

Clinical study of seven patients with special syndrome of post-epileptic dysfunction persisting over 24 hours

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Abstract. – OBJECTIVE: Todd's paralysis is the most common complication after epileptic seizures, especially status epilepticus, but other disabilities deriving from the postictal state are poorly understood. There is relatively little information on the underlying parameters that affect clinical features of post-epileptic dysfunction. The aim of this paper is to investigate clinical features of special post-epileptic dysfunction persisting over 24 hours.

PATIENTS AND METHODS: Seven patients with special syndromes of post-epileptic dysfunction were retrospectively analyzed and the related literature was reviewed.

RESULTS: Six patients with post-epileptic dysfunction experienced status epilepticus. Of the seven patients, six had underlying structural brain lesions. Post-epileptic dysfunction has different syndromes, including post-epileptic paralysis, post-epileptic aphasia, cognitive disorder, gaze palsy and hemianopsia. The duration of the dysfunction in these patients lasted from 2 days to 3 months.

CONCLUSIONS: The great majority of patients with post-epileptic dysfunction experience status epilepticus and have underlying structural brain lesions. Post-epileptic dysfunction includes various syndromes and can last from several days to 3 months with a good prognosis.

Key Words:

Epilepsy, Post-epileptic dysfunction, Todd's paralysis.

Introduction

Todd's paralysis is a special syndrome of post-epileptic transient motor dysfunction, and manifests as multiple or single limb paralysis¹. Todd's paralysis is the most common form of post-epileptic dysfunction (PED). However the other PED syndromes, for example post-epilep-

tic aphasia, hemianopsia, unilateral sensory disturbance and cognitive disorder haven't been given much attention. Furthermore, the incidence, potential etiology and pathogenesis of PED are not known. This study retrospectively analyzed seven patients with special PED syndromes persisting over 24h in the Department of Neurology of Zhongshan Hospital, (affiliated to Guangzhou University of Chinese Medicine) and the clinical characteristics were noted for the seven PED cases.

Patients and Methods

Seven patients with special PED were retrospectively evaluated. Among them, 5 patients with epileptic seizure were hospitalized at the first symptom; 2 patients were admitted due to non-neurological disorders during which they had episode of seizures. Six were first misdiagnosed as having acute cerebral infarction because they had PED symptoms such as post-epileptic paralysis, post-epileptic aphasia, gaze palsy, cognitive disorder and disturbance of consciousness. All neurological deficits persisted over 24h. Cranial MRI scan of multiple sequences (including T1WI, T2WI, DWI and Flair) were performed 48h after seizure and the diagnosis of acute cerebrovascular disease was excluded.

There were 5 male and 2 female patients and the average age was 67.86 ± 15.02 years old accounting for 3.83 (7/183) of the hospitalized epileptic patients in the same period. The patients had cranial CT scans before admission to hospital. Blood tests were performed 24h after hospitalization and the cranial MRI of multiple sequences (including T1WI, T2WI, Flair and DWI) and video EEG taken 48 h after hospitalization.

Results

PED Seizure Frequency and Manifestations

All the patients had completed multiple sequences cranial MRIs 48h after hospitalization, which excluded the possibility of neurological deficit caused by acute cerebral infarction and cerebral hemorrhage as well as neurological symptoms caused by systemic diseases. The PED seizure frequency of different patients varied depending on their individual conditions. The typical case was that PED occurred at the first epileptic seizure (3/7) as was the case for Case 2, Case 5 and Case 6. Six patients experienced PED after status epilepticus (SE) (6/7). Case 2 had PED after SE and upon oral medication of antiepileptic drugs, the seizure never occurred. Case 5 had PED after the first SE and with standard treatment of antiepileptic drugs, there were 6 seizures in the following 3 months with manifestation as CPS for 2~3 min without PED. Case 6 had recurrent epileptic seizures during 2 months. Each time transient cardiac arrest was accompanied by epileptic seizure of PED. Upon multiple sequences cranial MRI, no abnormalities were revealed. On the previous 2 episodes, seizures ended with neurological

deficit resolving to some degree, but not completely back to normal status. After 2 months the patient died due to multiple organ failure. Case 1 had recurrent PED after two episodes of SE, and every time epileptic symptoms were the same with neurological dysfunction completely recovering to normal status. Case 3, Case 4 and Case 7 were patients with a history of 3-5 epileptic seizures without PED every year. The reason for hospitalization this time was that PED was accompanied by epileptic seizure which had worse related symptoms than before. The duration of PED varied. For the short-term PED, it could be back to normal status in 2 days, such as with Case 1 and Case 7. For the long-term PED, it could last as long as 2-3 months.

Clinical manifestations of PED took different forms but the most common syndrome was motor dysfunction. However the motor dysfunction of individual patients could manifest differently. Usually it manifested as hemiplegia, bilateral lower limbs paralysis or quadriplegia although it also presented with aphasia including complete aphasia, motor aphasia or sensory aphasia. For other manifestations, there were cognitive disorder, gaze palsy, loss of consciousness and hemianopsia, etc. (Table I).

Table I. Clinical characteristics of seven patients with special syndrome of post-epileptic dysfunction.

Case No	Sex	Age (yrs)	Epilepsy duration	Types of seizures	Cause	Clinical manifestations of PED	Duration of PED
1	Male	83	6 m	Secondarily generalized tonic-clonic seizures, SE	Cerebral infarction	Hemiplegia, complete aphasia, gaze palsy	2 d
2	Male	73	1 st onset	Secondarily generalized tonic-clonic seizures, SE	Cerebral infarction, meningiomas	Lower limb paralysis, complete aphasia, cognitive disorder	2 m
3	Female	78	1 y	Secondarily generalized tonic-clonic seizures, complex partial seizures	Cerebral infarction	Hemiplegia, sensory aphasia	2 m
4	Female	75	2 y	Secondarily generalized tonic-clonic seizures, myoclonic seizures, SE	Cerebral infarction, Cerebral hemorrhage	Quadriplegia, motor aphasia, gaze palsy, cognitive disorder	3 m
5	Male	45	1 st onset	Secondarily generalized tonic-clonic seizures, complex partial seizures, Tonic seizures, SE	Chronic alcoholism	Lower limb paralysis, complete aphasia, cognitive disorder	3 m
6	Male	73	1 st onset	Secondarily generalized tonic-clonic seizures, SE	Cerebral embolism	Hemiplegia, complete aphasia, disturbance of consciousness	2 m
7	Male	48	3 y	Secondarily generalized tonic-clonic seizures, Tonic seizures, SE	None	Complete aphasia, gaze palsy, hemianopsia	2 d

Imaging of Bilateral Reversible White Matter Damage

Seven cases went through a cranial scan of DWI after hospitalization. Case 5 had been confirmed to have bilateral reversible white matter damage and the rest of the 6 cases had no acute infarction lesion or white matter damage. In Case 5, the patient presented with generalized tonic-clonic status for 2h, followed by complete aphasia, cognitive disorder and bilateral lower limb paralysis. The next day Case 5 had cranial MR DWI performed, and was found to have acute white matter damage with bilateral subcortical white matter symmetry diffuse high signal. Five days after epileptic seizure, the patient received cranial MR DWI and imaging illustrated that bilateral subcortical white matter high signal had resolved, although the patient's clinical symptoms had not recovered completely. Ten days after seizure the patient went through CT perfusion scan and it demonstrated that bilateral cortical mean transit time (MTT) was prolonged and cortical cerebral blood volume (CBV) was reduced, indicating low perfusion of bilateral symmetry cortex (Figure 1).

Discussion

In 1827 Bravais² wrote the first report of one side paralysis followed by unilateral seizure, which was called *hemiplegia epileptica*, but it did not attract neurologists' attention, until 1849, when Todd independently reported the cases of

post-epilepsy hemiplegia: "A paralytic state remains sometimes after the epileptic convulsion. This is more particularly the case when the convulsion has affected only one side or one limb: that limb or limbs will remain paralytic for some hours, or even days, after the cessation of the paroxysm, but it will ultimately perfectly recover"¹. From then on the concept of Todd's paralysis has been accepted by the neurologists. But the limb paralysis that Todd described was in fact just one kind of post-epileptic symptom. Limb paralysis could not encompass all types of neurological deficit. In 1890 Jackson explored the research on this topic and described different symptoms as post-epileptic aphasia, post-epileptic sensory loss, post-epileptic numbness, and post-epileptic mania³. Since then, many scholars have reported other types of post-epileptic syndromes including post-epileptic hemianopsia, complete blindness, weakness, unilateral mydriasis, bulimia, and prolonged confusion^{4,5}, but all these descriptions were reported as cases. Therefore Todd's paralysis does not represent all other types of neurological dysfunction, and the range of post-epileptic disorders could be better defined as post-epileptic dysfunction.

After a review of related literature, we could find no reports of the epidemiological and clinical features of post-epileptic dysfunction. Rolak et al⁶ reported 229 cases of generalized seizures and 14 of them had transient symptoms of post-epileptic dysfunction with an incidence rate of 6.11%. Eight of them had pre-existing intracranial focal lesions related to post-epileptic dys-

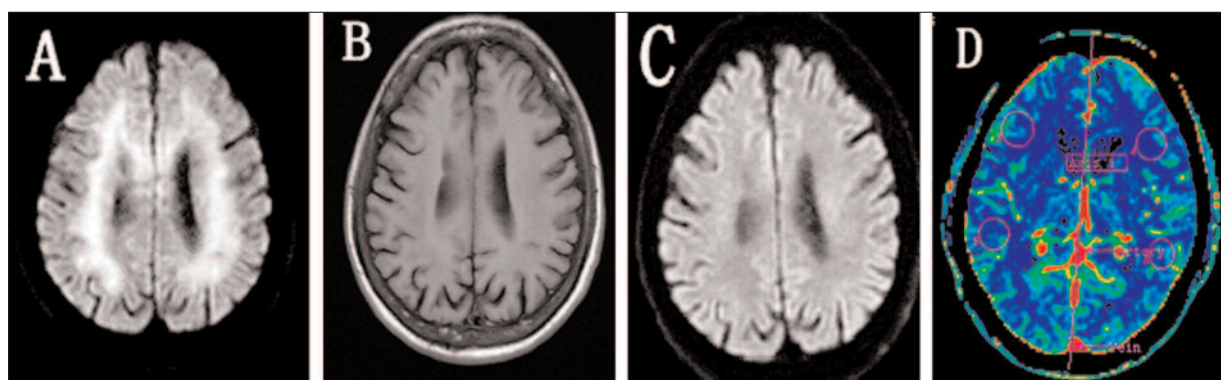


Figure 1. Case 5: post-epileptic dysfunction bilateral subcortical white reversible lesion and bilateral hemispheric hypoperfusion on CTA. Case 5, showing bilateral reversible white matter damage and bilateral cortical cerebral blood volume reduction. Image A 2d after the epileptic seizure MR DWI indication of bilateral subcortical white matter diffuse high signal; Image B 2d after the epileptic seizure MR T1 weighted and no obvious abnormalities; Image C 5d after the epileptic seizure MR DWI indication of bilateral subcortical white matter high signal disappeared; Image D 10d after the epileptic seizure CT perfusion with reduced bilateral cerebral blood volume.

function. The transient post-epileptic dysfunctions had diverse syndromes including post-epileptic aphasia, gaze palsy, inability and numbness which was rarely found. Motor deficits were also highly variable, ranging from very mild paresis to complete plegia, from flaccid status to spastic status and from focal lesion to one-side paralysis, but all these abnormal syndromes never exceeded 36 hours in duration. The patients had potential structural impairments but with 43% of them, no exact cause could be found.

This study demonstrated that 6 of 7 PED cases had experienced status epilepticus, and 5 cases had presence of underlying intracranial structural lesions before seizures as a basis for cerebral infarction, cerebral hemorrhage or meningioma. Compared with Rolak's study, the patients presented with different seizures, including partial, and secondary generalised tonic-clonic seizures, whereas Rolak et al excluded partial seizures or partial seizures with secondary generalisation.

At present, the pathogenesis of PED is not clear. Scholars have different hypotheses, but none of these hypotheses can explain all the clinical features of the various PEDs. The theories currently mooted include focal brain damage, severe seizure hypoxia or neuronal exhaustion induced by matrix depletion¹, and there may also be potential vascular disease susceptibilities which may predispose to insufficient metabolism of localized region. PED may also be caused by the excessive discharge of the inhibitory neurons or the release of endogenous inhibitors⁷ and the opening of an arteriovenous shunting⁸.

With the development of modern imaging techniques, recent studies^{9,10} have found that transient reversible cortex and subcortical white matter damage may be caused by epileptic seizures, especially when the patients have experienced continuous status epilepticus. It has also been found that hypoperfusion occurs in epileptogenic foci¹¹ or hemisphere¹² with epileptic seizures, but all these have been reported as case studies. All the PED patients in this study went through MR DWI. Case 5 went through DWI the day after seizure and was found to have bilateral subcortical white matter symmetry high signal, indicating bilateral symmetrical subcortical white matter lesions, while the other 6 cases had no such white matter lesions. Five days after epileptic seizure, the patient was rescanned by DWI and it was found that the bilateral subcortical high white matter signal had resolved completely, which suggested that bilateral subcortical white matter lesions could be re-

versible. Ten days after SE, cranial CT perfusion imaging indicated low bilateral cortical symmetry perfusion, furthermore, such syndromes as post-epileptic aphasia, cognitive disorder and post-epileptic paralysis had not yet completely resolved. Whereas the other 6 cases had DWI performed and were found to have no obvious change in the white matter signal. In summary, it is thought that PED may have a variety of pathogenesis and it is associated with different underlying diseases.

For PED duration, Todd suggests the maximum time period is 24h¹, but in the report by Rolak et al⁶ the duration of Todd's paralysis between 24 and 36 hours, Biton et al⁴ thinks PED can persist as long as 10 days, whereas Savard et al¹³ thinks PED can be improved significantly in a month. Scholars such as Rolak et al and Biton et al report that most of PED patients have pre-existing brain structural impairment for which the most common cause is cerebrovascular disease^{6,12}. The other most common cause is brain atrophy and chronic alcoholism, which are consistent with the conclusions of this study (see Table I). Structural lesions may be associated with the duration of the Todd's paralysis⁶.

Conclusions

It is indicated in our study that most of PED patients have underlying brain structural lesions and they have usually experienced status epilepticus. PED manifests as a variety of syndromes, such as post-epileptic paralysis, post-epileptic aphasia, cognitive disorder, disturbance of consciousness and hemianopsia most of which have favorable prognosis. However, the sample size in this study needs to be expanded upon for a more detailed research.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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