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A Case of Sotos Syndrome Treated with Distraction Osteogenesis in Maxilla and Mandible

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Abstract

Sotos syndrome is inherited in an autosomal-dominant manner and is characterized by increased birth weight, excessive growth, advanced bone age, and distinctive facial features, including dolichocephaly, hypertelorism, and a prominent mandible. We treated a jaw deformity due to Sotos syndrome consisting of malocclusion due to a narrow maxillary dental arch and mandibular retrusion from hypoplasia of the rami. The patient was a 17-year-old man. Malocclusion due to a narrow maxillary dental arch and mandibular retrusion was diagnosed. Rapid maxillary expansion with Lines corticotomy and mandibular advancement with distraction osteogenesis were performed. The maxilla was expanded laterally a total of 3 mm and the mandible prolonged 12 mm in the posterior area of the mandibular body. Subsequently, orthodontic treatment was continued. At present, 5 years after surgery, occlusion remains good and stable.

Key words: Sotos syndrome — Orthognathic treatment — Distraction osteogenesis

Introduction

Sotos syndrome, also known as cerebral gigantism, is a congenital disorder that was first reported by Sotos et al. in 1964[1]. Sotos syndrome is inherited in an autosomal dominant manner and is characterized by accelerated growth starting in the fetal period, a large head, dolichocephaly, frontal bossing, a high-arched palate, mandibular prognathism, large hands and feet, down-slanting palpebral fissures, ocular hypertelorism, strabismus, and nystagmus. Seizures and malignant tumors may also occur. Dyskinesia is usually not seen,
but mental retardation does occur, although
the degree of intellectual impairment varies
among patients.\(^{1-3,8}\)

The treatment of a patient with Sotos syn-
drome who had malocclusion due to a narrow
maxillary dental arch and mandibular retru-
sion caused by hypoplasia of the mandibular
rami is reported. Orthognathic surgery includ-
ing mandibular distraction was performed.

**Case**

The patient was a 17-year-old man who
was evaluated for orthodontic treatment at
our hospital at age 14 years with the chief
complaint of malocclusion and functional
dysphonia.\(^{13}\) Sotos syndrome was diagnosed
based on tall stature, typical facial abnormali-
ties and developmental delay in infancy. The
patient was treated for dental caries and the
occlusal relationship examined. At age 16
years, malocclusion due to a narrow maxillary
dental arch and mandibular retrusion was
diagnosed. He was referred to our department
of oral and maxillofacial surgery for orthog-
nathic surgery (Figs. 1–3). His medical history
was significant for Sotos syndrome, seizures,
and hydronephrosis (surgeries at age 1 year
6 months and 3 years). The patient was on
anticonvulsant therapy and had mild mental
retardation. There was no family history of
the syndrome.

On evaluation, his height was 185 cm and
weight was 52 kg. Facial examination revealed
dolichocephaly, left-right symmetry, maxillary
protrusion, and mandibular retrusion. Occlu-
sion was Angle Class II, with overjet of 14 mm
and overbite of −1 mm. There was open bite,
with crossbite in the molar region. The results
of laboratory studies, including blood tests,
electrocardiogram, and pulmonary function
tests, showed nothing remarkable. Cephalo-
metrics demonstrated maxillary protrusion
and mandibular retrusion with an SNA of
73° and SNB of 68°. Lower facial height was
increased, and the facial axis and depth were
decreased.

The diagnosis was malocclusion due to
mandibular retrusion caused by hypoplasia
of the mandibular rami and a narrow maxil-
lar dental arch. Rapid maxillary expansion
combined with corticotomy and mandibular
advancement with distraction osteogenesis
was planned. The surgical treatment plan was
explained to the patient and his mother and
informed consent obtained.

**Treatment and Clinical Course**

Since the seizures were well controlled and
cardiac function normal, surgery under gen-
eral anesthesia was deemed possible after
consultation with the attending internist and
dental anesthesiologist. Therefore, at age 16
years, preoperative orthodontic treatment
was started. At age 17 years, Lines cortico-

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Fig. 1  Facial findings at age 17 years
Facial symmetry, dolichocephaly, mild hypertelorism, maxillary protrusion, and
mandibular retrusion were observed.
Fig. 2  Oral findings before orthognathic treatment with malocclusion
Angle Class II, anterior open bite and posterior crossbite.

Fig. 3  Cephalograms and panoramic radiograph before treatment
Maxillary protrusion and mandibular retrusion were revealed.
(Le Fort I type) was performed under general anesthesia (Fig. 4). During surgery, the pyriform aperture was identified by an incision in the maxillary vestibule, and the inferior part of the nasal mucosa dissected. The cortical bone from the subzygomatic crest to the lateral margin of the pyriform aperture was then cut with a bone saw. In addition, the pterygomaxillary raphes were separated with a chisel. Next, the mucosa in the midline of the palate was stripped in a tunnel-like fashion with a periosteal elevator, and the median palatine raphe and anterior nasal spine separated with a bone saw and chisel. After mobility of the left-right bone segments was confirmed, the mucosa was sutured and closed. Operative time was 40 min, anesthesia time 1 hr 50 min, and blood loss 30 ml. There were no intraoperative complications, and the postoperative course was stable, without seizures or wound infection. On postoperative day 8, the patient was discharged. On day 14 after surgery, a rapid maxillary expansion device (skeleton type) was fitted and the maxilla expanded laterally a total of 3 mm at a rate of 0.5 mm per day over 6 days (Fig. 5).

At age 19 years, when preoperative orthodontic treatment was completed, mandibular distraction osteogenesis was performed under general anesthesia. Using a 3-D plaster model based on preoperative computed tomography, the insertion position of the mandibular distractor was established. Transnasal endotracheal intubation was performed under general anesthesia with propofol and fentanyl and application of vecuronium for muscle relaxation. General anesthesia was maintained with a target-controlled infusion of propofol at a predicted blood concentration of 3.0–5.0 μg/ml with nitrous oxide and
oxygen. During surgery, a mucosal incision was made along the external oblique ridge of the anterior border of the mandibular ramus. Then, after stripping the periosteum from the lateral border of the mandibular ramus and exposing the bone surface, the distractor was adjusted and fixed with screws. After removing the distractors, the mandible was cut at these sites with a bone saw and transected with chisels while preserving the inferior alveolar neurovascular bundle. The distractors were then inserted again, mobility of the bone segments confirmed and suturing and closure performed (Fig. 6). Operative time was 1 hr 40 min, anesthesia time 2 hr 50 min, and intraoperative blood loss 30 ml. There were no intraoperative complications.

The patient was hospitalized for 8 days after surgery, after which he was discharged; his clinical course was stable, without seizures or wound infection.

Starting on postoperative day 8, distraction was performed at a rate of 1 mm daily (0.5 mm in the morning and evening) for a total of 12 mm over 12 days (Fig. 7). Thereafter, the distractor was left in place to maintain distraction. Subsequently, orthodontic treatment was continued. At 1 year 3 months after surgery, active treatment was completed, and a retainer inserted. At 1 year 6 months after surgery, the distractors were removed under general anesthesia. Osteogenesis of the distracted region was good. At present, 5 years 2 months after mandibular distraction, occlusion remains good and stable and the patient is doing well (Figs. 8, 9).

**Discussion**

Sotos syndrome, also known as cerebral gigantism, is characterized by increased birth weight and height, large head size, and prominent face. It is an autosomal dominant disorder caused by mutations in the *CDKL5* gene. The clinical features of Sotos syndrome, including macrocephaly, broad forehead, hypertelorism, micrognathia, and ptosis, were observed in this patient. The mandibular distraction provided by the Ilizarov technique resulted in a significant improvement in facial and dental aesthetics. The patient’s speech and swallowing functions were also improved.

**Fig. 6 Intraoperative findings on mandibular distraction**
A: mandible body was cut while preserving inferior alveolar neurovascular bundle; B: distractor was set and mobility of bone segments confirmed.

**Fig. 7 Panoramic radiograph after distraction osteogenesis of mandible at age 19 years**
weight, excessive growth during the first 4 years of life, advanced bone age, and distinctive facial features, including dolichocephaly, hypertelorism, and prominent mandible.\(^1\) With respect to maxillofacial features, dolichocephaly is almost always present, and increased mandibular length with pointed chin, highly-arched palate, and premature eruption of the deciduous teeth are observed in over 50% of such cases. In occlusion, there is a tendency for anterior crossbite with mandibular prognathism and maxillary retrusion.\(^1\)

Dolichocephaly, mild hypertelorism, a highly-arched palate, and a narrow mandibu-

Fig. 8 Oral findings after orthognathic treatment
Malocclusion improved and occlusion remains good and stable.

Fig. 9 Cephalograms after orthognathic treatment
New bone formation was found in distracted region.
lar dental arch were observed in the present patient. However, there was also mandibular retrusion due to hypoplasia of the mandibular rami, with lateral crossbite and anterior open bite.

According to recent studies, 80–90% of patients with Sotos syndrome had mutations and deletions of NSD1, which encodes a histone methyltransferase implicated in chromatin regulation\(^7\). More recently, the NSD1 mutational spectrum has been defined\(^{14-16}\).

Cases of familial expression have been reported, but in the present patient the family history was unremarkable.

Patients with Sotos syndrome may have coexisting congenital heart and genitourinary anomalies, and careful attention must be paid to surgical planning. Patients may have attention deficit hyperactivity disorder, and intelligence can range from normal to severe mental retardation\(^8\). Surgery for scoliosis and intensive dental treatment under general anesthesia in such patients has previously been reported. To our knowledge, however, no reports have been published on aggressive orthognathic surgery including distraction osteogenesis in such cases, possibly due to the factors described above.

Distraction osteogenesis, which was indicated in the present patient, involves applying an external force with gentle traction during the callus formation stage of fracture healing to promote osteogenesis between the bone segments to lengthen bone. Since being developed by Ilizarov in 1989, distraction osteogenesis has been widely used in orthopedics to lengthen limbs and for treatment of nonunion\(^{5,6}\). In maxillofacial surgery, after Snyder et al.\(^{11}\) reported studies of mandibular distraction in dogs, McCarthy et al. performed mandibular distraction in patients with hemifacial microsomia and micrognathia\(^{10}\).

Subsequently, mandibular distraction has been performed to treat a variety of conditions, and it is particularly useful in cases such as in the present patient where there are severe developmental defects of the mandible. Initially, transcutaneous extraoral devices were used, but recently many types of intraoral device that do not require a skin incision have become available. These can also be used for expansion of a narrow maxillary dental arch. These methods involve relatively little operative time and blood loss, but because a bulky device is inserted into the oral cavity, attention must be paid to oral hygiene during treatment. In addition, after surgery, the patients themselves must manipulate the distractor every day for a few days to a few weeks, depending on the amount of lengthening required. Therefore, patient and family cooperation is important. After distraction, long-term retention with distracters or metal plates is required to prevent relapse.

The present patient had mild mental retardation but could independently perform daily activities. Treatment went according to plan, with the help of good patient and family communication and thorough instruction on oral hygiene. Furthermore, careful planning of preoperative and postoperative management, including general anesthesia, was undertaken to prevent seizures during surgery. Currently, the mandibular position is stable, without any marked retrusion. Careful follow-up and oral hygiene will be needed to prevent dental caries and periodontal disease. In addition, the patient should be monitored for gingival hyperplasia, a possible side effect of anticonvulsant drugs.

**Conclusion**

Mandibular distraction may be indicated to improve occlusion in patients with Sotos syndrome associated with malocclusion caused by a narrow maxillary dental arch and mandibular retrusion. Patient and family cooperation throughout the often lengthy period that orthognathic treatment requires is particu-
larly important in patients with mental retardation, including during surgery, inpatient treatment, and oral hygiene management.

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References


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