Unilateral cortical thickening and hyper-intensity due to mitochondrial encephalopathy, lactic acidosis, and stroke like episodes (MELAS)

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ABSTRACT

Patients with mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) present with recurrent and partially reversible neurological deficits. Lesions of MELAS classically cause a signal change in both the grey and white matter, predominantly in the occipital and parietal lobes. These lesions mimic infarction. Here, we reported a case of MELAS with rare neuroimaging finding of hemispheric cortical thickening on T2/FLAIR images with intracortical nodular gadolinium enhancement; then we discussed the clinical and radiological differential diagnoses of it.

Keywords:

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CASE REPORT

We have investigated the case of a 20-year-old man who presented with acute onset of progressive headache and right hemiparesis that occurred in the evening when he was doing his usual daily activities. The symptoms progressed over the first three days when poor verbal expression forced the family to seek medical attention. His past history included an episode of transient aphasia for one day in the last year and one attack of fever, headache and confusion that was empirically treated with intravenous Acyclovir, not confirmed by HSV-PCR testing.

Neurological examination initially showed mutism and writing and reading impairment. He was alert but unable to comprehend complex instructions. Cranial nerves except mild right peripheral 7th nerve palsy were intact. There was power of grade 3 of 5 on right side (distal = proximal and upper= lower) along with right hyper-reflexia and extensor plantar response. Otherwise, his examination findings were normal except mild neck stiffness. After three days, one attack of generalized tonic-clonicseizure occurred.

Laboratory evaluation revealed an ESR level of 22and creatine phosphokinasevalue of 1750 U/L (Nl value of up to 195 U/L).

The cerebrospinal fluid (CSF) analysis was normal. No oligoclonal band was detected and IgG index of the CSF was in its normal range.HSV-PCR and TB-PCR returned negative.

Noncontrast CT scan revealed bilaterally symmetric hyperattenuating areas in the caudate and lentiform nuclei, corticomedullary junction and thalami suggestive for calcification, in addition to mild gyral effacement in the left hemisphere (Figure 1). The patient was then examined with 1.5-T magnetic resonance (MR) system that showed global differences in cortical thickening and signal intensity between the two hemispheres (left cortical thickening) (Figure 2). Gadolinium-enhanced T1-weighted image showed left intracortical nodular enhancing lesions (Figure 3). MR-Venography and MR-Angiography were unremarkable.

MELAS syndrome was suspected and blood was

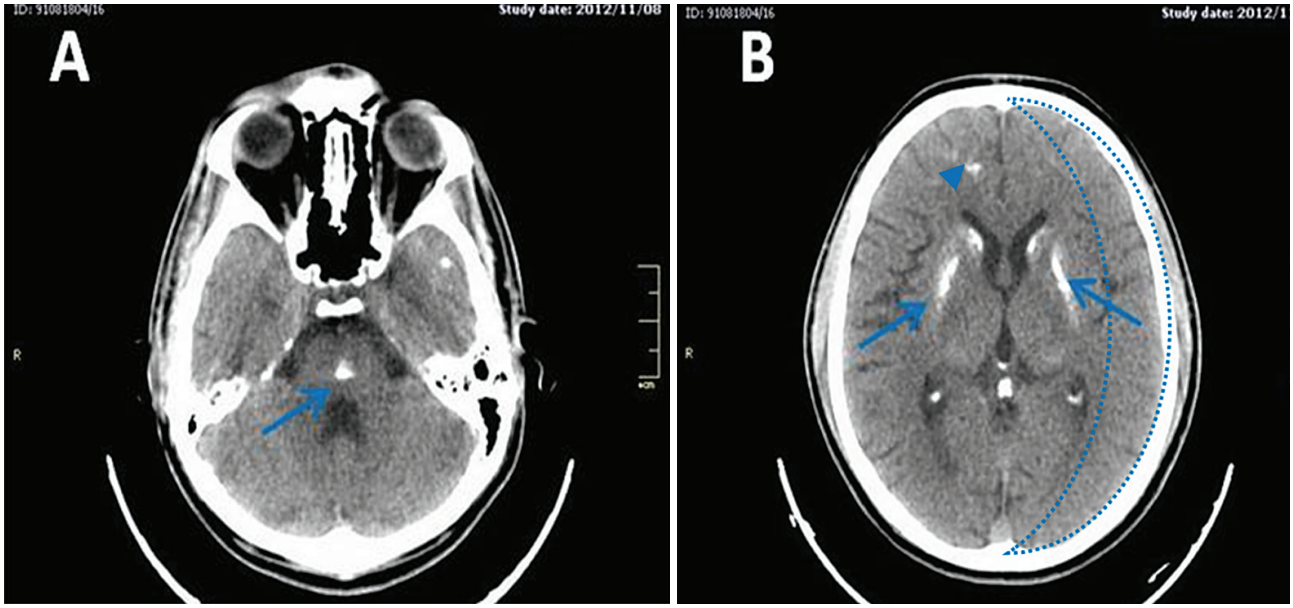

Figure 1. Axial noncontrast CT-scan of a 20 year-old man with MELAS syndrome demonstrates areas of calcification in the Pons (A), bilaterally symmetric calcification in the caudate and lentiform nuclei (arrows), corticomedullary junction (arrow head) and thalami in addition to mild gyral effacement in left side (en-dashes) (B).

drawn to measure lactate levels. Two-times elevated blood lactate levels were detected in ictusand inter-ictus state 62 and 22 respectively(Reference Interval: 4.5-19.8 mg/dL).

L-Carnitine and coenzyme Q10 were advised as a supplement. Levetiracetam was given for control of seizure. Hemiparesis improved gradually over the following two weeks. After a one year follow-up, the patient's condition improved and his speech became fluent with normal comprehension and repetition; However, Serial 7 subtraction test and delayed recall remained somewhat impaired (MMSE=26/30).

DISCUSSION

Mitochondrial encephalopathy, lactic-acidosis and stroke-like episodes (MELAS) is a type of mitochondrial disorder with heterogenous clinical and radiological findings (Table 1, 2).Our MR finding of "Hemispheric asymmetries in cortical thickening and heperintensity" with normal white matter on T2/FLAIR images and "intracortical nodular enhancement" of lesions after administration of Gadolinium is rarely reported in previous cases[1, 2].

In addition to the details mentioned in each item of the Tables 1 and 2, the main diagnostic cluesto rule out

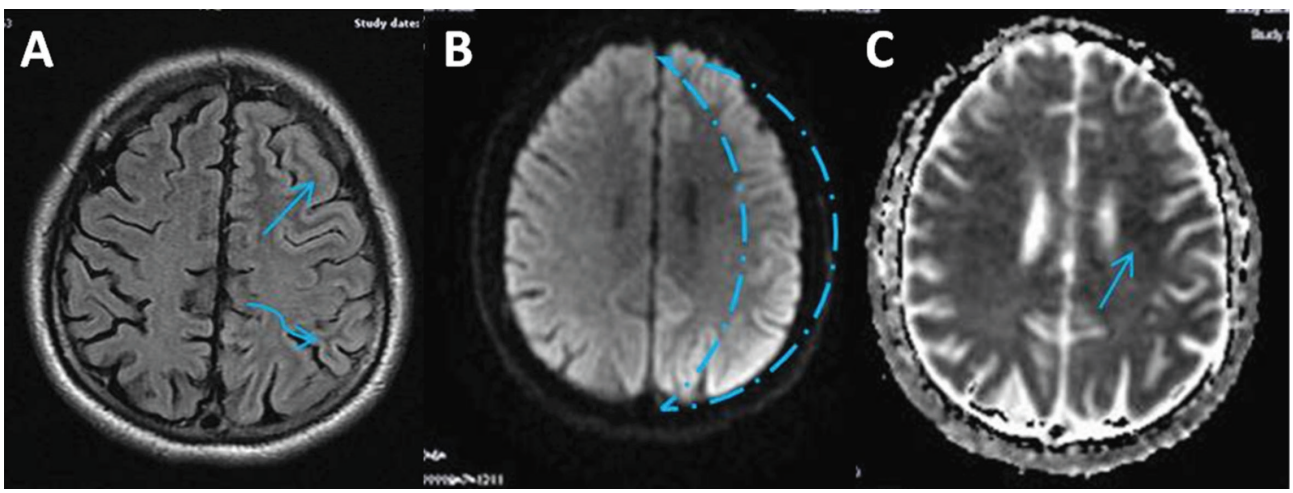

Figure 2. Axial FLAIR (A) and Diffusion-MR image (B,C) of the brain of a 20 year-old MELAS case show global left hemispheric cortical thickening and hyperintensity.

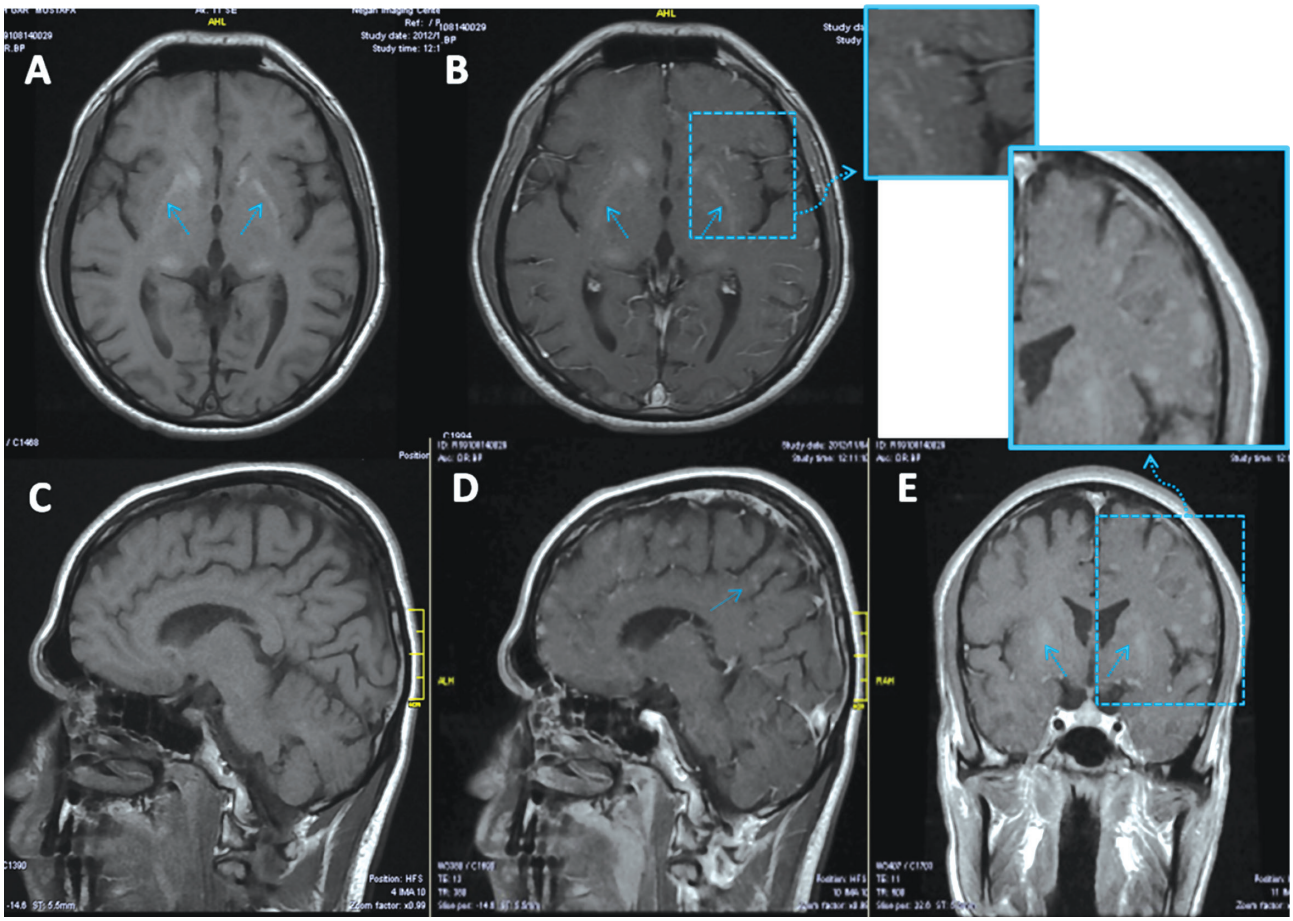

Figure 3. T1-weighted 1.5 T MR-images of the brain of a 20-year-old MELAS case (A:axial view, C:sagittal view), after Gadolinium-enhancement showed nodular cortical enhanced lesions (B:axial view, D:sagittal view and E:coronal view). Bilateral basal ganglia calcification is also shown on the images (arrows in A, B and E).

other diagnoses in our case were the recurrent episodes of transient focal neurologic deficits, important neuroimaging finding of bilateral basal ganglia calcification and high serum lactate levels.

Table 1. Neuroradiological differential diagnosis for MELAS.

Entity	MR image findings
MELAS	MR Signal change in both the grey and white matter, predominantly in the occipital and parietal lobes, which mimics infarction. However, distribution of the lesions does not follow vascular territories and often shows a slowly progressive spread with both decreased and increased ADC values in both the grey and white matter (with both vasogenic and cytotoxic edema), Findings of cortical thickening and hyperintensity (similar to our case) is rarely reported previously[1-3]
Acute Ischemic Stroke	MR finding of Hyperintense lesions with decreased ADC values (cytotoxic edema)
Chronic infarction	MR finding of Hyperintense lesions with normal or increased ADC values
Peritumoral lesions	Cerebral vasogenic edema (with increased ADC values), fluid-filled cysts and mass effect
Reversible posterior leukoencephalopathy syndrome (RPLS)	Cortical and subcortical bilateral occipitoparietal, frontal and sometimes brainstem lesions with occasional hemorrhage[4]
Hypoglycemia	Serial MR-imaging is necessary to detect new lesions. Immediate brain DW image mostly manifest hyperintense lesions over subcortical white matter. However, new hyperintense grey matter lesions might appear only later on DW image while previous subcortical lesions has disappeared[5]
Familial/sporadic hemiplegic migraine (FHM/SHM)	Variable ADC with normal T1W/T2W images[6,7]; Diffuse cortical thickening and lateralized cortical hyperintensity on T2W/FLAIR images, with no restricted diffusion is also reported[8]
The syndrome of transient headache and neurologic deficits with cerebrospinal fluid lymphocytosis (HaNDL)	Normal neuroimaging, recent studies suggest decreased ADC[9]

Table 2. Differential diagnosis of Post-Gadolinium enhanced T1-weighted MR findings of MELAS.

Entity	Diagnoses and description
Cortical gyral enhancement	• MELAS: cortical gyral enhancement at sites of infarction[10] • Vasodilatation after reperfusion of ischemic brain • Vasodilatation phase of migraine headache • Posterior reversible encephalopathy syndrom (PRES) • Vasodilatation with seizures • Meningitis and encephalitis (esp. Herpes virus encephalitis)
Cortical nodular enhancement	MELAS: cortical patchy enhancement of lesions[2]

MELAS is a rare disorder and here we reported an unusual MR finding for it. The study of DNA helps diagnosing many patients with MELAS. However, in cases where genetic testing cannot be easily performed, knowing such rare radiological features are useful.

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