and a tyrosine deficiency [2]. The prevalence of this disease is linked to the number of family marriages [3]. Phenylketonuria (PKU) has been linked to autistic symptoms in the past. Since the emergence of early testing and therapy for phenylalanine hydroxylase (PAH) deficiency, this link has practically dissipated. The possibility that autism and worse control are linked to dopamine insufficiency [3].

Types

A blood Phenylalanine concentration over the standard range (20-130 umol/L depending on age) is considered hyper phenyl alaninemia. Different classification approaches exist for PKU subtypes based on the severity of the clinical, biochemical, and/or molecular phenotype [3]. Patients with moderate hyperphenylalaninemia have a blood Phenylalanine concentration that is more than 200 umol/L (10 mg/dL) but less than 200 umol/L (10 mg/dL) without dietary treatment. Significant PKU is defined as a Phenylalanine concentration of greater than 200 umol/L (20 mg/dL) despite a normal protein consumption. Inherited abnormalities in the production or recycling of tetrahydrobiopterin (BH4), a cofactor in

the PAH reaction3, might cause an elevated blood Phenylalanine content in rare cases [3].

Pathogenesis

The hepatic enzyme phenylalanine hydroxylase (PAH) catalyses the conversion of phenylalanine to tyrosine, an essential amino acid. In addition to molecular oxygen and iron, tetrahydrobiopterin (BH4) is a cofactor necessary for PAH action. This route is responsible for the majority of catabolism and disposes of around 75% of dietary phenylalanine, with the rest being used for protein synthesis. PAH insufficiency is the cause of PKU. Phenylalanine and its metabolites, phenylacetate and phenyl lactate, are found in higher concentrations in the blood and urine as a result of this. Tyrosine concentrations are usually in the normal range, while low quantities do occur rarely. Approximately 2% of patients with increased phenylalanine levels have BH4 metabolism problems.

Symptoms

Severe to profound IQ issues, intellectual disability, mental retardation, seizures, autistic-like behaviours, micro cephal, rashes, hypopigmentation, and a musty body odour (phenyl acetic acid), as well as abnormal brain development and autism3 are all symptoms of PKU.

Diagnosis

Every patient who showed up at our clinic with symptoms and signs that might indicate an ASD underwent a thorough medical history and physical evaluation. An electroencephalogram (EEG) with a sleep sample was obtained in order to identify electrical status epilepticus while awake or asleep 4.To identify any hearing loss brought on by epileptic encephalopathy, an ABR hearing test was conducted. These examinations were made to rule out conditions that would call for extra forms of care.

Pharmacological therapy was recommended if the ABR and EEG were both normal. There is no proof of a genetic disorder (e.g., no family history of genetic disorders, no dysmorphic features) no global developmental delay or abnormal genetic test result), no global developmental delay or abnormal genetic test result Based on DSM-5 criteria, CARS2-ST, a CGI-S score of 4, and concurrent persistent behavioural problems, an ASD diagnosis is made. The diagnoses came from a doctor.

Management

Families who made the decision to start taking aripiprazole (patients started on 1 mg at night and this dose was gradually increased every 1 to 2 weeks to the maximum dose (10 mg, nighttime) or the maximum dose tolerated. When giving patients risperidone or aripiprazole for ongoing concurrent behavioural disorders, the regimens for these medications were followed [7, 8]. Risperidone was suggested as the first-line therapy since it has been studied more thoroughly in kids with ASD.

Aripiprazole is a different option that some families select. Off-label use and potential adverse effects were discussed with the children's parents and legal guardians. One class of antipsychotic drug is the antipsychotic drug. Because this study was a retrospective case study, there was no control group.

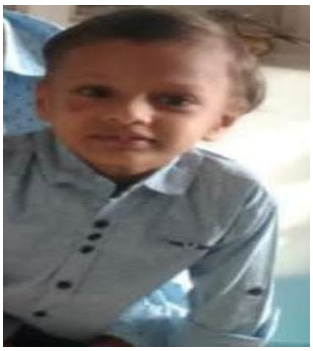
There were two options: randomization or placebo therapy. Depression was frequently treated with risperidone. The maximum dose was attained after a steady dose increase starting at 0.25 mg taken orally at night and continuing every 1 to 2 weeks. Dosage (0.5 mg at night and 2 mg in the morning) or the maximum amount tolerable In 8 out of 10 situations, this beneficial method was implemented (all except cases 2 and 4). Families who made the decision for the patient improved with each dose increase and experienced no negative consequences [4].

Case Study

An 8 years old male patient came to the hospital, with the complaints of seizures, delayed in speech and language, myoclonic jerks, development with developmental delay. Hypopigmented hair, skin rash and photosensitive, general behaviour and hyperactive since 8 years. His past medical history of present known complaints for 8 years. When he was in 6 months he was diagnosed with hypsarrhythmia and treated same. His past medication history includes anti-epileptics [ex: lanzol etc.], Ointments for skin rashes and nutrients are used. The family consulted a registered medical practioner, she gave symptomatic relief treatment to the patient.

Patient was now referred to our government general hospital. The patient presented the with chronic symptoms histological examination showed signs of phenylketonuria. Appetite was decreased, sleeplessness bowel and bladder habits are normal. Blood group O+ve, Blood tests were performed showed the White blood cells [WBC]:7800 cells/mm3, Packed cell volume (PCV):36.5vol%, MCH:25.4 pg/cell, Neutrophils: 24%, Lympocytes:66%, Eosinophils:8%. In peripheral smear test, RBC- Normocytic normochromic, WBC-

morphology normal with lymphocytic predominance no abnormal cells seen. Platelets- adequate. Chlorides: 108m.mol/L, Bili (D):0.4 mg/dl, SGPT: 98 u/L, ALP: 103 u/L, phenylalanine: 1014 nmoles/ml, Lysine: 36.4nmoles/ml. phenytoin serum: less than 0.50ug/ml. The histological examination of the patient verified as Phenyl ketonuria. Additionally, the patient was treated with Tab.Wysolone-10mg (after food) OD, for 2 weeks, Tab. Lanzol jr.-1.5 mg before food OD for 6 weeks, Tab. Lonazep-0.25mg for 3 weeks and for allergies Vencesia max cream (BD) full body, Flutibact ointment (OD) night at rashes, Dermadeu baby soap, Inj. ACTH (2vials) ice pack-0.6ml alternative days for 15 doses, physiotherapy and speech stimulation at home. He is recommended for phenyl alamine restricted diet to be initiated and kept on regular anti-epileptic medications and recommended for physiotherapy and speech therapy.



Discussion

About 1 in 100 youngsters are thought to be autistic worldwide. Environmental and genetic variables, among others, may increase a child's risk of developing autism. There is no proof that any additional childhood vaccinations may raise the risk of autism. Autism symptoms frequently manifest in childhood. Although autism is not a disease, early intervention can prepare kids to handle some of the unique obstacles they could encounter in the outside world. A young child may not articulate words by the age of 16 months, and they may not respond when adults talk to them, but they may react to other sounds.

Does not like to be cuddled, does not make eye contact, and does not play with others. Three-year-olds who struggle to start conversations, use repetitious vocabulary, or become excessively enthused about particular subjects or things may exhibit signs of autism. Additionally, greater risk conditions among autistic people include depression, anxiety, OCD, sleep difficulties, obesity, high blood pressure, diabetes, and seizures. Although autism spectrum disorder (ASD) is a chronic condition, numerous interventions, including medication and counselling, can help patients manage the difficulties they may encounter. Why ASD occurs is still a mystery to researchers.

Factors

ASD affects nearly twice as many men as women due to genetics, environmental factors, and early disturbance of brain development, preterm birth, and being a guy.

Conclusion

Rare metabolic condition PKU is frequently found at birth. The important amino acid phenylalanine cannot be metabolized properly as a result, which may lead to the condition. PKU is often identified at birth by new-born screening tests, at which point dietary therapy is initiated under the guidance of a nutritionist and a geneticist/metabolism specialist. However, if the new-born hasn't taken any protein, mild instances of PKU may go unnoticed. In PKU patients, it's important to keep an eye on their long-term nutritional needs, physical activity, growth, and cognitive abilities.

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