Para/Post Infectious Recovering Encephalitis with Localized Basal Ganglia Involvement

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Neurological dysfunction in children associated with bilateral hypodense lesions of the basal ganglia is seen in disorders like Huntington's chorea, Wilson's disease, Hallervorden Spatz syndrome, Leigh's disease, infantile striatal necrosis, hypoxia, ischemia and various intoxications(l). Goutieres and Aicardi described in 1982 a new neuroradiological syndrome characterized by a rapid clinical onset of striatal symptoms following an infectious illness, associated with similar hypodense basal ganglia lesions, but with a far better outcome than seen with the conditions mentioned above(2). Since then very few cases of this new disorder have been reported(3-6). We describe a series of 10 patients seen by us over the last 3 years who fit into the clinical and imaging features of this syndrome.

Case Reports

The clinical and investigative profile of the cases is summarized in *Table I.* Neuroradiological studies revealed a normal CT in 3, but revealed bilateral low density lesions of the caudate and putamen in 3 *(Fig. 1),* of the gl6bus pallidus in 1, and thalamus and mid brain in one. MRI was done in 7 children, including the 3 with normal CT scans, and showed increased signal intensity on T2 weighted images in the caudate and putamen *(Fig. 2)* in all except one. Involvement was bilateral in 5 and unilateral in one. One child had a CT done at the time of illness which was abnormal and then recovered to such an extent that her MRI after 1 year was totally normal. Two illustrative cases are described below.

Case 1: A 10-year-old male child was referred from another city with a history of febrile illness 1 month earlier, during which he developed alterations in sensorium, became unconscious and developed weakness in all 4 limbs. He slowly improved in consciousness but remained quadriplegic. One month later, when first seen by us, he was fully conscious, had visual fixation and following, and a mask like face. The child was mute and obeyed 1 step commands, albeit after a time lag. Tongue movements were spastic and glabellar tap was positive. He had quadriplegia with lead pipe rigidity, hyperreflexia, clonus, and extensor plantars. Over the next week he regained movements of the left side, but then developed dystonic spasms consisting of retrocollis, opisthotonus, with abnormal posturing of the left sided extremities. These attacks were accompanied by moaning sounds and autonomic disturbances in the form of sweating, hypertension and tachycardia. Normal investigations included complete blood count, ESR, platelet count, blood glucose, liver function tests, electrolytes, cortisol and ceruloplasmin. Plasma lactate was 9.1 (normal: 5.7-22.2 mg/dl). CSF analysis revealed proteins of 50 mg/dl, glucose 60 mg/dl and no cells. CSF IgG was greater than 1.1 IU/ml (nor-

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TABLE I - *Summary of Cases in the Present Series and Comparison with Other Reports*

Parameter	Current study (n=10)	Reported studies(2,4,7) (n=8)
Age [Mean (range)]	7.63 (4mo-14yr)	4 (12 mo-7 yr)
Sex M:F	3:2	5:3
Onset		
Acute	9	8
Subacute	1	0
Preceding infective illness	8 (Epidemic-2)	7
Altered sensorium/Coma	8	8
Tone		
Hypotonia	0	4
Hypertonia	8	3
Normal	2	1
Convulsions	2	5
Behavior changes	7	6
Pseudobulbar palsy	7	4
Motor weakness		
Quadri	4	6
Hemi	3	0
Mono	1	0
Movement disorder		
Tics	3	1
Dystonia	5	4
Hemiballismus/Akathasia	2	0
Akinetic rigid syndrome	5	4
Chorea/A thetosis	3	2
Abnormal CSF	4 (Asep men 3, Tprot 1)	5 (Asep men 4, RBCs 1)
Lactate/Pyruvate	8/8 normal	4/4 normal
Ceruloplasmin	4/4 normal	3/3 normal
Viral studies	3/3 negative	l/4positive-CMV
CT Scan	5/8 abnormal	7/8 abnormal
MRI	*7/7* abnormal	8/8 abnormal
Follow up		
Complete/Good recovery	7	6
Poor recovery	1	1
Died	1	1

Details regarding motor weakness were not available for one case in reported studies.
Asep men-Aseptic meningitis.
The follow up details of one case in the present series are not available.

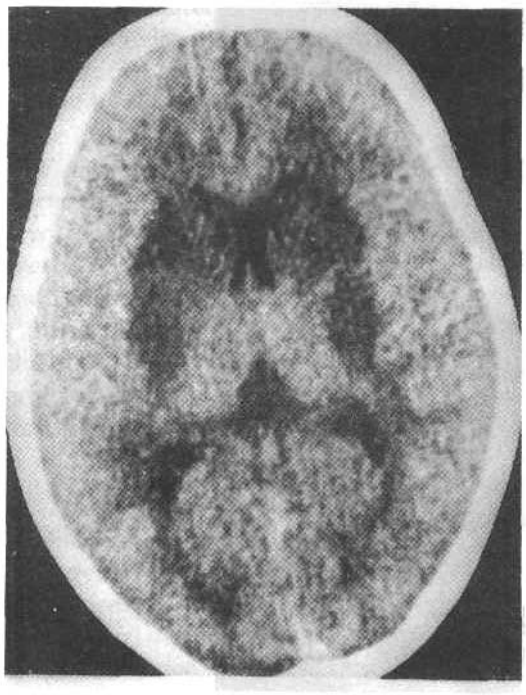

Fig. 1. CT scan showing bilateral low density lesions of the caudate and putamen.

mal upto 0.32 IU/ml). Brain-stem auditory evoked potentials were normal. Tibial somatosensory evoked potentials showed central slowing in somatosensory pathways. Nerve conduction studies were normal. EEG showed diffuse nonspecific slowing. MRI revealed hyperintensity of the caudate and putamen bilaterally. The child was treated with combinations of high dose oral diazepam (upto 100 mg/day), trihexyphenidyl (upto 12 mg/day), baclofen (upto 60 mg/day) and a short trial of pimozide. Pulse therapy of methyl prednisolone was tried. His spasms slowly subsided and he was discharged from the hospital on high doses of diazepam, baclofen and trihexyphenidyl.

Seen 3 months later, he had recovered remarkably, could walk independently with a mild hemiparesis of the right side, with minimal left sided dystonia. Some speech had been regained, though dysarthric. Behavioral disturbances such as hyperactivity, attention deficit and aggression were noted.

Case 2: An 8 year old male was seen with restless leg movements, disturbance of normal sleep, emotional lability, deterioration in writing and motor and vocal tics. The child had suffered an attack of mumps 3 weeks earlier. Four days after the attack, he developed severe headache and altered sensorium for a few days, when he was clinically diagnosed as aseptic meningitis elsewhere, without a lumbar puncture. He also developed stereotypic repititive movements of the hands and face, along with sudden grunts. His sleep cycle had been reversed.

CNS examination revealed normal higher functions except for poor attention span; normal cranial nerves, akathasia, simple and complex motor and vocal tics and a positive glabellar tap. His gait was normal. CSF was normal with an elevated IgG of 0.44 IU/ml. Other normal investigations included serum prolactim and ceruloplasmin. His CT scan revealed bilateral low density lesions in the caudate and putamen. He was treated with pimozide for tics and developed an acute parkinsonian state, which improved on reducing the dose of pimozide and adding trihexyphenidyl. Over the next few weeks his akathasia and tics disappeared, though the mild parkinsonian rigidity persisted. Three months later, he had no movement disorder but did have mild attention deficit hyperactivity disorder. One year later he developed a transient dystonic posturing of the right foot, with stammering, which resolved spontaneously in a few weeks.

Discussion

In the 10 patients described, a more or less stereotypic clinical picture was noted. Most of the children were more than 3

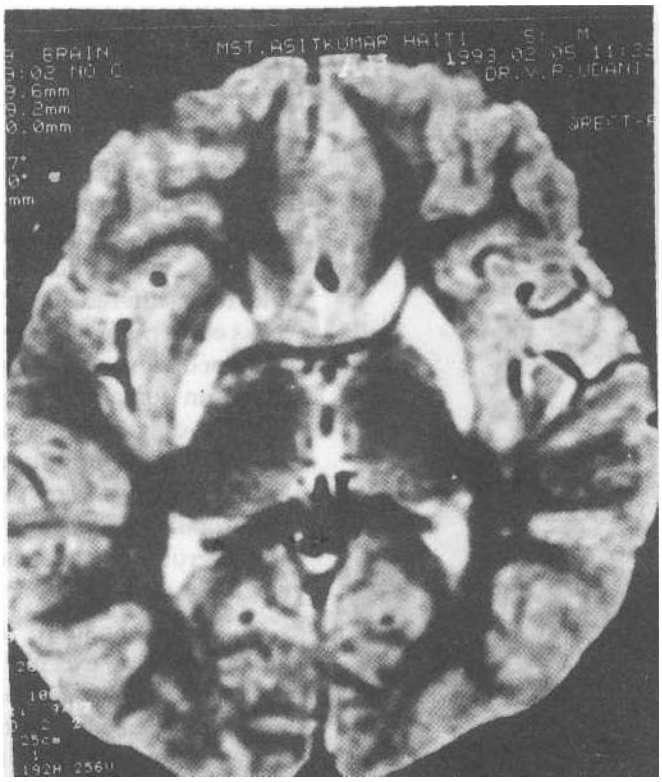

Fig. 2. MRI (T2 weighted image) showing increased signal intensity in caudate and putamen bilaterally.

years of age and had an acute onset of neurologic dysfunction following a febrile illness. The illness was characterized clinically by altered sensorium, supranuclear eranial nerve dysfunction, various types of movement disorders and spastic/rigid weakness. Imaging uniformly showed predominantly striatal lesions and in most cases there was good to complete recovery. Extended follow up in most revealed the illness to be monophasic in nature.

We believe these cases to be examples of post/para infectious "basal ganglia encephalitis" for the following reasons; (*i*) There was a rapid onset of a monophasic neurologic disease; *(ii)* Two of our subjects came as part of a cluster of 5 cases in the last 2 months of 1991, which clinically looked like an epidemic of viral encephalitis. The other 3 had normal MRIs; *(iii)* Measles and mumps were antecedent illnesses in 2 cases; *(iv)* Of the 10 children, 7 demonstrated either aseptic meningitis or elevated CSF IgG indicating that these were CNS inflammatory disorders. Of the remaining 3, two were part of the epidemic (as above), in which CSF can be normal(l). CSF IgG could not be estimated in these 3 cases; and *(v)* Partial or complete recovery was seen in 9/10 of our cases. The one patient who died had extensive white matter involvement similar to that seen in acute disseminated encephalomyelitis (ADEM), along with striatal lesions and elevated CSF IgG. This suggests that basal ganglia encephalitis could be similar to ADEM.

Approximately a dozen probably similar cases exist in literature(2-9), of which the clinical and radiological details were available to us for 8 cases (2-4,7). From *Table I* it is evident that the clinical profile, CSF picture and neuroimaging in these reports was similar to this series except for a few minor differences. Thus, convulsions were more frequent and hypotonia common in the previous cases, whereas our patients mostly had increased tone. Three of the 8 had normal CSF, which was also noted in our series. Three of the previous cases had definite serological evidence of viral/ mycoplasmal infection.

Friede coined a pathological term "infantile bilateral striatal necrosis"(10), which includes two subgroups now believed to be etiologically different from each other, namely, *(i)* familial genetic disorders like Leigh's disease and other mitochondrial cytopathies, and (n) non familial acute cases seen in older children which probably represent acute post infectious basal ganglia encephalitis.

We do not believe that our cases represent Leigh's or other mitochondrial cytopathies because: (*i*) These disorders are not monophasic and show only poor and incomplete recovery, though they may follow acute febrile illnesses; *(ii)* Blood/CSF lactate was normal in all 8 cases where it was done; *(iii)* Brainstem involvement is seen in 98% of cases of Leigh's disease(2), but was documented in only 1 case of ours. The only child in our series with an insidious onset and poor recovery had elevated CSF IgG, suggesting an inflammatory process, and normal lactate values, which went against the diagnosis of Leigh's disease. Necrosis was a prominent feature in the cases cited by Friede, but in two earlier subjects(3,4) as well as in one of our cases, there was complete resolution on subsequent imaging. This strongly suggests that edema is probably the part of the pathology, which subsequently resolves.

Cerebral malaria, which is seen in our country has been associated with basal ganglia lesions (unpublished observations). One of the children had severe associated hypoglycemia, which is common in cerebral malaria. However, this patient did not have fever at any time, repeated smears were negative for malarial parasite, and the child improved without antimalarial therapy. Some workers have seen(ll-13), as we also have (submitted for publication) extra pontine myelinolysis with predominantly basal ganglia involvement. Absence of the usually associated pontine involvement and lack of electrolyte abnormalities were points against this diagnosis. It is of interest to know that the case of Mathieson *et al.(8),* believed by Goutieres and Aicardi(2) to be one of the earliest cases of post infectious basal ganglia disease, had central pontine myelinolysis on autopsy. It is possible that this case may actually have had extra pontine myelinolysis.

In conclusion, we believe that these cases represent an acute post infectious basal ganglia encephalitis, a disorder which is probably immune mediated with good neurological recovery. This separates it from the prognostically poorer familial cases of infantile bilateral striatal necrosis. More cases are probably being identified now with the advent of MRI.

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