Analysis of Leigh Disease with Seizures and Co-Morbid Metabolic Conditions

Leigh Disease
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Abstract - Leigh disease is a relatively terrible disorder that is “neurometabolic” in nature and is found to occur in young children and new-borns. It is also sometimes called Juvenile Subacute Necrotizing Encephalopathy (JSNE). Leigh disease is an evolved/advanced disorder and it works by attacking the nervous system. It usually manifests in neonates and young children and it presents symptoms such as cough, cold, usual hallucinations, respiratory disorders, and difficulty in swallowing. Seizures is also a very common occurrence. Usually, it is known to manifest in children between 3 months – 2 years. But infrequently it is seen in teenagers and adults. Leigh syndrome occurs as a result of a flaw in the general functioning of the mitochondrial DNA.

The central nervous system due to the absence of energy in the cells, triphosphate which occurs as a result of the obstruction of the action of the thiamine diphosphate kinase in the manifestation of Leigh disease. Alternative treatments involve the use of sodium citrate or sodium bicarbonate which has been found to help combat lactic acidosis. (Dichloroacetate is also considered albeit is still in the research phase).

For metabolic disorders, diet is regulated, and in the causative event due to X-linked recessive inheritance, a low carbohydrate diet is highly advised.

Keywords - Leigh disease, Seizures, Thiamine/Vitamin B1 deficiency, metabolic disorders.

1. INTRODUCTION

Leigh disease is a neurological and metabolic disorder that is mostly found to manifest in childhood but can also, in rare cases occur in teenage and adulthood. It is usually identified on an MRI by the presence of dead/dying tissues which present as lesions on the brain of the inflicted. It causes symptoms such as Nausea, Seizures, Dysphagia and Lactic acidosis. Advanced stages of Leigh disease show degeneration of the muscular system, and its disconnection from the brain which leads to muscular complications. It also affects some major organs (heart, lungs, etc.) Overall manifestation is characterized by the presence of seizures and metabolic disorders like RTI, complex of phytosom.

2. CASE REPORT

A 3 months old male baby was presented to the paediatric department with fever with cold and cough for 15 days. A seizure episode activity with up rolling of eyes, tonic posture of limbs, groaning, head nodding towards one side, acidotic breathing. His CT scan showed bilateral symmetrical hypodensities in bilateral caudate and lentiform nucleus. MRI scan showed prominent sulcal spaces in the bilateral frontotemporal region. Upon admission in to the ward, he experienced intermittent airflow blockage and was assessed with ventricular support. Patient has metabolic disorders since birth, which is related to mitochondrial defective complications. His echo showed his respiratory rate to be 50 cycles per minute, detecting no abnormalities. His pulse was 150 beats per minute and blood pressure 80/50 mmHg. His weight was 4.7kg and height 57cm, peripheral capillary oxygen saturation levels was 98%, his routine hemogram reports showed that his haemoglobin levels are 7.5gm%. Total leucocyte count is 27900 cells per cubic metres, CRFT – 4 seconds, bicarbonate levels, 8.8mEq/L. [Urine out: 0.9/ml/kg]. Packed cell volume was found to be 26.8%. CSF lactate was noted 8.9mmol/L and his creatinine kinase levels were 340U/L. His liver function test revealed a mild abnormality with ALT, AST, ALP levels found to be 48IU/L, 56IU/L and 107IU/L respectively.

Arterial blood analysis revealed metabolic acidosis and blood and urine cultures were negative. After administration into the hospital and the correspondence of diagnosis, treatment was initiated and the protocol is observed in the table below.
3. DISCUSSION

Leigh disease can be defined as a progressive neurometabolic disease that is characterized by the presence of a blemished mitochondria. It also occurs as a result of the manifestation of defective pyruvate metabolism in young children, which results in seizures impaired vision, ataxia, regressive psychomotor capabilities. Leigh syndrome is generally progressed by research procedures that include testing and clinical laboratory findings, which is denoted by the presence of increased alanine levels in the blood or lactic acidosis, which are common indicators of Leigh disease. Due to the fact that Leigh syndrome occurs as a result of a defective metabolic and mitochondrial pathway, it can be sometimes be mistaken for similar conditions, due to the parallel clinical symptoms. Some of these conditions include thiamine deficiency and encephalitis.

Leigh disease also has a profound causative factor in the defect of gene mutations, specifically in the mitochondrial DNA (mt. DNA), which can affect the basic metabolic process of generation of Adenosine triphosphate (ATP) and disrupt energy transference in cells.

A deficit in the pyruvate dehydrogenase complex, specifically the intricate part of it that is encoded by an X-linked gene is one of the causative factors of Leigh disease, and it manifests as focal lesions in specific regions of the brain, which take on different forms, one of which is Demyelination. Demyelination is characterized by the loss/destruction of the myelin that covers the axons of neurons which in turn inhibits the relationship with other neurons. The focal lesions caused in the brain (which is a consequence of demyelination), affects the brain stem which results in the manifestation of a lot of the symptoms seen in Leigh disease.

Oxidative phosphorylation (OP) is a major step in the production of ATP, and a defective step in the general OP process, would lead to an accretion of pyruvate, which causes lactic acidosis associated with Leigh disease. To combat Leigh disease, its major symptoms, such as seizures, metabolic acidosis etc. are extensively managed with medication. Also, a decrease in the administration of drug or food that is not metabolized befittingly is initiated so as to curb the progression of the inherited metabolic disorder. Metabolic products in blood that cause metabolic disorders associated with Leigh disease are countered by the purification of blood, with chemicals that specifically prevent their build-up. Chelating agents also deter the accretion of toxic metabolites. Progression of the ruination of the cerebral tissue accounts for the deaths encountered in Leigh disease. To combat this occurrence, treatment patterns are applied to elevate the process of ATP reduction and reduce the overall lactate concentration.

A combination of mitochondrial essentials consisting of Vitamin B1, B12, Coenzyme Q, L-Carnitine and L-arginine is employed in the treatment of mitochondrial defect. With regards to the patient, as treatment with riboflavin improved the adenosine triphosphate production. Sodium bicarbonate is useful in the management of acidosis. Mannitol used to decrease intracranial pressure. Potassium chloride used for the management of hypokalaemia. Phenytoin is used for the treatment of seizures, including Midazolam infusion which is preferred to Diazepam due to its faster onset of action in the treatment of status epilepticus. Adrenaline is used in the management of blood pressure in emergency.

4. CONCLUSION

It is concluded that the current treatment goal of Leigh disease is to minimize or reduce the progression and advancement of its manifestation, ascertain elevated efficacy of drug, deter the hospitalization of the patient, and probable surgery, improve overall quality of life and the introduction of a more suitable treatment for patients with dire prognosis.
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