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Atypical early presentation of subacute sclerosing panencephalitis in children: A case series

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ABSTRACT

Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative disease of children and young adults that may occur as an uncommon complication 7–10 years after a measles infection. In measles – endemic countries like India, the incidence of this fatal disease is high and more number of new cases are detected in recent times. In this case series, we have presented three cases of SSPE between the 4 and 5 years age group, presented with abnormal movement and neuroregression and diagnosed by characteristic clinical features, raised anti-measles antibody titer in CSF, and typical Electroencephalography findings. All of them had a history of measles infection before the vaccination and very short latency period between measles infection and the development of SSPE. They were discharged in stable condition after the treatment with oral Isoprinosine and intrathecal Interferon alfa 2b. Early age of presentation, short latency period, and apparently good response to treatment for the time being prompted us to present these cases.

Key words: Children; Measles; Subacute sclerosing panencephalitis

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INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a slowly progressive degenerative disease of the central nervous system due to persistence of defective measles virus in the CNS after a previous measles infection. The latent period between measles infection and SSPE is normally 7–10 years. SSPE is characterized by progressive cognitive decline, myoclonic jerk, raised anti-measles antibody titer in the cerebrospinal fluid (CSF), and typical electroencephalography (EEG) findings of generalized and synchronous bursts of sharp–slow wave complexes.[1,2] The disease has a gradual downhill course, leading to death in most cases within 1–3 years of diagnosis. Here, we have presented three cases with this deadly disease that have presented with a very short latency period.

CASE REPORTS

Case 1

A 5-year-old boy was admitted with chief complaints of abnormal jerky movements of all four limbs and recurrent falls during walking for the past 7 days associated with low-grade fever. There was no associated abnormality in speech, loss of consciousness, or any history of similar episodes in the past. The child has history of fever with exanthematous rash at age of 8 months. Positive clinical findings were power 4/5 in all limbs, occasional myoclonic jerks of four limbs, and recurrent flexor movements during walking with support. Injection Valproate and tablet Clonazepam were started. MRI brain was normal. CSF shows normal cell count and protein with CSF/serum measles-specific IgG quotient positive. His EEG showed bursts of spikes and sharp waves followed by

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suppression pattern with interburst interval of 2–5 s. The child was diagnosed as a case SSPE and started on oral tablet Isoprinosine (Inosine pranobex). He was discharged in a stable condition.

Case 2

A 5-year-old boy was admitted with chief complaints of multiple episodes of convulsions associated with low-grade fever and vomiting for 1 day. He was well up to the age of 2.5 years since then had multiple episodes of convulsions and gradual neuroregression. At present, the child is bedridden, unable to talk, and has continuous choreiform movement. He had a history of fever with exanthematous rash at age of 6 months. On examination, his power was 2/5 in all limbs. Treatment was started with injection Valproate, Levetiracetam, oral Trihexyphenidyl, and Clonazepam but choreiform movements were not controlled. His MRI brain showed diffuse brain atrophy. CSF study showed normal cell count and protein, CSF/serum measles specific IgG quotient positive. His EEG showed paroxysmal high voltage generalized burst of slow wave discharges. He was diagnosed as a case of SSPE and started oral Isoprinosine. He was discharged in a stable condition with control of choreiform movements and seizures. He was readmitted and was given intrathecal Interferon alfa 2b and discharged in a stable condition with almost complete control of choreiform movements.

Table 1: History and clinical presentation of three cases

Features	Case 1	Case 2	Case 3
Age	5 year	5 year	4 year
Sex	Male	Male	Male
Myoclonic Jerks	+	-	+
Recurrent fall during walking	+	-	+
Fever	+	+	-
Convulsion	-	+	-
Choreiform movements	-	+	-
Unable to walk and talk	-	+	-
Birth history	Uneventful	Uneventful	Uneventful
Immunization history	Immunized till date	Immunized till date	Immunized till date
History of fever with exanthematous rash	At 8 months	At 6 months	At 31 days

Table 2: Important clinical findings

Features	Case 1	Case 2	Case 3
Motor system	No muscle atrophy	Muscle atrophy	No Muscle atrophy
Muscle power	4/5 in all 4 limbs	2/5 in all 4 limbs	4/5 in all 4 limbs
Muscle tone	Normal	Increased	Normal
Deep reflex and cranial nerves	Normal	Normal	Normal
Planter response	Normal	Extensor (B/L)	Normal
Sensory and autonomic system	Normal	Normal	Normal
Cerebellar system	Normal	Normal	Normal
Meningeal sign	Absent	Absent	Absent

Table 3: Relevent investigations

Investigation	Case 1	Case 2	Case 3
HB/TLC/Platelet	11.5/11500/4,60,000	12.8/7300/296000	11.4/9800/396000
SGPT/SG0T/ALP	40/36/190	37/39/156	12/37/269
Urea/Creatinine	21/0.7	21/0.6	27/0.9
Na/k	140/4.2	136/3.5	139/4
CSF: Cell count/protein/sugar	05/34/51	<05/43/70	<05/41/60
Serum total IgG	1595 mg/dL	2248 mg/dL	1534 mg/dL
CSF total IgG	4.52 mg/dL	2.95 mg/dL	7.53 mg/dL
Serum IgG measles**	17563 U/mL	78 U/mL	7446.5 U/mL
CSF IgG measles**	16428.4 U/mL	97.2 U/mL	6952 U/mL
CSF/Serum quotient reference**	4.25, positive	5.08, positive	4.64, positive
MRI brain	Normal study	Diffuse brain atrophy	Normal study
EEG	Bursts suppression pattern	Interictal discharges of generalized seizure.	Stereotypical periodic discharges

Interpretation: **Measles specific IgG in serum (dilution 1:404) & CSF (dilution 1:2) is tested using measles specific IgG ELISA kit having higher sensitivity (measuring range 5–100 U/mL) for which there are no established reference ranges. The results reported are further to be multiplied by the dilution factor as mentioned above followed by calculation of CSF/Serum Measles specific IgG quotient (Q IgG Measles specific). CSFQ ref Normal: <1.3 CSFQ ref Equivocal: 1.3–1.5 CSFQ ref Positive: >1.5**. Serum total IgG reference value: 700–1600, CSF total IgG reference value: 0–3.4

Table 4: Treatment of three cases

Drugs	Case 1	Case 2	Case 3
Tab. Isoprinosine (Inosine pranobex)	Yes	Yes	Yes
Intrathecal interferon Alfa 2b	No	Yes (6 million unit weekly)	No
Supportive treatment:	Yes	Yes	Yes
Sodium Valproate	Yes	Yes	Yes
Levetiracetam	No	Yes	No
Clonazepam	Yes	Yes	Yes
Trihexyphenidyl	No	Yes	No

Case 3

A 4-year-old boy was admitted with chief complaints of frequent fall during walking, jerky movements of neck and body, and drooling of saliva since the past 10 days not associated with convulsions, loss of consciousness, or fever. Jerky movements are gradually increasing in frequency. The child had a history of fever with exanthematous rash at age of 31 days. Power in all four limbs 4/5, recurrent flexor movements during walking, and myoclonic jerks. His MRI brain was normal, EEG showed stereotypical periodic discharges, CSF study showed normal cell count and protein, and SF/serum measles specific IgG quotient positive. Hence, a diagnosis of SSPE was made and patient was discharged with tab. Isoprinosine, Valproate, and clonazepam in a stable condition. Presentations of the three cases have been summarized in Tables 1-4.

DISCUSSION

SSPE is a chronic complication of measles which appears to result from persistent infection with an altered measles virus that remain dormant in the CNS for several years. After 7–10 years, the virus regains its virulence and attacks cell in CNS. Either defective measles virus or defective or immature immune system may be responsible for the lack of clearance of the virus from the body. SSPE has four stages: Stage (1): Poor scholastic performance, irritability, temper outbursts, Stage (2): Myoclonus with intact consciousness, Stage (3): Choreoathetosis, dystonia, lead pipe rigidity, and dementia, stupor then coma, Stage (4): Loss of critical centers of brain controlling breathing, heart rate, and blood pressure with impending death. Diagnosis is done by compatible clinical course and at least one of the following findings: (1). Measles antibody detected in CSF, (2). characteristic electroencephalographic finding of suppression burst pattern, (3). typical histological findings in and/or isolation of virus or viral antigen from brain tissue obtained by biopsy or postmortem examination.[3,4] Management of SSPE is mainly supportive. Clinical trials using Isoprinosine with or without Interferon suggest significant benefit.[5] Most of the patients with SSPE have a history of primary measles infection at an early age with 50% below 2 years and the latent period between measles infection and SSPE is around 6–8 years.[6] However, in our case series, all the child had latent period between 2 and 4 years which was much lower than expected.[7] Early onset SSPE with short latency is generally associated with congenital and neonatal measles infection which is present in our third case.[8-10] It is seen that earlier the age of measles infection, shorter will be the latency for the development of SSPE. In our cases, measles infection occurred at 1, 6, and 8 months of age of the baby which is before his first scheduled measles vaccination at 9 months. Although they all have been vaccinated with measles at scheduled date but still developed SSPE due to previous measles infection before vaccination. Hence, an early measles vaccination around 6 months of age in measles-endemic countries like India may be an option to prevent this deadly disease.

CONCLUSION

This case series shows that firstly a fatal disease like SSPE is occurring with a very short latency period from primary measles infection in contrary to the previous belief and secondly in babies who got measles even before getting the chance of first dose measles vaccination. Hence, eradication or elimination of measles through extensive vaccination coverage is the only way to save our children from this deadly disease.

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