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CASE REPORT

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Young onset mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome: a case report.

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ABSTRACT

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes Syndrome (MELAS) is a rare mitochondrial disorder characterised by diverse neurological and systemic manifestations. The key underlying mechanism of the disease is related to protein synthesis, energy depletion, and nitric oxide defciency. We present a case from a tertiary care hospital of a 19-year-old male with a history of seizure disorder and progressive neurological deficits. The patient was evaluated using clinical evaluations, laboratory tests, and radiological imaging to rule out the most serious complications. His symptoms included bilateral sensorineural hearing loss, visual disturbances, and recurrent headaches associated with vomiting. Neurological examination revealed signs of bilateral sensorineural hearing loss, visual field deficits, and asymmetric weakness in the four limbs. Diagnostic workup, including MRI findings of parieto-occipital lesions and elevated lactate levels, supported the diagnosis of MELAS syndrome. Genetic testing confirmed the presence of the m.3243A>G mutation in mitochondrial DNA. After a 2-week hospital stay, the patient was discharged with a follow-up plan. The main goals of treatment are to effectively manage disease complications and to enhance the patient's overall quality of life. Management involved the adjustment of antiepileptic therapy and initiation of mitochondrial supplements. This case underscores the clinical spectrum and diagnostic challenges of MELAS syndrome, emphasising the importance of early recognition and tailored treatment strategies to optimise patient outcomes.

KEY WORDS: Mitochondrial encephalopathy, stroke-like episode, lactic acidosis.

INTRODUCTION

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) syndrome is a rare mitochondrial disorder with a profound impact on patients' health and quality of life. It is characterised by stroke-like episodes, muscle weakness, and lactic acidosis, among other symptoms. Typically presenting in childhood or early adulthood (between the ages of two and fifteen), MELAS can often lead to significant morbidity due to its progressive nature and the severity of its neurological manifestations [1]. Stroke-like episodes, one of the hallmarks of MELAS syndrome, often present as acute focal neurological deficits that do not conform to typical vascular distributions. These episodes can include transient hemiparesis, cortical blindness, altered consciousness, seizures, and severe headaches that often accompany them [2]. Early-onset stroke is an alarming clinical finding that requires a thorough investigation of possible underlying causes, particularly when traditional risk factors such as hypertension, diabetes, and hyperlipidemia are absent. MELAS syndrome should be considered in the differential diagnosis of young patients with stroke-like episodes, especially when accompanied by other systemic or neurological symptoms.

This case report aims to highlight the importance of considering MELAS as a potential aetiology in young-onset stroke (nineteen years of age) and to emphasize the role of comprehensive diagnostic evaluation in these patients.

CASE REPORT

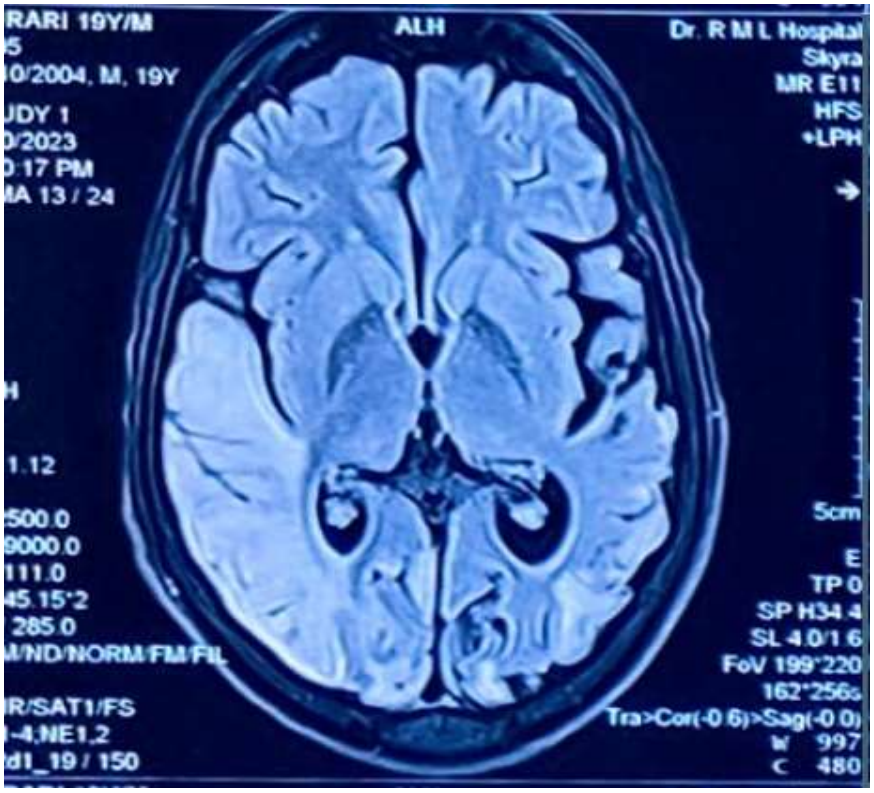
PATIENT INFORMATION: A 19-year-old young man came to the emergency department with compliances seizure disorder characterised by myoclonic jerks with secondary generalisation, weakness in his lower limbs more than in his upper limbs, bilateral hearing loss, and blurring of vision. The patient presented with a 15-day history of headache, frontal type with photophobia, and vomiting. During this period, his hearing loss and vision progressively worsened.

CLINICAL FINDINGS: Vital signs blood pressure, heart rate, respiratory rate and saturation were within normal limits. The patient presents with a seizure disorder characterised by myoclonic jerks with secondary generalised tonic–clonic seizure (GTCS). Neurological examination revealed a normal Glasgow Coma Scale (GCS) score, bilateral sensorineural hearing loss (SNHL), reduced visual fields in the left side of both eyes and bilateral plantar flexor responses. The patient exhibited delayed secondary sexual characteristics, including lack of axillary hair, absence of a moustache, and short stature.

TIMELINE: Patient with a history of seizure disorder characterised by myoclonic jerks with secondary generalisation generalized tonic–clonic seizure for the past 5 years, weakness in all four limbs, and bilateral sensorineural hearing loss (SNHL) for the past 4 years, blurred vision for the past 2 years and patient with headache and progressive decline in vision and hearing for the past 1 year.

DIAGNOSTIC ASSESSMENT: CBC, LFT, KFT and serum electrolytes including calcium were within normal limits. A hormonal profile was performed due to short stature that showed LH, FSH, prolactin, and thyroid function within the normal range. Testosterone levels were low (0.91 ng / ml) and vitamin D3 levels were normal. The CSF studies were normal. A fundoscopy was performed showing a normal fundus. Serum lactate showed high levels (11.6 mmol/L). Muscle enzymes showed elevated creatine kinase (CK): 509 U/L, CK-MB: 76 U/L, LDH: 290 U/L. Visual Evoked Potential (VEP) showed left-sided visual pathway dysfunction. The head of NCCT showed bilateral basal ganglia calcification and occipital infarctions. Magnetic resonance imaging showed abnormal gyral diffusion restriction in the bilateral basal ganglia (Figure 1). Lactate peak on magnetic resonance spectroscopy (MRS). Echocardiography did not show thrombus and carotid Doppler did not show internal cerebral artery stenosis. Muscle biopsy showed normal histology. Genetic testing for the m.3243A>G mutation m.3243A> G in mitochondrial DNA confirmed the diagnosis of MELAS syndrome.

Figure 1. Magnetic resonance imaging showed abnormal gyral diffusion restriction in bilateral basal ganglia (T2-weighted hyperintensities in bilateral parieto-occipital lobes).



FOLLOW-UP AND FUTHER RESULTS: The patient was treated with levetiracetam for seizures, and valproate was gradually withdrawn. Supplements including carnitine, arginine, biotin, riboflavin, coenzyme Q10 and benfotiamine (vitamin B1) were initiated. The antiepileptic medication was adjusted based on subsequent episodes of seizures. The patient had reduced seizure episodes with no further decline in vision and hearing and no further stroke episodes. After a 2-week hospital stay, the patient was discharged with a follow-up plan.

DISCUSSION

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes syndrome (MELAS) is one of the most common maternally inherited mitochondrial disorders. This condition is mainly related to a mutation involving an adenine-to-guanine transition at position 3243 of mtDNA (m.3243A>G) within the MT-TL1 gene, which encodes tRNALeu (UUR) [3-5]. The MELAS study group committee has established diagnostic criteria that incorporate clinical, laboratory, and genetic testing parameters [6]. Category A: Clinical Findings of episodes similar to stroke, headache with vomiting, seizures, hemiplegia, cortical blindness, and acute focal lesion observed by brain imaging. Category B: Evidence of mitochondrial dysfunction, such as high lactate levels in plasma and cerebral spinal fluid or deficiency of mitochondrial-related enzyme activities, mitochondrial abnormalities in muscle biopsy, definitive gene mutation related to MELAS. Definitive diagnosis of MELAS: Two items of Category A and two items from Category B (four items or more) Suspicion of the diagnosis of MELAS: One item from Category A with two items from Category B (at least three items).

Our patient had a definitive diagnosis of MELAS, presented with headache and vomiting, seizures, high plasma lactate levels, and the definitive gene mutation m.3243A>G. This mutation disrupts mitochondrial protein synthesis, leading to reduced energy production and multi-organ dysfunction. Energy deficiency can stimulate mitochondrial proliferation, which in blood vessels causes angiopathy, impairs blood flow and leading to complications such as stroke-like episodes. Furthermore, deficiency of nitric oxide (NO), resulting from decreased precursors such as arginine and citrulline, oxidative stress, and mitochondrial dysfunction, exacerbates these issues by altering vascular function [2]. In a study by Cox BC et al. [1], a total of 81 patients were analysed, including those with MELAS and those with positive genetic markers but not meeting the full clinical criteria. Patients were divided into MELAS, non-MELAS symptomatic and asymptomatic groups based on their symptoms and genetic findings. MELAS was also classified as ‘standard-onset’ if the initial stroke-like episode occurred before age 40, and as ‘late-onset’ otherwise. It revealed that MELAS patients had a significantly lower BMI. MELAS also showed a trend toward higher serum heteroplasmy levels. Symptomatic non-MELAS patients often presented sensorineural hearing loss as an initial symptom, while MELAS patients had higher rates of seizures and a shorter survival time. Standard-onset MELAS was associated with greater neurological involvement at onset. Furthermore, patients with late-onset MELAS had higher rates of diabetes and nephropathy and were affected in more organ systems. In this patient, seizures followed by hearing loss followed by stroke-like episodes.

Although mitochondrial mutations should theoretically affect all offspring of a female carrier, our patient had 1 older brother who was not affected. This can be explained by the heteroplasmic mutation or de novo mutation in our patient. The m.3243A>G mutation is associated with a wide spectrum of phenotypes, ranging from severe MELAS syndrome in about 10% of individuals with the mutation to asymptomatic carrier status in another 10%. Between these extremes are intermediate phenotypes, including single-organ involvement (e.g., cardiomyopathy or diabetes mellitus) and multiorgan involvement with various combinations of symptoms (e.g., myopathy, diabetes, and deafness).

Our patient refused genetic testing for the siblings, preventing us from determining the extent of the mutation. Our patient had a severe phenotype that is seen when 60-90% of mitochondrial DNA shows this mutation [7-9]. Moreover, in this patient, the importance of having a suspect of MELAS early, due to the complexity of the treatment. Valproic acid should be avoided in the treatment of seizures in MELAS syndrome due to its detrimental effects on mitochondrial function, potentially worsening seizures [10]. Other antiepileptic drugs that can affect mitochondrial metabolism include phenobarbital, carbamazepine, phenytoin, oxcarbazepine, ethosuximide, zonisamide, topiramate, gabapentin, and vigabatrin [11]. In this patient, valproate was started before the diagnosis which could be an attributing factor for seizure-like episodes

PATIENT PERSPECTIVE: By understanding these aspects of MELAS syndrome, clinicians can enhance their diagnosis, treatment, and treatment of affected patients, while also avoiding potential medication-related issues in the future.

CONCLUSIONS

MELAS is a rare, inherited, and progressive disease that affects multiple organ systems. Awareness of this condition is essential when evaluating stroke-like episodes in young patients. The timely diagnosis, genetic counseling, comprehensive evaluations, and regular follow-up are crucial to improving the quality of life for affected patients. Reporting a rare case such as MELAS syndrome is crucial to helping physicians with limited experience in such conditions, providing them valuable insights and guidance on appropriate treatment strategies.

SUPPLEMENTARY INFORMATION

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