Radiology Case Reports 19 (2024) 6347–6353

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Moyamoya syndrome secondary to MELAS syndrome in a child: A case report and literature revue ☆

Fatima Zohra Benbrahim, MD, Siham El Haddad, PhD, Nazik Allali, PhD, Latifa Chat, PhD*

Department of Radiology, Children Hospital of Rabat, Ibn Sina University Hospital, Mohammed V University, Rabat, Morocco

ARTICLE INFO

Article history:
Received 2 August 2024
Revised 27 August 2024
Accepted 29 August 2024

Keywords:
Recurrent strokes
MELAS
Moyamoya
Magnetic resonance imaging

ABSTRACT

Mitochondrial myopathy with lactic acidosis and stroke-like episodes is a rare mitochondrial disorder, most often revealed by symptoms and signs that typically include mitochondrial myopathy, encephalopathy with stroke-like episodes, seizures and/or dementia, and lactic acidosis. Imaging findings, although diverse, usually present characteristic features that help differentiate these disorders from vascular syndromes. We present a case of a 2-year and 4-month-old girl with recurrent ischemic strokes associated with nonterritorial cortico-subcortical foci on brain imaging, along with stenosis of the terminal portion of the internal carotid arteries associated with a neovascular network. An elevated serum lactate level was found in the biological assessment. This article provides an overview of the various neuroimaging modalities available and the advent of new imaging techniques used in these disorders. It highlights the importance of considering a diagnosis of hereditary mitochondrial disorder in the presence of recurrent atypical stroke-like episodes when neuroimaging is inconsistent with ischemic infarction and reports an exceptional association with Moyamoya syndrome.

Introduction

Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) is a maternally inherited mitochondrial metabolic disorder caused by diffuse and multisystemic mutations in mitochondrial DNA (mtDNA) [1]. This mitochondrial deficiency is involved in the pathogenesis of Moyamoya syndrome (MMS). Mitochondrial dysfunction can lead to defects in the respiratory chain, rendering the mi-

Abbreviations: MRI, Magnetic Resonance Imaging; MRS, Magnetic Resonance Spectroscopy; SLEs, Stroke-like episodes; MELAS, Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes; AIS, Acute Ischemic Stroke; TOF, Time-of-Flight; NAA, N-acetylaspartate; ECFCs, Endothelial Colony-Forming Cells; MMS, Moyamoya syndrome; ADC, Apparent Diffusion Coefficient.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: fzohrabenbrahim93@gmail.com (F.Z. Benbrahim).

https://doi.org/10.1016/j.radcr.2024.08.159

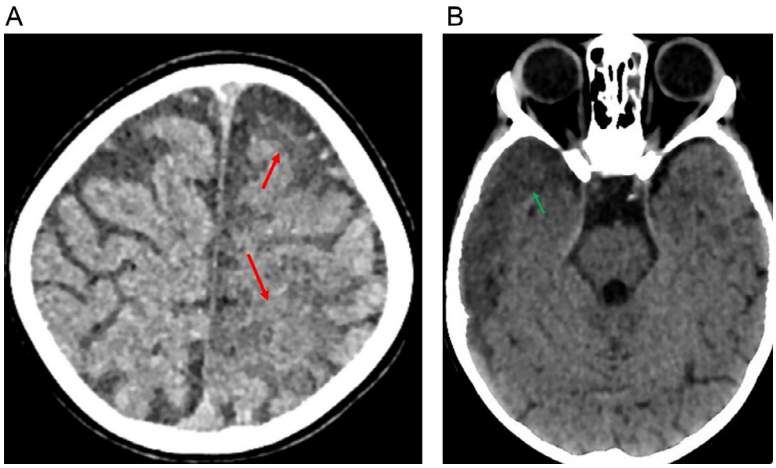

Fig. 1 – (A) Noncontrast axial brain CT scan showing cortico-subcortical hypodensities in the left fronto-parietal regions that do not correspond to any vascular territory. (B) Noncontrast axial brain CT scan in axial cuts, performed after 3 weeks, showing a right cortico-subcortical temporal hypodensity not observed in the previous exam that do not correspond to any vascular territory (green arrow).

tochondria unable to generate sufficient energy to meet the needs of various organs [2], resulting in mitochondrial proliferation within smooth muscle cells and endothelial cells of small blood vessels, causing angiopathy and impaired organ perfusion. MMS is a rare chronic intracranial arteriopathy characterized by stenotic-occlusive lesions at the bifurcation of the terminal internal carotid arteries, with the presence of a neovascular network nearby, creating a "puff of smoke" appearance, which is where the Japanese name Moyamoya comes from.

Stroke-like episodes (SLEs) are the most distinctive manifestations of MELAS [3], and they are very similar to those of acute ischemic stroke. Since SLEs resemble acute cerebral infarction, clinical diagnosis remains difficult and extremely complex in acute situations. Neuroimaging complements the clinical examination to assess the location of various lesions, particularly MRI and magnetic resonance spectroscopy (MRS), which are not commonly performed at an early stage in these patients. Lesions in MELAS are generally located in the temporal, parietal, or occipital lobes. These lesions do not follow any vascular territory, unlike the distribution of ischemic lesions [4,5].

In clinical practice, many patients presenting with a first SLE are misdiagnosed as having acute ischemic stroke (AIS), or less commonly, as viral or autoimmune encephalitis, or central nervous system vasculitis.

We report here a rare case of a 2-year and 4-month-old girl presenting with recurrent episodes of hemiplegia, in whom neuroimaging led to the diagnosis of MELAS associated with bilateral MMS.

Case presentation

A 2-year and 4-month-old girl, born to nonconsanguineous parents, who had a previous history of a brief episode of sudden onset right-sided hemiplegia that spontaneously resolved within 30 minutes. A week later, the girl experienced a second episode of hemiplegia on the same side that did not resolve associated with vomiting, prompting her emergency consultation at our department.

At admission, the girl was conscious, afebrile, hemodynamically, and respiratorily stable with stunted growth (-2SD). Neurological examination revealed right hemiplegia with inability to walk and brisk osteotendinous reflexes.

An emergency brain CT scan (Fig. 1A) showed a cortico-subcortical hypodense area in the left fronto-parietal region, not corresponding to any vascular system.

Subsequently, a brain MRI (Fig. 2) was performed, confirming the presence of the cortico-subcortical hypointense area in the left fronto-parietal region, restricted diffusion associated with ischemic lesions in the periventricular subcortical white matter. Contrast-enhanced sequences and Time-of-Flight (TOF) MR angiography (Fig. 3) revealed multiple tight stenoses at the terminations of the internal carotid arteries and proximal segments of the anterior and middle cerebral arteries bilaterally, more pronounced on the right side, replaced by an abnormal nearby network creating a "puff of smoke" appearance. MRI spectroscopy (Fig. 4) showed decreased NAA with a large lactate peak.

An electroencephalogram (EEG) was performed. No abnormalities or epileptiform activity were detected.

Cerebrospinal fluid analysis revealed a protein level of 0.57 g/L, a normal glucose level, an increased lactate level at 4.78 mmol/L (normal range between 1.2 and 2.1), with no cellular reaction. Laboratory tests were normal, except for elevated serum lactate levels measured at 3.35 mmol/L (normal range 1 to 1.78 mmol/L). There was no inflammatory syndrome or presence of antinuclear antibodies.

During hospitalization, clinical progression included incomplete recovery of the right lower limb and development of left hemiparesis. A follow-up brain CT scan (Fig. 1B) showed

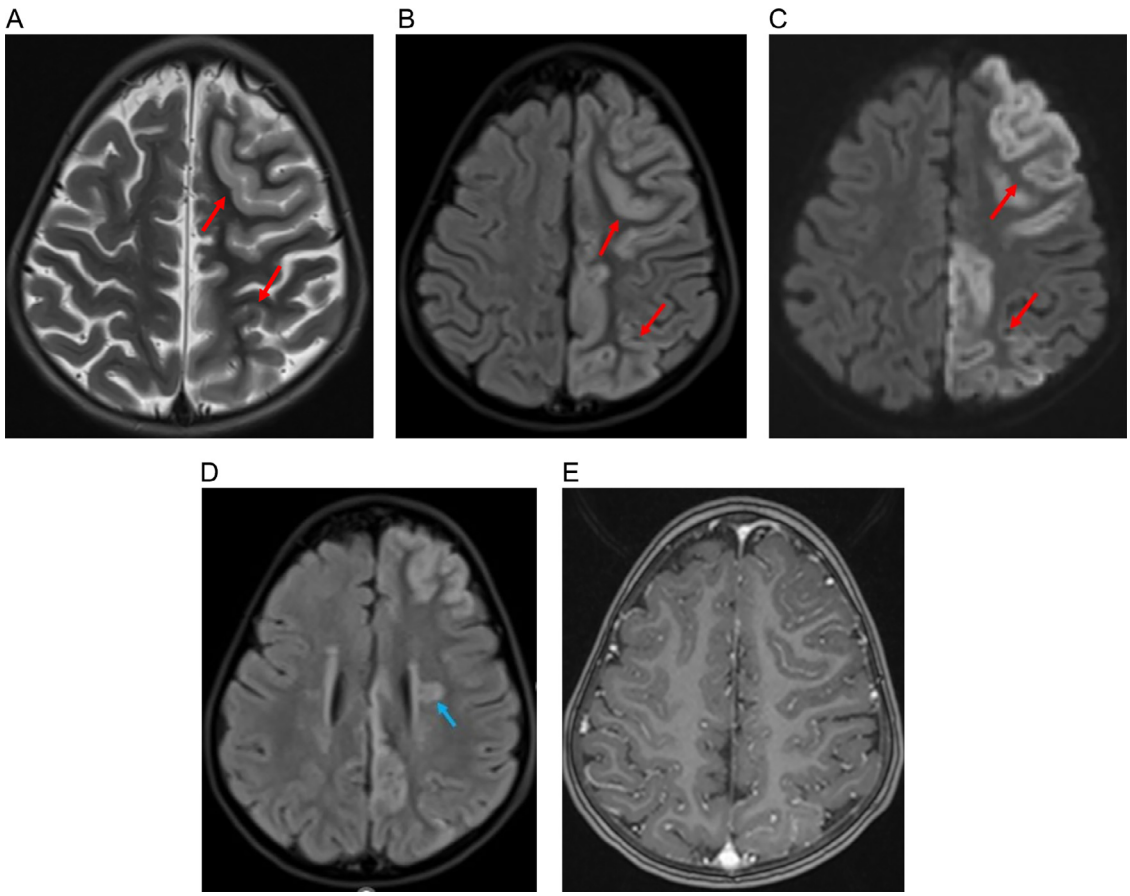

Fig. 2 – Axial MRI images in T2 (A), FLAIR (B and C), diffusion (D), and postgadolinium contrast (E) sequences reveal signal abnormalities in the left fronto-parietal cortico-subcortical regions (red arrows) and the left periventricular white matter (blue arrow). These abnormalities appear hyperintense on T2 and FLAIR sequences, exhibit restricted diffusion, and do not enhance after Gadolinium injection.

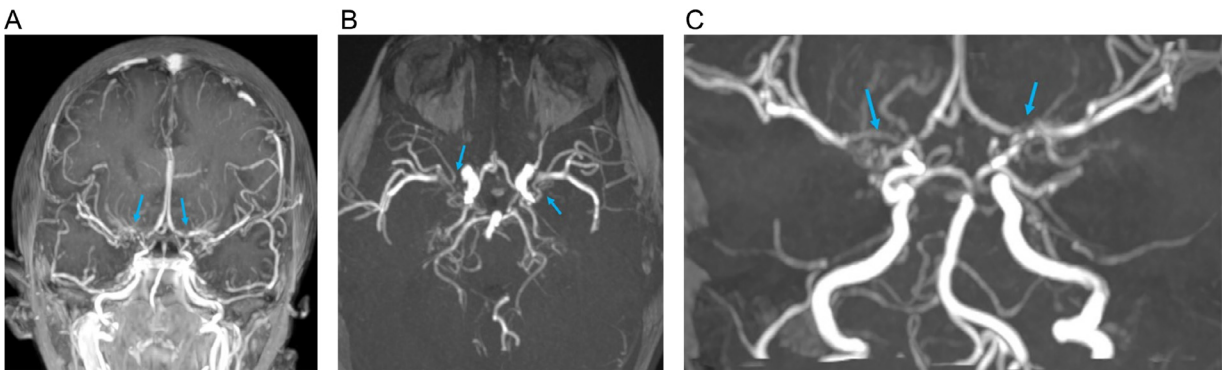

Fig. 3 – Brain MRI in T1 contrast-enhanced coronal sequence (Fig. A) and TOF sequences in axial (Fig. B) and coronal (Fig. C) views show severe stenosis of the terminal portions of the carotid arteries and the proximal portions of the middle cerebral arteries bilaterally, more pronounced on the right with hypertrophy of the adjacent perforating arteries creating a 'smoke-like' appearance (blue arrows).

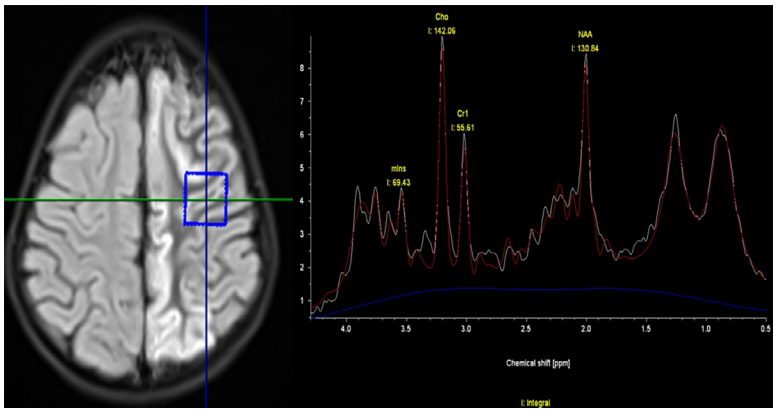

Fig. 4 – MRI spectroscopy showing a decrease in NAA with a large lactate peak (white arrow).

a hypodense cortico-subcortical lesion in the right temporal and frontal region.

The diagnosis of MELAS was suspected due to the clinical presentation dominated by stroke-like episodes, the elevated lactate levels in the cerebrospinal fluid and serum, as well as imaging findings and clinical evolution. A genetic test was ordered, which was positive, in the form of the m.3243A>G mutation. The diagnosis of MELAS syndrome associated with MMS was confirmed.

The patient was started on symptomatic treatment with intravenous L-arginine. Over a follow-up period of 6 months, she showed progressive motor recovery without the occurrence of additional episodes.

Discussion

MELAS, or mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes, is a rare genetic disorder characterized by a respiratory chain dysfunction that affects the nervous system and muscles. It is caused by a mutation in mitochondrial DNA (mtDNA). The most common mutation associated with MELAS is the m.3243A>G mutation, found in approximately 80% of cases [6]. Mitochondrial mutations are passed down through generations exclusively from affected females. The prevalence of this mutation varies from 0.95 to 236 per 100,000 individuals. It is also known that the clinical spectrum associated with the m.3243A>G mutation is broad, involving varying degrees of deafness, maternally inherited diabetes, and progressive external ophthalmoplegia [7].

On an epidemiological level, MELAS affects both sexes equally, with onset typically occurring early, generally between 2 and 15 years of age. Approximately 75% of cases occur before the age of twenty; However, the disease can begin at any age [3,8]. Yatsuga et al. [9] found that MELAS in young individuals is associated with significantly higher mortality and a faster disease progression compared to adults.

In MELAS, energy deficiency can stimulate the proliferation of mitochondria in smooth muscle cells and small vascular endothelial cells. Similarly, various factors can lead to a lack of nitric oxide, which is necessary to maintain vascular smooth muscle relaxation function. These 2 processes can cause microvascular blood perfusion impairments, resulting in stroke-like episodes and other complications [8].

A comprehensive study by Choi et al. revealed that mitochondria in Endothelial Colony-Forming Cells (ECFCs) from patients with MMS were both functionally and morphologically impaired, exhibiting elevated levels of reactive oxygen species compared to control groups [10]. The study found that ECFCs are involved in pathological angiogenesis, highlighting a strong link between dysfunctional ECFCs and MMS [10]. Choi's findings of defective mitochondria in ECFCs among Moyamoya patients strongly suggest that MMS may be a mitochondrial disorder [10]. In light of this, we believe that mitochondrial dysfunction was indeed the underlying cause of MMS in our patient. However, further research is required to elucidate the association between the 2.

Moyamoya disease (MMD) is characterized by the progressive and bilateral occlusion of the internal carotid artery and its major branches, leading to the formation of arterial collateral vessels at the base of the brain. The underlying neuropathological changes in MELAS syndrome include spongiform degeneration, neuronal loss, glial proliferation, and demyelination [11,12]. However, there is only 1 documented case in the literature of MMS secondary to a mitochondrial disorder in a patient with trisomy 13q14 [13].

The clinical manifestations of MELAS syndrome are highly variable and can appear at any age, with earlier onset often linked to a more severe disease course [14]. Stroke-like episodes (SLEs) represent one of the cardinal symptoms, typically presenting as acute hemianopsia, hemiparesis, or cortical blindness. These episodes tend to recur and can result in significant long-term effects, such as neurodegeneration and cognitive decline [15]. SLEs are frequently accompanied by migraine-like headaches, vomiting, seizures—often in the form of status epilepticus—hearing loss, stunted growth, and neuropsychiatric issues that usually differ from typical ischemic conditions [16]. Migraines are strongly associated with hereditary stroke-related disorders, including MELAS, CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), and hereditary hemorrhagic telangiectasia [17]. Recognizing these clinical features during the initial assessment aids clinicians

in distinguishing pseudo-stroke symptoms from ischemic events. Additionally, complications such as cardiomyopathy, nephrotic syndrome, and diabetes may also occur [6,18].

Various imaging techniques have been developed to identify the characteristics and location of lesions associated with mitochondrial disorders. Computed tomography (CT), commonly used as an initial imaging method, regularly reveals bilateral calcifications in the basal ganglia and thalamus [19,20]. It can also detect cortical hypodensities, often located in the occipital or parietal lobes, which do not correspond to any vascular territory, thus distinguishing them from ischemic lesions [21].

Research on the neuroimaging features of SLEs has mainly utilized MRI and magnetic resonance spectroscopy (MRS) [22,23]. However, many patients with their first SLE are often initially misdiagnosed as having an acute ischemic stroke (AIS) [24,25], and MRI is infrequently performed in acute situations. Despite this, MRI remains the gold standard for assessing metabolic disorders due to its superior spatial resolution and capacity to provide detailed characterization through various imaging sequences. On T2-weighted images, lesions appear hyperintense with a tendency to affect the cerebral cortex and do not match any arterial territory. SLEs typically localize to the cortical areas, most commonly involving the occipital and parietal lobes, although deep gray matter structures such as the thalamus can also be affected [26]. Some studies have reported bilateral and symmetric abnormalities in deep gray matter and the brainstem [22], as well as diffuse white matter changes with associated cerebral and cerebellar atrophy [27].

Diffusion-weighted imaging, while commonly used for ischemic conditions, has also proven valuable for diagnosing nonischemic lesions, including mitochondrial disorders that may mimic cerebral ischemia [28]. During the acute phase, diffusion-weighted imaging typically shows hyperintensity. However, several studies have explored the apparent diffusion coefficient (ADC) to assess vasogenic or cytotoxic edema in MELAS patients [29]. Yoneda et al. [30] found that ADC maps might display similar or reduced values compared to diffusion imaging, indicating vasogenic edema as a probable mechanism in MELAS. Conversely, other studies have reported decreased ADC signals, suggesting cytotoxic edema, particularly during the acute phase of SLEs [29,31]. The literature is still divided on this issue, and further research is needed to clarify these findings.

Magnetic Resonance Spectroscopy (MRS) is a non-invasive method used to evaluate chemical information of brain tissue in various metabolic disorders. A decrease in N-acetylaspartate (NAA) on MRS accompanied by an increase in lactate peak has proven useful for diagnosing patients with MELAS [32,33]. However, these changes are not specific and can be seen in other metabolic disorders. The lactate peaks observed on MRS reflect anaerobic metabolism and tend to vary depending on the different phases of the disease.

Cerebral angiography was infrequently used to evaluate vessel permeability because large vessels were seen as the main targets of mitochondrial defects in MELAS patients. However, MR angiography can identify dilation or stenosis of large cerebral vessels during both acute and chronic stages of the disease. According to Gramegna et al. [34], MR angiography revealed that the prevalence of stenosis and dilation of large cerebral vessels was 40% and 19%, respectively, with the middle cerebral artery being the most commonly affected. Notably, 88% of the dilations were linked to stroke-like episodes (SLEs), while only a few rare cases of stenosis were associated with SLEs. Furthermore, MR angiography has occasionally detected vasodilation up to 35 months before the onset of SLEs [35,36], underscoring its potential in predicting SLEs in carefully selected patients.

MRI and MR angiography (MRA) are currently the preferred imaging modalities for detecting MMS and can suffice for diagnosis. Ischemic lesions appear as T1 hypointensity, T2 hyperintensity, and FLAIR hyperintensity, with variable diffusion characteristics depending on their age. Hemorrhagic lesions exhibit variable T1 and T2 signals based on their age and constant T2* hypointensity [37]. Leptomeningeal enhancement or the "ivy sign" is typically observed on FLAIR and postcontrast T1 sequences with gadolinium injection.

Three-dimensional time-of-flight MR angiography (3D TOF) is the cornerstone examination with excellent spatial resolution for detecting stenotic lesions at the terminal portion of the internal carotid artery and/or proximal portion of the anterior cerebral artery and/or middle cerebral artery. It also visualizes abnormal vascular networks adjacent to stenoocclusive lesions, creating the characteristic "puff of smoke" appearance known as Moyamoya in Japanese, and demonstrates the bilateral nature of these anomalies [38]. The 3D TOF sequence is also valuable for disease monitoring, especially after surgical treatment, to assess the patency of anastomoses and neovascularization.

Both perfusion-weighted imaging (PWI) and arterial spin labeling (ASL) provide detailed hemodynamic information about the brain and assess cerebral perfusion. Typically, hyperperfusion is observed during the acute phase, while hypoperfusion is seen in the chronic phase of stroke-like episodes (SLEs) [39].

Diagnosing MELAS involves a combination of clinical features, elevated serum or cerebrospinal fluid lactate levels, and brain imaging. When MELAS is suspected clinically, genetic analysis for the m.3243A>G mutation in blood or other tissue samples (such as skin, urine, or muscle biopsies) should confirm the diagnosis [6,18].

Currently, no curative treatment exists for MELAS, and management is primarily symptomatic. This includes antiplatelet therapy for ischemic stroke episodes and anticonvulsants for seizures related to MELAS. A Cochrane review from 2012 found no evidence supporting specific interventions for mitochondrial diseases. However, some treatment centers use L-arginine for managing encephalopathy crises [6,18,40].

Conclusion

The MELAS syndrome is a rare condition characterized by stroke-like episodes, often misdiagnosed as a stroke. Its association with MMS is a rare event. Here, we report a case of MMS secondary to MELAS syndrome in a 2-year and 4-month-

old girl, emphasizing the role of neuroimaging in diagnosing MELAS syndrome.

Author contribution

All the authors contributed to study concept, data analysis and writing the paper.

Patient consent

Written informed consent for the publication of this case report was obtained from the patient.

REFERENCES

[1] Pavlakis SG, Phillips PC, DiMauro S, De Vivo DC, Rowland LP. Mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes: a distinctive clinical syndrome. Ann Neurol 1984;16(4):481–8. doi:10.1002/ana.410160409.

[2] Dimauro S, Houston H. Mitochondrial encephalomyopathies: what next ? J lnher Metab Dis 1996;19:489–503.

[3] Wang YX, Le WD. Progress in diagnosing mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes. Chin Med J 2015;128:1820–5. doi:10.4103/0366-6999.1593605.

[4] ItoH MK, Kagami S. Neuroimaging of stroke-like episodes in MELAS. Brain Dev 2011;33(4):283–8. doi:10.1016/j.braindev.2010.06.010.10.

[5] Haas R, Dietrich R. Neuroimaging of mitochondrial disorders. Mitochondrion 2004;4(5–6):471–90. doi:10.1016/j.mito.2004.07.008.11.

[6] Aurangzeb S, Vale T, Tofaris G, Poulton J, Turner MR. Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) in the older adult. Pract Neurol 2014;14:432–6. doi:10.1136/practneurol-2014-000853.

[7] Nesbitt V, Pitceathly RD, Turnbull DM, Taylor RW, Sweeney MG, Mudanohwo EE, et al. The UK MRC Mitochondrial Disease Patient Cohort Study: clinical phenotypes associated with the m.3243A>G mutation–implications for diagnosis and management. J Neurol Neurosurg Psychiatry 2013;84:936–8. doi:10.1136/jnnp-2012-303528.

[8] El-Hattab A, Adesina A, Jones J, Scaglia F. MELAS syndrome: clinical manifestations, pathogenesis, treatment options. Mol Genet Metab 2015;116:4–12. doi:10.1016/j.ymgme.2015.06.0042.

[9] Yatsuga S, Povalko N, Nishioka J, Katayama K, Kakimoto N, Matsuishi T, et al. MELAS: a nationwide prospective cohort study of 96 patients in Japan. Biochim Biophys Acta 2012;1820(5):619–24. doi:10.1016/j.bbagen.2011.03.015.

[10] Choi JW, Son SM, Mook-Jung I, Moon YJ, Lee JY, Wang KC, et al. Mitochondrial abnormalities related to the dysfunction of circulating endothelial colony-forming cells in moyamoya disease. J Neurosurg 2018;129(5):1151–9.

[11] Alston CL, Rocha MC, Lax NZ, Turnbull DM, Taylor RW. The genetics and pathology of mitochondrial disease. J Pathol 2017;241:236–50. doi:10.1002/path.4809.

[12] Chen H, Hu Q, Raza HK, Chansysouphanthong T, Singh S, Rai P, et al. An analysis of the clinical and imaging features of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS). Somatosens Mot Res 2020;37:45–9. doi:10.1080/08990220.2020.1720636.

[13] Abdul Rab S, Arabi TZ, Raheel HM, Sabbah BN, Zain AlAbidien NH, Alsemari A. Moyamoya syndrome secondary to mitochondrial disease in a patient with partial trisomy 13q14 and 13q31: a novel case report and literature review. Heliyon 2023;9(2):e13466. doi:10.1016/j.heliyon.2023.e13466.

[14] Ahmed ST, Craven L, Russell OM, Turnbull DM, Vincent AE. Diagnosis and treatment of mitochondrial myopathies. Neurotherapeutics 2018;15:943–53. doi:10.1007/s13311-018-00674-4.

[15] Pizzamiglio C, Bugiardini E, Macken WL, Woodward CE, Hanna MG, Pitceathly RDS. Mitochondrial strokes: diagnostic challenges and chameleons. Genes 2021;12:1643. doi:10.3390/genes12101643.

[16] Johnson EC, West TW, Ko NU, Strober JB. A 41-year-old man with new headache and altered mental status. Neurohospitalist 2011;1(1):48–54. doi:10.1177/1941875210385948.

[17] Jamieson DG, Cheng NT, Skliut M. Headache and acute stroke. Curr Pain Headache Rep 2014;18(9):444. doi:10.1007/s11916-014-0444-1.

[18] MELAS Syndrome - NORD (National Organization for Rare Disorders). (2011). Accessed September 1, 2020 https://rarediseases.org/rare-diseases/melas-syndrome.

[19] Kim IO, Kim JH, Kim WS, Hwang YS, Yeon KM, Han MC. Mitochondrial myopathy-encephalopathy-lactic acidosis-and strokelike episodes (MELAS) syndrome: CT and MR findings in seven children. AJR Am J Roentgenol 1996;166(3):641–5. doi:10.2214/ajr.166.3.8623642.

[20] Chung SH, Chen SC, Chen WJ, Lee CC. Symmetric basal ganglia calcification in a 9-year-old child with MELAS. Neurology 2005;65(9):E19. doi:10.1212/01.wnl.0000184112.34211.d1.

[21] Hirano M, Pavlakis SG. Mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes (MELAS): current concepts. J Child Neurol 1994;9(1):4–13.

[22] Castillo M, Kwock L, Green C. MELAS syndrome: imaging and proton MR spectroscopic findings. AJNR Am J Neuroradiol 1995;16(2):233–9.

[23] Bhatia KD, Krishnan P, Kortman H, Klostranec J, Krings T. Acute cortical lesions in MELAS syndrome: anatomic distribution, symmetry, and evolution. AJNR Am J Neuroradiol 2020;41(1):167–73. doi:10.3174/ajnr.A6325.

[24] Sinnecker T, Andelova M, Mayr M, Rüegg S, Sinnreich M, Hench J, et al. Diagnosis of adult-onset MELAS syndrome in a 63-year-old patient with suspected recurrent strokes: a case report. BMC Neurol 2019;19(1):91. doi:10.1186/s12883-019-1306-6.

[25] Jameel I, Sreh A, Das P. Recurrent stroke events secondary to a late presentation of mitochondrial encephalomyopathy with lactic acidosis and stroke-like symptoms (MELAS) syndrome. Cureus 2020;12(12):e11839. doi:10.7759/cureus.11839.

[26] Goodfellow JA, Dani K, Stewart W, Santosh C, McLean J, Mulhern S, et al. Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes: an important cause of stroke in young people. Postgrad Med J 2012;88(1040):326–34. doi:10.1136/postgradmedj2011-130326.

[27] Moroni I, Bugiani M, Bizzi A, Castelli G, Lamantea E, Uziel G. Cerebral white matter involvement in children with mitochondrial encephalopathies. Neuropediatrics 2002;33(2):79–85. doi:10.1055/s2002-32372.

[28] Pauli W, Zarzycki A, Krzysztalowski A, Walecka A. CT and MRI imaging of the brain in MELAS syndrome. Pol J Radiol 2013;78(3):61–5. doi:10.12659/pjr.884010.

[29] Wang XY, Noguchi K, Takashima S, Hayashi N, Ogawa S, Seto H. Serial diffusion-weighted imaging in a patient with

MELAS and presumed cytotoxic oedema. Neuroradiology 2003;45(9):640–3. doi:10.1007/s00234-003-1029-6.
[30] Yoneda M, Maeda M, Kimura H, Fujii A, Katayama K, Kuriyama M. Vasogenic edema on MELAS: a serial study with diffusion-weighted MR imaging. Neurology 1999;53(9):2182–4.
[31] Jian-Ren L. Precipitation of stroke-like event by chickenpox in a child with MELAS syndrome. Neurol India 2005;53(3):323–5.
[32] Chinnery PF. Mitochondrial disorders overview. GeneReviews(R). Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, editors. Seattle (WA): University of Washington; 1993.
[33] Saneto RP, Friedman SD, Shaw DW. Neuroimaging of mitochondrial disease. Mitochondrion 2008;8(5–6):396–413. doi:10.1016/j.mito.2008.05.003.
[34] Gramegna LL, Cortesi I, Mitolo M, Evangelisti S, Lia T, Cirillo L, et al. Major cerebral vessels involvement in patients with MELAS syndrome: worth a scan ? A systematic review. J Neuroradiol 2021;48:359–66. doi:10.1016/j.neurad.2021.02.002.
[35] Ikawa M, Yoneda M, Muramatsu T, Matsunaga A, Tsujikawa T, Yamamoto T, et al. Detection of preclinically latent hyperperfusion due to strokelike episodes by arterial spin-labeling perfusion MRI in MELAS patients. Mitochondrion 2013;13:676–80. doi:10.1016/j.mito.2013.09.007.
[36] Li Y, Xu W, Sun C, Lin J, Qu J, Cao J, et al. Reversible dilation of cerebral macrovascular changes in MELAS episodes. Clin Neuroradiol 2019;29:321–9. doi:10.1007/s00062-018-0662-8.
[37] Kikuta KI, Takagi Y, Nozaki K, Hanakawa T, Okada T, Mikuni N, et al. Asymptomatic microbleeds in Moya-Moya disease: T2*- weighted gradient-echo magnetic resonance imaging study. J Neurosurg 2005;102(3):470–5.
[38] Hashimoto N, Tominaga T, Miyamoto S, Nagata I, Houkin K, Suzuki K, et al. Guidelines for diagnosis and treatment of Moya-Moya disease (spontaneous occlusion of the circle of Willis). Neurol Med Chir (Tokyo) 2012;52(5):245–66.
[39] Kim JH, Lim MK, Jeon TY, Rha JH, Eo H, Yoo S-Y, 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. doi:10.3348/kjr.2011.12.1.15.
[40] Malhotra K, Liebeskind DS. Imaging of MELAS. Curr Pain Headache Rep 2016;20:54. doi:10.1007/s11916-016-0583-7.