Case report

EEG and seizure exacerbation induced by carbamazepine in Panayiotopoulos syndrome

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ABSTRACT – We report on a 4-year 8-month-old boy with Panayiotopoulos syndrome who showed atypical evolution with newly developed absence seizures and EEG exacerbation induced by carbamazepine. Soon after the introduction of carbamazepine, EEGs began to worsen, and finally absence seizures and myoclonic seizures appeared. Immediately after we discontinued carbamazepine, the seizures disappeared and the EEG improved. Carbamazepine may induce unusual electroclinical features, electrophysiologically explained by bilateral synchrony. This case provides more evidence of the close links between Panayiotopoulos syndrome and benign childhood epilepsy with centrotemporal spikes.

Key words: Panayiotopoulos syndrome, carbamazepine, absence, benign partial epilepsy, seizure exacerbation

Panayiotopoulos syndrome (PS) is a type of benign partial epilepsy of childhood (Panayiotopoulos 2002a, Panayiotopoulos 2002b, Caraballo et al. 2000). Recently, the relationship between benign childhood epilepsy with centrotemporal spike (BECTS), another representative type of benign partial epilepsy of childhood, and PS has been investigated from various standpoints, and attention has been drawn to the pathophysiological similarity of these two syndromes (Caraballo et al. 2000, Yoshinaga et al. 2005). One of the common characteristics of these two syndromes is that some patients demonstrate similar, atypical evolutions in which absence seizures and myoclonic seizures appear concomitantly with a worsening of the EEG (Caraballo et al. 2001, Ferrie et al. 2002).

CBZ is the drug of choice for benign partial epilepsy. However, CBZ has been reported to cause atypical evolutions associated with a deteriorating EEG in BECTS (Perucca et al. 1998, Nanba and Maegaki 1999). To the best of our knowledge, a similar exacerbation with CBZ has not been previously reported in a patient with PS. This is the first report of a boy with PS who showed EEG and seizure exacerbation induced by CBZ.

Case report

The patient was born uneventfully to non-consanguineous parents, and his development was normal. His younger sister had experienced febrile convulsions. His first seizure occurred at age 4 years and 3 months during
nocturnal sleep. The patient woke suddenly and began walking around, unable to answer questions. He remained unresponsive, vomiting repeatedly for 45 minutes, and then had a right-sided hemiconvulsion lasting for half an hour. The hemiconvulsion was suppressed by an intravenous diazepam infusion. Neurological examinations and routine laboratory investigations, including brain CT scan, MRI, and MRA, revealed no abnormal findings. His interictal EEG showed left occipital spikes during sleep (figure 1A). CBZ at about 10 mg/kg/day was initiated under the diagnosis of partial epilepsy, but the compliance was poor. He was referred to us at age 4 years and 8 months. We diagnosed PS and advised his family administer the medicine regularly. At age 4 years and 11 months, in spite of a regular intake of CBZ, his second seizure occurred during nocturnal sleep. He woke up, coughing and vomiting, and finally had a right-sided hemiconvulsion. A few minutes later, the hemiconvulsion terminated spontaneously, but he remained unresponsive, with repeated vomiting for 40 minutes. We increased the CBZ dose to about 22 mg/kg/day. Soon after, he began to experience episodes of unresponsiveness lasting for 10-20 seconds while awake. His newly developed seizures were characterized by abrupt onset and cessation and a brief interruption of his ongoing activities.

Any other features such as automatisms or myoclonic phenomena were not observed during the attacks. The attacks occurred several times a day. Also, he began to suffer from a twitching of limbs during wakefulness and sleep, especially just after falling asleep. His peak blood level of CBZ was 8.6 μg/mL.

The evolution of his EEG is shown in figure 1, and figure 1A shows his initial EEG. At age 4 years and 8 months, following the introduction of CBZ, his interictal EEG showed repetitive spike and waves, so-called clonid-like repetitive complexes described by Panayiotopoulos, in the left posterior head area associated with generalization (figure 1B). At age 5 years, his interictal EEG showed a further worsening, with diffuse slow spike and waves when awake and asleep. As shown in figure 1C, diffuse slow spike and waves were particularly numerous during sleep; however, the diffuse spike and waves were not as frequent as those seen in typical continuous spike and waves during slow sleep (CSWS). As shown in figure 1D, we frequently observed diffuse slow spike and wave bursts lasting for several seconds in awake EEG recordings. Because of the characteristic seizure and EEG manifestations, we presumed that he was experiencing absence seizures. We performed a polygraphic study to evaluate whether his myoclonus was epileptic, and found a myoclonus accompanied with a diffuse slow spike-wave burst while awake (figure 1E). We attributed this worsening of the EEG and the appearance of absence seizures and epileptic myoclonus, to CBZ. Therefore we gradually replaced CBZ by valproate (VPA). After complete replacement, the episodes of brief spells disappeared. The VPA dose was 300 mg/day, and the VPA blood level was 53.6 μg/mL. His EEG improved dramatically, with infrequent spike waves involving the left temporal-occipital area (figure 1F). The frequency and amplitude of spike discharges decreased, and the generalization of the spike-wave discharges disappeared. After the replacement of CBZ by VPA, he became alert as regards movements and expression, and his appetite also improved.

**Discussion**

Because of the typical clinical symptoms and the characteristic EEG findings, we concluded that our patient was suffering from PS, a type of benign partial epilepsy of childhood. PS occurs in normally developed children, with a peak age-at-onset of 4 or 5 years with no abnormal findings on neuroimaging examinations. The most characteristic seizure manifestations of PS are the existence of autonomic symptoms, mainly emetic, often accompanied by a deviation of the eyes and/or unresponsiveness. The seizure frequency is usually low, but prolonged seizures and complex partial status epilepticus, as in our case, are not unusual. Nevertheless, PS has a good neurological outcome. Intercital EEG predominantly shows occipital spikes. Although PS was first described as an early-onset childhood epilepsy with occipital paroxysms (CEOP), in contrast to a late-onset CEOP described by Gastaut, it has been recently thought that PS has closer links with BCECS than with the Gastaut type of CEOP. Several patients with PS have been reported whose seizure manifestations changed with age from typical PS seizures to Sylvian seizures. Taking all these findings together, Panayiotopoulos and his colleagues proposed a unified concept for benign childhood partial epilepsy, that is, benign childhood seizures susceptibility syndrome, including PS as the earliest type and BCECS as another type.

It is well known that 19% of patients with Panayiotopoulos syndrome show diffuse epileptic discharges in their EEG evolution. However, absence seizures are rarely observed in PS (Caraballo et al. 2004). Although we could not record the ictal EEG of our patient’s brief spells, diffuse slow spike and wave bursts lasting several seconds in his interictal EEG strongly indicate that these episodes were absence seizures. Atypical evolutions of BCECS with absence seizures are well known as atypical benign partial epilepsy. Several cases of PS patients reportedly showed similar, atypical evolutions in their clinical courses (Caraballo et al. 2001, Ferrie et al. 2002). In 2001, Caraballo et al. reported two patients with PS who began to have absence seizures and myoclonic seizures associated with mental regressions. The EEGs of both patients changed to CSWS (Caraballo et al. 2001). Although our patient had absence seizures and epileptic myoclonus along with the appearance of diffuse slow spike and waves, his EEGs did not display typical CSWS. In 2002, Ferrie et al. reported a
Figure 1. A) An EEG after the first complex partial status epilepticus at age 4 years and 3 months. It shows left occipital spikes during sleep. B) An EEG during sleep, after the introduction of CBZ at age 4 years and 8 months. It shows so-called cloned-like repetitive complexes in the left posterior head area associated with slight generalization. C) An EEG during sleep, after the regular intake of CBZ at age 5 years. Cloned-like, repetitive, multifocal spike-wave complexes increased and showed a strong tendency toward generalization. D) An EEG during wakefulness at age 5 years. It shows diffuse slow spike and wave bursts that continued for about three seconds, suggesting the existence of absence seizures. However, no clinical manifestations were noticed at this EEG recording. E) An EEG-EMG polygraphic recording performed at the same age as figures 1C and D. Note that the spike component of the generalized spike and wave discharges is time-locked with the myoclonic jerks (indicated by the arrow) recorded from the deltoids. F) An EEG during wakefulness at age 5 years and 1 month, when the patient took only VPA after discontinuing CBZ.
girl with PS who began to have absence seizures and absence status. She initially had clinical features typical of PS, followed by sylvian seizures two months later. She then began to have absence seizures (Ferrie et al. 2002). As in our patient, she took CBZ at the time of the appearance of absence seizures. However, her absence seizures did not disappear with the discontinuation of CBZ. In contrast, our case showed a dramatic improvement on the EEG and a disappearance of the absence seizures immediately after CBZ was stopped. In conclusion, although our patient shared similar clinical and EEG evolution with those reported by other authors (Caraballo et al. 2001, Ferrie et al. 2002), he was characterized by the closer relationship between his evolutional change and CBZ treatment.

Seizure exacerbations induced by CBZ were initially reported in cases that had generalized seizures, such as absence seizures and generalized tonic-clonic seizures (Shields and Saslow 1983). However, Talwar et al. found eight cases of symptomatic, localization-related epilepsy among a total of 26 cases that displayed EEG exacerbation at an age of less than 6 years (Talwar et al. 1994). Regarding benign partial epilepsy and seizure exacerbations by CBZ, Lerman (1986) first reported a patient with BCECS that began to have drop spells after the initiation of CBZ. Nanba and Maegaki also reported a patient with BCECS who began to have epileptic negative myoclonus and appearances of diffuse slow spike and waves in the EEG that were induced by CBZ (Nanba and Maegaki 1999). Similar to our patient, all these cases showed EEG improvement and seizure cessation immediately after the discontinuation of CBZ.

To the best of our knowledge, this is the first report of a boy with PS who showed EEG and seizure exacerbation induced by CBZ. We believe this case provides more evidence of the close links between PS and BCECS. Although CBZ is a drug of choice for PS, we should consider the possibility of exacerbation and observe carefully the clinical changes and EEG evolutions during CBZ therapy.

References


