Case Report

Carbamazepine-Induced Incomplete Stevens-Johnson Syndrome: Report of a Case in Children without *Mycoplasma pneumoniae* Infection

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*Incomplete Stevens-Johnson syndrome (SJS) is a rare reactive skin condition. Most cases are occurred in children and all are associated with Mycoplasma pneumoniae (M. pneumoniae) infection. We reported an unusual case of a 6-year-old boy who developed the presentation of isolated mucosal erosion with a lack of skin findings, which indicated incomplete SJS after two weeks of carbamazepine (CBZ) administration. Findings of positive HLA-B*1502 allele supported a possible causative influence of carbamazepine inducing SJS. Interestingly, this patient was tested negatively for M. pneumoniae. This is a significant finding since there is no previous report of incomplete SJS without M. pneumoniae infection. Discontinuation of CBZ and administration of systemic corticosteroids were accomplished to treat SJS, which resulted in complete recovery. Our interesting findings highlighted the manifestation of incomplete SJS, which can present with other causes rather than M. pneumoniae infection. Early manifestation of mucosal change without typical skin lesions should not be neglected in the diagnosis of incomplete SJS.*

Keywords: *Incomplete/Atypical Stevens-Johnson syndrome, Mycoplasma pneumoniae*

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Stevens-Johnson syndrome (SJS) is a severe life-threatening skin condition[1] with high morbidity and mortality. The typical findings usually present with target-like skin lesions with at least two or more mucosal involved[2]. Incomplete SJS or atypical SJS is another form of cutaneous reaction that is defined as a lack of target-like skin, typically found in SJS but presenting only mucosal manifestation[3-8]. The etiology of incomplete form is still unknown; however, many authors reported series of cases and believed that these can be associated with *M. pneumoniae* infection[5,7,9-13]. In contrast to those, classic SJS is mostly caused by drugs[2]. Most cases of incomplete SJS were presented in children and young adults and had evidences of *M. pneumoniae* infection. Because of its association of this infection, treatment with antimicrobial against *M. pneumoniae* is recommended.

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Nevertheless, Vanfleteren et al[8] reported one case in a 14-year-old boy of incomplete SJS without evidence of *M. pneumoniae* infection. The patient had no other possible causes supporting the manifestation of isolated mucosal findings. In this study, oral antimicrobial against *M. pneumoniae* was given and significant clearing of mucosal lesions was found. Thus, the author proved that without any evidence of *M. pneumoniae* infection, it could not completely rule out this organism in the manifestation of incomplete SJS.

Similarly to our case that illustrated the manifestation of incomplete SJS, our patient (a 6-year-old boy) also showed no evidence of *M. pneumoniae* infection. However, our patient had a complex partial seizure and was treated with oral carbamazepine (CBZ), which has been shown to be highly suggestive cause of incomplete SJS.

Our current report aimed to investigate the manifestation of a rare incomplete SJS, which can result from other causes without any evidence of *M. pneumoniae* infection. The study was approved by the Institutional ethical board review (Project No. HE571305), Khon Kaen University, Thailand.

Case Report

A six-year-old boy was referred to our department with erythematous cracked lips (Fig. 1), injected conjunctiva, and some erosions on his penis for two days. Two weeks prior to the onset of the mucosal changes, he had been treated for a complex partial seizure by taking 10 mg/kg/day of oral CBZ. His seizures were controlled; however, he developed some erosive changes on his mucosal areas as described. His cutaneous finding was normal. Neither target-like lesions nor denuded skin was found. Ocular examination was performed by an ophthalmologist right after he was hospitalized. The results showed early mucosal involvement of SJS.

According to a lack of cutaneous findings but with isolated mucosal involvement, incomplete form of SJS was diagnosed. CBZ was suspected as the primary cause of his mucosal changes. However, further investigations were performed to explore the possibility of *M. pneumoniae* infection.

All blood tests were done with negative results. The lesion on his oral mucosa was scraped and tested negatively for herpes and bacterial infection. No evidence of leukocytosis or infection was found. The patient was also tested negatively for *M. pneumoniae* from the serology testing in conjunction with normal chest radiograph. Four-fold rising and four-fold down of his blood serology for *M. pneumoniae* were performed and yielded negative results as well.

According to the recent findings of HLA allele B*1502 expression, which shown to be a marker for carbamazepine-induced SJS syndrome in many literatures, we performed blood testing to evaluate B*1502 allele using RT-PCR. The result was positive. Therefore, we firmly believed that CBZ was the culprit drug in this case.

Even though we found negative evidence of *M. pneumoniae* infection, we could not completely rule out this organism in the manifestation of incomplete SJS. However, we decided to treat this patient with prednisolone in combination with discontinuation of CBZ due to the fact that positive HLA allele B*1502 was highly associated with SJS. The anti-epileptic drug was changed to Valproate according to the symptoms of a complex partial seizure.

Prednisolone 1 mg/kg/day orally was prescribed for five days. His mucosal lesions improved and complete recovery was noticed at a two-week follow-up (Fig. 2).

Discussion

Incomplete SJS was defined as a lack of the typical skin manifestations found in classic SJS is characterized by erythematous, target-like, or denuded skin, with the presentation of two or more mucosal changes in oral, ocular, and genital area. Most reported

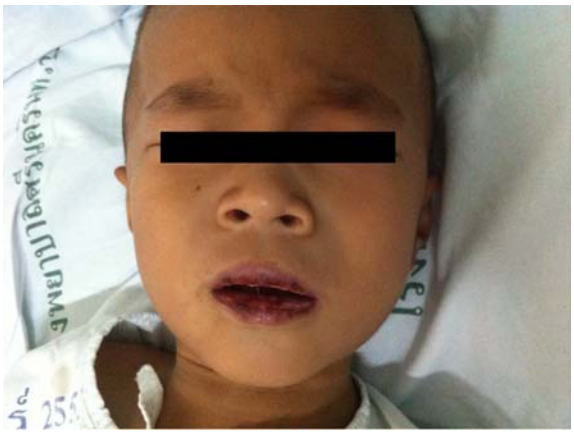

Fig. 1 Isolated cracked erythematous lips with a lack of skin findingssuggested incomplete SJS.

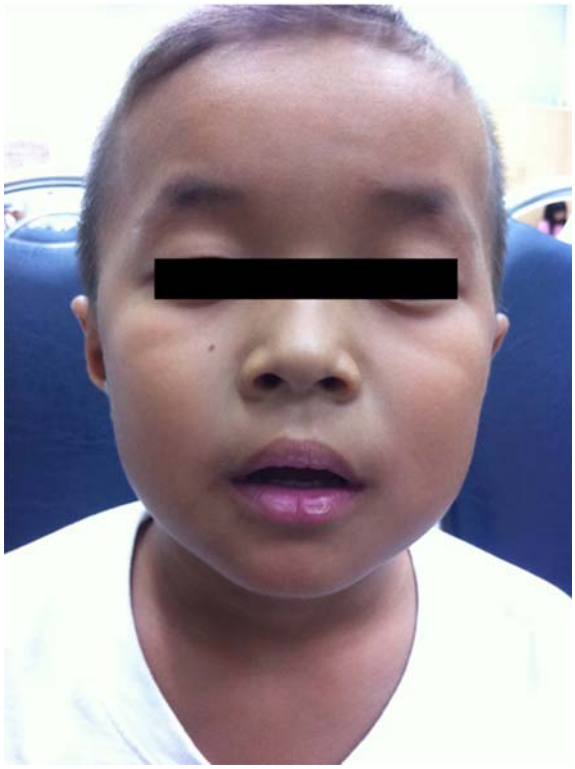

Fig. 2 Complete recovery of the mucosal changed at two-week follow-up after a five-day-course of 1 mg/kg/day oral prednisolone.

cases occurred in children and all were related to *M. pneumoniae* infection[3-6,12,14]. Some rare reported cases were found in adults[13] and the evidences of *M. pneumoniae* infection were documented as well.

Our case demonstrated a manifestation of incomplete SJS with no evidence of *M. pneumoniae* infection. Carbamazepine, the only exposed drug, was the possible cause in this case. Positive HLA allele B*1502 expression also supported the hypothesis of CBZ-induced SJS since a strong association between HLA-B*1502 and CBZ-induced SJS[15] has been reported in literature[16-19].

The difference between other SJS cases with positive HLA allele B*1502 and our case is the severity of the cutaneous findings. CBZ-induced SJS with positive HLA allele B*1502 are usually severe with extensive denuded skin[17]. In contrast, our case presented as incomplete form and had mild mucosal involvement only. This might result from an early detection and awareness of SJS cases in our practice. As mentioned above, antimicrobial against *M. pneumoniae* was used in the treatment of incomplete SJS in previous reported cases. However, this was not applied in our case since the patient was tested negatively for *M. pneumoniae* infection. We prescribed 1 mg/kg/day prednisolone orally for five days in conjunction with discontinuation of CBZ. Complete recovery was noticed at two-week follow-up, hence further indicated that CBZ was the culprit drug. This finding also supported the hypothesis of drug-induced incomplete SJS rather than infection.

Our interesting finding enhanced the notion that incomplete SJS can present with other causes rather than *M. pneumoniae* infection, even in the patient with positive HLA allele B*1502, which is highly associated with severe SJS. Moreover, complete recovery by stopping CBZ in combination with administration of oral prednisolone supported this incomplete form of SJS from CBZ without *M. pneumoniae* infection. Early manifestation of mucosal changes without typical skin lesions should not be neglected in the diagnosis of incomplete SJS. We suggested systemic corticosteroids as the treatment option in drug-induced incomplete SJS.

Conclusion

Incomplete SJS can present with other causes rather than *M. pneumoniae* infection, even in the patient positive for HLA allele B*1502, which is highly associated with severe SJS. The manifestation of isolated mucosal involvement without cutaneous findings is challenged and should not be neglected in the diagnosis of incomplete SJS.

What is already known on this topic ?

Incomplete SJS is the presentation of isolated mucosal lesion with a lack of cutaneous findings like those in classic SJS. *M. pneumoniae* was described as the cause of this manifestation.

What this study adds ?

Incomplete SJS can present with other causes rather than *M. pneumoniae* infection, even in the patient with positive HLA allele B*1502, which is highly associated with severe SJS. Systemic corticosteroids can be used as the treatment option in drug-induced incomplete SJS.

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Potential conflicts of interest

None.

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รายงานผู้ป่วย Stevens-Johnson syndrome ที่มีอาการทางผิวหนังไม่สมบูรณ์ที่เกิดจากยา carbamazepine และไม่สัมพันธ์กับการติดเชื้อ Mycoplasma pneumoniae

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*Stevens-Johnson syndrome ที่มีอาการทางผิวหนังไม่สมบูรณ์ (incomplete Stevens-Johnson syndrome) เป็นภาวะที่พบได้ไม่บ่อยนัก ส่วนใหญ่พบในผู้ป่วยเด็กและสัมพันธ์กับการติดเชื้อ Mycoplasma pneumonia การรายงานนี้พบในผู้ป่วยเด็กอายุ 6 ปี ที่มีอาการแสดงของเยื่อบุในร่างกายแต่ไม่มีอาการแสดงทางผิวหนัง ซึ่งเข้าได้กับการวินิจฉัย incomplete SJS โดยสาเหตุของ incomplete SJS ในผู้ป่วยรายนี้เป็นผลจากยา carbamazepine ที่ใช้รักษาภาวะชักในผู้ป่วยซึ่งมีประวัติได้รับยาก่อนเกิดอาการ 2 สัปดาห์ นอกจากนี้การตรวจพบ HLA-B*1502 ในผู้ป่วยรายนี้ยังช่วยสนับสนุนสมมติฐานสาเหตุการเกิด incomplete SJS ว่าเป็นจากยา carbamazepine อีกด้วย ผู้ป่วยได้รับการตรวจเพื่อหาหลักฐานการติดเชื้อ Mycoplasma pneumoniae เนื่องจากรายงานผู้ป่วยที่ผ่านมาของ incomplete SJS นั้นสัมพันธ์กับการติดเชื้อดังกล่าวทั้งสิ้นอย่างไรก็ตาม ไม่พบหลักฐานการติดเชื้อ Mycoplasma pneumoniae ในผู้ป่วยรายนี้แต่อย่างใด ผู้ป่วยได้รับการรักษาด้วยการหยุดยา carbamazepine ที่เป็นสาเหตุร่วมกับรับประทานยา corticosteroid ผลการรักษาพบว่าผู้ป่วยมีอาการหายเป็นปกติหลังติดตามการรักษา 2 สัปดาห์*