소아의 재발성 톨로사 헌트 증후군 1례

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Recurrent Tolosa-Hunt syndrome in a child : A Case Report

Tolosa-Hunt Syndrome (THS) is characterized by painful ophthalmoplegia caused by nonspecific granulomatous inflammation in the cavernous sinus. It shows a prompt response to steroids. However, there is a lack of data regarding the recurrence of THS and no guidelines yet exist for the optimal duration of steroid therapy, especially in children. A 6-year-old boy with headache, ptosis, and oculomotor palsy visited the pediatric emergency room with no other evidence which could account for the etiology of disease in terms of clinical symptoms or laboratory data. Upon brain magnetic resonance imaging (MRI), multiple small-sized enhancing nodules were observed around the left cavernous sinus. He improved with prednisolone treatment. Six months later, his painful ophthalmoplegia relapsed; however, no progressive lesion was visible on the brain MRI, and the symptoms were relieved by repeated steroid therapy. Herein, we report a case of recurrent pediatric Tolosa-Hunt syndrome, which is rare in Korea.

Key Words: Tolosa-Hunt syndrome, Child, Recurrence

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Introduction

Tolosa-Hunt syndrome (THS) is characterized by painful ophthalmoplegia or headache with oculomotor nerve palsy¹⁾. It is caused by nonspecific inflammation of the cavernous sinus, and shows a prompt response to steroids.

The syndrome was first described in 1954 by Tolosa²⁾ as a case of left-sided ophthalmoplegia with granulomatous inflammation, based on autopsy findings which were interpreted as periarteritis of the cavernous carotid artery. In 1961, Hunt³⁾ described six cases of remittent unilateral orbital pain with extraocular palsy, which improved promptly with corticosteroid therapy. In 1966, Smith and Texdal⁴⁾ reported five cases of painful ophthalmoplegia, first labeling it as "Tolosa-Hunt syndrome".

THS is a rare disease, especially in the pediatric population⁵⁻⁷⁾. A few case reports of pediatric THS in Korea were made after the introduction of the International Headache Society (IHS) criteria in 2004⁸⁻¹¹⁾. Recurrence of THS in children is even rarer, with only one reported case in Korea⁸⁾. We encountered recurrent THS in a 6-year-old boy with painful ophthalmoplegia. Therefore, herein we report a case of recurrent pediatric THS.

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Case

A 6-year-old boy visited the pediatric emergency room (ER) of Samsung Medical Center for acute onset of ptosis in the left eyelid and diplopia on October 4th, 2010. His initial symptoms were unilateral headache with vomiting, which started 10 days before visiting the ER and was relieved without medication. After four days, left ocular pain was developed, followed by diplopia and left-sided ptosis on the very next day. When visiting a local ophthalmologic clinic, the case was treated as allergic conjunctivitis. Three days later, the symptoms had not improved and the ophthalmologist found limitation of the median movement of left eye, prompting the patient to be referred to this institution.

In the ER, he complained of headache with ptosis and diplopia. He had previously been healthy and had no recent history of injury, fever or infection. In terms of family history, his father

was diagnosed with neurofibromatosis type I (NF-1). The child had had three hypopigmented spots on his back, chest, and leg when at the age of one; however, they had disappeared and were not observed upon physical examination. He did not fulfill the criteria of having NF-1. Vital signs and physical examination were also within the normal limits. Upon neurologic examination, he was found to be alert and showed limitation in medial gaze with ptosis in the left eye (Fig. 1). Otherwise, he showed up normal on examination of the other cranial nerves. He also had normal motor and sensory function, deep tendon reflex, cerebellar function and coordination without pathologic reflexes. The complete blood count, serum chemistry, erythrocyte sedimentation rate, C-reactive protein, and serum protein electrophoresis were all normal. No abnormalities were observed when testing autoantibodies, including fluorescent treponemal antibody (IgM), fluorescent antinuclear antibody, anti-smooth muscle antibody, and anti-dsDNA antibody.

Fig.1. On initial neurologic examination, the median movement of left eye was restricted and the ptosis of left eye was also found.

Fig.2. Brain magnetic resonance imaging (MRI) showed multiple small-sized tiny nodules of high signal intensity around the left cavernous sinus on the coronal view of T2-weighted image (A) and the coronal post contrast view of T1-weighted image (B). There was no difference in the follow-up brain MRI in the coronal post contrast view of T1-weighted image (C).

Upon brain and orbit MRI, multiple small-sized enhancing nodules were observed around the left cavernous sinus (Fig. 2A, 2B). There were cystic lesions in the left frontal lobe and basal ganglia, which was assumed to be associated with NF-1.

With the clinical diagnosis of THS, steroid therapy was started using prednisolone (30 mg, 1 mg/kg). The ptosis and limitation in the medial gaze of the left eye improved after two days of treatment. He was treated with prednisolone for 10 days, after which he was gradually weaned off over a month. His eye movement became nearly normal after a month of treatment. At a 5-month follow-up visit, no clinical symptoms were observed, and the follow-up orbit MRI showed no interval change of the previously recorded enhancing nodules near the left cavernous sinus.

A month later (6 months after the onset of disease), he visited the outpatient clinic with recurred headache, ptosis and diplopia. His headache had started four days before the visit and was followed by left oculomotor palsy 3 days later. Upon neurologic examination, ptosis of the left eye and limitation in both upper and lower gazes was found. No deficit was found on examination of the other cranial nerves. He also had normal motor and sensory function tests, deep tendon reflexes, cerebellar function and coordination without pathologic reflexes. On the brain MRI, no significant changes from the previous images were evident (Fig. 2C). The patient was administered the same dose of prednisolone (30 mg, 1 mg/kg) for 2 weeks, and then gradually weaned off over a month. His symptoms improved within two days of beginning the treatment. Since then, he was followed up for 2 years without showing symptoms of recurrence.

Discussion

THS is a rare disease characterized as painful ophthalmoplegia caused by nonspecific granulomatous inflammation in the cavernous sinus, superior orbital fissure, or orbital apex, and is highly sensitive to corticosteroid treatment. The literature reports indicate a recurrence rate of 30–40% in adults, with large variability over time and clinical conditions^{6,12,13}. There is also a recent report which showed the recurrence of adult THS to be higher in younger patients¹³. However, there are only a few reports of the recurrence of pediatric THS^{7,14}. This case illustrated a relatively rare recurrent case in a pediatric patient, which recurred within a year and showed good response to oral steroid treatment during both episodes.

There were two recurrent pediatric THS cases in which the patient presented with headache and diplopia or facial palsy and

required prolonged steroid treatment^{7,14}. In 2006, Kim et al.⁸ reported an unusual chronic variant of an 11-year-old girl who required low-dose steroids for 11 months due to incomplete remission during the tapering phase after the oral administration of 1 mg/kg prednisolone per day. In comparison with that case, the patient in this report had complete remission with oral prednisolone and recurred in 6 months. In the reported cases of recurrent pediatric THS, relapse was found within 2 years and prolonged steroid treatment was performed^{7,8,14}. However, steroid therapy of the relapse episode in this case did not require prolonged treatment, and additional recurrence of the disease for the next 2 years was not found.

THS is ameliorated with corticosteroid therapy in several weeks or months and sometimes relapses. Other treatment options have been considered, such as immune suppressors, immune therapy and radiotherapy^{14,15}. One of the recommended doses for the treatment of THS is prednisolone, 1–1.5 mg/kg per day. The typical steroid response in pediatric patients with THS was reported by Koul and Jain¹⁶ in 2003. After the administration of 1 mg/kg per day of prednisolone, the pain was found to subside within 72 hours and the neurological signs regressed after three weeks, with complete MRI normalization. Yeung et al.⁵ treated a 9-year-old who complained of headache, left eye pain, and third and fourth nerve palsy with high-dose steroid (2 mg/kg per day of prednisolone), resulting in complete resolution of the neurological signs within two weeks. The authors observed that a higher amount of steroid might be crucial for the success of the therapy. In 2013, Na et al.⁹ reported a Korean case in which a 12-year-old girl presented with left periorbital pain followed by oculomotor palsy, with a hypointense lesion at the left cavernous sinus on the brain MRI. It took a week for her to experience full recovery from the pain and neurological symptoms after the administration of 30 mg/kg of methylprednisolone followed by 0.6 mg/kg of dexamethasone. She recovered almost completely after the fifth day of treatment, and recurrence was not reported for ten months.

THS has diagnostic criteria which emphasizes the exclusion of other conditions such as infection, true neoplasm, lymphoma, leukaemic infiltration, sarcoidosis, arteriovenous fistula, or thyroid disease¹. Painful ophthalmoplegia should be differentiated from ophthalmoplegic migraine, carotid aneurysm, and arteriovenous fistula at the level of the cavernous sinus. Differentiating ophthalmoplegic migraines from THS is difficult because of their similar features, including headache, periorbital pain, and oculomotor palsy. In addition, ophthalmoplegic migraines also respond well to steroid treatment. In terms of MRI findings, ophthalmoplegic migraines show hyperintense

lesions on the oculomotor nerve, whereas THS shows granulomatous lesions on the cavernous sinus. Although there was a family history of NF-1 and cystic lesions upon brain MRI, the patient did not have any dermatologic or neuro-radiologic evidences of NF-1.

At present, the most sensitive modality for revealing signs of the typical granulomatous lesions involving the cavernous sinus is thin segmented brain MRI. After reviewing all cases published between 1988 and 2002 which met the clinical criteria, La Mantia et al.¹⁾ concluded MRI to be mandatory for correct diagnosis. Colnaghi et al.¹⁷⁾ emphasized the importance of the localization and extension of the inflammatory tissue on MRI as prognostic factors. The disappearance of abnormal soft tissue from the MRI after steroid therapy in pediatric cases has been reported in THS¹⁶⁾. However, in the present case, the pathologic signs did not completely disappear on the follow-up brain MRI compared to the initial MRI, but they did not progress either, as would be expected in malignancy.

Although ophthalmoplegia is a rare symptom in children, if there is no apparent cause of disease, Tolosa-Hunt syndrome could be considered as a differential diagnosis. Since the clinical criteria of THS involves the exclusion of other conditions, an initial close evaluation of the patient is very important for diagnosis. MRI findings and clinical changes of symptoms with steroid therapy are essential to fulfill the diagnostic criteria; neurologic and ophthalmologic evaluations should be performed advertently. Because there is a lack of data regarding the recurrence of pediatric THS, it is recommended to have one or two years of close follow-up evaluation with brain MRI.

In conclusion, the patient in this case fulfilled all the diagnostic criteria, including positive findings on the brain MRI. He went into complete remission after steroid therapy but experienced recurrence 6 months later. However, his relapsed symptoms were relieved with the same dose and duration of steroid therapy, and did not require prolonged steroid therapy. Therefore, we reported a case of recurrent pediatric THS.

요약

Tolosa-Hunt 증후군은 안와 주위의 통증과 안구운동 마비를 특징으로 하는 드문 질환으로 해면동 주위를 침범하는 비특이적인 염증 소견을 보이며 스테로이드 치료에 반응을 잘하는 것으로 알려져 있다. Tolosa-Hunt 증후군은 그 예후가 양호한 편이나 어른의 경우 30-40%에서 재발을 하는 것으로 알려져 있으며 소아에서의 재발에 대한 보고는 매우 드물다. 저자들은 6세 남아에서 Tolosa-Hunt 증후군으로 진단되어 스테로이드 치료 후 특별한 후유증 없이 회복되었으나

6개월 후 재발을 경험하여 다시 스테로이드 치료가 필요했던 증례를 경험하였기에 이를 보고한다.

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