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UNEXPLAINED SMALL VESSEL DISEASE IN A WOMAN

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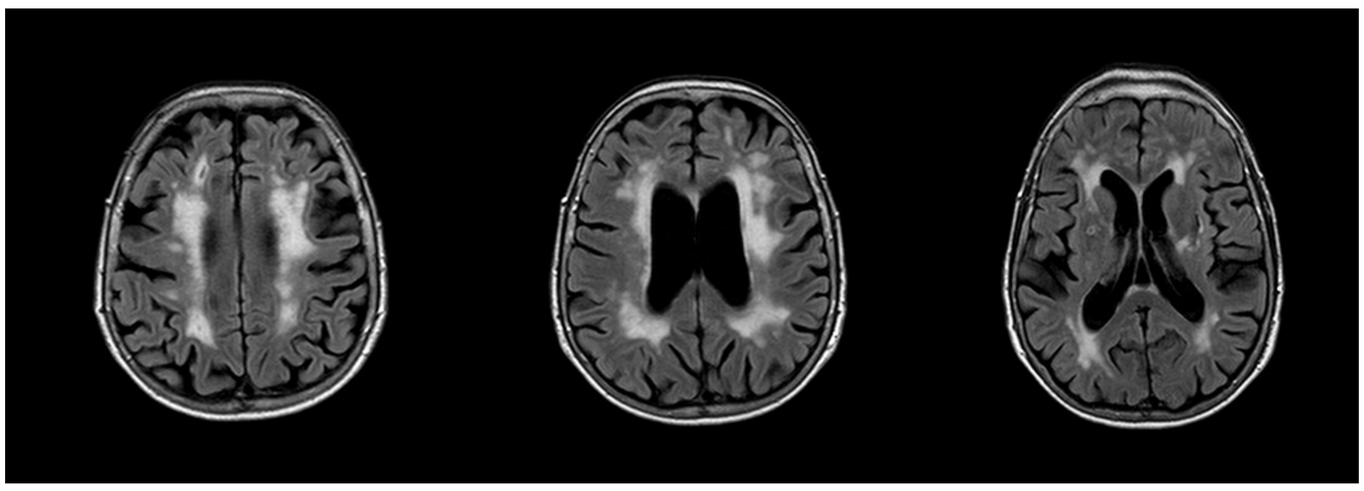

Fig. 1: MRI T2/FLAIR sequences: multifocal, confluent hyperintensities in the deep and periventricular white matter

Discussion - Fabry disease is an X-linked rare lysosomal storage disorder with an estimated incidence of 1 in 50,000 males that results from the deficiency of the enzyme α-galactosidase A. Affected hemizygous males may display all the characteristic signs of the disease; more recently, late-onset variant have been described with isolated cardiac, cerebrovascular, and/or renal disease. Disease in female has milder clinical manifestations, but recent studies showed that cardiac, cerebrovascular or abnormal renal function were present in about 91% of mutation-carrier females. The mutation present in our patient is a missense mutation described during a Italian screening among 37,104 consecutive newborn males. Apparently the carrier mother was asymptomatic, but her age was not reported. On the contrary, in our patient the mutation was associated with a quite severe phenotype. Early detection would have prompted therapeutic intervention in order to delay or prevent complications of the disease, especially renal and cardiac involvement. This case highlights the relevance of considering, in the presence of unexplained leukoencephalopathy, the diagnosis of Fabry also in women in whom the disease is still commonly under-evaluated.

Background - Small vessel disease refers to a group of pathological processes affecting arteries and veins, whose consequences on brain parenchima neuroimaging present as lacunar infarct, diffuse white matter lesions and haemorrhages. Hypertension and cerebral amyloid angiopathy are the more frequent causes in elderly.

Case Report - A caucasian 73-year old female was admitted to our Department for the acute onset of confusional state and fall to the ground. Familial history was un-remarking. The patient had a history of seizures from youth, transient ischemic attack, kidney transplant for renal failure since the age of 60; classical cerebrovascular risk factors were absent. At admission neurological examination was otherwise normal except for slow thinking and poor judgment, and reduction of tendon reflexes; she complained pain and distal numbness at the extremities. Lipid profile, glycemia, homocysteine and screening for thrombophilia were normal. MRI showed multifocal, discrete and confluent T2/FLAIR hyperintensities in the deep and periventricular white matter due to small vessels involvement, with no contrast enhancement. T2 GE did not show typical features of cerebral amyloid angiopathy (Fig 1) . Re-evaluation of antecedent MR, performed when patient was 50 years-old because of epilepsy, revealed similar, though less pronounced, findings. Considering the history of renal failure, the presence of painful peripheral neuropathy and the neuroradiological evidence of diffuse leukoencephalopathy, genetics for Fabry disease was performed revealing a heterozygous mutation (c.197A>G p.E66G) mutation in the GLA gene.

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