INTERFERON BETA (IFN-ß) THERAPY IN TWO CHILDREN WITH SSPE: A CASE STUDY

SSPE'Lİ İKİ ÇOCUKTA İNTERFERON BETA (IFN-ß) TEDAVİSİ: VAKA ÇALIŞMASI

M. Özlem HERGÜNER, M.D., Şakir ALTUNBAŞAK, M.D., Mürüvet ELKAY, M.D., Vildan BAYTOK, M.D.

Çukurova University, Faculty of Medicine, Department of Pediatric Neurology, Adana-Turkey
Gazi Medical Journal 2003; 14: 89-91

SUMMARY: We treated two patients with SSPE by using intramuscular interferon beta (IFN-ß) and oral isoprinosine for 5 and 6 months. However, we found no effect on the clinical course, magnetic resonance findings and measles antibody titers of the cerebrospinal fluid. The different responses to the therapy may be explained by the changes of virus subtypes responsible in recent years or the differences of the immunity capabilities of the hosts. Further multicenter collaborative controlled studies are needed to determine the efficacy of (IFN-ß).

Key Words: *Subacute Sclerosing Panencephalitis And ß-Interferon And Therapy.*

ÖZET: *Bu çalışmada SSPE tanısı alan iki çocuğu 5 ve 6 ay boyunca interferon beta (IFN-ß) ile tedavi ettik. Ancak klinik gidiş, magnetik rezonans bulguları ve beyin-omurilik sıvısı kızamık antikor düzeyleri üzerinde olumlu etki göremedik. Tedaviye karşı gelişen farklı cevapların, yıllar içinde virüs subtiplerindeki veya konağın immunolojik durumundaki değişikliklerle açıklanabileceğini düşünüyoruz. Ancak kesin bir karar için çok merkezli kontrollü çalışmalar yapılmalıdır.*

Anahtar Kelimeler: *Subakut Sklerozan Panensefalit, ß-İnterferon, ve Tedavi.*

INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a progressive and fatal central nervous system disorder caused by persistent infection with the measles virus. Affected patients usually have behavioral changes, myoclonus, mental deterioration, seizures, extrapyramidal dysfunction and visual disturbances. Spontaneous remission is rare, and the disease eventually has a progressive course, leading to death within a few years.

There is currently no specific, definite therapy protocol for SSPE, although several therapeutic agents are used with some beneficial effects in patients. There are many studies which report that the combined therapy of oral isoprinosine and intraventricular interferon alpha (IFN-α) is the most effective treatment for SSPE (1-3). However because many patients cannot receive this regimen for various reasons, particularly the need for a surgical procedure and hospitalization, investigators have looked for alternative treatment methods. interferon beta (IFN-ß) has a similar effect to IFN-α and has an easier administration. Therefore, in recent years some studies about the administration of IFN-ß- in SSPE have been reported (4).

This report concerns the follow-up of two patients with SSPE, which were treated with IFN-ß1a, plus oral isoprinosine.

PATIENTS AND METHODS

Two patients were diagnosed with SSPE at Çukurova University's Department of Pediatric Neurology in 1999-2000. The diagnosis was

based on the history, typical EEG findings and a positive cerebrospinal fluid (CSF) measles antibody titer using the complement fixation method. None of them had disorders other than SSPE. Staging was done according to Risk and Haddad (5). Intramuscular IFN-ß1a was given, 3 million units, twice per week for 5 and 6 months. Both of them also received oral isoprinosine 100mg/kg per day.

At the time of diagnosis, during the treatment every month and at the end of the treatment, the patients' neurologic examinations, neurologic disability index (NDI) scores, stages and renal, hepatic and hematological parameters were recorded. Additionally, at the beginning and end of the treatment, cerebral magnetic resonance imaging (MRI) and cerebrospinal fluid measles antibody titers were obtained in both patients.

RESULTS

Patient 1, a six-year-old boy, was admitted with ataxia and myoclonic jerks. His neurological symptoms had begun three months previously. He had mild spasticity and dementia suggesting stage IIA of SSPE. An axial T2-weighted MRI demonstrated cerebral and cerebellar atrophy and hyperintense lesions on the mesencephalon, basal ganglia and subcortical white matter. His NDI score was 17. He received IFN-ß1a plus isoprinosine for 5 months without any side effects. Although there was no change in the MRI, his neurologic status deteriorated steadily and his NDI score changed from 17 to 49 (Fig. 1), and his stage changed from IIA to IIIB. At the beginning of the therapy, the CSF measles antibody titers was 1/16. Moreover, at the end of the therapy it was measured at 1/512.

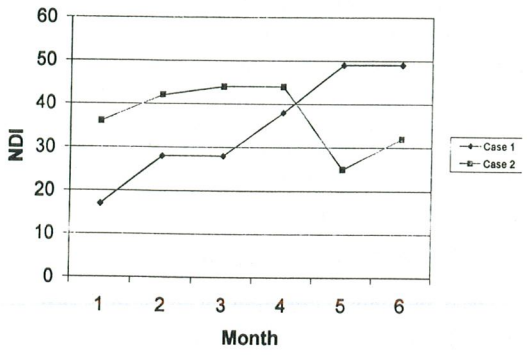

Fig. 1: Neurological disability indexes of patients.

Patient 2, a 6.5-year-old girl, was also admitted with myoclonic jerks and dementia. She had shown a loss of interest in normal daily activities over a 1-year period. On admission, the neurologic examination revealed mental deterioration, mild pyramidal signs and extremity ataxia. A T2-weighted MRI showed cerebral and cerebellar atrophy and hyperintense lesions on the basal ganglia. Her NDI score was 36, and the stage pointed to IIIB of SSPE. She was given IFN-ß1a therapy for 6 months and developed fevers and headaches after some doses. At the end of the treatment, the score changed to 32 and the stage was IIIA (Fig. 1). The CNS measles antibody titers were 1/16 and remained the same in the MRI findings. One month after the cessation of treatment, her neurological status progressively deteriorated. She was treated again with the same regimen. However, she unfortunately died 2 months later because of an additional infection.

DISCUSSION

SSPE is a rare childhood disease that usually begins with personality and behavioral changes, followed by myoclonic seizures and progressive mental and motor deterioration and finally leads to death in approximately 2 to 3 years. In previous studies, intraventricular IFN-α combined with oral isoprinosine was reported as the most effective agent in treatment. Because of some drawbacks, however, alternative therapies are needed.

IFN-ß is similar to IFN-α with its structural and biological status. It can be used in systemic ways. In addition, its safety and adverse effects are well-established in the treatment of multiple sclerosis (6). The action of IFN-ß may be related to its anti-inflammatory effect and its ability to modify the immune response.

In our first case, the patient's neurologic status deteriorated steadily despite therapy. But the second one showed some improvement at the end of 6 months. The remission state in the second patient may have been due to the disease's slower progression rate. Her therapy was stopped after 6 months, but her clinical state began to worsen. Although she was treated again with the

same regimen, her status deteriorated very progressively. Resistance to IFN-ß or the presence of antibodies to IFN-ß may have caused this deterioration. The drug should not be stopped in patients who have shown clinical improvement with therapy.

The pathophysiology of remissions and relapses in SSPE is unknown. The stable state may depend on a balance between viral replication and the immune response, and the immune system possibly has an effect in remissions.

In a previous study, subcutaneous IFN-ß was given to 7 pediatric patients (4). Three showed some improvement or stabilization, especially after 2 months. In some patients the effect of IFN-ß might continue for a few months after treatment was stopped. But in our patients, IFN-ß appears to be ineffective.

In Turkey, especially after 1995, the age of onset and the latent period of SSPE decreased significantly without a significant change in the age at onset of measles (7). But the real factors affecting them are unknown. This may be due to the changes of measles virus subtypes responsible for SSPE within the last decade or differences in the immune capabilities of individuals. The different responses to IFN-ß therapy may also be explained this way. But to assess the effectiveness of IFN-ß, more reports are needed.

In conclusion, intraventricular IFN-α therapy appears to be the most efficient therapeutic agent in SSPE. However, because of some of this therapy's limitations, it is necessary to determine alternative treatments. In our two cases, IFN-ß showed no effects. Multicenter colloborative controlled studies must be done in the treatment of SSPE.

Correspondence to: M. Özlem HERGÜNER, M.D.
Çukurova Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları
Anabilim Dalı
Neroloji Bilim Dalı
01330 ADANA - TÜRKİYE
Phone : 332 - 338 60 60 / 3155
e-mail: oherguner@hotmail.com

REFERENCES

1. Anlar B, Yalaz K, Öktem F, Köse G. Long-term follow-up of patients with subacute sclerosing panencephalitis treated with intraventricular α-interferon. Neurology 1997; 48: 526-528.
2. Gökçil Z, Odabaşı Z, Demirkaya Ş, Eroğlu E, Vural O. α-interferon and isoprinosine in adult-onset subacute sclerosing panencephalitis. J Neurol Sci 1999; 162: 62-64.
3. Tomoda A, Shirashi S, Hosoya M, Hamada A, Miike T. Combined treatment with interferon-alpha and ribavirin for subacute sclerosing panencephalitis. Pediatr Neurol 2001; 24: 54-59.
4. Anlar B, Yalaz K, Köse G, Saygı S. ß-interferon plus inosiplex in the treatment of subacute sclerosing panencephalitis. J Child Neurol 1998; 13: 557-559.
5. Risk WS, Haddad WS, Chemali S. Substantial spontaneous long-term improvement in subacute sclerosing panencephalitis: Six cases from the middle east and a review of the literature. Arch Neurol 1978; 35: 494-502.
6. The IFN-ß Multipl Sclerosis Study Group and the University of British Columbia MS/MRI Analysis Group. Interferon beta-1b in the treatment of multiple sclerosis: Final outcome of the randomized controlled trial. Neurology 1995; 45: 1277-1285.
7. Anlar B, Köse G, Gürer Y, Altunbaşak Ş, Haspolat S, Okan M. Changing epidemiological features of subacute sclerosing panencephalitis. Infection 2001; 29: 192-195.