ORIGINAL ARTICLE

Assessment Of Neurodevelopmental And Neuroimaging Outcome Of Patients Of Infantile Tremor Syndrome After 6 Months Of Treatment On Follow-Up

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ABSTRACT

BACKGROUND: Of the total 30 patients 16 had tremors and were given drugs and other had prodromal phase. MRI and DASII were done in all the patients after admission. 16 patients were followed and repeat MRI and DASII were done after 6 months. Delayed or regression of milestones were present in most patients (93.3%). Of 30 patients 6 had normal MRI findings on admission. Others had cortical atrophy,ventricular dilatation, increased subarachnoid space,thinning of corpus callosum,subdural effusion, hyperintensity in cortical areas suggestive of demyelination. MRI done after 6 months of treatment in 13 patients who had some abnormal finding on admission, all the patients showed disappearance of earlier findings. Of the 16 patients who had come for follow-up,2 patients achieved normal motor an mental development after 6 months while in other 14 patients, had variable amount of motor and mental delay on follow-up. Probably some degree of neurological damage persisted though radiologically MRI showed disappearance of all the findings in almost all the patients who have suffered from ITS in past.

Keywords: infantile tremor syndrome, MRI, developmental delay.

INTRODUCTION

Infantile tremor syndrome is an obscure entity which is characterized by tetrad of mental & motor changes, pigmentary disturbances of skin & hair, pallor and tremors in subjects around 1 year of age. Different investigations carried out by different researchers failed to prove particular etiology authentically. Hypotheses put forth include nutritional deficiency, viral infection, and degenerative process. Classically the presence of tremors has been attributed to structural and functional alterations of extra pyramidal system due to various causes, like excitatory activity in basal ganglia occurring by means of thalamocortical pathway. Vitamin B12 is one of the micronutrient implicated in the etiology of ITS. Treatment of ITS is aimed at correction of anemia, nutritional deficiency, treatment of infections, control of tremors and good nursing care.

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MATERIALS AND METHODS

The study was conducted in indoor patients of pediatric ward of medical college. Total 30 patients were admitted. Patients were selected on basis of having anemia, pigmentation, delayed milestones, and tremors. A detailed history and physical examination was carried out including complete haemogram investigation. Developmental quotient of the patient was scored on the basis of DASII test. DASII was done by experts at KGP hospital and the scores were noted. The test was repeated after 6 months for comparative study.MRI was done on admission and after 6 months on follow up .This was be done at neuroimaging centre affliated with the hospital. The reporting of the MRI was done by expert radiologist.

RESULTS

The study comprised of 30 patients of infantile tremor syndrome as well as pre ITS. MRI and DASII were done in all the patients after admission. 16 patients were followed and repeat MRI and DASII were done after 6 months. Most of the patients in our study were in age group of 5-12 months with equal male and female ratio.Incidence of ITS was high in Hindu

families. Out of 30 patients 22 were exclusively breast fed while other 8 were started with improper complementary feeds at the age 9-12 months with some water or cow milk not fortified with vitamin supplements. The most frequent presenting complaint in this study is respiratory tract infection (cough and cold or pneumonia), next was acute gastroenteritis. Delayed or regression of milestones were present in most patients (93.3%). Pallor of various degrees was observed in 25 patients (83.3%) of the patients.Pigmentary changes were seen in 90% of patients with 43.33%having knuckle pigmentation, 13.3% having reticular thigh changes, while 33.33%have both knuckle as well as reticular pigmentation.Hair changes were seen in 86.6 %(26/30), isolated sparse hair were present in 20% while hypopigmented hair were present in 10% both sparse and hypopigmented hair were present in 56.67% patients.Vacant facial expression were seen 76.67% of patients, while 86.67% of patients lost interest in surroundings. Drooling of saliva was present in 53.3 %of cases.Tremors were present in 16/30 (53.33%) of patients. Which varied in the form of some having generalised, focal involving hands only or some having perioral as well as tongue tremors.Chubby look was present in 43.33% while 33.33% of patients had wasted look and 23.33% had normal baby look.

40% of patients had haemoglobin level <= 5 and 17 of 30 (56.67%) children required blood transfusion with 2 patients requiring transfusion twice during the course of hospitalization. Most patients of ITS have significant pallor. Commonest peripheral smear picture is not yet clear, equal evidence for normochromic normocytic, microscopic microcytic as well as for macrocytic. Thrombocytopenia and leucopenia is present when changes of macrocytic or megaloblastic anemia are present. In this study most of the patients (93.3%) had some degree of protein energy malnutrition, with maximum having grade II. After initiating the treatment tremors usually disappear by average of 7 days; as most of our patients also had protein energy malnutrition weight monitoring was done and discharged by 2nd or 3rd week of admission. MRI done in patients maximum of 32 % has cotical atrophy(32%) followed by ventricular dilatation(21%) ; thinning of corpus callosum in 19%; subdural effusion seen in 9% and increased subarachnoid space seen in 2%; 4% cases showing miscellaneous findings such as hypenintensity seen in cortical areas which may suggest demyelinating changes. However 13% of the patients showed normal MRI. MRI was done after 6 months of treatment in 13 patients who had some abnormal finding on admission. All the patients showed disappearance of earlier finding. It was remarkable that all the patients who earlier had abnormal findings on MRI scan showed complete recovery on follow-up MRI scan. There was not a single MRI scan finding on follow up.

Patient no	MRI findings on admission	MRI findings on follow up
1	Mild diffuse dilatation of bilateral sulci, ventricles & cisterns	Normal
2	Prominence of subarachnoid spaces along bilateral fronto temporal lobe , corpus callosum is thinned out, mild restricteddiffusion of both hippocampi and both para hippocampal gyrus	Normal
3	Mild diffuse dilatation of bilateral cerebral sulci, ventricles and cisterns, possibility of aatrophic changes is likely	Normal
4	Mild prominence of sulci and CSF spaces along bilateral fronto temporal region , thinning of corpus callosum with relative sparing of splenium	Normal
5	Subtle poorly defined abnormal signal intensity in bilateral periventriculaar and subcortical white	Normal

	matter of both cerebral hemispheres, mild diffuse prominence of ventricles, cerebral sulci &cisterns	
6	Mild prominence of ventricles, bilateral cerebral sulci and cisterns	Normal
7	Dilatation of extraaxial CSF spaces and sulci along bilateralfronto temporal lobes , mild thinning of corpus callosum	Normal
8	Dilatation of extra axial spaces along bifronto parietal region , thinning of corpus callosum	Normal
9	Mild dilatation of subarchnoid spaces along bilateral fronto-temporo-parietal lobes and ventricles, mild thinning of anterior part of corpus callosum,mild decrease in volume of midbrain and pons.	Normal
10	Bilateral subdural collections with few hemorrhagic foci along right frontal and left fronto parietal lobes extending into interhemispheric pressures	Normal
11	Dilatation of ventricles, sulci and gyri are prominent, thinning of corpus callosum	Normal
12	Subdural collection of protein rich fluid in fonto temporal regions	Normal
13	Dilatation of cerebral and cerebellar sulci &cisterns s/o atrophic changes	Normal

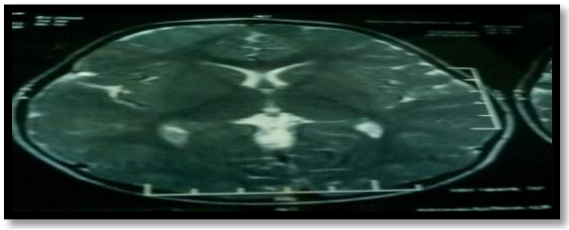
Of the 16 patients who had come for follow-up,2 patients achieved normal motor an mental development after 6 months while in other 14 patients, had variable amount of motor and mental delay on follow-up. Probably some degree of neurological damage persisted though radiologically MRI showed disappearance of all the findings in almost all the patients who have suffered from ITS in past.

Developmental score of all the patients by DASII on discharge and follow-up.

Table 8 - Development Assemssment Of All Patients By Abridged Dasii On Discharge And At The Time Of Follow Up (N=30)

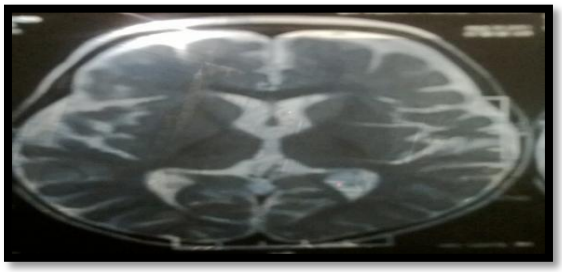
SR. NO.	Motor quotient at 50% pass level		Mental quotient at 50%pass level	
	Initially	On Follow-up	Initially	On Follow-up
N1	40	74	45	78
N2	26	55	32	60
N3	42	85	48	78
N4	47	76	52	80
N5	52	88	50	80
N6	32	74	34	78
N7	38	70	46	75
N9	36	66	48	64
N12	28	56	32	58
N13	28	56	34	54
N14	40	78	48	84
N16	48	84	46	88
N17	30	74	42	78
N23	48	72	52	78
N25	48	74	44	70
N30	28	58	32	62
Mean (Average)	38	71	43	73

Patient No:1



Here the MRI on the left side shows ventricular dilatation and increased subarachnoid space which becomes normalized after 6 months.

Patient No.2



MRI of the patient showing cortical atrophy and ventricular dilatation which disappeared after 6 months.

DISCUSSION: In this study most of the patients (93.3%) had some degree of protein energy malnutrition, with maximum having grade II. Though child with ITS are commonly described in literature as chubby but most of our patients had protein energy malnutrition along with other micronutrient

deficiencies. This is as the result of poor environmental factors leading to deficiency of all the factors leading to protein energy malnutrition as well as micronutrient deficiencies. Most of the Hindu families, of lower socioeconomic status in rural areas of are vegetarian. Vegetarian diet is a poor source of vitamin B12. So a mother of vitamin B12 deficiency has breast milk which is deficient in vitamin B12. Supplementation of vitamin B12 remains the treatment of choice. As persisting neurodisability is of great concern so it should be primarily be prevented rather than cured. For this results supplementing mother with vitaminB12 during pregnancy or fortifying complementary feeds with vitamin B12 should be done. Taking an inference from the available recent studies vitamin B12 seems to be the etiological factor in ITS. Though earlier data opposed this theory but vitamin B12 deficiency recorded in most patients of ITS, infants with vitamin B12 deficiency showing neuroregression and feature similar to ITS and the fact that vitamin B12 is involved in evolution of DNA and myelinating changes, the dispute on etiological factor can be resolved in favour of vitamin B12**.** In infants, vitamin B12 deficiency has been associated with demyelination and brain atrophy. Therefore, retardation of myelination of the brain in infancy leads to delayed acquisition of cognitive skills, and brain atrophy leads to regression of these skills. Neuroimaging findings in patients of ITS, most of the patients have shown some abnormalities, while normal MRI/ CT has also been reported. The most common finding in all the studies are correlating with cortical atrophy. With some reports specifically pointing on demyelinating changes.Whether cortical atrophy present in this patients are due to decreased number of neurons or due to demyelination occurring is yet to be found out, however MRI findings of demyelinating changes in ITS direct us more in favor of demyelination. Although neurological injury is thought to be classically described as irreversible, patients of stroke and other injuries usually has recovery with gliosis or porencephalic cyst, patients of ITS shows complete recovery. The cortical atrophy present earlier heal or recover without scarring. Patients of ITS have persisting neurodisability in the form that their IQ are on lower side when compared to the patients of the same age, while some may achieve normal development some months after treatment. The degree of improvement may be related to the time of presentation. It was observed that patient when treated at early stage of disease or at younger age group show greater improvement in development and less chances of persisting neurodisability. Probably as the brain is still a developing organ and myelination continues. till 2 years of age early intervention leads to less damage to the brain and so less chances of neurodisability.Probably some degree of neurological damage persisted though radiologically MRI showed disappearance of all the findings in almost all the patients who have suffered from ITS in past. It is not easy to establish whether the reported persistence of residual developmental delay is on account of permanent & irreversible damage of acute insult or because of persistant influence of nutritional, socioeconomic and environmental factors that the child continues to be exposed to. Our finding of near complete resolution of MRI findings of cortical atrophy, ventricular dilatation, demyelination, increased subarachnoid space, etc would suggest possibility to near complete reversibility of the neurological abnormalities and support recommendation of vigorous attempts for rehabilitation of the patient.

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