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REPORT CASE: CADASIL SYNDROME, A QUICK EVALUATIVE CASE IN ICU

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ABSTRACT

CADASIL is an arteriopathy that is due to NOTCH3 mutation that is mainly underestimated and misdiagnosed.

We will report a case of a 59-year-old female that was admitted to the ICU due to rapid evolution of the neurological symptoms, which is unusual for this particular pathology within tachycardia that's not usually found

The exact mechanism of the rapid evolution, still a mystery and could be related to either a new mutation that led to a quicker evolution or another mutation that emphasized the NOTCH3 mutation

Category: Neurology, emergency medicine. Genetic pathology.

KEYWORDS: ***Intensive care, rare illness, stroke, microangiopathy, dementia, CADASIL, notch3, genetic***

INTRODUCTION

CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is a micro vessel pathology that led to multiple strokes. This arteriopathy is due to a mutation in the NOTCH3 gene.

Analysis of several large, well-characterized CADASIL families demonstrated genetic linkage to a single disease locus on chromosome 19q12. (1)

The most common symptoms of CADASIL are small ischemic strokes, transient ischemic attacks, encephalopathy, epilepsy, depression, apathy and cognitive impairment, appearing in middle age, that may progress to frank vascular dementia(2)

Although CADASIL is thought to be a rare disease with a prevalence in the United Kingdom of 4 in, 100000 (3) and the estimated prevalence of the disease is 1 in 25,000–50,000 (4).

Actually, there is no estimation of CADASIL mortality.
The main source of concern is the cardiovascular risk secondary to it (5) it's frequently misdiagnosed due to it polymorphous clinical features (6).

Now, today, there are no guidelines and no treatment for micro vessel injuries secondary to NOTCH3 mutations. (7)

Reported Case

A 59-year-old female patient with a familial history of strokes at a young age and a personal history of transitory strokes since 2017.

She was presented to the emergency department following an abolition of swallowing reflex , dementia and tachycardia.

All deep tendon reflexes were symmetrically exaggerated. She didn't present cranial nerve palsies or cerebellar signs.

A CT scan was performed describing multiples lacunar images in thalamic and nucleus areas hypodense referring to squealer repetitive ischemic strokes (Fig 1)

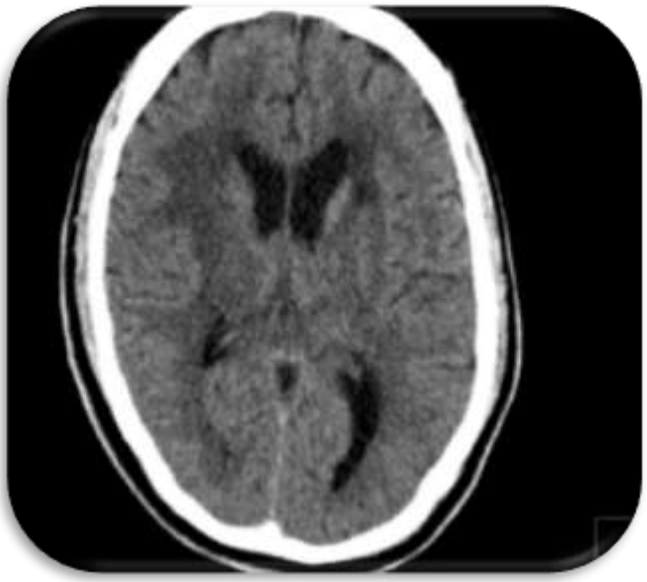

Fig 1: CT Scan of the PATIENT

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An initial biological exploration was performed (tab)

HB	14
WC	8x10*3
gly	1
urea	2
crea	12
CRP	20
asat	38
alat	54
K+	3.5
Na+	139
Ca2+	86
VIH	negative
HBV	negative
HCV	negative

Tab : Biological Exams Undertook

CSF direct exam showed leukocyte <5 a Glycemic =0.5 protein at 300.

A PCR of CSF liquid didn't find any trace of herpes
The EKG interpretation was sinusal tachycardia with a frequency of 125.

An MRI was performed reveals areas of T1 hypo intensity and hyperintensity on T2 and FLAIR on thalamic and nucleus areas associated with small lacunar infarcts. Extensive white matter abnormalities that are reattached to a CADASIL syndrome.

As for the therapy approach, we treated it as a ischemic stroke that was not t.so, we administrated aspirin100mg and worked on preventing secondary brain insults of systemic origin (SBISOs). The patient was transferred to the neurological ward for further explorations

DISCUSSION

CADASIL is a dominant autonomic illness that's pretty challenging to diagnose and for the majority of cases is undiagnosed. Secondary to the NOTCH 3 gene, which encodes a transmembrane receptor. Mutations are highly stereotyped and occur in the extracellular portion of the protein, and add or remove a cysteine residue resulting in disruption of a disulfide bond in one of the epidermal growth factors like (EGF) repeats (8).

Usually, patients manifest the condition before the age of 60 years(9), which is the case for our patient.

We excluded different differential diagnoses such as infectious encephalitis and meningitis with CSF, MRI and biological exam, a metabolic encephalitis secondary to perturbation of urea by biological exam. We left out hepatitis encephalopathy possibility according to biological exam and clinical exam. Furthermore, we also excluded an ionic disorder as a reason for her consciousness status.

in our case , our patient's MRI lesions were concurring with the literal MRI (10). In literature many methods for diagnosing CADASIL have been suggested. The (MRI) (10), the presence of Granular Osmiophilic Material (GOM) in capillary blood vessels of the skin and muscle on biopsy (11). Finally, genetic of NOTCH3 gene studies play a key diagnostic role (7).

However, the genetic study and skin biopsy were not available in our case.

As mentioned before, there is no guidelines proper to CADASIL. as it generates small ischemic strokes it was treated as an acute ischemic stroke. That was none thrombolyzed we used aspirin as recommended in guidelines (13,14)

Hypnotically, we can suppose that the tachycardia is secondary to the NOTCH 3 mutation since it impacts the EGF sequence, which plays an important role in revascularization. That leads us to think that CADASIL syndrome may be a multisystemic syndrome with a neurological predominant clinical, especially there is a study that concluded to a potential cardiac risk (12).

CONCLUSION

CADASIL is an atypical pathology and specially in the ICU that is secondary to a mutation of transmembrane receptor that affects EGF repeats, mainly the hypothesis of a systemic effects of CADASIL is a path to explore.

The exact mechanism of the rapid evolution still a mystery and could be related to either a new mutation that led to a quicker evolution or and another mutation that emphasized the NOTCH3 mutation.

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