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Tonic seizures in subacute sclerosing panencephalitis: a video-illustration of two cases

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ABSTRACT – Subacute sclerosing panencephalitis is a progressive disorder which also presents with various types of seizures, mainly myoclonic jerks, atonic attacks and tonic-clonic seizures. We report two cases, documented by video-EEG that during the course of the disease also presented with tonic seizures. The differential diagnosis of non-epileptic paroxysmal events might prove to be a problem.
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Key words: subacute sclerosing panencephalitis, tonic seizures, SSPE, myoclonus, measles

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Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative and inflammatory disease of the central nervous system caused by a persistent measles virus infection occurring mostly in early childhood. The disease has an incubation period of several years. The majority of patients with SSPE exhibit neurological deterioration, which usually proceeds from psycho-behavioural disturbances, myoclonus, long-tract signs, epileptic seizures, autonomic failure, dementia and mutism, to coma and death (Kubota *et al.* 2003). Recognition of the disease is not difficult when axial myoclonia leading to falls and periodic complexes in the electroencephalogram (EEG) appear, during clinical stage II (Jabbour *et al.* 1969; see discussion below). A diagnostic difficulty, however, may exist during the initial stage when such signs are minimal or absent, or when there are atypical features. Tonic seizures during the course of SSPE have not been reported before, apart from a single case with tonic posturing of upper limbs during a myoclonic seizure (Parthiv and Amal 2003). A video-EEG demonstration of seizures, with predominantly tonic components in two patients with SSPE, is presented.

Case study

Case 1

A 10-year-old boy was admitted to our department because of seizures. He

was the 2nd child of a non-consanguineous marriage, born at term following an uncomplicated pregnancy and delivery. His medical history was unremarkable, except for measles at 6 months of age. The family history was negative for neurological disorders. The patient had been healthy until two months before hospitalization, when head drops started, followed by drop attacks and global myoclonic jerks, rapidly increasing in frequency to several times a day. He was given valproic acid. Despite treatment, the myoclonia particularly, became more abundant, and, additional levetiracetam and topiramate proved to be of no benefit. Slurred speech and some regression in behaviour were apparent by the second month from onset. At the time of admission, the patient was reported to be suffering from tonic attacks, in addition to the previous types of seizure. Neurological examination revealed mild psychomotor retardation and generalized spasticity, with increased deep-tendon reflexes. Inspection disclosed repetitive myoclonic jerks reminiscent of SSPE. EEGs of the patient while awake and during sleep also revealed findings suggestive of SSPE. Cerebral magnetic resonance imaging (MRI) was normal. The IgG antibody titres against measles were positive in blood and CSF. All other biochemical and microbiological investigations revealed negative results. Diagnosis of SSPE was determined on the basis of clinical, EEG and CSF findings. The patient was classified as having stage II (Jabbour *et al.* 1969) disease. Valproic acid, topiramate, carbamazepine, levetiracetam, in various combinations, and isoprinosine along with alpha-interferon had no notable effect on the clinical course.

A tonic seizure was recorded in one of the video-EEGs of the patient during his stay on the ward (see video sequences). While the patient was awake and in a resting state, a sudden jerk characterized by eye-opening, symmetrical extension of the arms and some flexion of the legs at the knees occurred. The eyes then deviated upwards, and the arms were extended with elevation and some adduction. Following a 10-second tonic phase in that position, a series of myoclonic attacks started. They had a repeating frequency consisting of one per 1.5-3 seconds, the episode lasting for about 1 minute. Jerks associated with the periodic complexes in the EEG were prominent in the arms, and superimposed on the increased muscles tonus. The position of the arms was sustained, with forward extension at the shoulder level. The patient also had some minor oral automatisms during this tonic-myoclonic phase. EEG finding concomitant with the initial myoclonic jerk consisted of a single, bilateral diffuse spike-slow wave complex, with high voltage (300µm) *(figure 1)*. Tonic phase of the seizure started with a generalized desynchronization in the EEG, with superimposed muscle activity on all channels along with 8-10 Hz regular rhythm apparent on bi-parieto-occipital regions, more frequently on the left. This phase lasted for about 10 seconds, and was followed by the periodic complexes. These consisted of high voltage, mono-phasic slow complexes with quasi-rhythmic repetition. As was apparent on the EEG channels, the muscle tonus remained increased until cessation of myoclonic activity. The EMG channels yielded no information because of technical difficulties. This seizure may be described as presenting myoclonic, tonic and tonic-myoclonic sequences, based on clinical and EEG data (see CD for complete ictal EEG).

Interictal EEG changes during awakening included high amplitude, variable duration, quasi-periodic, bilateral, diffuse, mono or-biphasic delta waves, sometimes followed by rhythmic delta paroxysms (1-1.5 Hz) localized mainly in frontal areas. Background activity while awake was normal. Frontally localized delta activity had a tendency to become generalized during NREM sleep, and mixed with fast discharges as its amplitude increased. Runs of very small multiple spikes were seen independently in either fronto-central or parieto-occipital regions. There were no recognizable sleep spindles.

Case 2

A 7-year-old girl was referred to our department because of seizures. She was the first child of non-consanguineous parents, born at term following an uncomplicated pregnancy and delivery. Her medical history revealed measles infection at 10 months of age. Family history was unremarkable. The parents noticed behavioural changes and mild cognitive decline that had appeared about one year earlier. Three months before hospitalization, she presented with falls while standing or walking. They were followed by some jerks, initially during sleep, and later during the day too. About two months later, the parents noticed absence-like seizures, 10 to 15 times per day, lasting for a few seconds. When tonic attacks became apparent about 15 days later, the patient was taken to a medical centre, where valproic acid was initiated. The child was brought to our clinic, because of continuing absence seizures and myoclonia, despite treatment. The neurological examination revealed moderate psychomotor retardation, increased deep tendon reflexes and rare myoclonic attacks, sometimes in succession. The EEG showed changes suggestive of SSPE. Laboratory examinations were unremarkable, except for increased levels of measles

IgG in blood and CSF. The MRI was normal. She was diagnosed as having stage II SSPE. A combination of valproic acid, carbamazepine and isoprinosine was ineffective.

A tonic seizure was recorded during one of the video-EEGs of the patient while she was in the ward (see video sequences). Clinically, the initial event was limited to eye-opening. Along with a gradual increase in muscle tone, there was abduction of the arms and elevation of the forearms. Asymmetrical, dystonic posturing involving the hands was then apparent. Forearms took a position to the left as erratic myoclonia with left predominance, began.

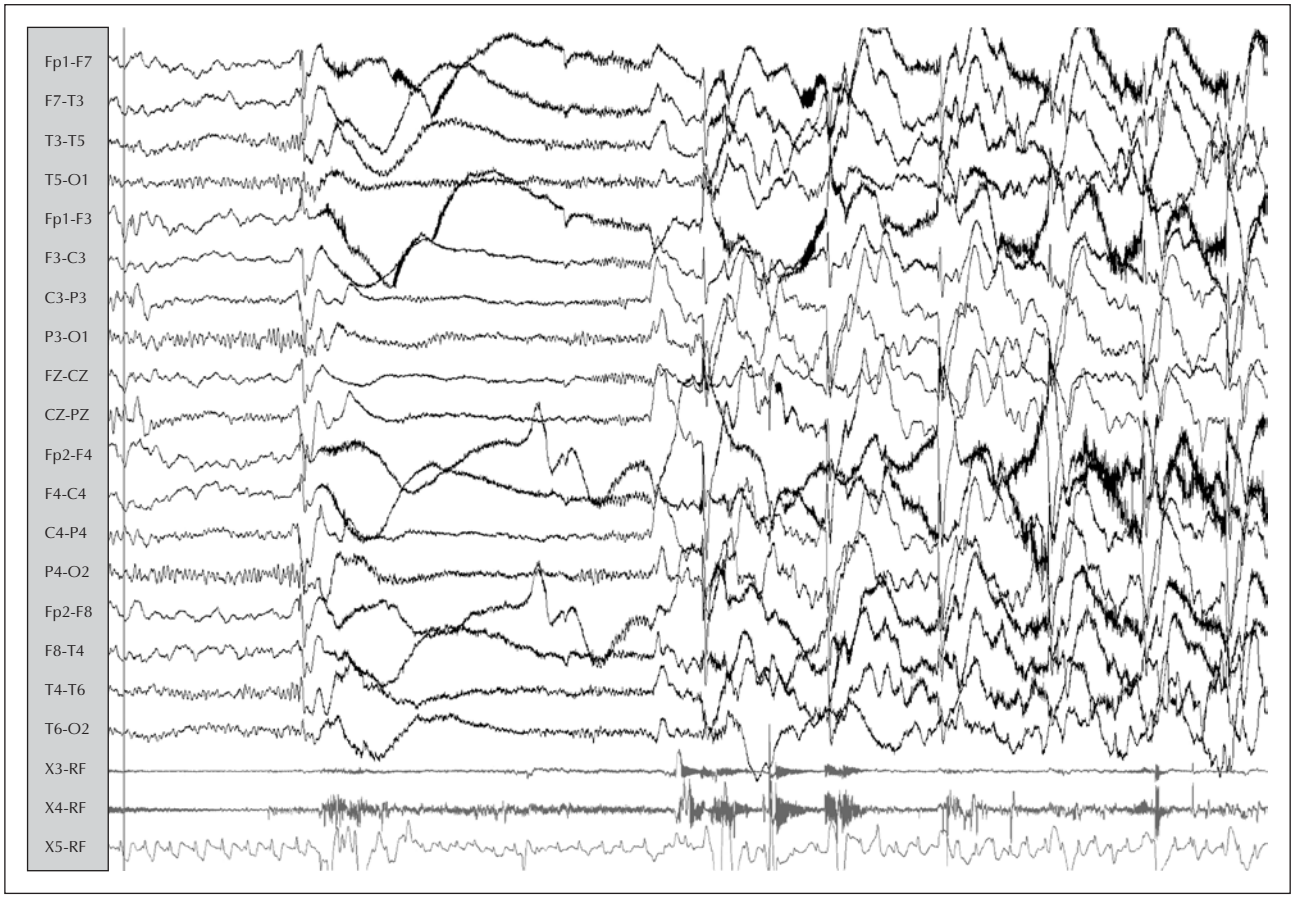

Figure 1. Ictal EEG (**case 1**). Bilateral diffuse spike-slow wave complex with high voltage (initial myoclonic jerk), followed by generalized desynchronization with superimposed muscle activity on all channels along with some 8-10 Hz regular rhythm apparent on bi-parieto-occipital regions, more, on the left (tonic phase), followed by high voltage, mono-phasic slow complexes with quasi-rhythmic repetition (myoclonic attacks).

The patient then brought her arms back to the original position. Following this sequence, which lasted for 10 seconds, there seemed to be a slow eye deviation to the left side, and the patient seemed less alert (10 sec). Consciousness returned following a brisk myoclonic jerk of her right arm (see the EMG channels in *figure 2A*; 3 seconds before the end). The total duration of the seizure was 20 seconds.

Seizure onset in the EEG *(figure 2A)* corresponded to a bilateral, diffuse discharge composed of a sharp-and-slow wave which was followed by an eight second desynchronization, with superimposed muscle activity, associated with the clinical, tonic phase. Following this activity, a diffuse, regular delta activity with right-sided and somewhat posterior predominance was seen, which accompanied the eye-deviation to left. There was a bilateral paroxysmal complex superimposed during the third second, on this 15 second delta activity. A phasic activity on the EMG channel marked the termination of the delta activity and the clinical seizure. Electro-clinical features of the seizure may be described as presenting tonic, tonic-myoclonic, partial (possibly, complex) and myoclonic sequences.

Interictal EEG *(figure 2B)* was composed of high voltage (500 µv), bi-phasic, quasi-periodic complexes repeating at 10-15 second intervals, random delta waves with a frequency of 3 Hz, and of moderate voltage with parieto-occipital localization along with normal alpha activity. Abnormalities were more pronounced during sleep. The frequency and the duration of the periodic complexes were increased; a discrete spike-and-wave activity on the right parieto-occipital region became apparent *(figure 2C)*. In some periods of NREM sleep, either symmetrical, or asymmetrical, long-lasting (10-11 seconds) bursts of bilateral, fast discharges were present, in addition to focal abnormalities. No sleep spindles were recognized.

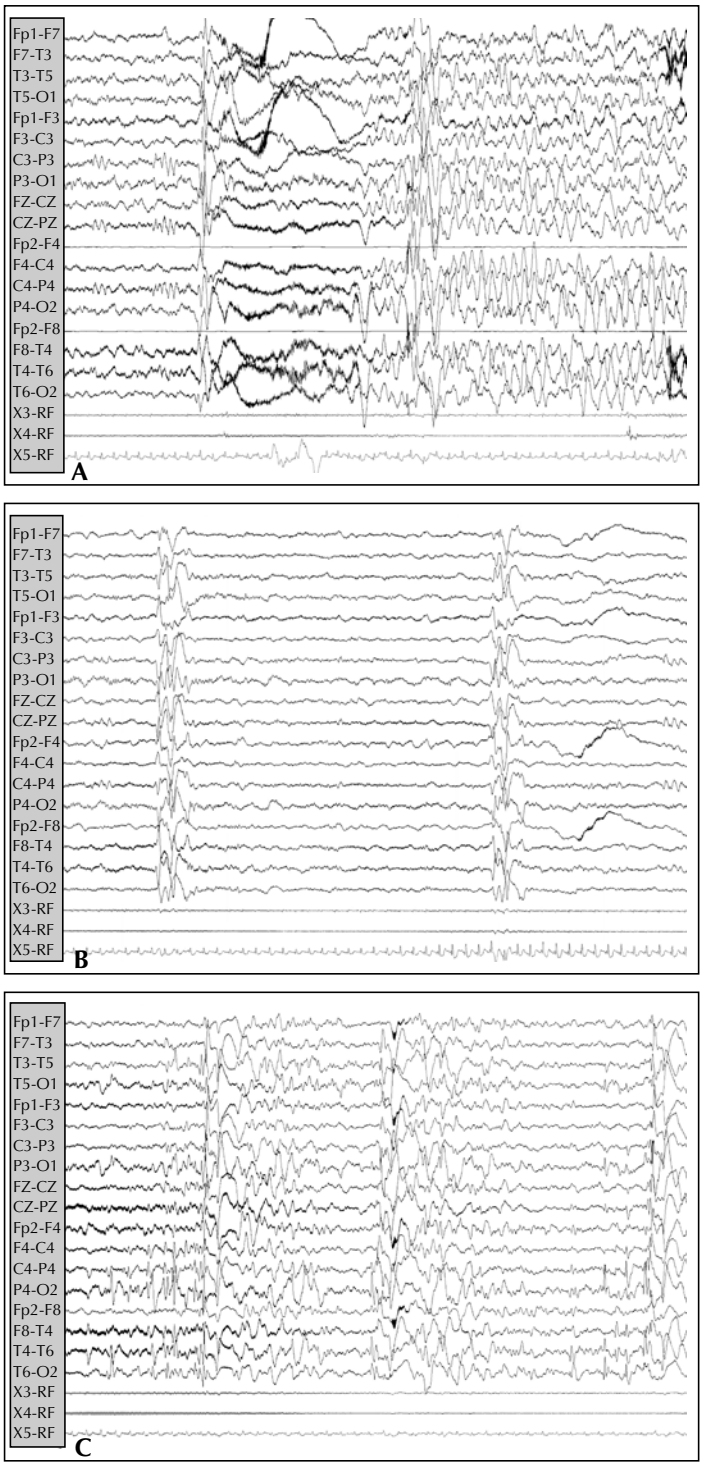

Figure 2. A) Ictal EEG (**case 2**). Bilateral, diffuse sharp-and-slow wave complex followed by an eight-second-lasting desynchronization with superimposed muscle activity (tonic phase). Later, a diffuse, regular delta activity with right-sided and somewhat posterior predominance accompanied by eye-deviation to left. At the third second, there was a bilateral paroxysmal complex, superimposed on this 15 seconds-lasting delta activity. **B**) Interictal EEG while awake (case 2). High voltage bi-phasic quasi-periodic complexes repeating with 10-15 seconds intervals, random delta waves with a frequency of 3 Hz and of moderate voltage with parieto-occipital localization along with normal alpha activity. **C**) Interictal EEG during NREM sleep (case 2). The frequency and the duration of the periodic complexes were increased in sleep; spike-and-wave activity on right parieto-occipital region became apparent.

Discussion

Subacute sclerosing panencephalitis is a late manifestation of measles virus infection and a disease with insidious onset. Decreased school performance (59%) and myoclonus (33%) were found to be the most common presenting symptoms (Lekhra *et al.* 1996). Affected children show irritability, distractability, decreased attention, lethargy, forgetfulness, regressive or slurred speech, which are attributable to the first stage of the disease (Jabbour *et al.* 1969). Stage II is defined as the presence of convulsive motor signs, myoclonus of the head, limbs, and trunk, poor coordination of trunk and limbs, dyskinesia-choreoathetoid movements and tremor (Jabbour *et al.* 1969). The characteristic symptom of this stage is myoclonic jerks.

Epileptic phenomena associated with SSPE were found to be partial seizures, generalized tonic-clonic seizures, atypical absences (Kissani *et al.* 2001, Lekhra *et al.* 1996) and myoclonic-atonic attacks (Dimova and Bojinova 2004), with varying frequency and degrees of severity. Tonic seizures have not been reported during the course of SSPE, except in a recent description of a single case (Parthiv and Amal 2003), in which the motor phenomena described may be similar to the condition in the present cases.

The two patients with SSPE presented here, had clinically evident tonic seizures as recognized by the parents initially, and documented by video-EEG in our laboratory.

Non-epileptic paroxysmal events such as dystonic, or rarely, opisthotonic posturing, may pose a real problem in the differential diagnosis of tonic seizures, even in conditions with ictal video-EEG data. Rhythmic EEG activity, within the 10-11 Hz frequency, accompanying the tonic phase in the first patient seems to be a reliable indicator of a tonic seizure. This is not the case in the second patient. Clinical symptoms, in this case, eye-opening, concurrent myoclonic jerks, and a partial seizure following the tonic posturing may provide evidence of a tonic event of an epileptic nature. An additional, inter-ictal finding in both patients, is the fast activity, either alone or intermixed with slow paroxysms during NREM stage, which resembles the fast activity in sleep EEG of patients with Lennox-Gastaut syndrome (LGS), and is well-known to be related to tonic seizures (Beaumanoir and Blume 2002).

Since SSPE is a disease with diffuse involvement of both grey and white matter, it is not unreasonable to expect any kind of seizure phenomena, either partial or generalized. Furthermore, association of tonic posturing with myoclonic phenomena, either sequentially as in LGS (Beaumanoir and Blume 2002), or, synchronously, as in myoclonic absence epilepsy (Bureau and Tassinari 2002) may be encountered in various epilepsy syndromes. Although they are mostly focal or unilateral and without ictal EEG concomitants (Clanet and Azais-Vuillemin 1997), tonic spasms, as a feature of multiple sclerosis, might also be considered in the differential diagnosis in cases of SSPE with tonic seizures, if other clinical and/or imaging similarities exist.

As in the reported studies in the related literature, tonic seizures in SSPE was not a well-known concept to the present authors, despite the frequency of the disorder in our region, as compared to industrialized countries. Possible explanations for the situation may be that, tonic seizures may be unnoticed if they are rare, not severe, short-lasting, or limited to sleep. They may also be considered as dystonic phenomena, especially if they start later in the course of stage II, as was the case in our patients. The presence of tonic seizures seems to have no negative influence on the diagnosis of SSPE. However, diagnostic difficulty may be encountered in cases with atypical presentations, or suspicious laboratory findings. Therefore, awareness of the presence of tonic seizures during the clinical course of SSPE may be important in order to avoid unnecessary investigations. □

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