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AN INTERESTING CASE OF RECURRENT STROKE

Neurology

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ABSTRACT

Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) is a mitochondrial cytopathy caused by mutations in mitochondrial DNA. Clinical manifestation occurs before the age of 40. We present the case of a 52 year-old female who was initially Diagnosed as episodes of recurrent ischemic strokes. Brain imaging including MRI, clinical and laboratory findings that lent cues to the diagnosis of MELAS.

KEYWORDS

MELAS, Recurrent ischemic strokes MRI

INTRODUCTION

The clinical syndrome of MELAS (mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes) is caused by mutations in mitochondrial (DNA) and subsequent respiratory chain deficiency. Symptoms and signs typically comprise mitochondrial myopathy, encephalopathy with stroke-like episodes, seizures and/or dementia, and lactic acidosis. Clinical manifestation typically occurs before the age of 40. Although MELAS is a rare disease, the present case clinical presentations and imaging findings may mimic stroke.

Case Report

A 52 year-old woman of short stature was first admitted to our hospital three days after onset of acute aphasia, headache and a moderate right-sided hemiparesis.

Medical history included type 2 diabetes, arterial hypertension, and past smoking. The patient had no history of mental retardation or cognitive decline up to the time of her acute illness. she had developed hearing loss and diabetes at the age of 45years. She was also diagnosed with cardiomyopathy that was initially thought to be of hypertensive aetiology, and had a history of chronic obstructive pulmonary disease (COPD) and renal insufficiency. Of note, the patient had two miscarriages, and one newborn child died within the first hours after birth. There was no history of previous frequent headaches.

On admission, she presented with moderate fluent aphasia and moderate weakness of the right arm and leg. Laboratory testing revealed hyponatremia (118mmol/l) and hyperglycaemia. Plasma osmolality was low (294mmol/kg), whereas urine osmolality (467mmol/kg),.In addition, serum lactate and serum creatine kinase levels were elevated.

Computed tomography (CT) on admission showed hypodense areas within the left temporal lobe without signs of haemorrhage. CT angiography showed few calcified plaques in both carotid bifurcations without a relevant stenosis or occlusion of intracranial or extracranial arteries . Magnetic resonance imaging (MRI) revealed fluid attenuated inversion recovery (FLAIR) hyperintensities within the cortical grey and white matter of the left temporal lobe .

The patient was diagnosed with ischaemic stroke in the territory of her left middle cerebral artery and transferred to the stroke unit. Duplex sonography confirmed moderate atheroma of the right and left carotid bifurcation without relevant stenosis, which was considered a possible cause. Transthoracic echocardiography revealed left ventricular hypertrophy, but no cardiac sources of embolism. Electrocardiogram (ECG) monitoring showed no atrial fibrillation. Glycated haemoglobin was elevated .

Antiplatelet therapy was switched from aspirin to clopidogrel, and the patient was discharged after two weeks . Two weeks later, the patient was readmitted due to recurrence of the right-sided hemiparesis which now also involved her face. MRI revealed enlarging FLAIR hyperintense signal changes in the mesiotemporal area extending towards the left parietal lobe. In addition, new FLAIR hyperintense signal changes were also present in the right temporal pole . CT angiography again showed no vessel occlusion. The patient was diagnosed with a recurrent stroke. Transoesophageal echocardiography did not reveal any patent foramen ovale or other cardiac source of embolism. Clopidogrel was stopped and oral anticoagulation was started. During the second hospitalization impaired consciousness, recurrent vomiting and disorientation occurred. Electroencephalography (EEG) showed generalized slowing, and frequent multifocal rhythmic epileptiform discharges. Clinical course and EEG findings improved under antiepileptic therapy with lacosamide and levetiracetam.

Cerebrospinal fluid (CSF) examination revealed normal cell count, normal protein, negative herpes simplex polymerase chain reaction (PCR) and elevated lactate levels. Laboratory screening for vasculitis turned out negative.

Paraneoplastic encephalitis was also considered, CT thorax was normal and paraneoplastic antineuronal antibodies in serum (Anti-Hu, Anti-Yo, Anti-Ri, Anti-CV2, Anti-Ma1, Anti-Ma2/Ta, Anti-Amphiphysin, Anti-VGCC, and Anti-NMDA-receptor antibodies) turned out negative. The patient was again discharged with residual aphasia.

Six months later, the patient presented at the emergency department with disorientation, aggression, mutism and refusal to eat, drink or take her medication. She was diagnosed with organic psychosis and admitted to a psychiatric hospital.

The patient was finally readmitted again 8 months after initial hospitalization with repeated falls and progressive apathy. On admission, the patient was mute. At this point, MRI showed progressive brain lesions involving both temporal and occipital lobes, characterized by a FLAIR-hyperintense oedema with signs of a local mass effect. These lesions crossed the boundaries of vascular territories. The parts of the lesions involving the cortex appeared hyperintense on diffusion-weighted imaging (DWI) and hypointense on apparent diffusion coefficient (ADC) maps, consistent with cytotoxic oedema. In contrast, subcortical regions appeared hyperintense on ADCmaps, consistent with vasogenic oedema.

Taking into account the clinical presentation with recurrent stroke-like episodes, encephalopathy, seizures, headache and lactic acidosis, as well as the medical history including hearing loss, short stature, cardiomyopathy and diabetes, we suspected MELAS as the underlying cause. A detailed family history revealed hearing loss in a brother, and transient visual disturbances as well as a history of acute hearing loss in a sister .

A biopsy of the vastus lateralis muscle showed signs of mitochondrial myopathy, including sub-sarcolemmal accumulation of mitochondria on Gomori trichrome staining , neutral fat deposits and prominent

cytochrome C oxidase (COX) negative and succinate dehydrogenase (SDH) hyperreactive muscle fibres.

Finally, the diagnosis of MELAS was confirmed by positive genetic testing for the mitochondrial DNA mutation in the MT-TL1-gene- the most common mutation in patients with MELAS- in peripheral blood as well as in the muscle biopsy.

The patient's state worsened rapidly. The diagnosis and the lack of curative treatment options were discussed with her family. The patient died shortly thereafter.

DISCUSSION

MELAS typically manifests before 40years of age with symptoms that may include cardiomyopathy, progressive (bilateral) sensorineural hearing loss, migraine-like headache, recurrent vomiting, peripheral neuropathy, ophthalmoplegia, pigmentary retinopathy, diabetes, hypoparathyroidism, ataxia, and short stature. The age of the first clinical presentation of stroke-like episodes in MELAS is highly variable, but first episodes usually occur before the age of 40. Although MELAS is a rare disease, the present case illustrates that the clinical presentations and imaging findings may mimic stroke, the most common acute brain disease. The educational value of our case lies in distinguishing findings on brain MRI, which have finally led to the correct diagnosis.

In our patient, stroke-like episodes first occurred at 52 years of age, which is highly unusual for MELAS. Indeed, our patient was misdiagnosed as having recurrent strokes of arterio-arterial embolic origin. The disease course, medical history, clinical and paraclinical signs of a mitochondrial encephalomyopathy and distinct MR imaging findings finally had led to the suspicion of MELAS which was confirmed by muscle biopsy and molecular genetic testing.

In our patient, distinct findings on brain MRI first raised the suspicion of MELAS. MELAS lesions are typically localized in the temporo-occipital cortex and may progress over time, extending to adjacent areas without respecting vascular arterial territories . Both grey and white matter are affected and appear hyperintense on FLAIR or T2w images as a sign of oedema, which may result in a pronounced local mass effect .

Another chameleon mimicking MELAS lesions is posterior reversible encephalopathy syndrome (**PRES**) that typically shows vasogenic oedema in subcortical areas of the occipital and temporal lobes. However, atypical presentations of PRES are increasingly recognized, including lesions with signs of restricted cortical diffusion or lesions in other brain areas . In these cases, clinical features such as the existence of predisposing conditions or the reversibility of symptoms may guide the way to the correct diagnosis.

Herpes encephalitis, may mimic MELAS lesions as it typically affects both cortical and subcortical temporal areas bilaterally, and because lesions may also exhibit a combination of restricted cortical diffusion and subcortical vasogenic oedema . However, “step-wise” progression of lesions is uncommon in herpes encephalitis, and lesions are typically located mesio-temporally .

PML is another differential diagnosis presenting with FLAIR-hyperintense lesions that expand continuously and centrifugally without respecting vascular territories . In contrast to MELAS, however, cortical areas are not typically affected in PML, resulting in a “flamelike” shape of subcortical lesions and a relatively good signal contrast between the lesion and the cortex.

Finally, as in our patient, stroke-like episodes in MELAS can be misdiagnosed as subacute **ischemic strokes.** Cerebral infarcts appear as FLAIR-hyperintense– and sometimes gadolinium-enhancing-lesions involving the grey and white matter Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (**CADASIL**) typically presents with recurrent subcortical infarcts and progressive ischemic white matter lesions predominantly affecting the anterior temporal pole. Although cortical microinfarcts have been demonstrated, macroscopic cortical infarcts are rare in CADASIL.

Current therapeutic options for MELAS are limited to supplementation of coenzyme Q10, L-carnitine and L-arginine, a non-essential amino acid involved in NO synthesis and endothelial-dependent vascular relaxation which may explain its benefit particularly in the acute phase of the disease.

CONCLUSION

In conclusion, this MELAS case with first stroke-like episodes at 52 years of age underscores the importance of considering inherited mitochondrial disorders as a potential cause of recurrent atypical stroke-like events, if MRI findings are inconsistent with ischemic infarction, even in adult or elderly patients.

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Conflict Of Interest- NIL

Consent – Consent was taken

REFERENCES

1. Lyuobi-Idrissi A, De Guio F, Chabriat H, Jouvent E. Focal macroscopic cortical lesions in cerebral autosomal-dominant Arteriopathy with subcortical infarcts and leukoencephalopathy. Stroke. 2017;48:1408–11.
2. Koenig MK, Emrick L, Karaa A, et al. Recommendations for the Management of Strokelike Episodes in patients with mitochondrial Encephalomyopathy, lactic acidosis, and Strokelike episodes. JAMA Neurol. 2016;73:591–4.
3. Nightingale H, Pfeffer G, Bargiela D, Horvath R, Chinnery PF. Emerging therapies for mitochondrial disorders. Brain. 2016;139:1633–48.
4. Gieraerts C, Demaerel P, Van Damme P, Wilms G. Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome mimicking herpes simplex encephalitis on imaging studies. J Comput Assist Tomogr. 2013;37:279–81.
5. Ito H, Mori K, Kagami S. Neuroimaging of stroke-like episodes in MELAS. Brain and Development. 2011;33:283–8.
6. Farrar MA, Lin CS, Krishnan AV, Park SB, Andrews PI, Kiernan MC. Acute, reversible axonal energy failure during stroke-like episodes in MELAS. Pediatrics. 2010;126:e734–9.
7. Kim JH, Lim MK, Jeon TY, et al. Diffusion and perfusion characteristics of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episode) in thirteen patients. Korean J Radiol. 2011;12:15–24.
8. Kubota H, Tanabe Y, Takanashi J, Kohno Y. Episodic hyponatremia in mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes (MELAS). J Child Neurol. 2005;20:116–20.
9. Harrison's principles of internal medicine 21st edition.
10. Adams and victor's principles of neurology 11th edition.