

Case Report

## Gingivectomy for gingival enlargement in a child with I-cell disease: a report of case

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**Abstract** I-cell disease is a rare autorecessive metabolic disorder that is classified as one of the lysosomal storage diseases. Gingival enlargement is a representative oral manifestation of patients with I-cell disease. This report describes a case with a satisfactory prognosis after gingivectomy for gingival enlargement accompanying I-cell disease in a 2-year-old boy. The chief complaints were both eating disorders and night terrors accompanied by gingival enlargement of both the maxillary and mandibular alveolar gingivae, especially in the region of the first deciduous molars. Although it was supposed that there were various hazards associated with gingivectomy caused by aortic incompetence, sigmoidal spinal curvature and hypertrophy of the laryngopharynx, gingivectomy with an internal bevel incision was performed under general anesthesia to improve the chief complaints. A piece of the enlarged gingivae dissected during the operation was examined histopathologically, and the histopathological diagnosis was gingival hyperplasia. The patient's signs and symptoms of the eating disorders and night terrors have improved since the gingivectomy operation. Recurrence of the gingival enlargement has not been identified up to 18 months after the surgery. It is therefore concluded that gingivectomy for gingival enlargement accompanying I-cell disease was effective for this 2-year-old boy.

**Key words**

Gingival hyperplasia,  
Gingivectomy,  
I-cell disease,  
Mucopolipidosis II

### Introduction

I-cell disease is a rare autorecessive metabolic disorder that is classified as one of the lysosomal storage diseases. The etiology of I-cell disease is a deficiency in the enzyme N-acetylglucosaminyl-phosphotransferase. Strikingly elevated levels of a number of lysosomal enzymes have been identified in body fluids from these patients. Furthermore, a marked reduction in the levels of several lysosomal enzymes can be observed within cultured fibroblasts derived from these individuals with a corresponding increase in the levels in the tissue culture medium. This multiple enzyme deficiency is thought to result in the accumulation and storage of a diverse group

of macromolecules within cells. This disease occurs when a specific "recognition marker", mannose 6-phosphate, fails to be added to lysosomal enzymes during their posttranslational processing. This recognition marker is necessary for the appropriate translocation of newly synthesized hydrolases in the lysosome. I-cell disease is manifested clinically within the first few months of life. Affected patients with this disorder exhibit clinical features of both lipidoses and mucopolysaccharidoses, and may have severe dysostosis multiplex, a short stature, generalized hypotonia, thick and tight skin, joint stiffness, flexion contracture, dislocated hips, hepatosplenomegaly, inguinal hernia, cardiovalvular hypertrophy, corneal opacity, mental retardation and gargoylism. Gargoylism is a typical orofacial feature seen in patients with mucopolysaccharidoses including exophthalmos, puffy eyelids and small

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orbits with flat supraorbital ridges, and becomes more conspicuous with age. Characteristic bone changes related to severe dysostosis multiplex occur, leading to a cloaking of the appearance of long tubular bones, shortening of the vertebral bodies, and other significant changes in the pelvis, hands, ribs and skull. Patients with I-cell disease usually pass away due to congestive heart failure or pneumonia at 2–8 years of age. Therefore, management is supportive with the prescription of antibiotics to control pneumonia. Bone marrow transplantation is a possible way of supplying a source of structurally normal lysosomal enzymes. Oral manifestations seen in I-cell disease patients may be gingival enlargement, a thick tongue, hypocalcified enamel and teeth eruption without a lamina dura. Obvious gingival enlargement also results in buried teeth and an open bite which is caused by earlier contact of the gingivae in the posterior regions than in the anterior regions during jaw closing. Although some authors have reported cases of I-cell disease with gingival enlargement causing an apparent open bite, gingivectomy was only performed in one case and recurrence of the gingival enlargement was confirmed within a few months after the surgery<sup>1–3</sup>). In the present case, we report a case of gingivectomy with a satisfactory prognosis for gingival enlargement accompanying I-cell disease. We explained the contents of this report to the patient's parents and informed consent was received.

## Case Report

This report describes a male Japanese infant who was introduced to the pediatric department of Nihon University Dental Hospital at the age of 2 years and 1 month. The chief complaints were both eating disorders and night terrors accompanied by gingival enlargement of both the maxillary and mandibular alveolar gingivae, especially in the region of the first deciduous molars. According to the mother's obstetrical records, there were no particular comments about the patient's family history. The patient was the first child of the mother, who had no problems except for serious hyperemesis gravidarum in the early stages of pregnancy. The patient was born by cesarean section due to fetal pathological rotation at the embryonal age of 39 weeks and 1 day, weighed 2,702 g and was 48 cm in stature. The patient's records indicated that I-cell disease was first suggested at the age of 5 months, after enzyme investigations

were performed when the patient was hospitalized for emaciation treatment caused by low suckling muscular strength for 2 months. Aortic incompetence was reported, and therefore medical treatment with digoxin was performed. The patient's developmental features were as follows. Head stability became possible at the age of 1 year and the anterior fontanel closed at 1 year and 6 months. Speech was confirmed at the age of 1 year and 8 months and the first word was 'Dakko' which means 'Pick me up' in Japanese. Single word sentences such as 'Mama' and 'Papa' became possible at the age of 2 years and 2 months. Mandibular deciduous central incisors erupted at the age of 8 months, followed by eruption of the maxillary deciduous central incisors at the age of 1 year. Gingival enlargement was symmetrically remarkable at the age of 1 year and 6 months. The physical features at the first visit to our hospital at the age of 2 years and 2 months were 80 cm stature, 7.5 kg weight, 43.3 cm head circumference and 41.2 cm chest circumference. Walking was impossible accompanied by muscular hypotonia, thickened skin, and joint stiffness and tightness of the knees, elbows, fingers and dorsum of the hands. There were two unusual observations in chest radiography in that the rachis was curved sigmoidally and the cardiothoracic ratio was increased. Most of the typical orofacial features of I-cell disease, gargoylism, were observed. Gargoylism includes exophthalmos, puffy eyelids and small orbits with flat supraorbital ridges, and is similar to that seen in Hurler's syndrome. Another remarkable orofacial feature, gingival enlargement, was observed symmetrically in both the maxillary and mandibular alveolar gingivae. Gingival enlargement with rubor was especially identified at the region of the first deciduous molars. The enlarged gingivae seemed to be considerably stable, and not like flabby gum tissue. Tooth eruptions were identified from the region of the central incisor to the first deciduous molar in both the maxilla and the mandible, but four of the first deciduous molars were at half-eruption caused by the gingival enlargement, at the first visit to our hospital (Fig. 1A). As a result of simple dental radiography, serious bone resorption was observed vertically and horizontally in the whole area of the alveolar bone in both the maxilla and the mandible, but the teeth did not appear to be loose. Neither signs of dental caries nor hypocalcified enamel, which is frequently observed in patients with I-cell disease, were identified. To improve

(A)



(B)

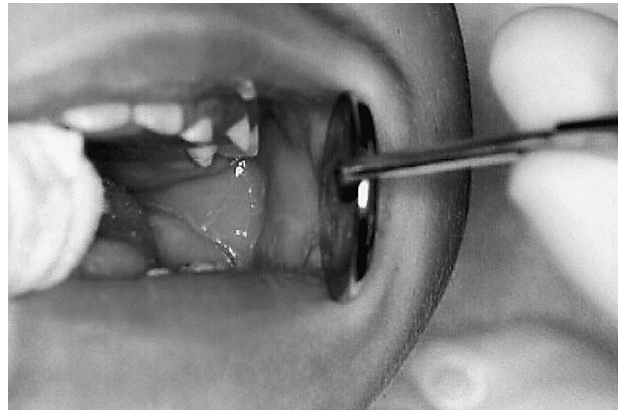


Fig. 1 (A) Gingival enlargement is especially identified at the region of the first deciduous molars and results in buried teeth before the gingivectomy operation.

(B) Recurrence of gingival enlargement is not identified up to 18 months after the gingivectomy operation.

the patient's chief complaints, gingivectomy was performed under general anesthesia. Gingivectomy at the region of the first deciduous molars in both the maxilla and the mandibular was performed under general inhalation anesthesia using sevoflurane with an O<sub>2</sub> and N<sub>2</sub>O gas mixture. The patient was hospitalized 1 day before the operation for premedical care. Premedications, 0.1 mg atropine sulfate and 5 mg hydroxyzine hydrochloride, were injected intramuscularly 2 hours prior to the general anesthesia. At the time of the intratracheal intubation, 25 mg thiopental sodium and 140 mg suxamethonium were injected. Endotracheal intubation was difficult due to the thickened skin, hypertrophic pharynx and head circumference with respect to the stature. General anesthesia was maintained using 1.5% sevoflurane with a 3.5 l/min O<sub>2</sub> and 3.5 l/min N<sub>2</sub>O gas mixture and 2 mg vecuronium bromide during the gingivectomy operation. Since both antiallergic and anti-inflammatory effects were expected, 100 mg prednisolone was used during the general anesthesia. In addition to the general anesthesia, 0.5% lidocaine hydrochloride including two-hundred-thousand-fold diluted epinephrine was used for local anesthesia since a styptic effect was expected during the gingivectomy operation. The excision of the enlarged gingivae was not only made with a scalpel but also with an electrocautery in an effort to prevent as much bleeding as possible. The wounds were sewn up with cotton thread after the surgery, and two threads were used for suturing each part of the

incision. As a result of these procedures, the total amount of bleeding was 29 ml. The total time of the general anesthesia was 2 hours and 30 minutes, 1 hour and 6 minutes of which was the actual operation time. After the operation, both amoxicillin and acetaminophen were given to prevent postoperative infection and pain. The day after the operation, the patient was approved to leave the hospital since the wounds seemed to be making satisfactory progress.

One week later, the threads suturing each part of the wounds were removed with a satisfactory prognosis. The signs and symptoms of the eating disorders and night terrors have improved since the removal of the threads. Recurrence of the gingival enlargement has not been identified up to 18 months after the gingivectomy (Fig. 1B).

### Histological Findings

A piece of the enlarged gingivae dissected at the operation was examined histopathologically (Fig. 2), and the histological diagnosis was gingival enlargement. The increases in fibroblasts and eosin chromophilic fibrous connective tissue were remarkable in the subepithelium, and the circumvascular subinflammatory cellular infiltration was mainly composed of lymphocytes, enlargement and an increase in the number of blood capillaries, mucous degeneration, edema, bleeding, Russell bodies and epithelial islands. Although this enlarged gingivae clinically resembled familial gingival enlargement,



Fig. 2 Microscopic view of the cut surface of the dissected enlarged gingivae. The increases in fibroblasts and eosin chromophilic fibrous connective tissue are remarkable in the subepithelium, and the circumvascular subinflammatory cellular infiltration is mainly composed of lymphocytes, enlargement and an increase in the number of blood capillaries, mucous degeneration, edema, bleeding, Russell bodies and epithelial islands (HE, original magnification  $\times 40$ , scale:  $100\mu\text{m}$ ).

there were basal cells, parabasal cells, physalis conglobation cytoplasm hemangioendothelioma and many granular inclusion cells in the cultured fibroblasts, which are not observed in sections of familial gingival enlargement.

## Discussion

I-cell disease is often confused with Hurler syndrome. Hurler syndrome is the most severe of the mucopolysaccharidoses caused by a deficiency in alpha-L-iduronidase, which leads to the accumulation of dermatan and heparin sulfates in tissues and urinary excretion. I-cell disease is distinguished from Hurler syndrome by very high levels of acid hydrolases, rapid psychomotor retardation and early death. Gingival enlargement is observed in Hurler's syndrome but is less pronounced, limited in its distribution to the maxillary anterior region and occurs later at about 2 years of age<sup>6</sup>. In this case, gingival enlargement was identified on the whole region of both the maxillary and mandibular alveolar gingivae, but it was especially pronounced in the region of the first deciduous molars. This gingival enlargement resulted in buried teeth in the region of

the first deciduous molars, but did not result in an open bite, as has been reported previously<sup>3</sup>. The provisional diagnosis of I-cell disease was initially made from the presenting gingival appearance since gingival enlargement of both the maxillary and mandibular alveolus gingivae is one of the most distinctive observations in this disease. Therefore, the identification of oral abnormalities by dentists could be an important contribution to the diagnosis of this fatal condition<sup>6</sup>. Gingival enlargement is also observed as a chronic side effect in patients with hypertension receiving calcium antagonists, immunosuppressive drugs or anti-epileptic drugs. Although the mechanisms of gingival enlargement are not well known, a recent pathological study with cathepsin-L-deficient mice revealed evidence that impaired cathepsin-L activity may play a key role in the establishment of the skin and gingival abnormalities seen in I-cell disease<sup>4</sup>. Furthermore, an apoptosis-related study using human skin fibroblasts obtained from an I-cell disease patient showed that lysosomal enzymes are important inducers/mediators of apoptosis, in which I-cells are resistant to the apoptosis induced by several unrelated apoptogenic agents, most likely due to the difference in activity

and/or compartmentalization of cathepsins<sup>7)</sup>. There are some clinical reports of the management of juvenile patients with gingival enlargement<sup>1-3,5,6)</sup>. It is difficult to estimate the recurrence of gingival enlargement after gingivectomy. In the present case, recurrence of gingival enlargement has not been identified up to 18 months after the gingivectomy adopting an internal bevel incision. An internal bevel incision has the advantage of preventing postoperative infection and pain due to less exposure of the wound compared to an external bevel incision, and furthermore it does not require a periodontal bandage after the surgery, which seems to be especially suitable for patients with mental retardation. Some authors have suggested from clinical observations of the recurrence of gingival enlargement that there is less chance of recurrence if the gingivectomy is delayed until the permanent dentition is in place<sup>1)</sup>. In addition, tooth eruption seems to promote the recurrence of gingival hypertrophy. However, in this case, recurrence of gingival enlargement has not been identified in any region in the mouth up to 18 months later even though the deciduous teeth were retained, and therefore these theories cannot be applied to all patients with gingival enlargement.

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