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Case Report

Long-term weekly ACTH therapy for relapsed West syndrome in tuberous sclerosis complex: A case report

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Abstract

Background: In Japan, adrenocorticotropic hormone (ACTH) therapy has been the mainstay of treatment of West syndrome. Conventional ACTH therapy is administered short-term with efficacy, yet the relapse rate is high. Relapse after initial ACTH therapy is a poor prognostic factor for long-term seizure control and outcome of cognitive function. Here, we report successful long-term weekly ACTH therapy for relapsed WS in a tuberous sclerosis complex (TSC) child after conventional ACTH therapy.

Patient: The patient had a series of epileptic spasms (ES) and hypsarrhythmia at age 3 months. She was diagnosed with WS associated with TSC, and was treated with conventional ACTH therapy at age 4 months, and a second course of ACTH therapy at age 8 months. Both courses of therapy were transiently effective. A third course of ACTH therapy was started at age 1 year and 2 months, and long-term weekly ACTH therapy was continued thereafter. During this therapy, both ES and hypsarrhythmia remained completely resolved. Therapy was continued, and dose reduction was started when the patient was 2 years and 10 months old. No serious adverse events had occurred during this therapy.

Conclusion: This case demonstrated that long-term weekly ACTH may be safe and effective. Although at present, this therapy may only be considered for relapsed symptomatic WS patients, it may be a good alternative therapy when frequent relapses occur after favorable response to conventional ACTH therapy.

Keywords: Long-term weekly ACTH therapy; West syndrome; Tuberous sclerosis complex; Relapse; Epileptic spasms; Hypsarrhythmia

1. Introduction

West syndrome (WS) is the most recognized epileptic encephalopathy in early infancy resulting in poor cognitive outcome. The disorder presents with a unique seizure type, epileptic spasms (ES), a characteristic electroencephalography (EEG) pattern known as hypsarrhythmia, and psychomotor regression. Early control of hypsarrhythmia is crucial for improved neurodevelopmental prognosis [1]. In addition, 60–70% of patients with WS have an associated underlying disorder [2]. Among them, tuberous sclerosis complex (TSC) is the most important cause of symptomatic WS.

Previous reports have highlighted the efficacy of vigabatrin (VGB) for WS, particularly for WS with TSC (WS-TSC) [3]. However, in Japan, adrenocorticotropic hormone (ACTH) therapy has been the mainstay of

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WS treatment with or without TSC, because VGB is not approved for use. The efficacy of conventional ACTH therapy administered short-term has been reported, but relapse rate is high [3,4]. Relapse after initial ACTH therapy is a poor prognostic factor for long-term seizure control and cognitive outcome, and is more frequently seen in symptomatic WS than cryptogenic one [5]. Recently, long-term weekly ACTH therapy was reported for relapsed WS patients [6,7]. Here, we report successful long-term weekly ACTH therapy for a relapsed WS child with TSC after conventional ACTH therapy. The present report suggested this unique therapy may be used as an alternative treatment for relapsed WS, when conventional ACTH therapy shows only transient efficacy.

2. Case

The patient was a girl born to non-consanguineous, healthy parents at 41 weeks gestation after an uneventful pregnancy. At age 3 months, she manifested a series of ES. Along with typical skin lesions, intracranial calcifications, multiple cortical tubers, and a cardiac mass confirmed the diagnosis of TSC. EEG demonstrated hypsarrhythmia (Fig. 1A), and she was ultimately diagnosed as WS-TSC.

After initial treatment failure with valproate and pyridoxal phosphate, conventional ACTH therapy was started when she was 4 months old. The protocol consisted of daily intramuscular injections of synthetic ACTH at a dose of 0.005 mg/kg for 2 weeks, which was then reduced gradually during the following 2 weeks (Table 1). ES was resolved on day 6, and hypsarrhythmia disappeared on day 12.

The second and third course of ACTH therapy were begun at age 8 months and 1 year, respectively, due to occurrence of ES and modified hypsarrhythmia (Fig. 1B). Both episodes immediately responded to conventional ACTH therapy, and ES were resolved within a week (Table 1). Thus, we selected long-term ACTH therapy to maintain its effects. Because the dose of the third course of ACTH therapy was 0.01 mg/kg daily for 2 weeks, the same dose was given weekly thereafter (Table 1). During this therapy, both ES and

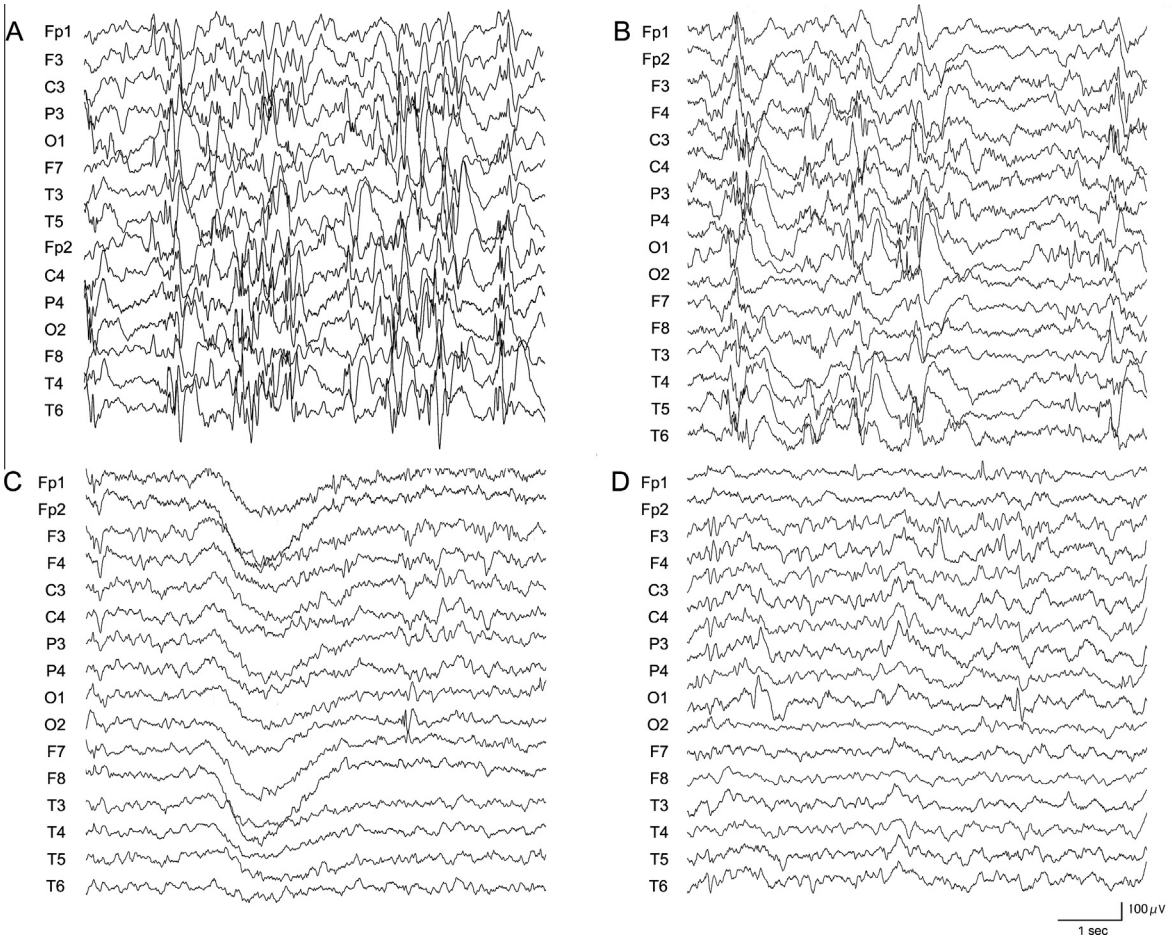

Fig. 1. Interictal sleep EEG. The EEG data revealed hypsarrhythmia at initial presentation (A) and before the third course of ACTH therapy (B), rare spikes in the occipital regions during long-term ACTH (C) and at age 3 years (D).