CASE REPORT

Recurrent Alternate-Sided Homonymous Hemianopia Due to Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-Like Episodes (MELAS): A Case Report

Kristen M. Krysko^a and Arun N. E. Sundaram^{a,b}

^aDivision of Neurology, University of Toronto, Toronto, Ontario, Canada; ^bDepartment of Ophthalmology and Visual Sciences, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

ABSTRACT

Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) can rarely cause alternate-sided homonymous hemianopia due to stroke-like episodes involving the occipital lobes, as reported in three previously published cases. The authors report an interesting case of a 16-year-old presenting with myoclonic epilepsy due to MELAS with the rare ND3 mitochondrial mutation T10191C, with recurrent alternate-sided homonymous hemianopia. Visual field and corresponding magnetic resonance imaging (MRI) findings are presented. To the authors' knowledge, this is the first report of recurrent alternate-sided homonymous hemianopia in MELAS with documented visual field and MRI findings with resolution between each episode.

ARTICLE HISTORY

Received 15 July 2016
Revised 9 August 2016
Accepted 10 August 2016

KEYWORDS

Case report; MELAS; mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes; recurrent alternate-sided homonymous hemianopia

Introduction

Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) is a multi-system mitochondrial maternally inherited disorder.^{1,2} Common initial manifestations include seizures, stroke-like episodes, recurrent headaches, cortical vision loss, weakness, and recurrent vomiting, with cortical vision loss being a common manifestation.³

Three case reports describe MELAS presenting with alternate-sided homonymous hemianopia, each presenting with homonymous hemianopia, followed by contralateral homonymous hemianopia with corresponding magnetic resonance imaging (MRI) changes in the occipital lobes.^{4–6} Su et al. presented a case with visual field loss in isolation but did not report the associated mitochondrial mutation.⁴ The other cases presented with homonymous hemianopia and seizures and carried the typical A3243G mitochondrial mutation.^{5,6}

We describe an interesting case of recurrent alternate-sided homonymous hemianopia in

MELAS related to the T10191C mitochondrial mutation, which has not been previously described.

Case report

A 16-year-old female with short stature, attention deficit hyperactivity disorder, and a learning disability presented with headaches and myoclonic epilepsy characterised by myoclonic jerks, focal sensory and motor seizures, and clusters of generalised myoclonic and tonic-clonic seizures. She did not report visual loss or hallucinations. She was an only child, with no family history of epilepsy or neurologic disease. She appeared well, with a height of 157 cm and a weight of 46 kg. She was alert and oriented. Neurologic examination revealed a left homonymous superior quadrantanopia and mild left leg weakness with associated spasticity, hyperreflexia, and extensor plantar response. Ophthalmoscopy did not reveal any abnormalities in the optic discs or the retina. Clinical seizures resolved with phenytoin treatment.

Goldmann perimetry confirmed a left homonymous superior quadrantanopia (Figure 1A). MRI brain revealed T2/fluid-attenuated inversion recovery (FLAIR) hyperintense non-enhancing right occipital and bilateral peri-rolandic lesions (Figure 2A), with elevated lactate on MR spectroscopy (MRS), suggestive of a mitochondrial disorder. There was no associated diffusion restriction. Electroencephalography (EEG) was normal in wakefulness and sleep. Serum lactate was normal (0.7 mmol/L, range: 0–2.4 mmol/L). Muscle biopsy was normal, with no ragged red fibres and normal mitochondrial enzyme assays. Nerve conduction studies were normal.

Initial investigations including karyotype and mitochondrial mutation testing (A3243G, T3271C, A3252G, C3256T, T3291C, G13513A, A8344G, T8356C, G8363A, A8296G, T8993G, and T8993C) were negative. Sequencing of the whole mitochondrial DNA revealed the ND3 mitochondrial mutation T10191C, with 74% heteroplasmy in muscle, 11.3% in fibroblasts, and 16% in blood. She was diagnosed with MELAS. Her mother's blood was negative for the mutation.

She was treated with carbamazepine and tapered off phenytoin, and her seizures were well controlled. Levetiracetam was added, with improvement in myoclonus. Several months later, her neurologic examination normalised and the visual field defect (Figure 1B) and MRI brain lesions (Figure 2B) improved. Coenzyme Q10 and vitamins A, C, and E were supplemented.

Seizures and myoclonus worsened the following year, although there were no new visual symptoms. EEG showed interictal activity with spike and wave discharges independently over the left and right centroparietal regions. Levetiracetam was increased and clonazepam was initiated. Carbamazepine was discontinued due to side effects.

Subsequently, about 2 years after the initial presentation, without a change in seizure frequency or anti-epileptic therapy, she developed worsening vision with a recurrent left homonymous hemianopia on Humphrey visual fields (Figure 1C), with associated left leg weakness. MRI brain demonstrated bilateral parietal T2/FLAIR hyperintense lesions (Figure 2C). Her mitochondrial supplementation was expanded to include coenzyme Q10, vitamins A, C and E, α -lipoic acid, creatine, and a multivitamin.

Figure 1. Visual fields (VF). (A) Goldmann VF at initial presentation with left homonymous superior quadrantanopia. (B) Goldmann VF with improvement 11 months later. (C) Humphrey VF with recurrent left homonymous hemianopia 2 years later. Mean deviation (MD): left -11.31 dB, right -8.89 dB. (D) Humphrey VF with improvement 5 months later. MD: left -2.93 dB, right -3.42 dB. (E) Humphrey VF with contralateral right homonymous hemianopia 3 years later. MD: left -25.06 dB, right -10.93 dB.

Figure 2. Magnetic resonance imaging (MRI) brain axial fluid-attenuated inversion recovery (FLAIR) sequences. (A) Initial presentation with hyperintensities in right occipital and bilateral peri-rolandic areas. (B) Improvement of lesions 9 months later. (C) New bilateral parietal lesions 1 year later. (D) Improvement of lesions 1.5 years later. (E) New left occipital hyperintense lesion 1 year later. (F) New left temporal, parietal, and perisylvian lesions 2.5 years later.

Repeat visual fields ([Figure 1D](#)) and MRI brain ([Figure 2D](#)) improved again several months later.

MRI brain 1 year later revealed a new large left occipital lesion ([Figure 2E](#)), without new neurologic or visual complaints. Visual field testing was not performed at this time, although this new left occipital lesion explains the interval development of an alternate-sided right homonymous hemianopia on subsequent Humphrey visual fields ([Figure 1E](#)). Two and a half years later, she also developed worsening headaches and increased frequency of complex partial motor seizures. Repeat MRI brain showed new T2/FLAIR hyperintensities in the left parietal, superior temporal, and posterior perisylvian cortex ([Figure 2F](#)). Levetiracetam was increased, although seizures and myoclonus remained refractory and increased in frequency. Her vision did not improve.

Within the next year, she developed progressive aphasia, cognitive impairment, dysarthria, dysphagia, ataxia, and cortical blindness. Visual field assessment was not possible due to the poor neurologic status. Seizure frequency increased despite the stepwise addition of primidone, phenytoin, topiramate, phenobarbital, perampanel, and the ketogenic diet. EEG demonstrated frequent interictal spike and wave discharges over the posterior hemispheres. Unfortunately, she entered terminal refractory status epilepticus despite appropriate optimisation of antiepileptic agents and mitochondrial supplementation.

Discussion

We present a rare case of recurrent alternate-sided homonymous hemianopia with corresponding

changes on MRI brain over several years attributed to MELAS. The initial presentation involved a left homonymous superior quadrantanopia with associated left hemiparesis and seizures that improved, followed by recurrent left homonymous hemianopia, which improved again. She subsequently developed an alternate-sided right homonymous hemianopia in association with increased seizure frequency and disease progression, which did not recover and she ultimately developed cortical blindness.

Other aetiologies of temporary visual field defects were considered, but given that the visual field defects lasted months on each occasion with no associated diffusion restriction, they were not due to strokes or transient ischaemic attacks. Posterior reversible encephalopathy syndrome (PRES) could cause temporary visual field defects, but the pattern of abnormalities on MRI would be atypical given the prominent cortical without white matter involvement and the elevated lactate on MRS, which were suggestive of MELAS despite the normal serum lactate and muscle biopsy. Identification of a mitochondrial mutation confirmed the diagnosis of MELAS.

The three previously reported cases of alternate-sided homonymous hemianopia occurred as the initial presentation of MELAS,^{4–6} either in isolation⁴ or in combination with seizures,^{5,6} and did not include the entire disease course. An interesting feature of our case involves documentation of the temporal evolution of visual field defects and corresponding MRI lesions throughout the course of disease. Although Su et al.⁴ described a case with two episodes of right homonymous hemianopia followed by a left homonymous hemianopia, the initial two episodes were only 1 month apart, without resolution between episodes, and without imaging at the time of the first episode. It is possible these two described episodes may have represented a single stroke-like episode. The current case importantly documents resolution of visual field defects between each episode and the development of new MRI lesions during each episode.

Visual involvement is common in MELAS, as there is a propensity for occipital involvement, which may be due to the susceptibility of the occipital cortex to mitochondrial dysfunction.⁷ Lesions on MRI brain often mimic ischaemia, but do not typically respect vascular territories and

tend to have cortical involvement with relative sparing of white matter, as observed in our case.

Our patient is unique, as she had the rare T10191C mutation in the ND3 gene, which was first described in 2001⁸ but has not been reported to cause alternate-sided homonymous hemianopia. This mutation has also been described in Leigh syndrome, but the current case presentation is more consistent with MELAS. The most common mitochondrial mutation in MELAS is the A3243G mutation,⁹ which was the causative mutation in two of the previously reported cases of this rare phenomenon.^{5,6}

Unfortunately, there is no definitive evidence for treatment of MELAS. Despite antiepileptic therapy and treatment with potentially beneficial supplements, neurologic deficits continued to accumulate, culminating in terminal refractory status epilepticus and cortical blindness in this aggressive case of MELAS, with death 8.5 years from onset.

Recurrent alternate-sided homonymous hemianopia in MELAS with documented visual field and MRI findings with resolution between each episode has not been previously reported to our knowledge. It is important to recognise that stroke-like episodes in MELAS may result in recurrent and/or alternate-sided homonymous hemianopia.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

References

- [1] Hirano M, Ricci E, Koenigsberger MR, Defendini R, Pavlakis SG, DeVivo DC, DiMauro S, Rowland LP. MELAS: an original case and clinical criteria for diagnosis. *Neuromuscul Disord* 1992;2:125–135.
- [2] Yatsuga S, Povalko N, Nishioka J, Katayama K, Kakimoto T, Matsuiishi T, Kakuma T, Koga Y, Matsuoka T, for the MELAS Study Group in Japan. MELAS: a nationwide prospective cohort study of 96 patients in Japan. *Biochem Biophys Acta* 2012;1820:619–624.
- [3] El-Hattab AW, Adesina AM, Jones J, Scaglia F. MELAS syndrome: clinical manifestations, pathogenesis, and treatment options. *Mol Genet Metab* 2015;116:4–12.

- [4] Su WY, Kao LY, Chen ST. Alternate-sided homonymous hemianopia as the solitary presentation of mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes syndrome. *Chang Gung Med J* 2003;26:199–203.
- [5] Bi WL, Baehring JM, Lesser RL. Evolution of brain imaging abnormalities in mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes. *J Neuroophthalmol* 2006;26:251–256.
- [6] Aaron S, Anupriya A, Sunithi M, Mathew V, Maya T, Goyal MK, Alexander M. MELAS: recurrent reversible hemianopia. *Neurol India* 2010;58:791–793.
- [7] Koo B, Becker LE, Chuang S, Merante F, Robinson BH, MacGregor D, Tei I, Ho VB, McGreal DA, Wherrett JR, Logan WJ. Mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes (MELAS): clinical, radiological, pathological and genetic observations. *Ann Neurol* 1993;34:25–32.
- [8] Taylor RW, Singh-Kler R, Hayes CM, Smith PE, Turnbull DM. Progressive mitochondrial disease resulting from a novel missense mutation in the mitochondrial DNA ND3 gene. *Ann Neurol* 2001;50:104–107.
- [9] Zhao D, Hong D, Zhang W, Yao S, Qi X, Lv H, Zheng R, Feng L, Huang Y, Yuan Y, Wang Z. Mutations in mitochondrially encoded complex I enzyme as the second common cause in a cohort of Chinese patients with mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes. *J Hum Genet* 2011;56:759–764.