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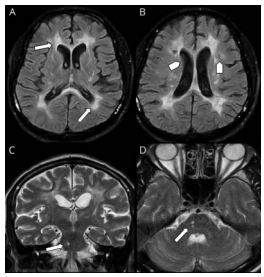
Abstracts

Papers appearing in the February 2019 issue

Cerebral small vessel disease due to a unique heterozygous *HTRA1* mutation in an African man



Objective To describe the case of an African patient who was diagnosed with cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL).

Methods Case report and literature review.

Results We present a 39-year-old Gabonese man who developed progressive gait difficulty at the age of 32, followed by insidious tetraparesis, urinary sphincter disturbance, spastic dysarthria, cognitive dysfunction, and seizures. Brain imaging was performed many years after disease onset and revealed diffuse confluent white matter lesions and lacunar infarcts. He tested negative for acquired white matter disease, but genetic screening detected a genetic variant of *HTRA1* gene (G283R), which has not been previously reported.

Conclusions CARASIL is a disease that usually affects Asian patients. This case report describes a unique case of an African patient diagnosed with CARASIL and a novel genetic mutation in *HTRA1* that has not been previously described in the literature.

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Early infantile epileptic-dyskinetic encephalopathy due to biallelic *PIGP* mutations

Objective To describe clinical, biochemical, and molecular genetic findings in a large inbred family in which 4 children with a severe early-onset epileptic-dyskinetic encephalopathy, with suppression burst EEG, harbored homozygous mutations of phosphatidylinositol glycan anchor biosynthesis, class P (*PIGP*), a member of the large glycosylphosphatidylinositol (GPI) anchor biosynthesis gene family.

Methods We studied clinical features, EEG, brain MRI scans, whole-exome sequencing (WES), and measured the expression of a subset of GPI-anchored proteins (GPI-APs) in circulating granulocytes using flow cytometry.

Results The 4 affected children exhibited a severe neurodevelopmental disorder featuring severe hypotonia with early dyskinesia progressing to quadriplegia, associated with infantile spasms, focal, tonic, and tonic-clonic seizures and a burst suppression EEG pattern. Two of the children died prematurely between age 2 and 12 years; the remaining 2 children are aged 2 years 7 months and 7 years 4 months. The homozygous c.384del variant of *PIGP*, present in the 4 patients, introduces a frame shift 6 codons before the expected stop signal and is predicted to result in the synthesis of a protein longer than the wild type, with impaired functionality. We demonstrated a reduced expression of the GPI-AP CD16 in the granulocytic membrane in affected individuals.

Conclusions *PIGP* mutations are consistently associated with an epileptic-dyskinetic encephalopathy with the features of early infantile epileptic encephalopathy with profound disability and premature death. CD16 is a valuable marker to support a genetic diagnosis of inherited GPI deficiencies.

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