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CT and MRI imaging of the brain in MELAS syndrome

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Summary

Background:	MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes) is a rare, multisystem disorder which belongs to a group of mitochondrial metabolic diseases. As other diseases in this group, it is inherited in the maternal line.
Case Report:	In this report, we discussed a case of a 10-year-old girl with clinical and radiological picture of MELAS syndrome. We would like to describe characteristic radiological features of MELAS syndrome in CT, MRI and MR spectroscopy of the brain and differential diagnosis.
Conclusions:	The rarity of this disorder and the complexity of its clinical presentation make MELAS patients among the most difficult to diagnose. Brain imaging studies require a wide differential diagnosis, primarily to distinguish between MELAS and ischemic stroke. Particularly helpful are the MRI and MR spectroscopy techniques.
Key words:	MELAS • encephalomyopathy • mitochondrial disease • differentiation • stroke-like lesions
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Background

MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes) is a multisystem disorder that belongs to a group of mitochondrial metabolic diseases. As other diseases in this group, it is inherited in the maternal line [1]. tRNA mutations lead to the absence or deficit of subunits of the respiratory chain protein complexes. This results in abnormal intracellular energy production, which in turn leads to impaired function of cells, or even to their death [2,3].

Onset of the disease usually manifests itself between 2 and 10 years of age and is preceded by normal psychomotor development [3].

Early symptoms of the disease are varied and nonspecific, which complicates diagnosis. It is very important to slow down the progression of the disease with the appropriate treatment.

The most characteristic clinical features of MELAS syndrome, also important from the point of view of diagnostic imaging, are the stroke-like episodes and corresponding CT or MR changes [4–6].

With their analysis, the radiologists are able to effectively guide the clinician to a correct diagnosis.

Case Report

A 10-year-old patient was admitted to hospital because of headaches, vomiting and elevated temperature. A study of cerebrospinal fluid samples excluded neuroinfection.

Due to persistent severe headaches, the patient underwent a CT examination of the brain.

CT scans showed areas of hypoattenuation in the left occipital and partially parietal lobe arousing the suspicion of ischemic changes (Figure 1A and 1B). In addition, there were bilateral hyperdense areas covering basal ganglia (Figure 2A and 2B). Those changes were accompanied by mass effect in the form of compression of the body, occipital and frontal horn of the left lateral ventricle, with effacement of the sulci on the surface of the left cerebral hemisphere. CT images were not conclusive to differentiate between the ischemic stroke, metabolic disease or proliferative process.



Figure 1AB. CT scan revealed hypodense areas in the left occipital and parietal lobe. There is also mass effect with effacement of the sulci on the surface of left cerebral hemisphere.

Therefore, extended diagnostic tests were performed – brain MRI with contrast medium. The MRI showed thickening of the cortex and areas of abnormal, high signal on Flair, PD and T2 images with loss of cortico-subcortical differentiation (Figure 3A and 3B), and reduction of signal intensity in these areas on T1 images (Figure 3C), and a clearly restricted diffusion in hypodense areas on CT images (Figure 4A and 4B). On ADC maps, there was no significant reduction in cortical signal intensity, and the signal decrease could be noticed within the adjacent white matter (Figure 4C and 4D). There were areas of increased signal intensity (Flair, PD, and T2) bilaterally in globus pallidus and the posterior part of the left thalamus, without restricted diffusion (Figure 5).

Pathological contrast enhancement was not found.

Single-voxel MR spectroscopy was carried out as well. In the left hemisphere, it revealed significantly elevated lactate peaks with decreased NAA spectrum and decreased NAA/Cr ratio.

Choline/Cr ratio was normal.

The nature of the spectrum reflected the severity of metabolic disorders suggesting disturbed anaerobic processes.

The whole clinical picture, results of tests carried out during hospitalization, as well as information from history-taking (short stature, WPW syndrome, episodes of headache, delayed intellectual development, rapid fatigue), CT and MR images of the brain were all suggestive of MELAS syndrome.

In a molecular study, a typical for MELAS syndrome mutation m.3243 A>G in MTTL1 was found [2].

The discussed patient is now under control of the Clinic of Metabolic Diseases and under the following medication: coenzyme Q10 and L-arginine, which were proved to support the metabolism of cells affected by mitochondrial tRNA mutation in MELAS syndrome [3,7,8].

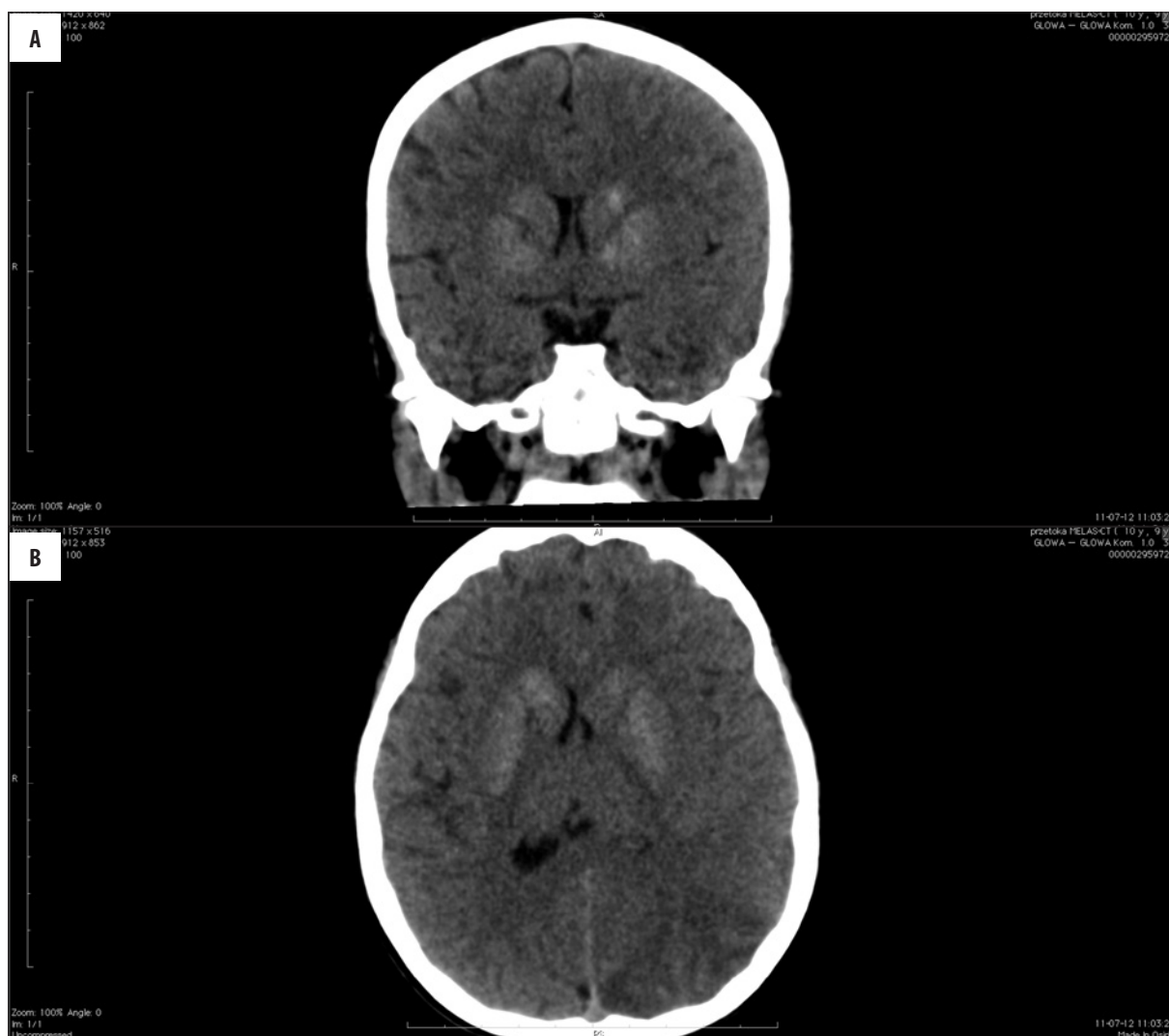


Figure 2AB. CT scans show hyperdense areas covering basal ganglia bilaterally and compression of the left lateral ventricle.

Discussion

MELAS syndrome was first described in 1984 by SG Pavlakis. It is a multisystem disorder with a special predilection for the nervous system and muscles [1].

The clinical diagnosis of MELAS is based on the following features: 1) stroke-like episodes occurring before the age of 40, 2) encephalopathy with seizures and/or dementia, 3) the presence of lactic acidosis, ragged red muscle fibres, as well as additional criteria such as recurrent headaches and recurrent vomiting. [1]

Typical changes in brain imaging include stroke-like areas, basal ganglia calcifications and brain atrophy [3,9–11].

Stroke-like lesions occur in approximately 90% of MELAS patients and correlate with focal neurological symptoms [12]. On CT scan, the disease appears as hypodense areas, therefore it can both clinically and radiologically mimic ischemic stroke.

Location of lesions, non-overlapping with areas of cerebral vasculature, as well as the age of patients argues against

stroke [5]. MELAS syndrome usually affects people under 40 years of age [3].

The stroke-like areas in MR studies show prolonged T1 and T2 relaxation times [4], which can be confusing and again suggest the diagnosis of stroke.

DWI and ADC sequences are very useful to distinguish between these two pathologies. In the ischemic areas of the brain, diffusion is restricted, which is caused by cytotoxic edema, and the signal on the ADC map is typically reduced [5,13]. However, in MELAS syndrome, lesions most often occur due to vasogenic edema, and the signal intensity on the ADC map is usually not reduced at all or less reduced than on DWI [5,14].

An additional tool is MR spectroscopy with a characteristic for MELAS large lactate peak at 1.3 ppm [5,14,15].

Stroke-like lesions can occur in any part of the brain with predilection to the parietal, temporal and occipital cortex [1,4,5,10,11]. Mass effect is associated with an acute or subacute phase. [4] In the subacute phase, there may

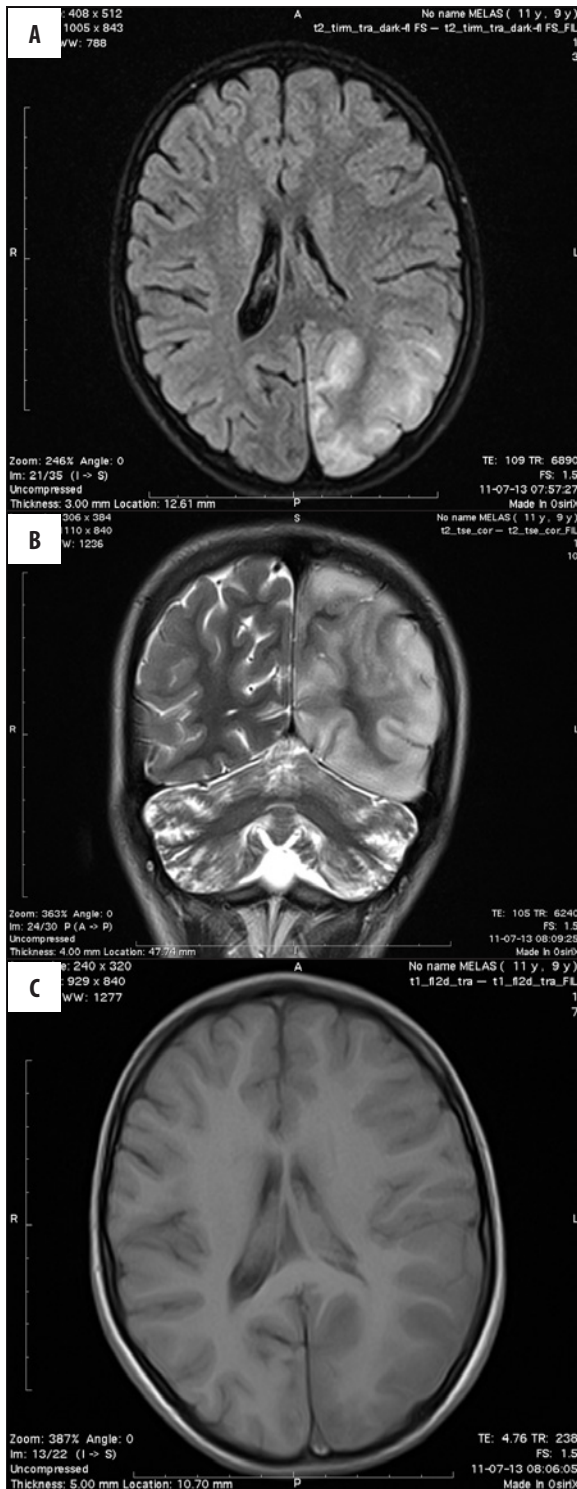


Figure 3A-C. 1.5T MRI scan revealed thickening of the cortex and abnormal, high Flair signal in the left occipital lobe. In the T1 sequences signal is decreased.

be contrast enhancement due to blood-brain barrier damage or as a result of congestion or reperfusion [4,10]. In the course of the disease, the lesions regress with obvious clinical improvement, often leaving atrophy of the brain tissue.

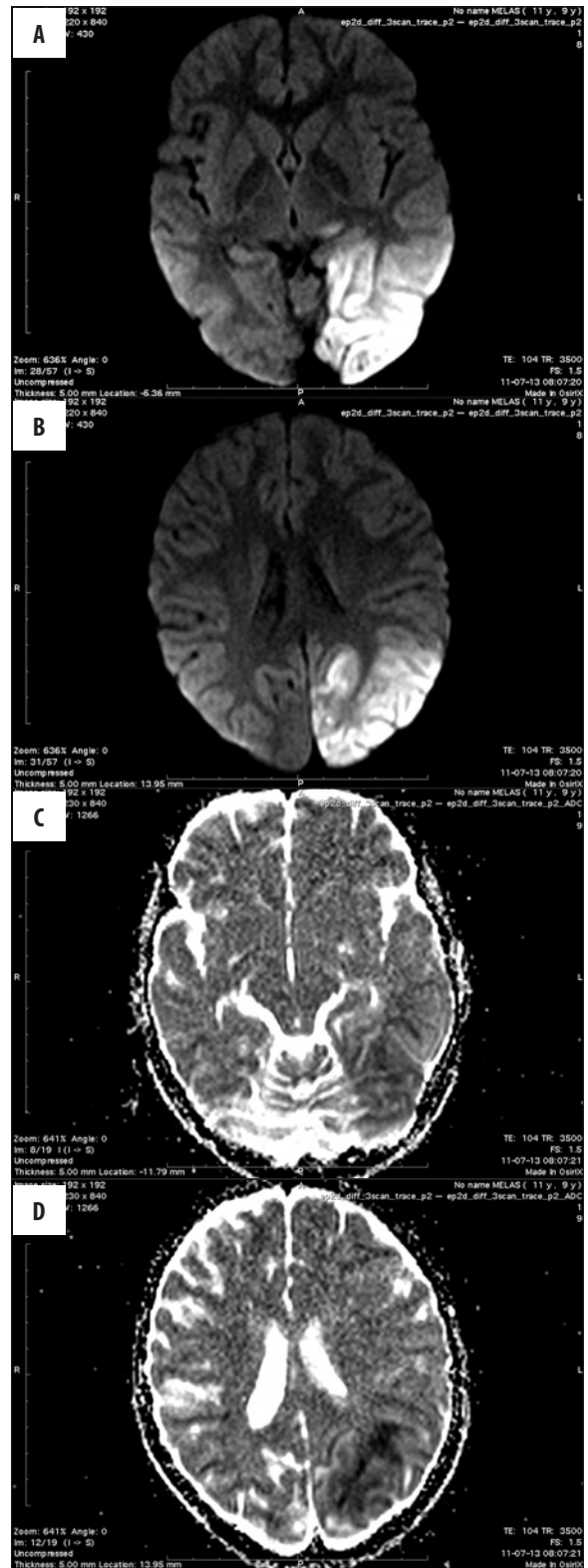


Figure 4A-C. There is restricted diffusion in areas which were hypodense on CT scan. On ADC maps there is no significant reduction in cortical signal intensity and the signal drop covers adjacent white matter.



Figure 5. MRI revealed (Flair) areas of increased signal bilaterally in globus pallidus and in posterior part of the left thalamus.

Lesions tend to appear in locations other than previously, which is a particularly characteristic symptom of MELAS syndrome [4,10,11,16].

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The differential diagnosis should include (besides the ischemic stroke) a viral infection and vasculitis (moyamoya disease, Kawasaki disease) [4]. Diseases associated with changes in the basal ganglia which should also be considered are other mitochondrial encephalomyopathies (Leigh's disease, Kearns-Sayre syndrome, myoclonic epilepsy with raggedred fibres), Wilson's disease, hypoxia and status epilepticus [4]

Conclusions

The present study described a patient with clinical and radiological picture of MELAS syndrome. The rarity of this disorder and the complexity of its clinical presentation make MELAS patients among the most difficult to diagnose. Brain imaging studies require a wide differential diagnosis, primarily to distinguish between MELAS syndrome and ischemic stroke. Particularly helpful are the MRI and MR spectroscopy techniques.