

# Extreme Tooth Abnormalities and Treatment under General Anesthesia in a Child with chronic GVHD Surviving Relapse of Acute Lymphoblastic Leukemia

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*Treatment for acute lymphoblastic leukemia (ALL) mainly consists of chemotherapy, irradiation and bone marrow transplantation. In terms of long-term treatment effects, dental abnormalities and chronic graft-versus host disease (GVHD) are problems. We present a patient surviving relapse of ALL at one year of age. He had extreme dental abnormalities and multiple caries. Most of his permanent teeth were abnormal, and multiple caries were observed. Since he had a strong vomiting reaction to dental treatment, general anesthesia was given. During the general anesthesia, much sputum was aspirated because of chronic GVHD. His dental condition was worse than other cases reported previously. Since the survival rate has increased recently, the dental effects of ALL treatment have become significant. Especially, in patients undergoing total body irradiation at under 2 years of age, it is highly likely that dental problems will occur in the future.*

**Keywords:** Teeth Abnormality Leukemia Graft vs Host Disease, children, General Anesthesia.

## INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common cancer in children and adolescents. Although the fatality due to ALL was higher in the past, progress in treatment of ALL has resulted in a steady improvement in outcomes. In the 1990s, the five-year event-free survival rates for childhood ALL was about 80 percent in developed countries, and the cure rate is expected to be almost 90 percent in the near future.<sup>1</sup> However, one long-term effect of chemotherapy treatment and irradiation is

dental abnormalities such as absent teeth, microdontia, incomplete calcification, foreshortening root and multiple caries<sup>2,3</sup> because the treatment does not differentiate between neoplastic cells and metabolically active normal cells.<sup>4</sup> At present, most long-term survivors of childhood ALL reported to have dental abnormalities were diagnosed between 2-15 years of age.<sup>2,3,5</sup> We report a patient who was diagnosed with ALL at one month of age, and he relapsed when he was 1 year old. His dental condition was underprivileged at 11 years of age, and dental treatment was performed under general anesthesia (GA) due to a strong vomiting reflex to dental treatment.

## Case Report

The patient was diagnosed with infant ALL within one month after birth, and unrelated cord blood transplantation (uCBT) and chemotherapy consisting of busulfan (BU) and cyclophosphamide (CY) were performed at 8 months of age. ALL relapsed at 1.5 years old, and he was treated with unrelated bone marrow transplantation (uBMT) and CY combined with 12 Gy total body irradiation (TBI). After that, he was mainly treated for chronic graft-versus host disease (GVHD) in the lungs and conjunctiva with immunosuppressive agents and steroids. He was diagnosed with pervasive developmental disorder at 9 years old, although no intellectual disability was involved. He was short for his age (11 years old, 115 cm tall, 19 kg), and was diagnosed with precocious puberty.

He was introduced to a department for pediatric dentistry from his responsible doctor at 9 years of age. His dental problems at that time were a microdont and a delay in tooth eruption after primary tooth fell out. Panoramic X-rays showed the following (Fig 1): 1) Primary canine first and second primary overretained teeth, but severe dental caries involving all teeth. Since root resorption was observed in primary teeth, the original root shapes were unknown. The root shapes of the maxillary primary teeth appeared abnormal. 2) Cuspids, first and second premo-

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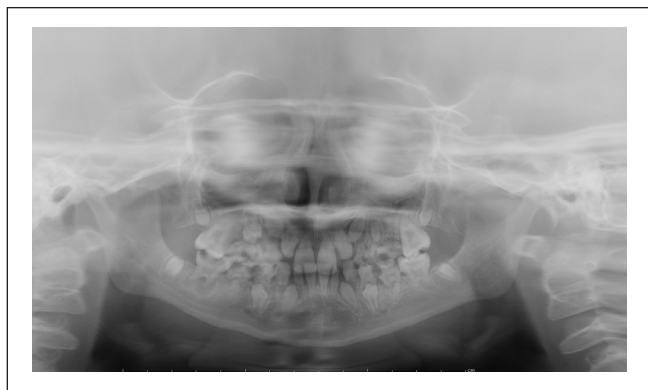
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**Figure 1.** Panoramic X-ray taken at 9 years of age. Serious caries were observed in most primary teeth.

lars and second molars were impacted, and microdonts. 3) Incisors first molars erupted normally, and crown shapes were considered almost normal. However, the roots were short. Severe caries was observed at the right lower first molar. Preventive dental treatment was mainly performed for 2 years, although other dental treatments were hard for him because of a strong vomiting reflex.

Finally, a general anesthesia was planned as dental treatment for molars when he was 11 years old. The findings from a panoramic X-rays at that time were follows (Fig 2): 1) Replacement teeth had grown from 2 years earlier, although the upper and lower second milk molar remained. 2) The roots of the first incisors, second incisors and first molars were short. The first molars were cone-shape. 3) Other permanent teeth were microdonts. 4) The right lower first molar had collapsed.

While active inflammatory changes were not observed on chest X-rays, slight ground glass opacity was observed on a chest CT scan. The patient coughed intermittently. Although he did not show any disturbances for activity of daily living (ADL), he had not exercised so much perhaps because he might cough severely. In a general screening blood test, there were no significantly abnormal values. SpO<sub>2</sub> was 97% in room air. The responsible doctor for ALL commented that there was no specific problem for general anesthesia. GA was maintained with nasal intubation using remifentanyl and propofol. Since the nasal space to insert the tracheal tube was narrow, a smaller tube was used. The respiratory rate was set at 15 times per minute, and the airway pressure was not beyond 20 cm H<sub>2</sub>O; nevertheless, the level of end tidal carbon dioxide was between the late thirties and fifty mmHg. During treatment, more sputum from tracheal tube was observed than from a healthy patient. The right lower molar was extracted, and caries in the other molars were filled with a dental composite resin. After the treatments, anesthetics were terminated, and the tracheal tube was removed. No significant episode was observed after that. On a chest CT scan taken 1 month after the general anesthesia, no significant changes were observed.

After that, the patient has been examined at fixed intervals, and no significant change is observed. Latest condition is shown in Fig 3 (left side) and 4 (right side). Tooth crowns of first incisors and first molars are almost normal, but rest of other teeth are microdonts.

## DISCUSSION

Dental abnormalities have been reported in long-time survivors of ALL, most of whom were diagnosed from 2-15 year of age.<sup>3,6-8</sup> This



**Figure 2.** Panoramic X-ray taken at 11 years of age. Most all permanent teeth are abnormal except for the crowns of the first and second incisors and first molars.

patient was diagnosed within 1 month after birth, when none of the milk teeth had erupted. This is the youngest case to be reported with dental abnormalities after ALL treatment, and his dental condition was worse than cases reported previously.

Of all the permanent teeth of this patient, the formation of the first molar and first and second incisor crowns was normal. On the other hand, the roots of the 3 teeth and all of the other permanent teeth were abnormal. According to the classification of dental stages,<sup>9,10</sup> calcification of the crowns is nearly complete by 2 years old. The first chemotherapy treatment was performed at 8 months of age, and the second treatment consisting of 12 Gy of TBI combined with chemotherapy after relapse began at 1 year and 10 months of age. Therefore, the treatment, including irradiation, was considered to strongly affect teeth formation in accordance with previous reports.<sup>6,11</sup> Thus, it is very likely that irradiation to patients younger than 2 years old causes severe dental problems.

Reports of general anesthesia for patients with chronic GVHD are rare. Although a child case with severe restrictive pulmonary dysfunction after BMT was reported,<sup>12</sup> no significant problem was noted in other reports of cases who underwent surgery under general anesthesia.<sup>13,14</sup> In addition, although our patient was treated for chronic GVHD, it did not disturb his ADL. Besides, pathological changes observed with chest X-ray and CT scans were limited and stable. Thus, we decided his condition was good enough for general anesthesia with tracheal intubation. However, a lot of sputum from the lungs was unexpected. Also, since his nose was narrow, we had to use smaller tracheal tube, leading to difficulties in aspiration of sputum during treatment. We should have anticipated a deterioration of respiratory system in reaction to general anesthesia for patients with chronic GVHD.

Since ALL has been notorious for its high fatality in the past, dental diseases were a comparatively minor problem. However, since the survival rate has increased in recent decades, the dental effects of ALL treatment have become significant. Especially, performing TBI in patients younger than 2 years old is considered to have a big impact on the formation of permanent teeth. In addition, dentin formation is influenced by chemotherapy for malignant tumors,<sup>15</sup> and significant enamel disturbance was observed in many patients surviving childhood cancer compared with controls,<sup>16</sup> leading to the formation of weaker teeth with greater caries risk. Thus, since a combination of a short root and incomplete calcification is consid-



**Figure 3.** Latest oral condition of this patient. A: left side, B: right side. Tooth crowns of first incisors and first molars are almost normal, but rest of other teeth are microdents.

ered to make teeth more vulnerable, preventative dental treatment is important. A support system for patients in cooperation with responsible doctors for ALL should be established. This will contribute to raising the quality of life of these patients in the future.

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