CADASIL in a Family from North-west India

A Panagariya*, Bhawana Sharma**, Shubhakaran***

Abstract
We here with report a family with two sibs having history of recurrent familial stroke. Neuroimaging revealed diffuse hyperintense signals in subcortical white matter and basal ganglia on MR images in younger sib suggestive of cerebral autosomal dominant arteriopathy with sub-cortical infarcts and leucoencephalopathy (CADASIL). The diagnosis was further strengthened on skin biopsy showing presence of PAS positive granules with thickening of dermal vessels.

INTRODUCTION
Cerebral autosomal dominant arteriopathy with sub-cortical infarcts and leucoencephalopathy (CADASIL) is a rare inherited cause of early stroke and dementia described first in the year 1977. Till date, around 400 families from countries around the world have been identified as carriers of the gene. The condition is believed to be largely undiagnosed with most of the earlier reports from West. Recently, we came across a case of young onset familial stroke almost fulfilling criteria for CADASIL. To the best of our knowledge this could be first case to be reported from India.

CASE REPORT
A 50 years right handed non-hypertensive, non-diabetic male was admitted with history of sudden onset right sided weakness five years back. In next one year there was history of partial improvement in motor power. In addition he also revealed recurrence of similar episodes in next 2-3 years. History of emotional lability and change in speech was also elicited. On interrogation his elder brother was noted to have history of transient ischaemic attacks. There was no history of the headaches or mood disturbances in either of the two. Neurological status examination revealed mild cognitive impairment (mini mental status examination score of 23), pseudobulbar palsy, upper motor neuron type of facial paresis with bilateral pyramidal signs (Right > Left) and 4/5 (MRC grade) power in right upper and lower limbs with hemiplegic gait.

His investigation revealed normal hemogram, blood biochemistry including serum lactic acid. Neuro-imaging revealed diffuse hypodensity over subcortical white matter on computerized axial tomography. Further, MRI showed diffuse hyperintense signals on T2 weighted images in subcortical white matter and basal ganglia (Figs. 1 and 2). To add, skin biopsy revealed thickening of dermal vessels with narrowing of the lumen. Many of the vessels showed collection of PAS positive granules in their wall consistent with CADASIL.

On basis of history of recurrent young strokes and mild dementia in index case and similar episodes in his sib, typical neuroimaging findings, a diagnosis of CADASIL was
considered and confirmed by skin biopsy findings. Other differentials like Binswanger’s (absence of history of hypertension, and familial nature in index case illness), mitochondrial (normal serum lactate) and demyelinating disease were excluded on basis of history and investigations.

**DISCUSSION**

CADASIL appears to be essentially a disorder of the arteries that is linked to single mis-sense mutation in the NOTCH-3 gene locus on chromosome-19. It is a hereditary (autosomal dominant) cause of early recurrent strokes (84%), dementia (80%), migraine with atypical aura (22%), and mood disorders (20%). The underlying lesion is a widespread vasculopathy distinct from arteriosclerotic and amyloid angiopathy generally affecting leptomeningeal and perforating arteries of the brain between 100-400 µm in diameter, producing deposition of osmophilic granules and electron dense material in media.

Magnetic resonance imaging is a crucial required tool for diagnosis in addition to genetic analysis as neuroimaging penetrance of CADASIL is complete by 30-40 years of age. On MRI typical findings include hyperintense signals in sub-cortical white matter and basal ganglia.

Exact prevalence of CADASIL is still not known as disease is largely undiagnosed. CADASIL experts stress that the "Diagnosis should be considered not only in patients with recurrent small sub-cortical infarcts leading to dementia, but also in patients with transient ischaemic attack, migraine with aura or severe mood disturbances whenever MRI reveals prominent signal abnormalities in sub-cortical white matter and basal ganglia, clinical and MRI investigations of family members are then crucial for the diagnosis, which can be confirmed by genetic analysis.

The basic purpose of reporting this case is to increase awareness for correct diagnosis of this clinical entity based on clinical symptoms and neuroradiological findings and screen susceptible family and provide them with presymptomatic genetic testing.

**REFERENCES**


---

**Announcement**

26th Annual Conference of Association of Physicians of India - UP Chapter on 20th and 21st November 2004 at Motilal Nehru Medical College, Allahabad.

Theme of the Conference: "Trials, Tribulations and Triumphs of Modern Medicine".

For further details contact Conference Secretariat: Dr. Sarita Bajaj, 3/6 Panna Lal Road, Allahabad 211 002.

Tel.: 0532 2600561, 0532 2606110; Fax: 0532 603866 e-mail: bajajak1945@yahoo.co.in