Isolated Mitochondrial Complex Iv (Cytochrome C Oxidase) Deficiency Mimicking ADEM

Amal Y. Kentab[1,2], Hamdy H. Hassan[3], Hisham El Khaldi[4]

[1]Department of Pediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia [akentab@ksu.edu.sa]
[2]Division of Pediatric Neurology, Department of Pediatrics, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia [akentab@ksu.edu.sa]
[3]Department of Radiology, Dar El Ashaa Center, Alexandria, Egypt. [hamdyct@hotmail.com]
[4]Departments of Pathology, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia [hishamkh@gmail.com]

ICNC 2024

BACKGROUND

Cytochrome C Oxidase deficiency is a rare inherited metabolic disorder characterized by deficiency of the enzyme cytochrome C oxidase; an essential enzyme active in oxidative phosphorylation.It is clinically heterogeneous, ranging from isolated myopathy to severe multisystem presentation. Acute disseminated encephalomyelitis (ADEM) is a monophasic polysymptomatic inflammatory condition of the CNS that principally involves the white matter although the grey matter may also be affected.

CASE REPORT

A 6-year-old boy, a product of a consanguineous marriage with a history of progressive weakness and convulsions noted at 2 years of age in his sister who died at the age of 5 years with no definite diagnosis. At the age of 2 years, he presented with fever, encephalopathy, and seizures, proceeded by varicella skin infection. Diagnosed as ADEM based on MRI. He showed slow recovery but remained with poor speech and ataxic gait. At 4 years of age, he developed the 2nd episode of ADEM, was admitted in a coma state and ventilated for 10 weeks. Progressive neurologic decline and frequent myoclonic seizures were noted despite full support with immunosuppressive therapy, antiviral treatment, antiepileptic drugs, and megavitamins. RI showed generalized cortical swelling and high signal intensity diffusely involving cerebral cortex, cerebellum, and deeper gray matter. He remained in a vegetative state with spastic quadriplegia. Muscle biopsy showed reduced cytochrome C oxidase activity and abnormal accumulation of mitochondria at the subsarcolemmal membrane.

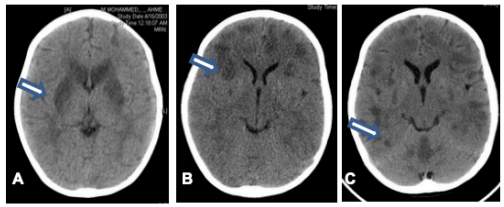

Figure 1: CT brain (Plain) : **At 2-years of age** Axial (A) showing hypodensities involving basal ganglia bilaterally. **At 4-years of age** Axial (B) showing multiple focal lesions of hypodensity scattered at frontal lobe of bilateral cerebral hemispheres predominantly at grey-white matter interface. **Follow- up 4 weeks later** Axial (C) showing similar lesions scattered at more multiple regions at bilateral cerebral hemispheres

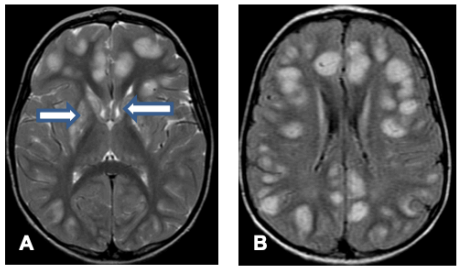

Figure 2: MRI brain **At 4-years of age** Axial T2WI (A) and axial FLAIR (B) demonstrating multiple focal lesions of high signal intensity scattered at bilateral cerebral hemispheres predominantly at grey-white matter interface.High signal intensity at bilateral basal ganglia arrows in (A) suggesting acute dissemintated encephalomyelitis (ADEM)

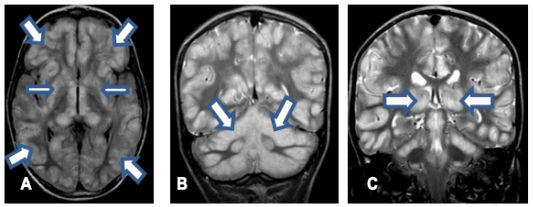

Figure 3: MRI brain ; **At follow-up 4 weeks later** , Axial FLAIR (A) and coronal T2WI (B & C) demonstrating swollen and abnormal high signal intensity diffusely involving bilateral cerebral cortex, cerebellum basal ganglia and thalami suggestive of acute mitochondrial encephalopathy.

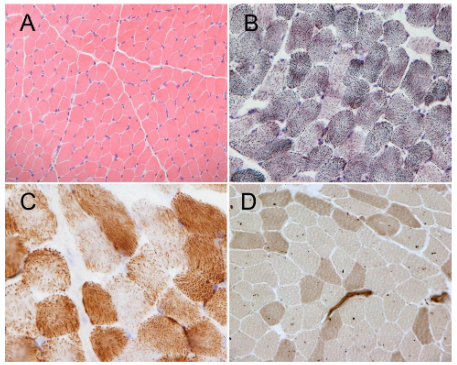

Figure 4: Histochemical staining of skeletal muscle. (A) Hematoxylin and eosin staining. No ragged red fiber was observed. (B) NADH staining. No darkly stained fibers were detected. (C) Cytochrome C - oxidase staining. The activity was reduced in some muscle fibers. (D) Adenosine triphosphate cyclase staining (pH 9.6). The type I muscle fibers exhibited dominance.

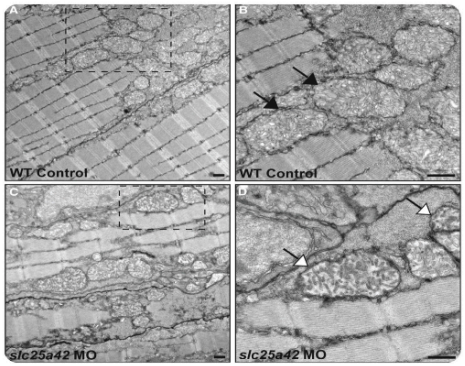

Figure 5: Cytochrome c oxidase (CXO) deficiency causes severe abnormalities in mitochondrial ultrastructure. **Longitudinal transmission electron micrographs of zebrafish skeletal muscle at 3 dpf. a, b** Wild-type controls show normal mitochondria (black arrows). **B** is an enlarged image of dashed box in **a. c, d** In contrast, Skeletal muscles of zebrafish injected with e3i3-MO contain mitochondria with swollen and dark inner membranes (white arrows). **d** is an enlarged image of dashed box in c. Scale bars 500 nm

CONCLUSION

This case serves as a reminder of the clinical heterogeneity of cytochrome C oxidase deficiency, and physicians should consider a broader differential diagnosis for ADEM.

CORRESPONDENCE

AMAL Y. KENTAB. MD
Associate Professor of Pediatrics & Consultant Pediatric Neurologist.

Amkentab@hotmail.com, akentab@ksu.edu.sa

CYTOCHROME C OXIDASE DEFICIENCY, COMPLEX IV, MITOCHONDRIAL DISORDERS, ACUTE DISSEMINATED ENCEPHALOMYELITIS, MRI, CHILDREN.