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CHILDHOOD LEUKODYSTROPHY PRESENTING AS SECONDARY BIPOLAR DISORDER

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ABSTRACT

Leukodystrophies are rare dysmyelinating disorders of the nervous system, which occasionally have an initial psychiatric presentation. This report describes a case of a 9-year-old boy whose initial presentation resembled a bipolar disorder but subsequent work-up revealed an underlying leukodystrophy, most likely Alexander's disease. The course of this rare disease along with the implications of making a diagnosis of leukodystrophy in a psychiatric setting is discussed.

Key words : Leukodystrophy, alexander's disease, course, bipolar disorder

A leukodystrophy is a condition in which absence of myelin is primary, i.e., it cannot be explained on the basis of secondary (Wallerian) degeneration (Poser,1996). Leukodystrophies are prototypes of dysmyelinating diseases and include diseases like metachromatic leukodystrophy, adrenoleukodystrophy, Krabbe's disease, Canavan's disease, Pelizaeus - Merzbacher disease and Alexander's disease. Alexander's disease (AD) is the rarest of the leukodystrophies which is pathologically characterized by Rosenthal fibers (also known as hyaline bodies or as fibrinoid degeneration of astrocytes) and pronounced myelin loss (dysmyelination) (Poser,1996). Diagnosis of AD is difficult because of its rarity and variable presentation. We describe the course over four years of a case of probable AD initially presenting as bipolar disorder.

CASE REPORT

Four years ago, a 9-year-old right-handed boy with normal birth and developmental history presented to us with a six months history of urinary incontinence, forgetfulness and a changing pattern of behavioural problems. Incontinence was the first symptom noticed by the parents and was mostly nocturnal. He tended to forget to finish his work at school and home and had difficulty finding his objects. His school teacher complained about his inattention and frequent and prolonged gazing. Moreover, he appeared quieter than usual and preferred solitude. A progressive neglect towards personal hygiene was also observed. His mood was described as sad with intermittent crying spells. Being symptomatic for three months, a consultation sought with a general practitioner saw the patient getting imipramine 25 mg at bedtime. Nocturnal enuresis was the diagnosis at that time.

Although his incontinence did not remit, a dramatic change in patient's behaviour became apparent over the ensuing weeks. He had become more talkative, speaking in a domineering fashion, the content being mostly grandiose. He was also hyperactive, restless and remained unduly cheerful. Interspersed with these were spells of irritability, abusive and assaultive behaviour and impulsivity wherein he would run away from home or would beat other children. Subsequent to this change, he was put on haloperidol, 7.5 mg/day along with a

benzodiazepine for sedation while imipramine was stopped. Having shown no improvement with these medications, he was referred to us.

Examination revealed a distractible, hyperactive and physically unkempt boy who attempted to leave the interview room several times. His neurological examination showed nothing significant other than bilateral hyperreflexia. Cranial nerves were intact, fundus was normal and no cerebellar signs were elicited. No dysarthria, dysphagia or movement disorders were noticed. He did not have macrocephaly. On mental status examination, his attention was poorly sustained, speech was pressured, affect was euphoric with marked lability and thought content revealed grandiose delusions of ability. His inattentiveness and hyperactivity made him neuropsychologically non-testable but grossly his other higher cognitive functions appeared intact. A tentative diagnosis of bipolar disorder was kept and patient was commenced on lithium carbonate, 600 mg/day, and haloperidol, 2.5 mg/day.

After admission, an EEG done under sedation showed generalized high amplitude sharp and slow waves in sleep background with photic stimulation producing a photic convulsive response. Cranial MRI disclosed T_2 weighted images showing bilaterally symmetrical, irregular hyperintense areas involving both the frontal white matter, caudate nucleus, and genu of corpus callosum. Similar signal changes were also noticed in the anterior limbs of the internal capsule, cerebral peduncles, and corticospinal tracts in the pons. These areas appeared hypointense on T_1 weighted images and were not associated with any mass effect. These findings were suggestive of leukodystrophy, most probably early Alexander's disease. The diagnosis was reviewed as bipolar disorder secondary to Alexander's disease (American Psychiatric Association, 1994). Lithium carbonate was stopped and sodium valproate was initiated and hiked to 400 mg/day. Patient was referred for further investigations and management to a neurological centre where he underwent repeat MRI showing similar findings. Urine and blood for arylsulfatase was negative and so was buffy coat for vacuolated lymphocytes. Brain biopsy was planned but was not consented for by patient's parents. A working diagnosis of juvenile onset Alexander's disease was kept and following an episode of complex partial seizures, valproate was hiked to 800 mg/day.

Despite medication patient has had a downhill course. Although his behavioural problems gradually decreased, neurological signs and symptoms became more apparent. Over a span of four years he has had isolated episodes of partial and generalized seizures and has progressively developed aphasia, dysphagia, double incontinence, quadriparesis and diminishing vision. He has bilateral optic atrophy, pyramidal signs and upgoing plantars. Presently he is bed-ridden and takes only liquids. Parents have been counseled regarding the fatal course of the illness.

DISCUSSION

A diagnosis of leukodystrophy has been entertained in the above case considering the typical white matter changes on MRI. Although the final diagnosis in such conditions rests on histopathology, neuroimaging can be utilized for making the generic diagnosis of leukodystrophy (Osborn, 1994). Alexander's disease (AD) is the most probable type of leukodystrophy in this case as evident by its predilection to involve bilateral frontal lobes (Osborn, 1994). Other factors favouring AD are the juvenile onset which is not present in all leukodystrophies, absence of any genetic loading which is peculiar to AD, and clinical features and laboratory studies not typical of any other leukodystrophy (Poser, 1996). Moreover, emergence of bulbar signs as the disease progressed is characteristic of AD (Borrett and Becker, 1985).

The aetiology of AD is not known and the difficulty in its diagnosis arises due to a symptomatology, which varies according to patient's age (Borrett and Becker, 1985). The clinical profile of our patient when viewed

longitudinally encompassed most of the features of a bipolar disorder. Although mania has been described in some forms of leukodystrophies (Cummings and Benson,1992), to our knowledge, neither mania nor bipolar disorder has been associated with AD. Secondary mania is a rare complication of brain lesions with 1/3rd cases having evidence of associated depression (Starkstein et al.,1991). This makes secondary bipolar disorder a still rarer entity. Patients with brain lesions presenting as bipolar disorder show a greater propensity for either subcortical or cortical-subcortical lesions whereas patients with pure mania usually have cortical lesions (Starkstein et al.,1991). This concurs with the MRI findings in our patient that revealed involvement of bilateral frontal lobes and caudate nuclei. The mechanism by which such lesions cause affective disorders and associated urinary incontinence is ascribed to dysfunction of frontal-subcortical circuitry and has been dealt in detail elsewhere (Cummings,1993).

In conclusion, leukodystrophies, including AD need to be kept in mind in the differential diagnosis of mania and bipolar disorder presenting in childhood. In early stages, these may present with subtle neurological signs and symptoms. A prompt neuroimaging in such cases can aid a physician in diagnosing leukodystrophy before going in for invasive procedures like brain biopsy. Moreover, an early diagnosis of leukodystrophy assumes significance in view of its grave prognosis. Inspite of this, a diagnosis of AD offers some consolation for parents of children with this untreatable disease because of its unclear pattern of inheritance (Borrett and Becker,1985).

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