CASE REPORT
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Long-term Complications of Stevens-Johnson Syndrome on Permanent Teeth : A Case Report

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Stevens-Johnson syndrome (SJS) is a severe adverse cutaneous drug reaction seen rarely in clinical practice. Although relatively rare, the condition can be fatal. Mainly, it is caused by side effects of certain medications. Previous reports have associated Stevens-Johnson syndrome with abnormal root development, but the other long-term dental complications have rarely been reported. In this case, the patient developed SJS at the age of 5, and abnormal root development of the maxillary and mandibular first molars and mandibular incisors was observed, as well as impaction of the mandibular canine and enamel hypomineralization of multiple teeth. Accordingly, appropriate restorative treatment and orthodontic treatment were performed, and the clinical characteristics of this symptoms and its treatment were discussed in more detail. We aim to highlight the need for dentists to be aware of the potential dental complications of SJS and to enable early diagnosis and management of the condition to avoid undesirable sequelae. [J Korean Dent Sci. 2024;17(2):75-83]

Key Words: Stevens-Johnson syndrome; Toxic epidermal necrolysis; Abnormal root development; Enamel hypomineralization; Impaction

Introduction

Stevens-Johnson syndrome (SJS) is a severe adverse cutaneous reaction to certain drugs in susceptible patients that mostly involve the skin and mucosal membranes[1]. SJS occurs across all age groups and the cause, although not clear, is generally attributed to hypersensitivity or adverse drug reactions in most cases. In some cases, bacterial infections may lead to SJS[2]. SJS can progress to toxic epidermal necrolysis (TEN). The difference is based on the extent of epidermis involvement. SJS involves less than 10% of the epidermis, while in TEN, more than 30% is affected. The prevalence of TEN is 1 - 2 cases per 1,000,000 population, and the prevalence of SJS is 1 - 6 cases per 1,000,000 population[3]. The initial symptoms of TEN and SJS

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can be non-specific, such as fever, eye irritation, and discomfort while swallowing. These are followed by a painful rash that spreads to form blisters on the mucous membranes of the mouth, nose, eyes, and genitals[4]. While skin involvement is most common, other organs, such as the eyes, cardiovascular, lung, stomach, and urinary system, can also be affected[5].

In adults, the oral symptoms of SJS are limited to the soft tissues including ulcerative lesions and blisters. In contrast, when a child is affected by SJS, teeth development may be affected, in addition to soft tissue invasions[6].

Oral soft tissue involvement related with SJS is well-reported in the literature. However, only a few studies have reported on the complications on permanent teeth development. The first report on abnormal root development was published in 1979 by De Man[7], followed by Ranalli et al.[8] in 1984, and by Brook[9] in 1994. Aside from these studies, dental complications of SJS were rarely been reported.

In this case report, we described a patient who experienced dental development complications, such as generalized enamel hypomineralization, mandibular canine impaction, and abnormal root development after experiencing SJS in early childhood. The patient underwent restorative treatment and orthodontic treatment. The symptoms, management, and outcomes are reported in this study.

Case Report

This study was conducted with the approval of the Institutional Review Board of Chosun National University Dental Hospital (IRB No: CUDHIRB 2402 001). Informed consent was obtained from the patient's legal guardian for the publication of this case report and any accompanying images.

A 9-year-old male patient presented to the dental hospital at Chosun University complaining of abnormal root development and tooth pain. The patient was diagnosed with SJS at age 5 years. At the time, the patient was prescribed a topical medication for a common cold accompanied by fever and headache. Two days after using the prescribed medication, blisters broke out all over the body. On the third day, the patient visited the emergency room at Chonnam National University Hospital with symptoms that were suggestive of mumps and pneumonia, spots appeared all over his body and his throat was swollen. SJS was confirmed. On day 5, the patient's condition worsened and the SJS progressed to TEN, with positive Nikolsky sign and additional symptoms, including exudate from both eyes, lesions in the mouth and on the external genitals, as well as neck swelling. Subsequently, the patient's condition improved with steroid treatment and antibiotics. However, symblepharon of the eye ball, cicatricial atrophy of the tongue surface, and vulvar urethra stricture persisted (Fig. 1).

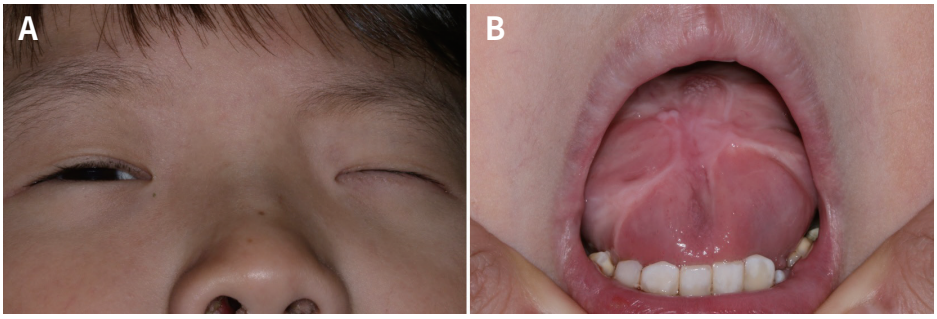


Fig. 1. One lasting effect of the disease in this patient. (A) Symblepharon of the left eyeball, (B) Cicatrizing atrophy of the tongue surface.

During a subsequent oral examination at this hospital, caries was observed on the occlusal surfaces of All permanent first molars, and the mesial, distal surfaces of maxillary right primary first molar and distal surface of mandibular left primary first molar and mesial surface of mandibular both permanent first molars (Fig. 2). Radiological examination showed abnormal root development affecting both permanent first molars and the mandibular permanent central and lateral incisors (Fig. 3). The short roots did not lead to clinical symptoms. Mobility and percussion tests were unremarkable. Additionally, the normal trabecular pattern in the periapical region indicated a healthy periodontium without external root resorption.

Appropriate restorative treatment was performed on each carious tooth. Among them, the mandibular left first molar, which complained of tooth pain, was in a state of severe caries, and it was judged that root canal treatment would be difficult due to abnormal root development and the patient's young age, so partial pulpotomy was performed for conservative treatment. After caries was removed, Biodentine™ (Septodont, Saint Maur des Fosses, France) was applied and composite resin was restored. In addition, composite resin restorations were performed on the permanent first molars, and preformed stainless-steel crown restorations were performed on the maxillary right primary first molar.

Two years later, at 11 years of age, the patient visited the hospital again for oral examination. On clinical examination, enamel hypomineralization was observed in the maxillary and mandibular first premolars, second premolars, and mandibular second molars (Fig. 4). Caries was observed in the occlusal surface of the mandibular permanent second molars. Considering the likelihood of crown breakdown due to enamel hypomineralization, a preformed stainless-steel crown was placed.

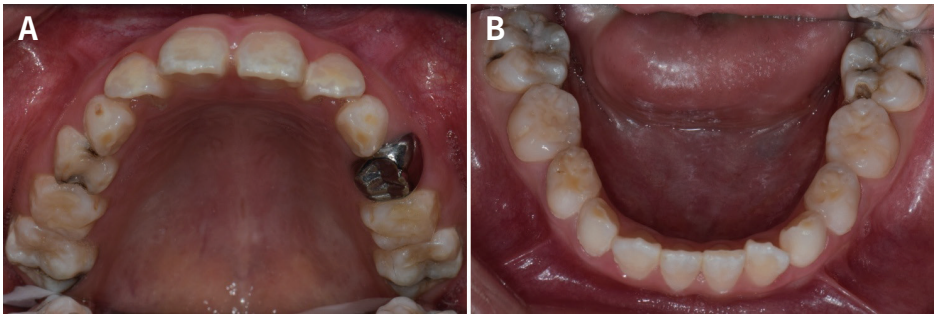


Fig. 2. Intraoral view at pretreatment. Nonspecific finding without dental caries. (A) Maxillary occlusal view. (B) Mandibular occlusal view.

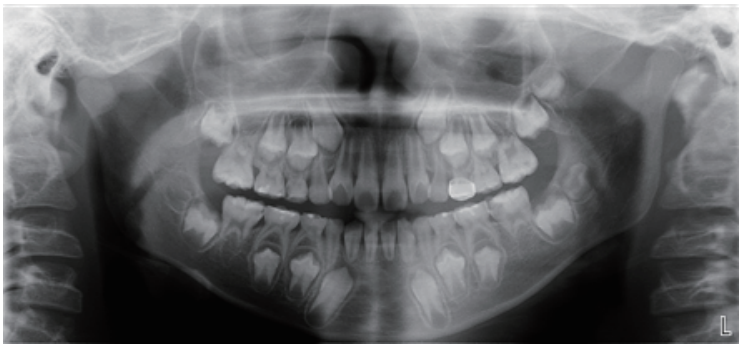


Fig. 3. Panoramic radiographic view at the initial visit shows abnormal root development of the maxillary both 1st molars, mandibular both 1st molars, and anterior mandibular teeth.

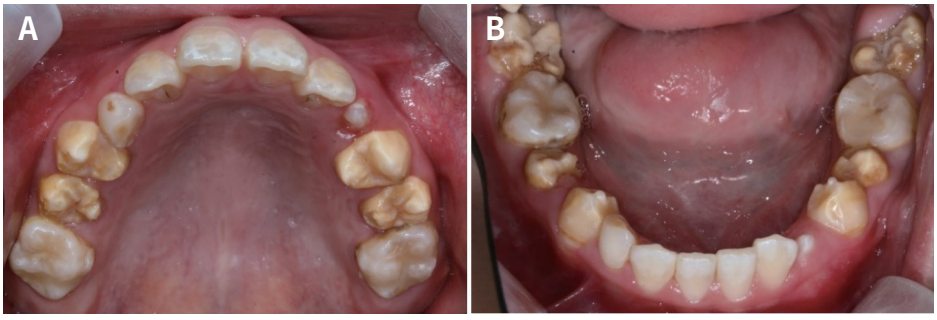


Fig. 4. Intraoral view at 11 years old shows enamel hypomineralization of the maxillary both premolars and mandibular both premolars, 2nd molars. (A) Maxillary occlusal view. (B) Mandibular occlusal view.

On radiological examination, impaction of the mandibular right canine was observed (Fig. 5). Cone-beam computed tomography (CBCT) imaging showed that the mandibular right canine was mesially tilted and was impacted against the lingual surface of the mandibular right lateral incisor. Moreover, well-defined and unilocular radiolucency surrounding the crown of the mandibular right canine was observed. This was subsequently diagnosed as a dentigerous cyst (Fig. 6). To treat the cystic lesion, decompression was performed after extraction of the mandibular right primary canine. The patient was followed up at the hospital every month for 6 months (Fig. 7). Six months later, the mandibular right canine erupted lingually. Orthodontic treatment was planned to align the teeth.

Before orthodontic treatment, aching symptoms developed in the mandibular both second premolars, which were enamel hypomineralization. Hence, pre-

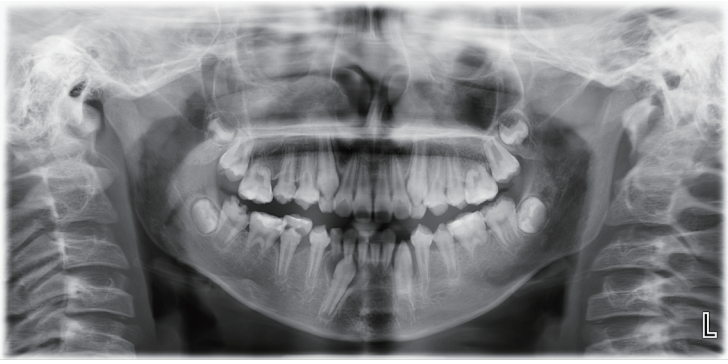


Fig. 5. Panoramic radiographic view at 11 years old shows impaction of the mandibular right canine.

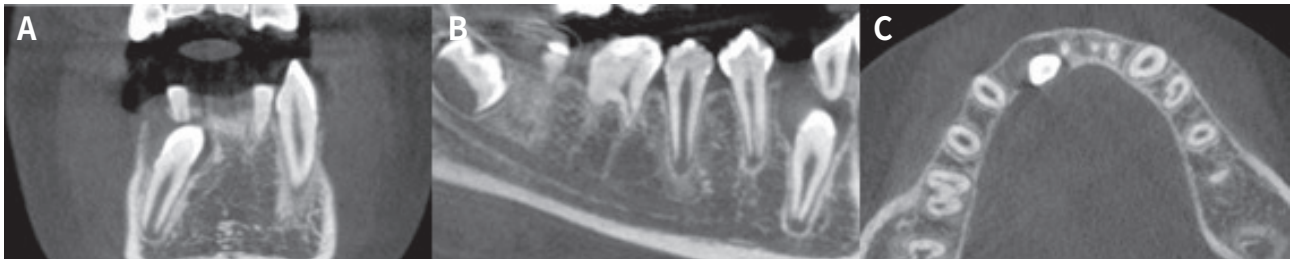


Fig. 6. Cone-beam computed tomography image for #43 impaction. (A) Coronal view. (B) Sagittal view. (C) Transverse view.

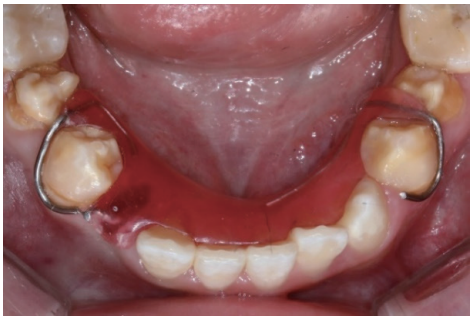


Fig. 7. Marsupialization was performed on the #43 impaction with removable appliance.

formed stainless-steel crowns were placed.

To ensure effective orthodontic treatment, a modified mandibular lingual arch appliance was used. An elastic thread was applied on the lingual hook of the mandibular right second primary molar to move the tooth distally, and another one was applied to the labial hook to move the tooth toward the labial and occlusal surfaces (Fig. 8). After 3 months, the mandibular right canine was aligned, and the appliance was removed.

Subsequently, hypersensitivity due to enamel hypomineralization occurred in the maxillary right second premolar and the maxillary left first and second premolars. These teeth were restored with preformed stainless-steel crowns. Preformed stainless-steel crowns were also placed on the maxillary both second permanent molars because of crown breakdown as these teeth were affected by enamel hypomineralization (Fig. 9, 10). We explained to the parents that the preformed stainless-steel crown should be removed and replaced with a cast crown when patient's occlusion of permanent dentition is completed.

At 16 years old, a panoramic radiograph showed that the roots of the maxillary and mandibular first molars and mandibular central and lateral incisors were still

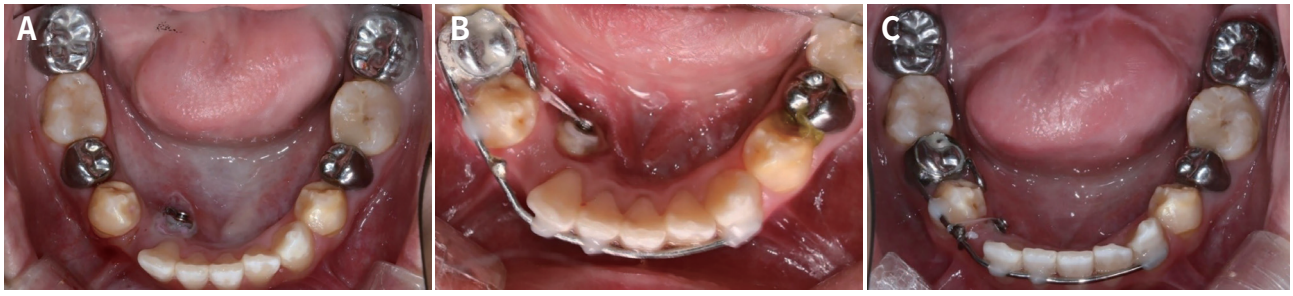
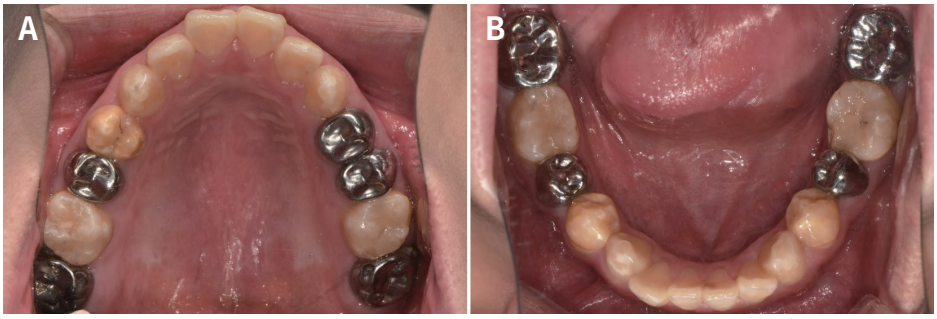


Fig. 8. Orthodontic traction of impacted canine with modified passive lingual arch. (A) Attaching a button to the lingual surface of #43. (B) Distal traction with applying elastic thread to the lingual hook of #85. (C) Labial traction with applying elastic thread to the labial hook.

Fig. 9. Post-treatment intraoral view at 16 years old. (A) Maxillary occlusal view. (B) Mandibular occlusal view.



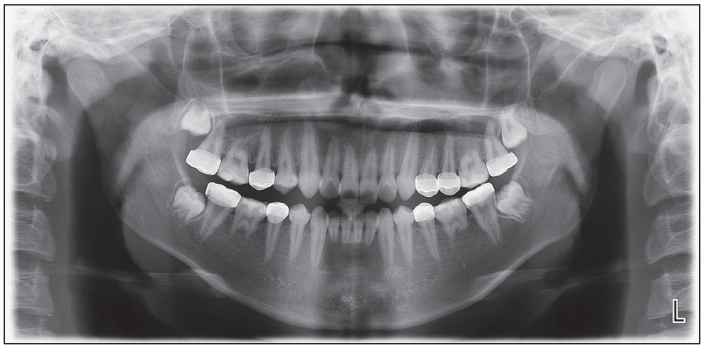


Fig. 10. Post-treatment panoramic radiograph at 16 years old.

stopped and shortened, and clinical examination showed negative mobility and percussion (Fig 10). The parents were notified that the prognosis of both first molars was bad, and if these were extracted, the possibility of replacement of the posterior second molar and uprighting of the mesially inclined third molar should be considered through orthodontic treatment.

Currently, the patient attends the hospital for regular dental examinations for follow-up check and preventive treatment, including applying periodic fluoride varnish, and for continuous management and long-term maintenance of the dentition.

Discussion

SJS and TEN, a form of acute severe mucocutaneous reaction, are rare diseases and the specific cause is still unknown. Drug exposure and a resulting hypersensitivity reaction is the cause of the very large majority of cases of SJS/TEN[1]. More than 100 drugs of various classes have been associated with SJS and TEN, but those most frequently implicated are sulfonamides, especially sulfamethoxazole; anticonvulsants (including carbamazepine, lamotrigine, phenobarbital, and phenytoin); non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids; the uric acid-lowering drug allopurinol, and nevirapine[10-12]. Drugs prescribed to treat other diseases may cause the syndrome, and causative drugs can only be confirmed by medical history. Therefore, finding a causative drug is not easy. Likewise, in this case, as the causative drug could not be defined at the time. So the use of dental medications was limited.

According to the study by Magina et al.[4], complications related to SJS have been reported to include hyper- and hypopigmentation of the skin, nail dystrophy, and eye complications. According to the study by Yip et al.[5], 50% of patients with TEN reported severe dry eyes, trichiasis, symblepharon, distichiasis, visual loss, entropion, ankyloblepharon, lagophthalmos, cornea ulceration as complications. Long-term complications involving the mucosal membrane occur in most patients in the acute phase, and mucosal complications typically invade the oral and esophageal mucosa and, to a lesser extent, the lung and genital mucosa[6].

As mentioned, systemic complications of SJS are recognized. However, abnormal root development as a dental complication of SJS has not been frequently reported[7-9]. A previous study reported that it is characteristic that the developed root length varies from tooth to tooth in relation to the time of onset of SJS. In other words, it can be assumed that tooth root development was stopped by some mechanism while the tooth root was developing. The main characteristic of SJS is a skin disease caused by necrosis of epidermal cells. This necrosis of epidermal cells affects the Hertwig's epithelial root sheath that develops the tooth root, inhibiting the differentiation of tooth papilla cells

into odontoblasts, thereby forming tooth root dentin. It can be assumed that an abnormality has occurred and the development of the tooth root has stopped[7,13]. Considering the timing of teeth development, this hypothesis is applicable in our case. For our patient, SJS occurred at 5 years of age. The timing consistent with root development of the mandibular permanent incisors and maxillary and mandibular first permanent molars. Similarly, the findings from Ranalli et al.[8], Gaultier et al.[14], Brook[9], and Thornton and Worley[15] concurred that SJS development was consistent with the time when root development stopped.

In the case of the patient, in addition to abnormal tooth root development, enamel hypomineralization was observed in the maxillary and mandibular first premolars, second premolars, and second molars. In severe enamel hypomineralization cases, the enamel may fracture due to the occlusal forces, thereby exposing dentin, and causing symptoms of post-eruption breakdown, rapid caries morbidity, and severe pain[16]. To effectively manage complication of SJS, early diagnosis is crucial, and appropriate restoration using preformed stainless-steel crowns is necessary. To date, the exact cause of enamel hypomineralization has not been identified, and it is assumed that various factors influence each other[17]. Long-term exposure to dioxins from breast milk[18], medical problems related to birth, postnatal nutritional status, fluoride intake[19], and childhood illness accompanied by high fever[20] have been associated with the increased frequency and severity of enamel defects. In our patient, it is possible that the enamel hypomineralization occurred due to ameloblast disruptions because of high fever and epidermal cell necrosis. Considering the timing of enamel development, and the age of the patient at the time, it is probable that the enamel hypomineralization may be related to SJS.

The patient also had an impacted the mandibular right canine and cystic lesion surrounding the tooth crown. Eruption failure of mandibular canines is relatively uncommon. Previous studies[21,22] suggest that generally, canines become impacted due to abnormal size or missing of lateral incisors. Brin et al.[23] reported that maxillary canine impaction was observed 10 times more often when the adjacent permanent lateral incisor was small, peg-shaped, or missing. This led to the "guidance theory," which states that canines erupt along the root surface of adjacent lateral incisors[24].

In our case, a reduced root-to-crown ratio was observed in the mandibular permanent lateral incisors due to abnormal root development. In addition, the abnormal roots had different degrees of root development. The impacted right mandibular permanent canine was mesially tilted and had complete root formation (Nolla stage 9), which suggests developmental disorders occur during the primary and early-mixed dentition periods. Such impaction typically occurs when there is root resorption of the lateral incisors, which can be explained with the guidance theory[24].

In Fig. 3, the degree of root development of both mandibular lateral incisors was the same, leading to the prediction that the differentiation paths of both mandibular canines would be similar. However, Figure 5 reveals a difference: radiograph show that the root development of mandibular left lateral incisor has progressed more than mandibular right lateral incisor and the impacted mandibular right canine and the normally erupted mandibular left canine. Therefore, it can be presumed that there was a high possibility of mandibular canine impaction due to abnormal root growth of the mandibular lateral incisor as well.

Erythema multiforme (EM) and SJS/TEN are distinct entities that lead the clinician to different investigations and management. The clinical appearance of cutaneous EM differs from that of SJS/TEN. The presentation of EM ranges from a self-limited, mild, exanthematous variant with minimal oral involvement (EM minor) to a progressive, fulminating, severe variant with extensive mucocutaneous epithelial necrosis (SJS/TEN), with EM major intermediate in severity[25]. Unlike EM minor, SJS/TEN is accompanied by systemic symptoms. Moderate leukocytosis, fluid and

electrolyte microalbuminuria, hyponatremia, elevated liver transaminase, hypoproteinuria and anemia also may be present. Additionaly, with EM the investigative focus is on identification of an infectious cause, particularly an HSV. With SJS/TEN the effort is to identify the causative drug[26]. So, when a dentist meets a patient suspected of having SJS/TEN in an outpatient clinic, It is necessary to recognize the diagnostic points of EM and SJS/TEN and consider appropriate management of the condition to avoid undesirable sequelae.

Conclusion

In conclusion, the dental developmental anomalies detected in our patient may be related to SJS at 5 years of age. Although the patient has recovered from the condition, complications including cicatricial atrophy of the tongue surface and eyelid adhesions have persisted. Furthermore, abnormal root development of the maxillary and mandibular first molars and mandibular incisors was noted on radiographs. Additionally, impaction of the mandibular canine due to short root of the mandibular lateral incisors and generalized enamel hypomineralization were also observed. This report aimed to enhance awareness of dental developmental complications associated with SJS.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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