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CADASIL syndrome (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) presenting as psychosis

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ABSTRACT

Cerebral autosomal dominant arteriopathy with subcortical infarct and leukoencephalopathy (CADASIL) is the most common monogenic form of cerebral small-vessel disease characterised by recurrent strokes. Behavioural disturbance also presents in a significant proportion of subjects as neurotic spectrum disorders and psychotic features are rarely reported. In this case report, we highlight a 32-year-old man with CADASIL syndrome, who had overt psychotic symptoms with neurological signs later on.

INTRODUCTION

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare genetic disorder due to the mutation in NOTCH-3 gene on chromosome 19q12, with autosomal dominant inheritance.[1 2] Clinically, it most frequently presents as recurrent ischaemic episodes, cognitive deficits, dementia with gait disturbance, urinary incontinence, pseudobulbar palsy, migraine and epileptic seizures. Behavioural disturbances are seen in approximately 30% of the cases,[3] with adjustment disorder, mood disorders, especially depression being the most frequent diagnosis.[4] Psychotic symptoms in CADASIL syndrome are rarely reported in literature. Thus, we present a case of CADASIL with psychotic symptoms at a tertiary-care psychiatric hospital.

CASE HISTORY

A 32-year-old man presented with suspiciousness, fearfulness, odd ritualistic behaviour, decline in academic performance, self-care and social functioning and occasionally complaint of urinary and faecal incontinence, with symptoms starting from 14 years of age and being gradually progressive in the course. He had a history of seizure episodes at the age of 8. For this reason he took antiepileptic medication for 4 years and since then there has been no recurrence of seizures. Futhermore, there was a family history of stroke in his father. The patient was treated with second-generation antipsychotics earlier, but there was no significant improvement in symptoms and also there was a history of developing extrapyramidal side effects with typical antipsychotics. His mental status examination revealed odd mannerisms, increased reaction time, retarded speech, shallow affect with decreased reactivity and delusion of persecution against the family member, with complete denial of illness by the patient. In addition, his neurological examination revealed ataxic gait while other parameters of physical examination were unremarkable. MRI brain imaging revealed confluent and discrete, fairly symmetric T2 hyperintense foci in the deep and subcortical white matter of the cerebral hemispheres, bilateral basal ganglia, brainstem, thalami and the subcortical white matter, suggesting the possibility of CADASIL syndrome. Thus, for confirmation, skin biopsy was performed which revealed granular osmophilic deposits in the basal lamina of a small blood vessel with degeneration and loss of smooth muscle cells under the electron microscope, as genetic testing was unavailable at our centre. The patient was given clozapine in view of his treatment history, which resulted in partial improvement of symptoms.

DISCUSSION

CADASIL is a rare genetic disorder, and the prevalence of CADASIL is unknown, but worldwide, pproximately 400 affected families

have been reported.[5] Notch protein family is composed of cell surface receptors that transduce signals between neighbouring cells. Notch3 is predominantly expressed in adult arterial smooth muscle cells in human and plays a critical role in maintaining the phenotypic stability of vascular smooth muscle cells.[6] Common presentation is silent or clinically evident ischaemic strokes, migraine, seizure and cognitive impairment as described earlier. Neurotic symptoms are reported to be mainly associated with this syndrome.[3] The exact pathophysiological mechanism underlying the association of psychotic symptoms with CADASIL syndrome is not clearly understood. One possible explanation is that multiple white matter infarcts particularly in the frontal region result in disruption of cortical–subcortical network which results in altered reality monitoring and genesis of psychotic symptoms. NNotch signalling pathways have a crucial role in neurodevelopment and altered Notch signalling is reported in schizophrenia, hence this may be a common dysfunction pathway between schizophrenia and CADASIL syndrome.[7–9] Therefore, we want to make readers aware of this unique presentation of psychotic behavioural symptoms associated with CADASIL syndrome. A high index of suspicion is required when associated neurological features are found alongside unusual behavioural symptoms with inadequate response to management as usual. The targeted investigation is helpful for identifying this syndrome. Neuroimaging is helpful for identification of suggestible features. Although genetic testing is definitive for confirmation of diagnosis, as per previous literature skin biopsy yields high results with high sensitivity and specificity.[10]

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