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Mandibular Distraction in a Patient with Type II Collagenopathy

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Abstract

Kniest dysplasia is an extremely rare form of type II collagenopathy associated with cleft palate, micrognathia, shortened trunk, arms, and legs, and club foot. We present a case of an infant with this disorder who also had micrognathia and respiratory distress for which mandibular distraction was performed. Although abnormal collagen and impaired endochondral ossification is noted with Kniest dysplasia, adequate bone formation was observed across the distraction gap. Nonetheless, despite stable mandibular advancement, failure to consider concomitant restrictive lung disease resulted in tracheostomy dependence. We demonstrate that while successful bone regeneration can be achieved through distraction of intramembranous facial bones, discretion must still be employed in patients with collagenopathies.

Keywords

Mandibular Distraction; micrognathia; Type II Collagenopathy; COL2A1; Kniest Dysplasia

Introduction

The COL2A1 gene, found on chromosome 12, encodes the alpha-1 chain of type II collagen, a fibrillar collagen found in cartilage and vitreous humor of the eye.(1) Type II collagen is essential for proper endochondral ossification, as this type of bone formation requires a cartilaginous intermediate.(2) Disorders arising from COL2A1 mutations, collectively termed type II collagenopathies, comprise a wide spectrum of conditions with highly variable phenotypes.(3, 4) Common clinical syndromes include Stickler dysplasia type I, Kniest dysplasia, and the spectrum of spondyloepiphyseal dysplasia.(3, 5, 6) Severity may range from lethal forms of spondyloepiphyseal dysplasia (i.e. achondrogenesis type II and hypochondrogenesis) to less severe midline clefting, osteoarthritis, and visual abnormalities seen in Stickler syndrome.(1)

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Missense and splice-site mutations resulting in exon skipping in the COL2A1 gene have been most frequently associated with Kniest dysplasia.(4, 7, 8) This autosomal dominant type II collagenopathy is extremely rare, with an estimated incidence of one out of every 1 million births, and presents with cleft palate, short neck, scoliosis, shortened arms and legs, club foot.(9–11) Midface and mandibular hypoplasia have also been reported in patients with Kniest dysplasia.(12) We present a female infant with micrognathia and respiratory distress shortly after birth in the setting of Kniest dysplasia. Successful bone formation and mandibular advancement was achieved through distraction, however failure to consider concomitant restrictive lung disease resulted in post-distraction tracheostomy dependence.

Case Report

A 38-year-old G4 P2-0-1-2 woman delivered a female infant at our hospital with skeletal dysplasia diagnosed prenatally. At birth, the infant was noted to have a U-shaped cleft palate, short neck, shortened long bones, bilateral club foot, and bilateral hip dislocation. No ocular or auricular/auditory abnormalities were noted. Immediate endotracheal intubation was performed for respiratory distress. A computed tomography (CT) scan was performed which demonstrated micrognathia, with narrowing of the airway in the region of the tongue base, and a maxillary-mandibular discrepancy of 11 mm (Figures 1A and B). Additionally, CT and MRI revealed foramen magnum and C1 spinal stenosis, as well as nonspecific cerebral underdevelopment.

Extubation was attempted at one week in conjunction with direct laryngoscopy, and no significant laryngomalacia was noted. Unfortunately, the patient quickly developed difficulty with breathing, particularly in the supine position. She required prone positioning along with supplemental oxygen via high-flow nasal cannula. An oximetry study was therefore performed which revealed multiple episodes of oxygen desaturation, worse in supine position, and an oxygen saturation nadir of 81%. However, no apneic episodes were noted.

Given the patient's difficulty with breathing in the setting of micrognathia and direct laryngoscopy and oximetry study results, the decision was made to proceed with mandibular distraction. On day of life 18, bilateral inverted "L" mandibular osteotomies were made and 15 mm end-driven neonatal distractors (KLS Martin; Tuttlingen, Germany) were placed (Figure 1C). Distraction began on postoperative day one, and the mandible was distracted bilaterally at 1 mm daily to a total of 15 mm. The patient was then extubated, but despite overcorrection of her maxillary-mandibular discrepancy, she again developed respiratory failure following removal of the endotracheal tube. The patient was found to have restrictive lung disease and pulmonary hypoplasia. Therefore, at three months of age, a tracheostomy was performed. Bronchoscopy at the time of tracheostomy revealed no tracheomalacia or lower airway obstruction.

After three months of consolidation, a CT scan was obtained demonstrating adequate bone regeneration across the distraction gap (Figures 2A and B). Bilateral mandibular distractors were removed without complication, and the regenerate appeared well-ossified, even overgrowing parts of the distractors (Figure 2C). Twelve months following tracheostomy, our patient remains ventilator-dependent due to her restrictive lung disease.

Discussion

Phenotypic expression of our patient's COL2A1 mutation included cleft palate and airway obstruction due to micrognathia and glossoptosis, consistent with the Pierre Robin sequence. Management with prone positioning or tongue-lip adhesion may be considered to prevent base of tongue obstruction, strategies that alleviate obstruction in 80% of cases.(13, 14) Patients who fail these measures have traditionally required a tracheostomy.(13) Alternatively, distraction osteogenesis of the mandible has been shown to eliminate the need for tracheostomy in over 91% of cases.(15, 16) However, patients with glottic or subglottic airway obstruction may still require tracheostomy, as mandibular distraction may be ineffective due to obstruction at multiple levels of the airway.(13, 16)

Although, to our knowledge, no previous reports of distraction in patients with type II collagenopathies exist in the literature, we hypothesized that distraction would be successful in our patient. Collagen type II constitutes the major protein in the extracellular matrix of cartilage, and transgenic mice in which the Col2a1 gene is knocked out exhibit a lethal phenotype, with complete absence of endochondral bone.(17) However, intramembranous bones including the splanchnocranium and sides and roof of the neurocranium are relatively spared despite the absence of type II collagen, as formation of these do not require a cartilaginous intermediate.(17)

During mandibular distraction, new bone is created through intramembranous ossification. (18–20) Therefore, our patient's impaired ability to assemble type II collagen would not be expected to interfere with mandibular bone regeneration. Following 15 mm of distraction and three months of consolidation, CT scan confirmed adequate ossification of the regenerate in our patient. And on removal of distractors, we noted firm bone across the distraction gap. Bone was even appreciated to overgrow parts of the distractor foot plates. We were therefore able to achieve stable advancement of the mandible despite our patient's type II collagenopathy.

However, our patient continued to have respiratory failure even after distraction, arising from restrictive lung pathology secondary to chest wall abnormalities. Although we were able to distract the mandible, and although laryngoscopy/bronchoscopy demonstrated no laryngomalacia or other forms airway obstruction, tracheostomy could not be avoided. Notwithstanding this failure, two important points may still be gleaned from this outcome. While endochondral bone formation is impaired, type II collagenopathies may not preclude successful distraction of intramembranous bones such as the mandible and midface. However, this strategy must be used judiciously, and full consideration of pulmonary chest wall mechanics must be made in concert with evaluation of laryngomalacia, tracheomalacia, or other airway pathologies before attempting mandibular distraction for micrognathia-related airway obstruction.

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Figure 1.

A) Lateral photograph of patient showing micrognathia. B) Three-dimensional reconstruction of CT scan done four days after birth demonstrating maxillary-mandibular discrepancy. C) Intraoperative photograph showing placement of neonatal mandibular distractor following inverted “L” osteotomy.

Figure 2.

A) Lateral photograph following 15 mm advancement of mandible through distraction. B) Three-dimensional reconstruction of CT scan after three months of consolidation demonstrated adequate bone formation in the distraction gap. C) Intraoperative photograph during removal of distractors. White arrow shows bone overgrowth on top of the distal footplate.