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MELAS Syndrome: An Uncommon Mitochondrial Inheritance

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Abstract: Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome is a progressive neurodegenerative disorder caused by mutations in the genes in the mitochondrial DNA. In most cases, the signs and symptoms of this disorder appear in childhood following a period of normal development. A 2 year old female child with global developmental delay presented with trauma to the paediatric OPD. On examination patient showed signs of microcephaly, hypotonia, reduced reflexes and abnormal vision. The child was hospitalized to evaluate reduced reflexes. Audiology evaluation reported affected receptive and expressive language. Low hemoglobin, elevated lactate: pyruvate ratio, reduced bicarbonate levels were found. Arterial blood gases analysis revealed metabolic acidosis.MRI of the brain showed acute infarction in basal ganglia and internal capsule. Based on the clinical and laboratory evaluation, patient was diagnosed as MELAS syndrome. Along with symptomatic treatment, Biotin and Coenzyme Q were supplemented to which patient responded progressively, thereby substantiating the diagnosis.
Keywords: MELAS, lactate: pyruvate, Mitochondrial inheritance, Neurodegeneration

INTRODUCTION

Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome is a progressive neurodegenerative disorder [1]. It is caused by mutations in the genes in mitochondrial DNA. In most cases, the signs and symptoms of this disorder appear in childhood following a period of normal development. Most people with MELAS have a buildup of lactic acid in their bodies, a condition called lactic acidosis. Increased acidity in the blood can lead to vomiting, abdominal pain, extreme tiredness (fatigue), muscle weakness, loss of bowel control, and difficulty breathing [2]. The most commonly involved pathogenic point mutations are A3243G and T3271C in the gene encoding the leucine Trna [3]. We are presenting a rare case of MELAS syndrome.

CASE REPORT

A 2 year old female child presented to our institute with a history of vaginal bleeding. Patient had global developmental delay and patient's mother gave history of injury by woodstick while playing.

On examination child had hypotonia, reduced reflexes and abnormal vision. Her head circumference was 42 cms indicating microcephaly. Child's audiology report showed affected receptive and expressive language. On ultrasonographic examination of abdomen and pelvis, a hematoma was found. On MRI of her head, acute infarction in basal ganglia and internal capsule was detected.

Patient's lab parameters showed following results:

On the day of admission patient's Hemoglobin was very low (4.9 g/dl) and total white blood cell counts were 19390, Serum Bicarbonate levels were significantly reduced (7.8 meq/L). AST was high (146 IU/L). Patient was in acidosis and hence treatment was started to treat acidosis. Patient was put on oxygen. Phenytoin was given to prevent seizures. Inspite of treatment, patient's bicarbonate levels did not improve much and Arterial blood gas analysis showed less improvement in acidosis. Geneticist's openion was taken and patient was suspected of having MELAS syndrome which is commonest amongst diseases with mitochondrial inheritance. For the confirmation of MELAS syndrome, Serum lactate/ pyruvate ratio was measured. Lactate levels were 35.9 mg/dl and pyruvate levels were 0.85 mg/dl, hence lactate/pyruvate ratio was increased.

Clinically patient's global developmental delay, abnormal vision and hearing, infarcts in the brain i.e. stroke and lactic acidosis lead to the diagnosis of MELAS syndrome which could not be further confirmed genetically due to financial constrains of the patient. Patient was started on biotin and Coenzyme Q and after improvement in acidosis, she was discharged.

DISCUSSION

As discussed previously MELAS syndrome is a neurodegenerative disorder associated with pathological point mutation in the genes of the mitochondrial DNA, leading to encephalopathy, lactic

acidosis and stroke. Approximately 80% of patients with the clinical characteristics of MELAS syndrome have a heteroplasmic A-to-G point mutation in the dihydrouridine loop of the transfer RNA (tRNA)Leu (UUR)gene at base pair (bp) 3243 (ie, 3243 A →G mutation) [4].

Some of the genes (MT-ND1, MT-ND5) related to MELAS provide instructions for making proteins involved in normal mitochondrial function. These proteins are a part of large enzyme complex (NADH dehydrogenase, also called complex I) in mitochondria that helps convert oxygen and glucose to energy.

Metabolic stroke like episodes may be nonvascular and due to transient oxidative phosphorylation (OXPHOS) dysfunction within the brain parenchyma which may be responsible for multisystem dysfunction in these patients.

Increased production of free radicals in along with OXPHOS defect leading to vasoconstriction may offset the effect of potent vasodilators (eg, nitric oxide). The unusual stroke like episodes and higher morbidity observed in these cases may be secondary to alterations in nitric oxide homeostasis that cause microvascular damage [1].

Early symptoms of this disease may include muscle weakness and pain, recurrent headaches, loss of appetite, vomiting, and seizures. Most affected individuals experience stroke-like episodes beginning before age 40. These episodes often involve temporary muscle weakness on one side of the body (hemiparesis), altered consciousness, vision abnormalities, seizures, and severe headaches resembling migraines. Repeated stroke-like episodes can progressively damage the brain, leading to vision loss, problems with movement, and a loss of intellectual function (dementia) [2].

Other abnormalities that may be observed are ventricular dilatation, cortical atrophy, and basal ganglia calcification. Psychiatric abnormality like altered mental status, schizophrenia, bipolar disorder may be observed in MELAS syndrome. Autism spectrum disorders (ASDs) with or without additional neurological features can be early presentations of the m.3243 A → G mutation. Myopathy may bedebilitating. The encephalopathy may progress to dementia; eventually, the clinical course rapidly declines, leadingto severe disability and premature death [1].

Though currently there is no definitive treatment modality is available for the disease, the following supplements have shown promise and given hope to MELAS patients.

CoQ10 has been helpful for some MELAS patients [5]. Riboflavin has been reported to improve the function of a patient with complex deficiency [6].

The administration of L-arginine during the acute and interictal periods may represent a potential new therapy for this syndrome to reduce brain damage due to impaired vasodilation in intracerebral arteries owing to nitric oxide depletion [7, 8].

Our case was presented with global developmental delay and hearing as well as vision abnormalities with episodes of stroke, hence it was already late to prevent the permanent damages. We started on biotin and Coenzyme Q as to lengthen the lifeline of the patient. We diagnosed on the basis of MRI picture, lactate pyruvate ratio and clinical features. But for the definitive diagnosis, Genetic analysis is needed which could not be done due to financial constrains of the patient.

REFERENCES

1. Fernando S, Bruce B editors; MELAS syndrome. Available from: http://emedicine.medscape.com/article/ 946864-overview
2. Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes. Available from: http://ghr.nlm.nih.gov/condition/mitochondrial-encephalomyopathy-lactic-acidosis-and-stroke-like-episodes
3. Kael S, Hanna M; Mitochondrial DNA and heritable traits and diseases. In Fauci A, Braunwald E, Kasper D, Stephen L, Hauser, Longo D, Loscalzo J editors; Principles of Internal Medicine by Harrisons, 17th edition, Volume 2, United States of America, McGraw-Hill, 2008: e311.
4. Mehrazin M, Shanske S, Kaufmann P, Wei Y, Coku J, Engelstad K; Longitudinal changes of mt DNA
A3243G mutation load and level of functioning in MELAS. Am J Med Genet A., 2009; 149A (4): 584-587.
5. Rodriguez MC, MacDonald JR, Mahoney DJ, Parise G, Beal MF, Tarnopolsky MA; Beneficial effects of creatine, CoQ10, and lipoic acid in mitochondrial disorders. Muscle Nerve, 2007; 35(2): 235–242.
6. Ogle RF, Christodoulou J, Fagan E, Blok RB, Kirby DM, Seller KL *et al*.; Mitochondrial myopathy with tRNA(Leu(UUR)) mutation and complex I deficiency responsive to riboflavin. J Pediatr., 1997; 130(1): 138–145.
7. Koga Y1, Povalko N, Nishioka J, Katayama K, Kakimoto N, Matsuishi T *et al*.; MELAS and L-arginine therapy. Mitochondrion 2007; 7(1-2): 133–139.

8. Hirata K, Akita Y, Povalko N, Nishioka J, Yatsuga S, Matsuishi T, *et al*.; Effect of l-arginine on synaptosomal mitochondrial function. Brain Dev., 2007; 30 (4): 238.