Case Report

Alexander disease - A case report

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Abstract Alexander disease is rare leucodystrophy with three recognized clinical forms- Infantile Juvenile and Adult. Alexander disease show specific radiological and histopathological features.
Key Word: Fibrinoid Leucodystrophy , Rosenthal Fibres, Macrocephaly

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INTRODUCTION

Alexander disease is rare non familial metabolic disorder due to heterozygous dominant mutation in GFAP gene which results in accumulation of GFAP aggregates .It accounts for just 1 – 2% of childhood inherited leucodystrophies. There are 3 recognized clinical forms of Alexander disease – Infantile, Juvenile and adult. We report a case of Adult form of Alexander disease.

CASE REPORT

A 21 year old male came with complaints of progressively increasing difficulty in walking and stiffness of both upper and lower limbs since 2 yrs. On further inquiry he admitted difficulty in swallowing and occasional double vision. Extent of ataxia was such that he had limited much of his mobility and preferred to sit in wheelchair impairing his daily activities. There was no prior major medical or surgical history in past. No history of similar complaints in family. Clinical examination revealed grade III power on bilateral upper and lower limbs and positive Babinski sign .Other clinical examination was unremarkable.

His most of the blood /serological work up was normal.

IMAGING WORKUP: CT Brain (plain and contrast) and MRI BRAIN was done

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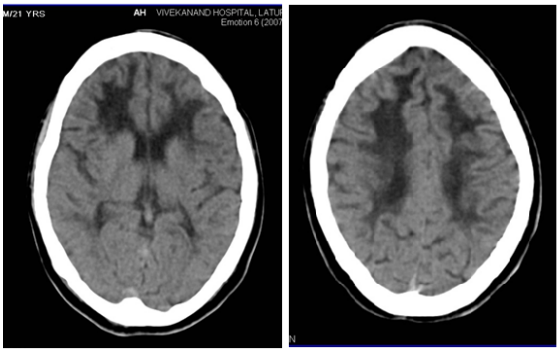

Figure 1

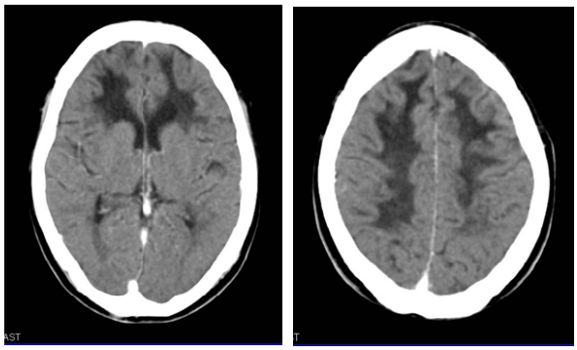

Figure 2

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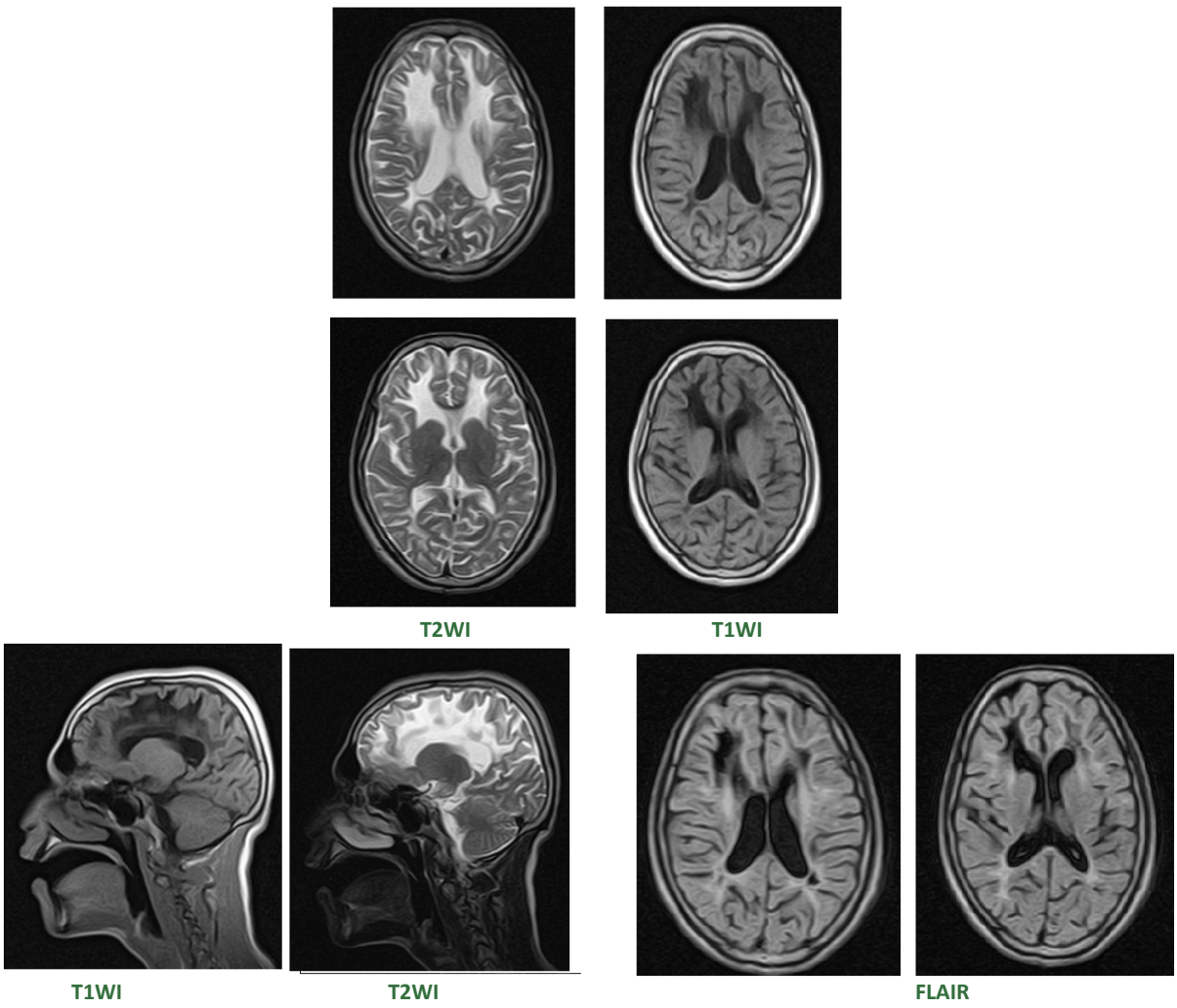

Legend

Figure 1: (NECT brain reveals bilateral symmetric white matter hypodensities)

Figure 2: (CECT brain reveals bilateral symmetric white matter hypodensities –same as that of plain ct)

MRI Brain: symmetrical areas of altered signal intensity involving bilateral frontal lobe white matter extending posteriorly. These ares are hypointense on T1WI and hyperintense on T2WI and FLAIR.MRI also reveled brainstem atrophy.

IMAGING FINDINGS

CECT revealed symmetric white matter hypodensities in frontal lobes that extends posteriorly. These findings were confirmed on MRI BRAIN, it revealed- symmetrical areas of altered signal intensity involving bilateral frontal lobe white matter extending posteriorly. These ares are hypointense on T1WI and hyperintense on T2WI and FLAIR.MRI also reveled brainstem atrophy.

DISCUSSION

Alexander disease (AD) is an infantile leucodystrophy first described in 1949 .It is characterized by macrocephaly, psychomotor regression, spasticity, ataxia and seizures leading to death in a few years . Parents of affected children can be neurologically normal. Alexanders disease is rare non familial metabolic disorder due to heterozygous dominant mutation in GFAP gene which results in accumulation of GFAP aggregates which begins during fetal life. This GFAP – GLIAL FIBRILLARY ACIDIC PROTEIN is expressed only in astrocytes. The striking loss of myelin seen in these patients is due to disrupted astrocyte derived myelination signaling. The brains of infants have markedly increased astrocytic density and are grossly enlarged. *Rosenthal fibers* -eosinophylic inclusions localized in astrocyte cytoplasm, are the pathologic hallmark of the disease and are mainly found in perivascular, periventricular and subpial spaces of cerebral hemispheres, cerebellum and brainstem. In typical infantile cases, MRI shows extensive white matter signal hyperintensities in T_2-weighted images, more marked in the frontal regions; a rim of periventricular T2 hypointensity; involvement of basal ganglia, thalami and brainstem. on contrast study

MRI brain reveals contrast enhancement particularly of periventricular regions and brainstem.

A few sporadic or familial cases of AD with later onset and predominant involvement of brainstem were pathologically diagnosed owing to Rosenthal fiber presence . *GFAP* mutations have been associated with the following: (i) typical infantile AD, with onset before age 2 years and rapid lethal course; (ii) the juvenile form of AD, characterized by onset between age 2 and 12 years, and running a slower course; (iii) adult-onset AD (AOAD), with symptoms beginning during adolescence or later (after age 12), predominant brainstem involvement and survival into adulthood. Patients with AOAD usually present with dysarthria, dysphonia, dysphagia, pyramidal signs and ataxia; palatal myoclonus is common . Their MRI is characterized by atrophy and changes in signal intensity in the medulla oblongata and upper spinal cord, with inconstant supratentorial periventricular white matter abnormalities.

GFAP mutations frequently occur *de novo*, particularly in infantile cases, while in AOAD both sporadic cases with *de novo* mutations and familial cases with autosomal dominant transmission have been described.

IMAGING FEATURES

CT

Hypodensities in frontal deep white matter extending into parietal region and internal capsule. Hypodensity at caudate head. It is one of the few inherited metabolic disorder that enhances after contrast administration. Contrast enhancement seen near tips of frontal horns in early stages.

MRI

MRI brain shows Extensive cerebral white matter altered signal intensities with frontal predominance. Classic finding is Periventricular rim- hyperintense on T2 and hypointense on T1WI.Abnormalities of basal ganglia (caudate head and anterior putamina) and thalami. Another unique finding is enlargement of caudate lobe and fornices which appear swollen and hyperintense. In more severe protracted cases FLAIR images may show areas of cystic encephalomalecia. on contrast study striking enhancement is seen on T1WI. The major differential diagnosis of Alexanders disease are other inherited leucodystrophies with macrocephaly. These primarily include canavan disease and mucopolysaccharidoses.prediliction of Alexanders disease to involve frontal lobes caudate nucleus and enhancement help to distinguish from others.

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