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CADASIL syndrome: Long-term follow-up on MRI

IMAGING

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CASE REPORT



ABSTRACT

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a hereditary vascular disorder inherited in an autosomal dominant manner. MRI plays a crucial role in the diagnosis and follow-up of patients. Characteristic MRI lesions include symmetric and bilateral white matter periventricular hyperintensities, lacunar infarcts and cerebral microbleeds. In our case report, we demonstrate a male patient with genetically confirmed CADASIL syndrome and the progression of symptoms with corresponding imaging findings throughout the years.

KEYWORDS

CADASIL, MRI, white matter hyperintensities, cerebral microbleeds, lacunar infarcts

Introduction

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a hereditary vascular disorder inherited in an autosomal dominant manner with a prevalence of 1.93 per 100,000 adults [1]. It develops due to mutations of the epidermal growth factor-like repeat domain of the NOTCH3 gene located on chromosome 19p13 [2]. Factors that contribute to clinical suspicion include 1) Early-onset of clinical symptoms (40–50 years); 2) Recurrent transient ischemic attack episodes without the presence of stroke risk factors; 3) Episodes of lacunar infarcts leading to clinical presentations of pseudobulbar palsy and dementia; 4) Migraine with atypical aura; 5) Familial history of typical clinical manifestations [3]. Diagnostic methods include Magnetic Resonance Imaging (MRI), presence of Granular Osmophilic Material in capillary blood vessels on skin biopsy and molecular genetic analysis [4].

Case

In 2004 a 44-year-old male patient presented with clinical signs corresponding to left sided middle cerebral artery transient ischemic attack (speech disturbance, right sided hemi-sensory loss). Due to recurrent suspected transient ischemic episodes MRI investigation was performed. Baseline MRI findings showed symmetric and bilateral white matter

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hyperintensities in the periventricular regions seen on T2W-TSE and FLAIR sequences. Because of recurrent attacks of additional symptoms (headache, memory disturbance and vertigo) control MRI investigations were performed in the following years, in which lesions from the primary MRI scans were unchanged. In 2014 CADASIL syndrome was genetically proven. In the following period, the patient presented with symptoms typical for CADASIL syndrome including mild cognitive impairment with executive dysfunction, attention deficit, psychomotor retardation and mood disturbances. The patient's mood disturbances progressed to a manic psychotic attack in 2019, in which he required psychiatric hospitalization. His neurological status in 2020 progressed compared to previous years with new neurological signs including: left sided hypoglossal paresis, bilateral lower extremity spasticity and frontal release signs. The latest MRI scan performed on the 22nd of September 2021 showed typical imaging characteristics of CADASIL syndrome. Lacunar infarcts and white matter hyperintensities were identified bilaterally in the subcortical and periventricular region on axial FLAIR images (Fig. 1). Predominant hyperintensities were also detected in the anterior

pole of the temporal lobes and in the external capsules (Fig. 1). Hemosiderin depositions, which correspond to cerebral microbleeds, were observed in the cerebellum, brainstem, basal ganglia, and cerebral subcortical regions as focal signal loss on SWI sequence (Fig. 2).

Currently, our patient is being treated by the neurology department outpatient unit. Despite the progression of his clinical symptoms and MRI lesions the Mini Mental State Examination score only declined from 28 to 26 over the years. Due to his recent symptoms (staring spells, episodes of confusion without impaired consciousness) a new diagnostic workup for epilepsy was initiated and anti-epileptic medication was introduced.

Discussion

Our case demonstrates the difficulty in the diagnosis of CADASIL syndrome. Due to the wide differential diagnoses with similar and overlapping clinical and imaging manifestations CADASIL syndrome remains a highly underdiagnosed

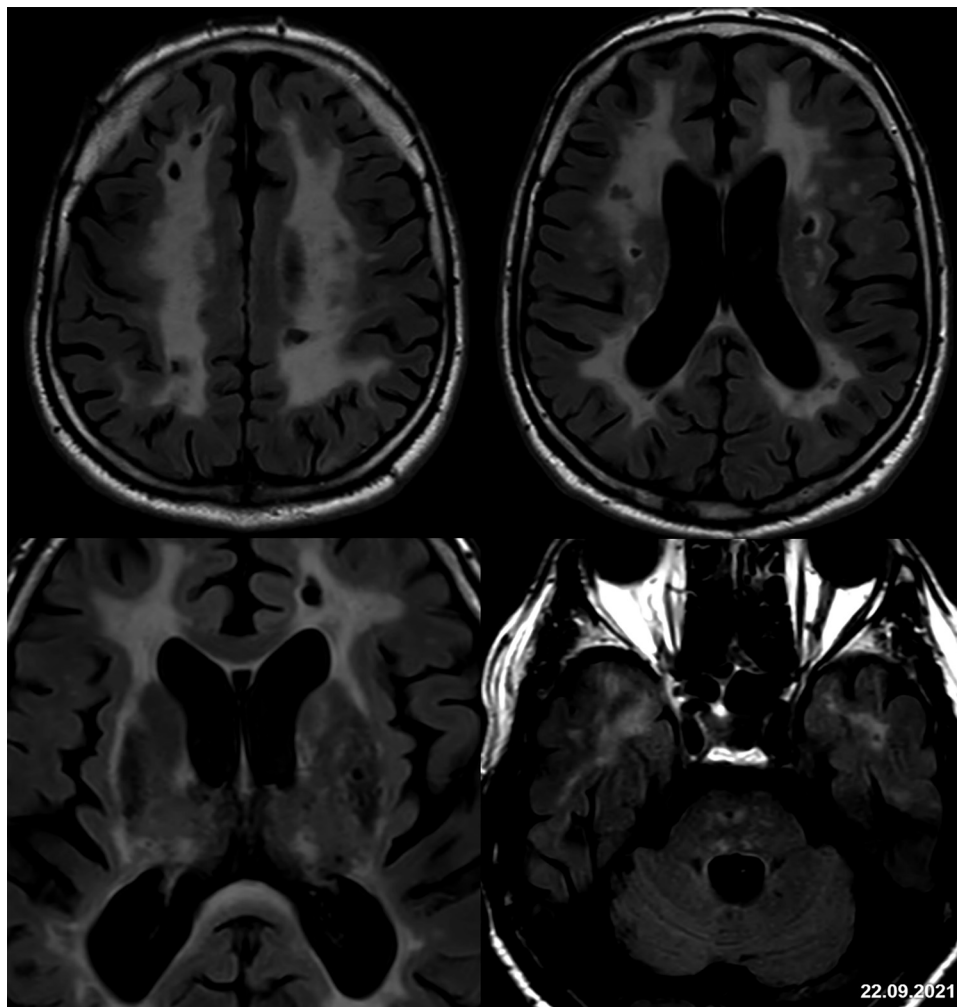


Fig. 1. Axial FLAIR images showing lacunar infarcts, symmetric and bilateral white matter hyperintensities emphasizing the anterior temporal lobe and external capsule regions

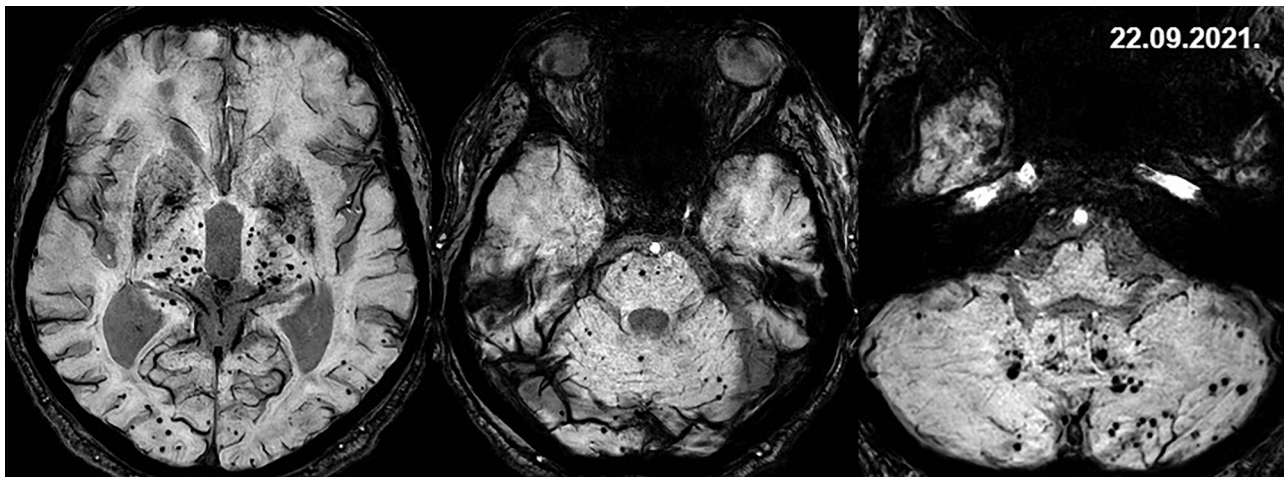


Fig. 2. Cerebral microbleeds in the basal ganglia, subcortical regions, brainstem, and cerebellum on SWI sequence

pathology. As displayed in our case, it may take years for physicians to assess and test for this entity. Diagnosis is further delayed when there is no typical family history of CADASIL syndrome.

Initially in our case, to rule out more common pathologies such as thromboembolic events, carotid doppler ultrasound, echocardiograms and ECGs were performed. Upon negative findings in these examinations, suspicion for less common disorders were raised and serial MRI images were performed. There are certain clinical and imaging features which can be used to differentiate CADASIL syndrome from pathologies with overlapping manifestations [3]. For example in comparison to multiple sclerosis, CADASIL syndrome more commonly displays temporopolar lesions with sparing of the spinal cord [5]. CARASIL patients experience extra-neurological findings (spondylosis and alopecia) with earlier clinical manifestations and imaging findings [6]. This includes high signal intensity in the middle cerebellar peduncles and in the pons on T2W scans, known as the arc sign [7]. MRI features of Binswanger's disease include widespread diffuse white matter lesions and scattered multiple lacunes, but cerebral microbleeds are rarely observed [8]. Our case displayed these differences which enabled a greater likelihood of the diagnosis of CADASIL syndrome.

As of today there is no proven treatment for CADASIL syndrome. However, the work of a multidisciplinary team for the medical and psychological care of patients with CADASIL syndrome is crucial in improving their quality of life.

Authors' contribution: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, writing or revision of the manuscript. Acquisition of images: KB, HB, IBK, DMF, EB, LO. Interpretation of literature: KB. Drafting the manuscript: KB, HB, IBK, DMF.

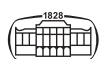
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