Role of Magnetic Resonance Imaging in Early Progressive Dementia in diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL)

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TITLE: Role of Magnetic Resonance Imaging in Early Progressive Dementia in diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL).

ABSTRACT: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) is an autosomal dominant vascular disorder. Diagnosis and follow-up in patients with CADASIL are based mainly on magnetic resonance imaging (MRI). MRI shows white matter hyperintensities (WMHs). WMHs lesions tend to be symmetrical and bilateral, distributed in the periventricular and deep white matter. The anterior temporal lobe and external capsules are predilection sites for WMHs, with higher specificity and sensitivity of anterior temporal lobe involvement compared to an external capsule involvement. Lacunar infarcts are presented by an imaging signal that has intensity of cerebrospinal fluid in all MRI sequences. They are localized within the semioval center, thalamus, basal ganglia and pons. CMBs are depicted as focal areas of signal loss on T2 images which increases in size on the T2*-weighted gradient echo planar images ("blooming effect").

KEY WORDS: CADASIL, MRI, computed tomography, white matter hyperintensities, cerebral microbleeds.

INTRODUCTION:
Clinically, cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL), a hereditary vascular condition, is characterized by a variety of the following symptoms: migraine with aura, mood disturbance, vascular dementia, ischemic stroke, and premature mortality (1,2,3,4). The prevalence rate of CADASIL is unknown. Many cases of CADASIL were mistakenly diagnosed as multiple sclerosis, Alzheimer's disease, or other neurological disorders before the discovery of genetic analysis for CADASIL in 2000. The most prevalent minor cerebral artery single-gene condition is called CADASIL. It arises from mutations in the NOTCH3 gene on chromosome 19p13's epidermal growth factor-like repeat domain [(5)]. The NOTCH3 gene encodes a 2,321 amino acid-long single-pass transmembrane receptor. There are four members of the NOTCH receptor family in mammals (NOTCH 1-4). A transmembrane domain, an intracellular domain, and a sizable extracellular domain (ECD) with 34 tandem epidermal growth factor (EGF)-like repeats and three Notch/Lin12 repeats make up this specific gene. Each EGF repeat has a length of about 40 amino acids. Each of the repetitions has six cysteine residues that assemble themselves into three highly structured sulphur bridges. A proteolytic cleavage brought on by ligand binding results in the translocation of the intracellular domain to the nucleus. A modest number of mutations in the ligand-binding domain result in a considerable decrease in transcriptional activity (EGF repeats 10 and 11) [(6,7,8)]

CASE DESCRIPTION:
CASE NO-1: 44 years old female patient presented with complaints of recurrent mood swings, dementia and loss of interest in daily activities and cognitive impairment came for further evaluation and was subjected to MRI brain without contrast.

Figure 1: FLAIR/T2 images showing diffuse and confluent periventricular hyper intensity, Multiple chronic lacunar infarcts and diffuse cerebral cortical atrophy with volume loss.

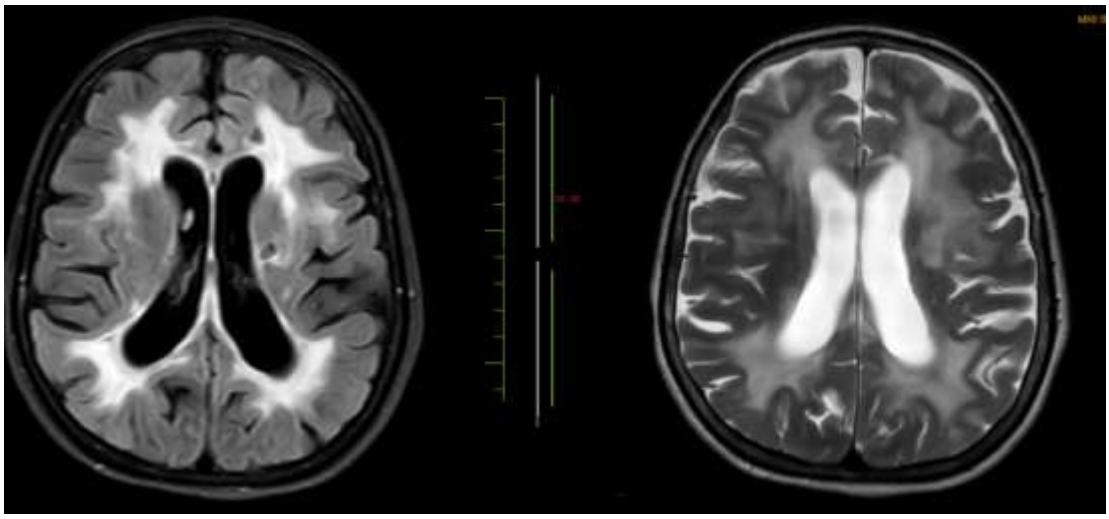
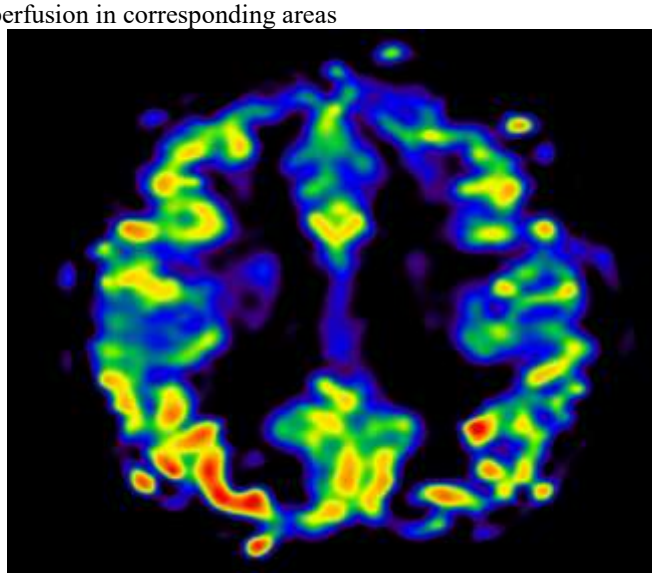
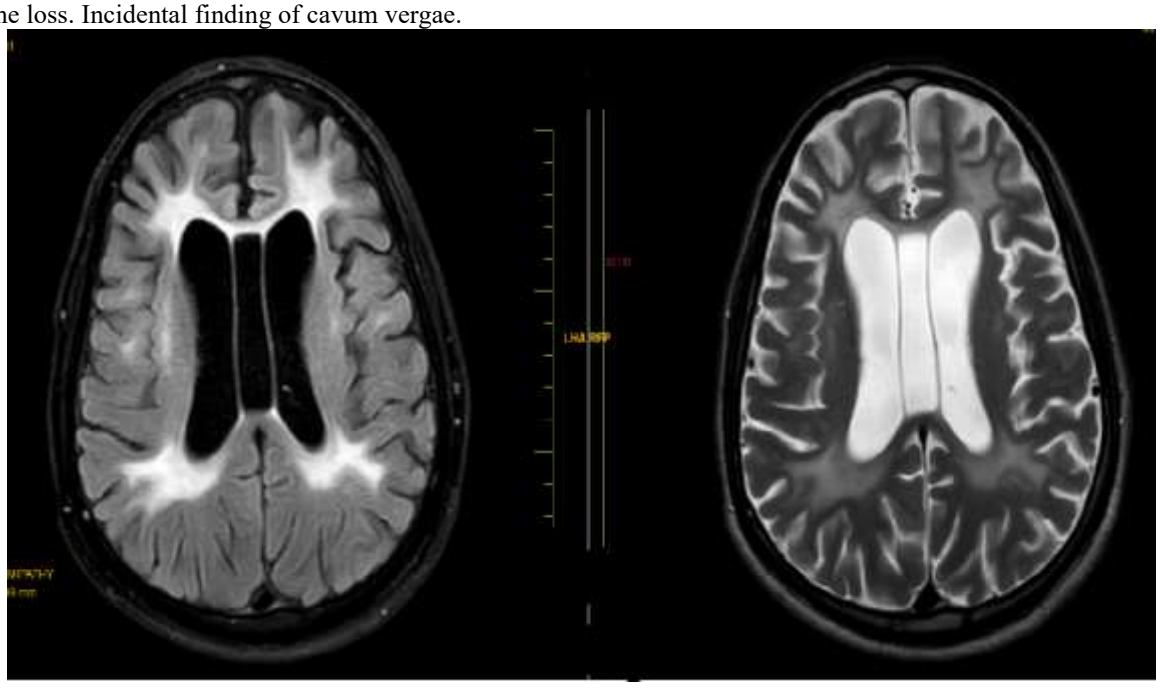


Figure 2: ASL showing reduced perfusion in corresponding areas



CASE NO-2: 42 years old male patient presented with progressive dementia , came for further evaluation and was subjected to MRI brain without contrast.

Figure 3: FLAIR/T2 images showing diffuse and confluent periventricular hyper intensity and diffuse cerebral cortical atrophy with volume loss. Incidental finding of cavum vergae.



DISCUSSION:

Patients with CADASIL reported greater lesion scores in the paramedian superior frontal WM and the temporal WM, primarily in the temporopolar area, where arcuate fibre involvement was noticeably more prevalent. In addition, it revealed symmetric areas of high signal intensity in the superior frontal WM. The distinct MR pattern in this study may be partially explained by a different lobar distribution of small vessel disease in CADASIL. Systematic regional vessel studies in CADASIL are needed to shed light on this matter. Cortical arteries in the superior frontal and anterior temporal areas may also be impacted in CADASIL, which would explain the involvement of standard arcuate fibres that have been noticed. Arcuate fibre involvement or cortical arterial involvement in temporopolar and superior frontal regions was presumably not the focus of earlier pathology investigations of CADASIL. [5,6,7,8] Moreover, the CADASIL have few lacunar lesions, which would result in low signal intensity regions on FLAIR images. Two MR investigations in individuals with chronic multiple sclerosis [9] and in children at high risk of cerebral infarction may provide one reason for this observation [10]. Increased ferrous or other pigments deposition in the brain has been seen in neuropathologic examinations of CADASIL patients [6,7]. If pigments deposition in CADASIL is the cause of the low signal intensity regions on MR imaging that were discovered in this study, further research is necessary to determine this.

CONCLUSION:

Patients with CADASIL are diagnosed and monitored primarily based on MRI results. Lacunar infarcts and WM hyperintensities are visible on neuroimaging. Lesions from WMHs are often bilateral, symmetrical, and dispersed in the periventricular and deep white matter. The anterior temporal lobe and external capsules are WMH preference areas, with anterior temporal lobe involvement showing more specificity. The pons, thalamus, semioval centre, and basal ganglia are the specific locations of lacunar infarcts in CADASIL. In individuals with CADASIL, the number of lacunar infarcts is a significant indicator of cognitive impairment.

ABBREVIATIONS AND ACRONYMS:

MRI	Magnetic Resonance Imaging
CADASIL	cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy
FLAIR	Fluid attenuation inversion recovery
WM	White Matter

CONFLICT OF INTEREST: NIL

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