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Case report

Successful treatment for West syndrome with severe combined immunodeficiency ☆

Mitsuo Motobayashi [a], Yuji Inaba [a,*], Tetsuhiro Fukuyama [b], Takashi Kurata [a], Taemi Niimi [a], Shoji Saito [a], Naoko Shiba [a], Takafumi Nishimura [a], Tomonari Shigemura [a], Yozo Nakazawa [a], Norimoto Kobayashi [a], Kazuo Sakashita [a], Kazunaga Agematsu [c], Motoki Ichikawa [d], Kenichi Koike [a]

[a] *Department of Pediatrics, Shinshu University School of Medicine, Matsumoto, Japan*
[b] *Department of Neuropediatrics, Nagano Children's Hospital, Azumino, Japan*
[c] *Department of Infection and Host Defense, Graduate School of Medicine, Shinshu University, Matsumoto, Japan*
[d] *Department of Family and Child Nursing, Shinshu University School of Medicine, Matsumoto, Japan*

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Abstract

Several immune mechanisms are suspected in the unknown etiology of West syndrome (WS). We report a male infant who suffered from WS and X-linked T−B+NK− severe combined immunodeficiency (X-SCID) with a missense mutation of the *IL2RG* gene (c.202G>A, p.Glu68Lys). He promptly began vitamin B6 and valproic acid treatment, but infantile spasms (IS) and hypsarrhythmia persisted. Administration of intravenous immunoglobulin and the change to topiramate (TPM) at 7 months of age resulted in the rapid resolution of IS. The CD4/8 ratio in his peripheral blood increased from 0.04–0.09 to 0.20–1.95 following unrelated cord blood transplantation (UCBT). *In vitro* lymphocyte proliferation in response to phytohemagglutinin or concanavalin A and the ability of B lymphocytes to produce antibodies improved as well. Electroencephalogram findings became normal 1 month after UCBT. Thus, we consider that T-cell dysfunction and/or impairments in T–B cell interactions due to X-SCID may have played important roles in the onset of WS. Immune-modulating therapies along with the administration of TPM effectively treated this severe epileptic syndrome in our patient.

Keywords: West syndrome; Severe combined immunodeficiency syndrome; CD4/8; Hematopoietic stem cell transplantation; Intravenous injection of immunoglobulin

1. Introduction

West syndrome (WS) is an intractable epileptic disorder that is characterized by infantile spasms (IS), specific interictal electroencephalogram (EEG) findings of hypsarrhythmia, and arrest or regression of psychomotor development [1]. While the etiology of WS remains unknown, several immune mechanisms are suspected on the basis that immune-modulating therapies, such as adrenocorticotropic hormone (ACTH), glucocorticoids, and intravenous immunoglobulin (IVIG) are effective [2,3],

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* Corresponding author. Address: Department of Pediatrics, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan. Tel.: +81 263 37 2642; fax: +81 263 37 3089.
E-mail address: inabay@shinshu-u.ac.jp (Y. Inaba).

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and that spontaneous WS remission following acute viral infections has been reported [4–7].

X-linked severe combined immunodeficiency (X-SCID) is a rare primary immunodeficiency syndrome caused by a mutation of the *IL2RG* gene on the X chromosome. X-SCID patients uniformly have low percentages of T and NK cells and a high percentage of B cells which have no capability to produce antibodies, and typically succumb early in life to severe and recurrent infections unless they receive suitable treatment. Hematopoietic stem cell transplantation (HSCT) is the only known curative option for such patients [8].

We report the clinical and immunological course of an infant with X-SCID complicated by WS who has been treated successfully with immunomodulatory therapies in addition to antiepileptic drugs.

2. Case report

The patient was the first boy of a healthy non-consanguineous 40-year-old mother and 46-year-old father. He had a family history suggestive of X-linked disease; many boys on his maternal side had died from unknown causes in early childhood. He was born spontaneously at term after an uneventful pregnancy. From 2 months after birth, he began to suffer from recurrent airway infections and was treated intermittently with antibiotics. IS (3–11 series/day) appeared at the age of 6 months. Interictal EEG findings revealed hypsarrhythmia (Fig. 1A). Immunological examinations showed hypogammaglobulinemia and decreased percentages of CD4+ cells (2%) and CD56+ cells (3%) (Table 1). Circulating CD8+ cells were detected at 48%, but 78% of these cells had derived from his mother according to X/Y fluorescent in situ hybridization analysis. DNA sequencing showed a missense mutation of the *IL2RG* gene (c.202G>A, p.Glu68Lys). Based on this evidence, he was diagnosed as having X-SCID (T−B+NK− SCID) complicated by WS. No pathogenic microbes were detected in specimens taken from blood, respiratory tract secretions, gastric fluid, urine, stools and cerebrospinal fluid (CSF). At the initial visit, his

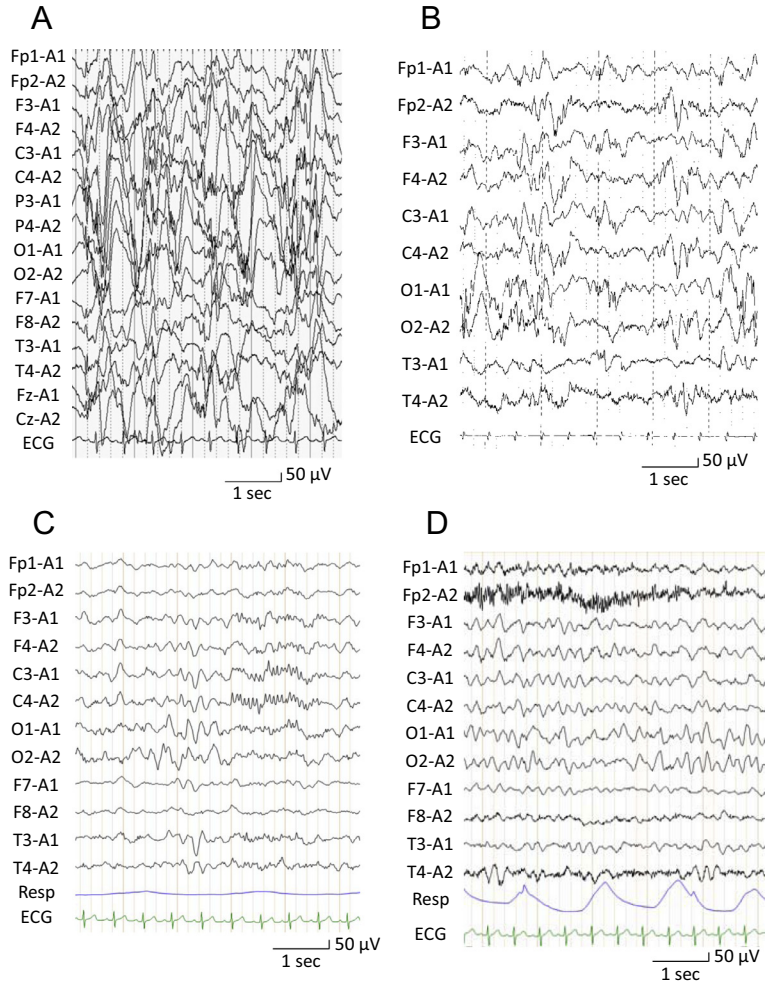

Fig. 1. Interictal EEG findings. (A) An interictal EEG during sleep at the age of 6 months showed high amplitude and irregular waves and spikes in a background of chaotic and disorganized activity (hypsarrhythmia). (B) Before UCBT, moderate EEG abnormalities persisted. (C and D) After UCBT, at the age of 9 months, EEG showed no epileptiform discharges with normal background activity during sleep (C) and wakefulness (D).