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Turkish Title: Akut Eş Zamanlı Subkortikal Infarktların Neden Olduğu Progresif Bulber Paralizi ile Prezente olan CADASIL Olgusu

Turkish Running Head: Eş Zamanlı İnfartlarla Prezente olan CADASIL

Title: A CADASIL Case Presenting with Progressive Bulbar Palsy Caused by Acute Simultaneous Multiple Subcortical Infarcts

Running Head: CADASIL Presenting With Simultaneous Infarcts

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Introduction

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), which is caused by the mutation in NOTCH3 gene, is the most common hereditary small vessel disease of the brain in adults. The main clinical features of this otosomal dominant inherited disease is recurrent transient ischemic attacks and stroke, migraine, mood disturbances and cognitive impairment(1). Transient ischaemic attacks and ischaemic strokes are the most frequent manifestations in CADASIL, occurring in up to 85% of patients(2). As being a small vessel disease, most of the ischemic events appears in the form of subcortical infarctions causing lacunar syndrome clinically. The uncommon clinical and radiological manifestations of CADASIL patients have been rarely reported in the literature. Here, we report a patient with a progressive bulber palsy and acute simultanously multiple subcortical infarctions as the first manifestation of CADASIL.

Case Report

A 35 year-old male man was admitted to our hospital with a complaint of worsening slurred speech for 6 hours. His past history was unremarkable including drug or substance use. No consanguineous marriage was present between the parents. His father had had ischemic stroke a few times and he had become bedridden 2 years before his death at 56 year-old age. Also, his two brothers and one sister had history of migraine headache. On admission, his blood pressure was 120/70 mmHg and heart rate was 82 bpm (regular), and body temperature was 36.8C. There was no abnormality in his electrocardiograhy. The neck was supple and Kernig sign was absent. Neurologically, he was alert and oriented. His speech was severely dyshartric . There was no facial paralysis or no tongue deviation. The soft palate elevation was good bilaterally. There was no sensory or motor deficit in his extremities and cerebellar examination was normal. His complete blood count, liver and kidney function tests, blood glucose, electrolytes and thyroid function test, and vasculitis panel was normal.

Brain Computed Tomography scanning disclosed periventricular chronic ischemic changes, predominantly in frontal regions. Diffusion Weighted magnetic resonance imaging (DWI- MRI) revealed multiple hyperintensities in bilateral subcortical white matter with low ADC values (Figure 1, A,B). Fluid-attenuated inversion recovery (FLAIR) images showed extensive ischemic gliotic changes in centrum semiovale, periventricular and subcortical white matter, basal ganglia, temporal lobes

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and also in pontin area bilaterally (Figure 1, C,D). He was hospitalized and started dual antiagregan treatment (asetylsalysililc acid 100 mg and clopidogrel 75 mg daily). 24 hour after his admission, he had a progression with anarthria and bilateral palsy of lower motor cranial nerves. Repeated DWI-MRG demonstrated enlargement of ischemic lesion as well as appearance of new ischemic infarctions in bilateral border-zone areas(Figure 2). There was no hypo-hypertensive episode during follow up period. Extra-intracranial CT Angiograhy, transthoracic and transesophageal echocardiography, 24-h Holter ECG analysis were all normal. He improved in 3 weeks with supportive treatment and antiagregan treatment. Because the patient had diffuse encephalopathy involving temporal lobes and also family history of migraine and stroke at young age, CADASIL is suspected and NOTCH3 gene mutation was found positive. Informed consent was taken from the patient fort his case report.

Discussion

As being a small vessel disease of the brain, ischaemic events are almost invariably subcortical and present in 67% of patients as lacunar syndromes such as pure motor, pure sensory or sensori-motor deficit, ataxic hemiparesis and dysarthria–clumsy hand syndrome in CADASIL(1). Generally, if there is acute simultaneous ischemic infarctions in a patient with stroke, the etiological cause is usually attributed to cardiac or carotid arterial emboli(3). However, etiological work-up was not demonstrated any evidence of embolic etiology in our patient.In the literature, there were 7 CADASIL cases with multifocal cerebral infarctions and these infarctions were supposed to be related with hemodynamic fluctuations(4-9). One of these reports, global white matter hypoperfusion was demonstrated in MRI perfusion study(6). To the best of our knowledge, there is no CADASIL case presenting with progressive bulbar palsy probably caused by acute bilateral subcortical lesions in the literature. There were no evidence of hemodynamic failure, as in cases in the published literature, in our patient. The precise pathophysiology of these infarcts remains unclear. In a recent study, small vessel disease of the brain have been proved to be an important cause of acute simultaneous small subcortical infarcts (10).

With this case , we emphasize that CADASIL patients may present with acute simultaneous infarctions and may show a progressive course in the early days. Family history should be taken in

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detail and brain MRI should be evaluated for diffuse leucoencepholopathy with temporal lobe involvement.

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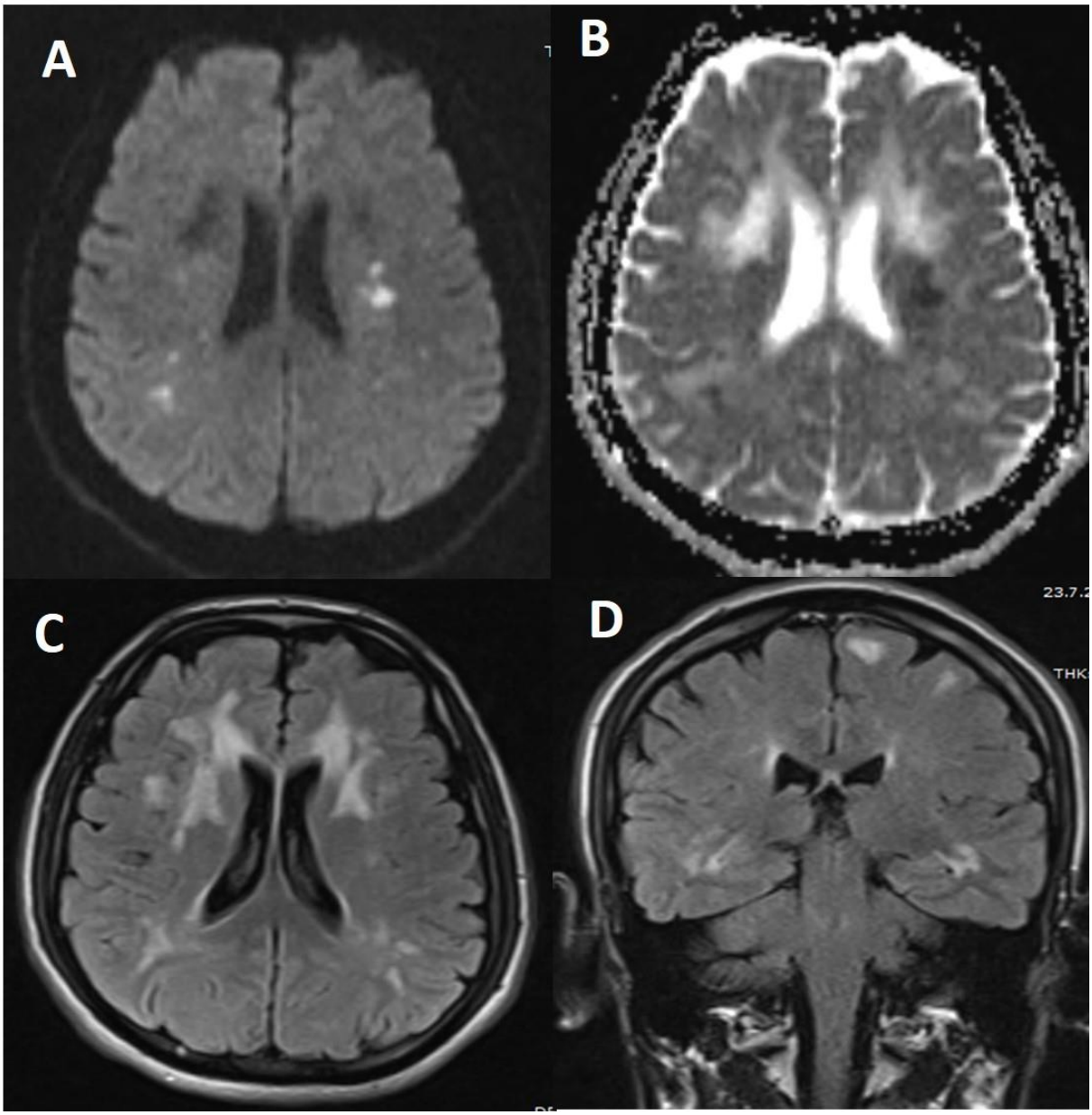

Figure 1

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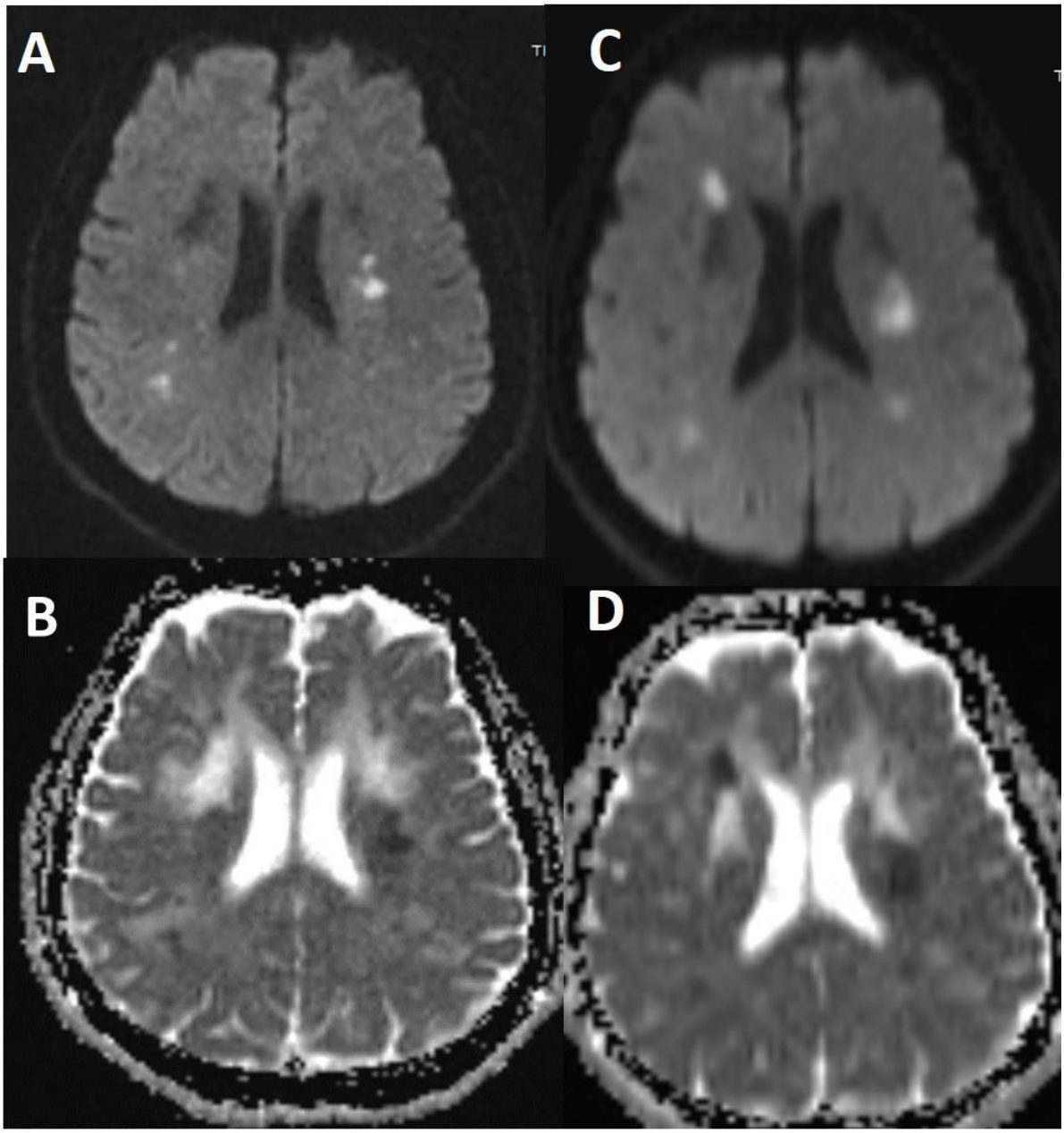

Figure 2

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