Subacute sclerosing panencephalitis presenting as rapidly progressive young-onset dementia

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Abstract

Onset of dementia before 65 years of age is termed as young-onset dementia (YOD). Very little literature exists regarding the clinical features and diagnoses of dementia in younger individuals. We present a case series of four patients of age 10 to 23 years with severe dementia within 18 months of clinical onset (rapidly progressive dementia). Three patients had generalised periodic complexes typical of subacute sclerosing panencephalitis (SSPE) on electroencephalogram (EEG). All patients had elevated cerebrospinal fluid (CSF) IgG measles antibodies. Our case series highlights that SSPE is an important cause of rapidly progressive YOD in developing countries like India.

Keywords: Young-onset dementia, Subacute sclerosing panencephalitis, Electroencephalogram.

Introduction

Subacute sclerosing panencephalitis (SSPE) is caused by a mutated measles virus and is characterised by cognitive deterioration, motor decline and myoclonus.[1] The onset is between 5 and 15 years of age with a progressive downhill course leading to death within two to four years. Though the incidence of SSPE has declined substantially after the introduction of an effective measles vaccine, the annual incidence of SSPE is still quite high but variable in developing countries.[2] Rapidly progressive global cognitive decline leading to severe dementia or death is a frequent presentation of SSPE. Severe dementia or death within 18 months of clinical onset is termed rapidly progressive dementia.[3] We present a profile of four patients of SSPE presenting as rapidly progressive young-onset dementia (RP-YOD). SSPE is an important cause of RP-YOD in developing countries as opposed to other causes seen in the developed countries.

Case-1

A 23-year-old carpenter presented with progressive cognitive decline for the preceding two years, change in personality since one year, disinhibited behaviour since six months and getting lost in familiar surroundings since three months. The patient was in his usual state of health two years ago when his relatives noticed that he had become apathetic, did not interact with relatives and had become inattentive. He was not able to calculate money and render appropriate change. He could not use tools and, hence, was not able to work and had given up his job. There were episodes when he would come out of the bathroom without clothes. Before presenting, he was not able to reach his home and was found wandering in the market. There was no history of forgetfulness, language disturbances, delusions, hallucinations, myoclonic jerks,

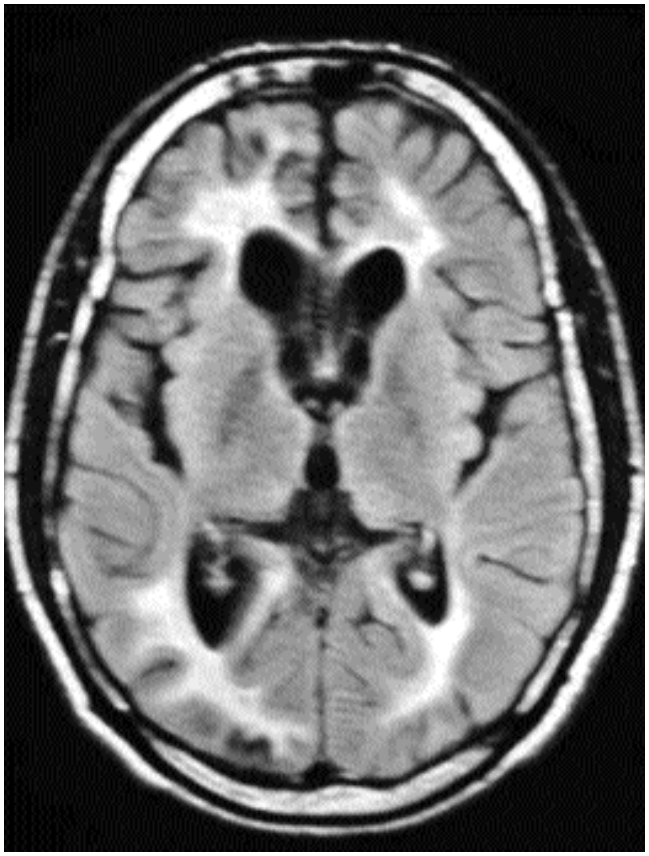

Figure-1: Flair axial magnetic resonance imaging of Case-1 showing confluent symmetrical white mater hyperintensity in bilateral periventricular region reaching up to the subcortical regions. It appears equally predominant in the anterior as well as posterior regions. The ventricles appear a little prominent.

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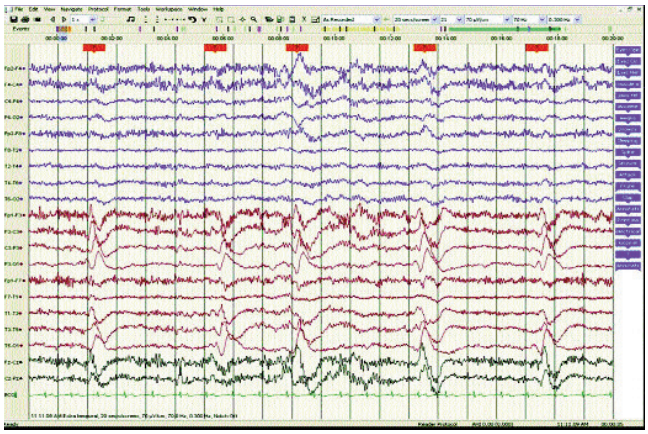

Figure-2: Electroencephalogram of Case-1 showing periodic lateralised epileptiform discharges from the left temporo-parietal region.

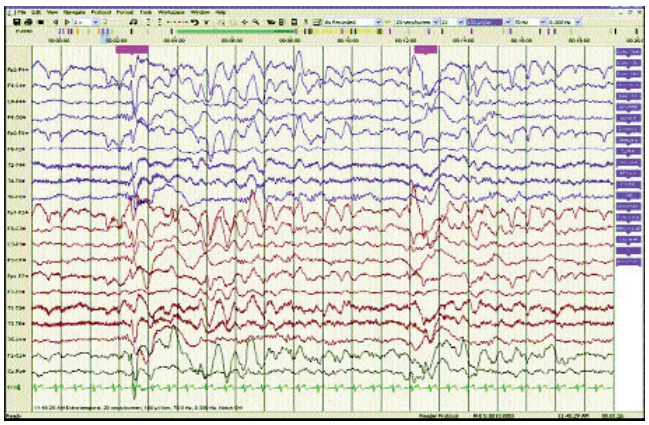

Figure-3: Electroencephalogram of Case-2 showing periodic complexes of slow waves intermixed with sharp waves every 10 seconds.

fever, headache, vomiting or head injury. There was no family history of similar complaints. He had measles at four years of age and had not received any vaccination.

His general physical examination was unremarkable. Higher mental function (HMF) examination revealed poor attention, impaired abstract thinking and judgment. Mini-mental status examination (MMSE) score was 16/30 (lost six points in orientation, five in calculations, and one point each in reading, writing and construction). Frontal assessment battery (FAB) score was 8/18 (lost three points each in similarities and lexical fluency, one point each in motor programming and conflicting instructions, and two points in go-no go test). He had difficulty in clock drawing. There was ideational and ideomotor apraxia. He had alexia, agraphia, acalculia but no finger agnosia, prosopagnosia, or visual agnosias. Cranial nerve examination revealed right hemianopia. Rest of the neurologic examination was normal. Magnetic resonance imaging (MRI) of the brain revealed symmetric T2 and Flair hyper-intense areas in the bilateral frontal and parieto-occipital white matter (Figure-1). Electroencephalogram (EEG) showed periodic lateralised epileptiform discharges (PLEDs) from the left temporo-parietal region (Figure-2). Cerebrospinal fluid (CSF) IgG measles antibody was 4.350 IU /ml (N < 0.08).

Case-2

A 14-year-old student presented with deteriorating school performance for three months, and aggressive behaviour and getting lost in familiar environment since one month. The patient was apparently normal three months earlier when the teachers noticed deteriorating scholastic performance. He could not do arithmetic calculations, and was not able to answer simple questions. He was not able to grasp lessons taught in the class. Once he had lost way while going to school. His friends complained that he had become aggressive and would quarrel on petty issues. He used to forget where his books were kept and had difficulty in passing on the messages told to him. There was no history of language disturbances, delusions, hallucinations, myoclonic jerks, fever, headache, vomiting or head injury. There was no family history of similar complaints. He had received measles immunisation and did not have measles.

HMF examination revealed poor attention, impaired abstract thinking and judgement. MMSE score was 14/30 (lost seven points in orientation, four points in calculation, three points in recall, and one point each in construction and writing). FAB score was 3/18 (lost three points each in similarities, lexical fluency, motor programming, conflicting instructions & go-no go test). Rest of the neurological examination was normal. EEG showed periodic discharges of slow waves intermixed with sharp waves of 1-2 seconds' duration every 10 seconds without clinical myoclonus (Figure-3). MRI of the brain was normal. CSF IgG measles antibody was 4.88 IU /ml.

Case-3

An 18-year-old girl presented with apathetic behaviour for six months, disinhibited behaviour and myoclonus since three months. She was apparently normal six months earlier when it was noticed that she had become less interested in going to work and in doing household chores. She was apathetic, less talkative and less interactive with family members. Three months later, she developed sudden jerky movements of hands with objects dropping, and sudden turning of the head occurring at regular intervals several times a minute. Subsequently, she developed disinhibited behaviour and inappropriate micturition. There was no family history of

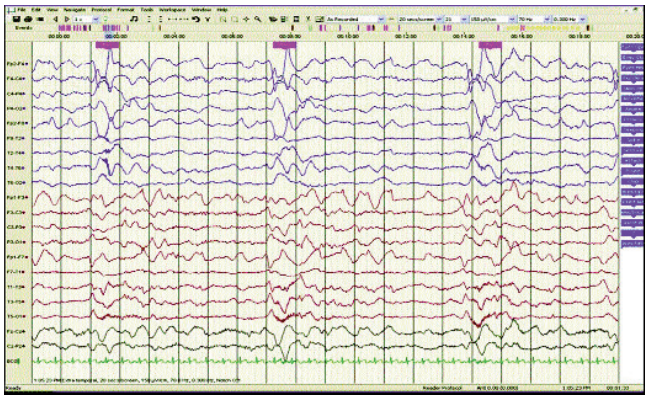

Figure-4: Electroencephalogram of Case-3 showing periodic complexes of slow waves intermixed with sharp waves every 6 to 7 seconds.

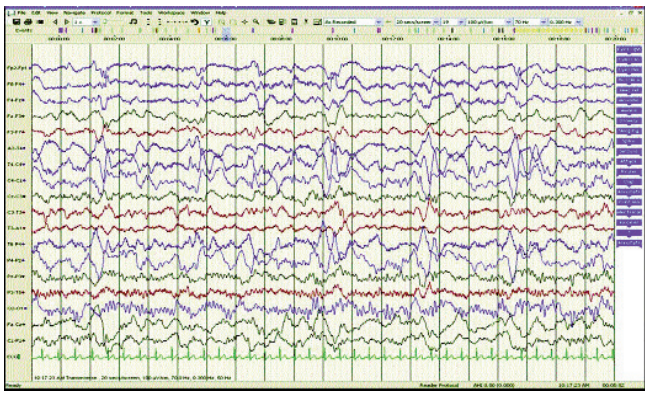

Figure-5: Electroencephalogram of Case-4 showing periodic complexes of slow waves intermixed with sharp waves every 3 seconds.

similar complaints. There was no history of forgetfulness, language disturbances, delusions, hallucinations, fever, headache, vomiting or head injury. She had measles at the age of two, and had not received any vaccination.

HMF examination revealed poor attention span, impaired judgement and abstract thinking. MMSE score was 8/30 (lost nine points in orientation, three points in recall, five points in calculation, one point each in reading, writing and construction, and two points in three-stage command). FAB score was 2/18 (lost three points each in similarities, lexical fluency, motor programming, conflicting instructions go-no go and one point in prehension behaviour). Other detailed lobar functions could not be performed due to poor attention span. Rest of the neurological examination was normal. She had myoclonus time locked with EEG paroxysms of periodic complexes of slow waves intermixed with sharp waves every 5 seconds (Figure-4). MRI brain showed T2 hyperintensities in bilateral frontal and fronto-parietal cortical and subcortical regions. CSF IgG measles antibodies were 4.693 IU/ml.

Case-4

A 10-year-old boy presented with deteriorating school performance for eight months, apathetic behaviour, muttering to self, getting lost in familiar environment and myoclonus since the preceding six months. He was apparently normal eight months earlier, when it was noticed that his school performance had deteriorated and he could not answer simple mathematics which he was able to do so earlier. The teachers also complained that he was less attentive. Over the next two months, he became less interested in going to school and used to get lost while going to school. He became apathetic, used to remain aloof and was found muttering to self. There was no history of language disturbances, delusions, hallucinations, fever, headache, vomiting or head injury. There was no family history of similar complaints. He had measles at the age of two, and had not received any vaccination.

On examination, attention and comprehension were severely impaired for detailed HMF testing and MMSE. FAB score was 2/18 (lost three points each in similarities, lexical fluency, motor programming, conflicting instructions, go-no go and one point in prehension behaviour). There were bilateral pyramidal signs on motor examination. Rest of the neurological examination was normal. He had myoclonus time locked with EEG paroxysms of slow waves intermixed with sharp waves every 3.5 to 4 seconds. On MRI brain, there were T2 hyperintensities in the right temporo-occipital and right posterior parietal regions. CSF IgG measles antibodies were 4.909 IU/ml.

Discussion

All the patients had rapidly progressive cognitive decline with predominant frontal lobe dysfunction. Case 1 presented with cognitive decline interfering with his work; cases 2 and 4 had deteriorating school performance; and case 3 had initial apathetic behaviour followed by disinhibited behaviour. All patients had an RP-YOD with onset between 10 to 23 years of age (mean age 16.25±5.56 years). There was no family history of similar complaints. Three of the four patients (75%) had history of measles and only one (25%) patient had received immunisation. Three (75%) patients had EEG with generalised periodic complexes of slow waves intermixed with sharp waves every 3 to 10 seconds characteristic of SSPE. Case one had PLEDs, which are not specific to SSPE. Periodic complexes in SSPE may be grossly asymmetrical and resemble PLEDs in some montages. All patients had elevated CSF IgG measles antibodies.

Conventionally, dementia with onset before 65 years of age is regarded as young-onset dementia (YOD).[4] Very little literature exists regarding the clinical features and diagnoses in younger individuals experiencing rapidly progressive dementia, primarily due to the rarity of the presentation. In a study of RP-YOD by Kelley et al, the age of onset and presentation of dementia was after 20 years of age.[3] There was no case of SSPE in their study. In another study of YOD with onset between 17-45 years Kelley et al found that the cause of dementia varied with age with inborn errors of metabolism being more common before age 30 years, and neurodegenerative aetiologies being more common after age 35.[5] In their study, the aetiology of YOD was neurodegenerative in 31.1%, autoimmune or inflammatory in 21.3%, metabolic in 10.6%, unknown in 18.7% and infectious in 4.7%. Prion disease,[6] human immunodeficiency virus (HIV) dementia,[3] progressive multifocal leukoencephalopathy[2] were the various infectious aetiologies.[5] They did not have any case of SSPE as a cause of YOD. Our case series highlights that SSPE is an important cause of YOD, especially RP-YOD, in developing countries like India.

The existence of the SSPE in high number in India could be multifactorial — improper vaccine coverage, failure of cold chain maintenance or circulating atypical measles virus strain can be the causes.[6] It is notable that only one patient in this series had received immunisation.

Conclusion

In developing countries, RP-YOD should alert one for the possibility of SSPE. Non-immunisation is an important factor for the existence of SSPE in developing countries.

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