Acta Med. Okayama, 2019
Vol. 73, No. 3, pp. 255-262

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Case Report

Improvement of Open Bite and Stomatognathic Function in an Axenfeld-Rieger Syndrome Patient by Orthodontic Sectional Arch Mechanics: Clinical Considerations and the Risk of Orthodontic Tooth Movement

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Orthodontists need to understand the orthodontic risks associated with systemic disorders. Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant disorder with genetic and morphological variability. The risks of orthodontic treatment in ARS patients have been unclear. Here we describe the correction of an anterior open bite in a 15-year-old Japanese female ARS patient by molar intrusion using sectional archwires with miniscrew implants. An undesirable development of external apical root resorption (EARR) was observed in all intrusive force-applied posterior teeth during the patient's orthodontic treatment, suggesting that ARS patients have a higher risk of EARR than the general population.

Key words: Axenfeld-Rieger syndrome, external apical root resorption, miniscrew implant, anterior open bite

Axenfeld-Rieger syndrome (ARS) is an autosomal dominant disorder with an incidence of 1 in 200,000 of the total population [1]. In ARS, an abnormal migration and differentiation of neural crest cells causes anomalies in ocular, craniofacial, and dental development [1, 2]. Mutations in the transcription factors Pitx2 and Foxc1 are associated with ARS [3]. The specific clinical features of ARS include defects and/or malformation of the ocular anterior segment, and glaucoma is observed in 50% of ARS patients [2].

Other systemic disorders — such as failure of the periumbilical skin to involute, anomalies of the pituitary gland, conduction deafness, and congenital heart defects — have been diagnosed in some ARS patients [2, 3]. The characteristic craniofacial features of ARS are maxillary hypoplasia, hypertelorism, a broad nasal bridge, and an enlarged sella turcica [1-4]. The specific dental manifestations of ARS are hypodontia, hypoplasia, microdontia, and taurodontism [3-5]. Malocclusions associated with skeletal mandibular protrusion and maxillary protrusion with anterior open bite have also been reported in ARS patients [4-6].

Patients with systemic disorders often have specific orthodontic risks associated with the systemic disorder. In one example, patients with poorly controlled diabetes mellitus have a risk of periodontal breakdown during orthodontic treatment [7]. Thus, the condition of diabetes mellitus must be controlled before orthodontic treatment to prevent periodontal breakdown [7]. Patients with Ehlers-Danlos syndrome type VIII, which is characterized by abnormalities of connective tissues leading to the fragility of skin and blood vessels, are thought to be at a higher risk of unfavorable rapid tooth

Received September 3, 2018; accepted December 26, 2018.
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Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

movement, increased tooth mobility, enhancement of external apical root resorption (EARR), and alveolar bone loss compared to the general population [8, 9]. These side effects may be caused by a collagen cross-linkage defect, which is the etiology of the syndrome [8, 9].

Therefore, when orthodontic treatment is performed for patients with systemic disorders, orthodontists need to understand the orthodontic risks associated with the systemic disorders, and they must carefully design orthodontic treatment plans and mechanics to minimize the risks. In ARS patients, the risks of orthodontic treatment have been unclear in part because there has been only one report of orthodontic treatment for an ARS patient.

The present case report describes, for the first time, the correction of an anterior open bite in an ARS patient by intrusion of the molars using miniscrew implants. During the intrusion, the orthodontic mechanics had to be changed because of the undesirable development of EARR of the premolars and molars. We discuss a causal relationship between ARS and EARR, and we note several points to keep in mind regarding orthodontic treatment for ARS patients based on the findings in our patient's case.

Case Report

A Japanese female aged 15 years and 8 months with ARS presented to the outpatient clinic of Tohoku University Hospital. Her chief complaint was an esthetic problem of the anterior open bite. She had been diagnosed with ARS by an ophthalmologist. The systemic findings observed in this patient were glaucoma, conduction deafness, and internal carotid artery dysplasia. Facial photographs showed hypertelorism, a broad nasal bridge, and a convex facial profile (Fig. 1). The mandibular dental midline was deviated 2.5 mm toward the left compared to the maxillary midline (Fig. 1). The molar relationships were Class III on the right side and Class II on the left side (Fig. 1). The overjet and overbite were 3.7 mm and −2.5 mm, respectively (Fig. 1). The maxillary canines and mandibular lateral incisors were not present (Fig. 1).

The posteroanterior cephalogram showed mandibular deviation of 1.5 mm toward the left, and the lateral cephalogram showed enlargement of the sella turcica (Fig. 2). A cephalometric analysis showed a skeletal Class II jaw-base relationship and a high mandibular plane angle (Fig. 2, Table 1) [10]. A panoramic radiograph revealed the absence of the maxillary and mandibular third molars, short roots on the mandibular canines, and taurodontism of the maxillary and mandibular molars (Fig. 3).

The patient was diagnosed as having a skeletal Class II jaw-base relationship, anterior open bite, and bilateral congenital absence of the maxillary canines and mandibular lateral incisors. A 6-degrees-of-freedom jaw movement recording system showed unstable tracings of the incisal path and an incisal path length of 3.6 mm during protrusive jaw movement (Fig. 4A). Occlusal force of 253 N and an occlusal contact area of 5.2 mm^2 were calculated by an occlusal force recording

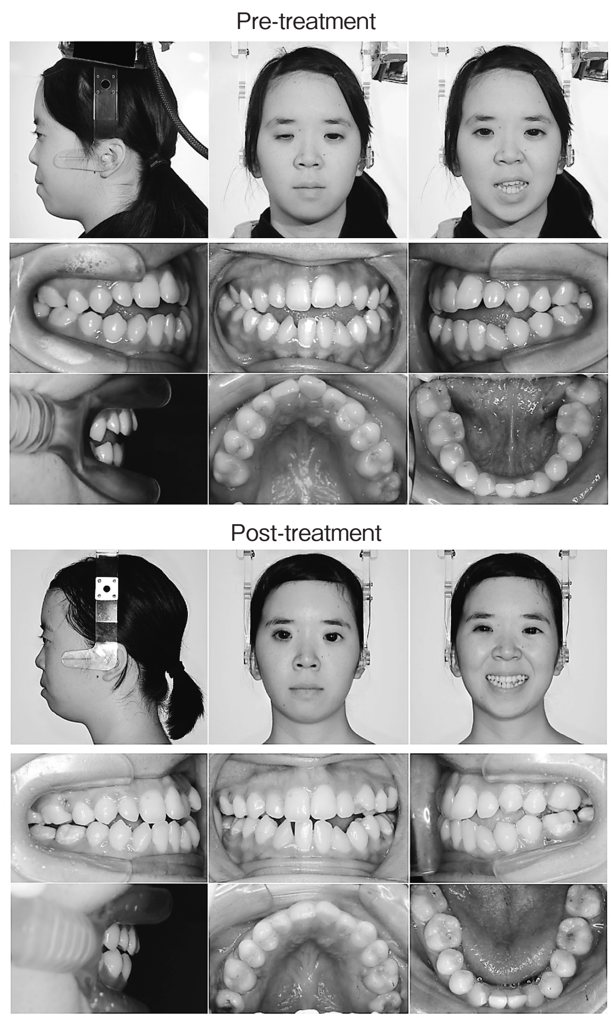

Fig. 1 Pre- and post-treatment facial and intraoral photographs.

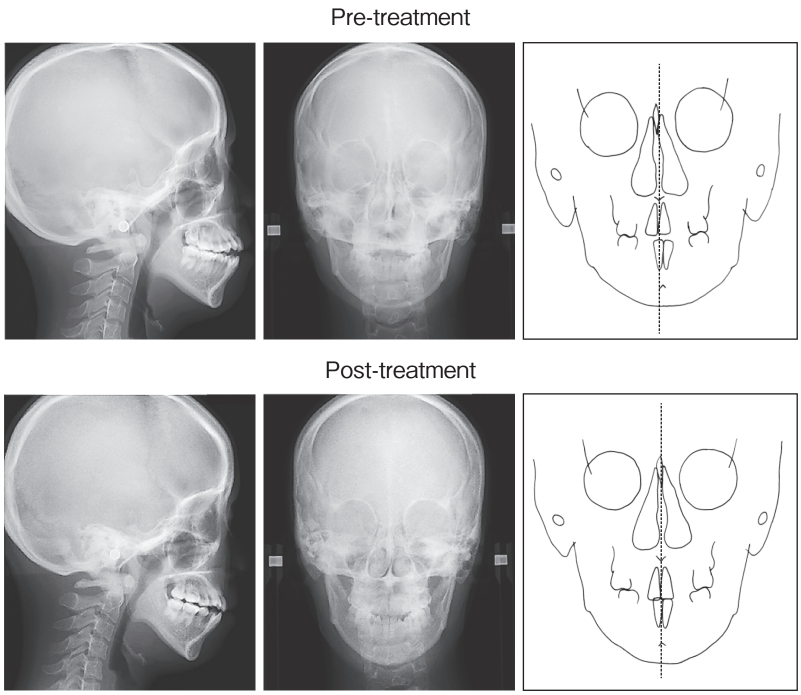

Fig. 2 Pre- and post-treatment lateral and posteroanterior cephalograms, and posteroanterior cephalometric trace lines. The *dotted line* shows the facial midline.

Table 1 Cephalometric summary

Measurements	Japanese Female Norm (Adult)		Pre-treatment	Post-treatment
	Mean	SD		
Angular (°)				
SNA	80.8	3.6	69.4	69.4
SNB	77.9	4.5	63.6	64.5
ANB	2.8	2.4	5.8	4.9
Mp-FH	30.5	3.6	40.9	39.3
Gonial A	122.1	5.3	125.7	125.8
U1-FH	112.3	8.2	108.0	108.2
L1-FH	56.0	8.1	49.6	51.6
L1-Mp	93.4	6.8	89.5	89.1
IIA	123.6	10.6	121.6	123.4
Linear (mm)				
S-N	67.9	3.7	70.6	70.6
N-Me	125.8	5.0	136.7	135.8
Me/NF	68.6	3.7	70.5	70.5
ANS-Ptm/NF	52.1	3.0	47.4	47.4
Go-Me	71.4	4.1	62.5	62.3
Ar-Go	47.3	3.3	41.9	42.3
Ar-Me	106.6	5.7	95.0	95.3
Overjet	3.1	1.1	3.7	2.0
Overbite	3.3	1.9	−2.5	0.8

The data are means and standard deviations from Wada *et al*. [10].

system (Fig. 4B, Table 2).

Considering that continuous management of the symptoms of her condition, such as glaucoma and hearing loss, had been indispensable, the patient and her parents hoped for minimal orthodontic intervention to correct anterior occlusion. Therefore, we chose to perform limited orthodontic treatment to correct the anterior open bite by intrusion of the molars using sectional archwires instead of using full fixed edgewise appliances.

After assessing the oral hygiene status and providing tooth brushing instruction, we placed 0.018 × 0.025-in. preadjusted edgewise appliances on the premolars and molars of both arches, and leveling and alignment were commenced using 0.014-in. nickel-titanium sectional archwires. Tooth alignment proceeded as we changed the sectional archwires sequentially, and 0.017 × 0.025-in. stainless-steel sectional archwires were placed to intrude the molars in both arches. Maxillary and mandibular miniscrew implants (1.4 mm in diameter and 6.0 mm in length) were placed into the buccal alveolar bone between the first and second molars on either side of the arch.

Four weeks after the implantation, 100 g of intrusion force was applied by elastic chains connecting the miniscrew implants and the sectional archwires. A transpalatal arch and a mandibular lingual arch were placed between the first molars to prevent buccal molar tipping caused by the intrusion force. During the molar intrusion, all miniscrew implants became mobile or dropped, and reimplantation was performed. After 12 months of intrusion, the patient had acquired an overbite of 0.8 mm (Fig. 5A). The panoramic and periapical radiographs taken at this point showed EARR involving one-third of the root length in the maxillary second premolars and first and second molars and slight EARR of the mandibular second premolars and first and second molars (Figs. 5B, 6A). Thus, we ceased to load any orthodontic force and monitored the condition of the EARR for 6 months. EARR had not progressed during the observation period, and then we started premolar extrusion. The maxillary and mandibular molars were ligated with miniscrew implants, and

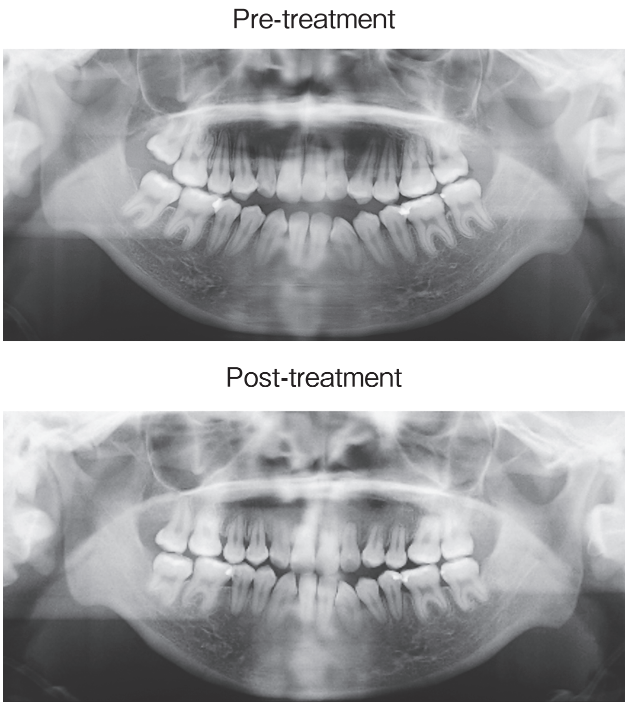

Fig. 3 Pre- and post-treatment panoramic radiographs.

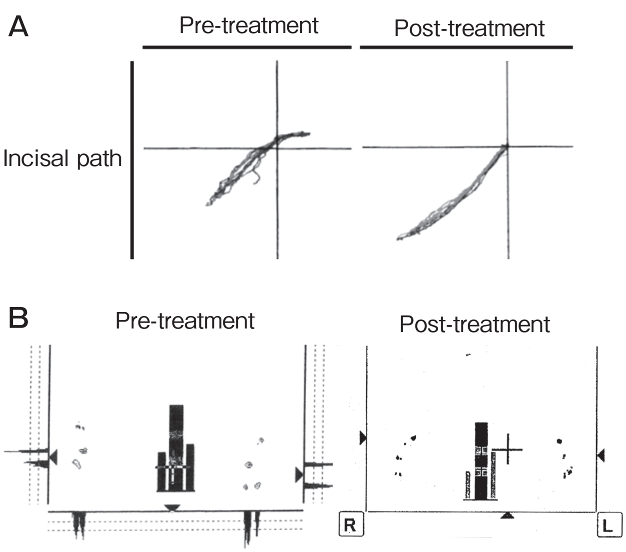

Fig. 4 Pre- and post-treatment stomatognathic function. A, Sagittal view of the patient's incisal path during protrusive jaw movement as detected using a 6-degrees-of-freedom jaw-movement recording system; B, Occlusal force and occlusal contact area recordings.

Table 2 Occlusal force and occlusal contact area

	Pre-treatment	Post-treatment
Occlusal force (N)	253	380.6
Occlusal contact area (mm^2)	5.2	7.8

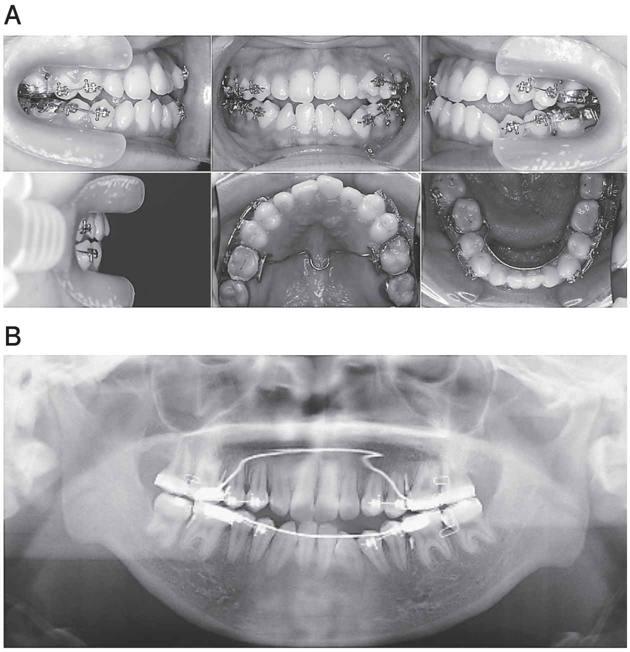

Fig. 5 Intraoral photographs (A) and panoramic radiograph (B) at the molar intrusion interruption.

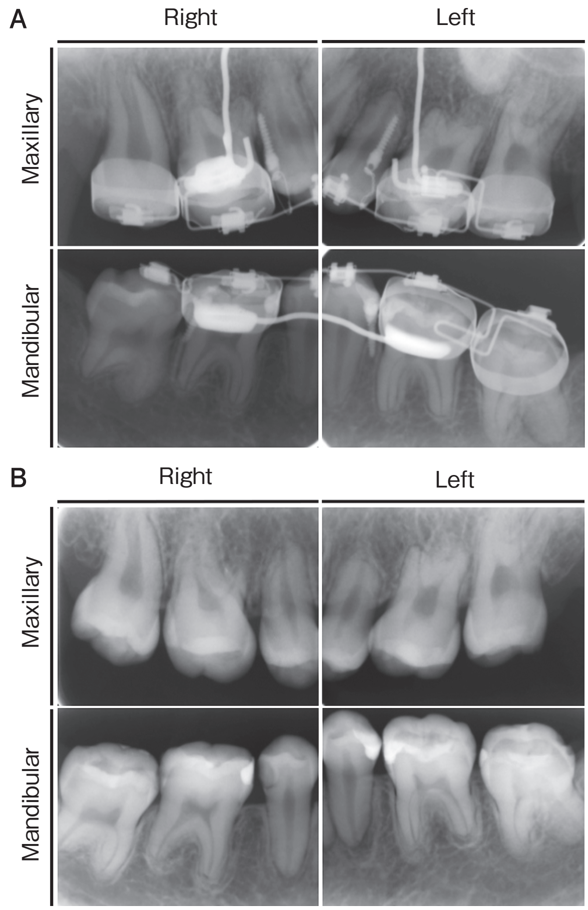

Fig. 6 Periapical radiographs. A, Molar intrusion interruption; B, Post-treatment.

extrusion of the maxillary and mandibular premolars was commenced for correction of the premolar open bite using vertical elastics. After 12 months of premolar extrusion, the open bite exhibited some improvement. The patient was moving to a distant city at this point in time. She and her parents were already satisfied with the treatment result and did not want further orthodontic treatment using full fixed appliances. We were also concerned that orthodontic treatment using full fixed appliances would aggravate the EARR. Thereafter, the edgewise appliances were removed and retention was commenced using clear plastic retainers.

Results

Miniscrew implants were initially placed into the buccal alveolar bone between our patient's first and second molar, but the miniscrew implants became mobile and fell out. Then, miniscrew implants were reimplanted between the buccal alveolar bone of the second premolar and first molar. Considering a center of resistance for efficient molar intrusion, preadjusted edgewise brackets were placed on the premolars and molars [11].

After active orthodontic treatment, the patient's anterior open bite improved, and the overjet and overbite became 2.0 mm and 0.8 mm, respectively (Fig. 1). The amount of mandibular deviation decreased by 1.0 mm, resulting in a deviation of 0.5 mm (Fig. 2). No significant EARR progression was observed since the intrusion of the molars was interrupted (Figs. 3, 5B, 6A, B). Enlarged periodontal spaces of mandibular second premolars were observed; this would be the result of the extrusion (Fig. 6B). The post-treatment cephalometric analysis showed that the ANB angle decreased from 5.8° to 4.9°, indicating improvement of the skeletal Class II jaw-base relationship (Figs. 2, 7A, Table 1). The maxillary and mandibular first molars were intruded by 1.5 mm and 0.5 mm, respectively (Fig. 7B, C). The maxillary and mandibular first premolars were extruded by 0.5 mm and 1.0 mm, respectively. The mandibular plane angle decreased by 1.6° with counterclockwise rotation of the mandible (Fig. 7A, Table 1). A 6-degrees-of-freedom jaw movement recording system

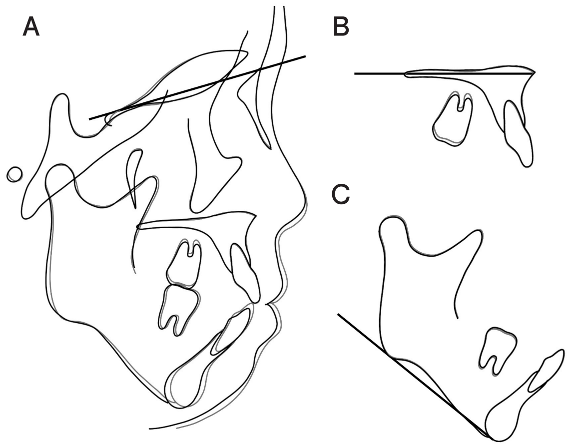

Fig. 7 Superimposed pre-treatment (*black line*) and post-treatment (*gray line*) cephalometric tracings. **A**, On the sella-nasion plane at sella; **B**, On the palatal plane at ANS; **C**, On the mandibular plane at the menton.

showed a smooth and stable incisal path and an increase of the incisal path length to 4.5 mm during protrusive jaw movement (Fig. 4A). Occlusal contact in the incisal region was obtained (Fig. 4B). The values of occlusal force and occlusal contact area exceeded those at pre-treatment (Fig. 4B, Table 2).

Discussion

The systemic disorders (ocular disease, hearing disability, and vascular disease) and craniofacial features in our patient were consistent with the specific features of ARS [1-3]. Dental anomalies such as agenesis of the permanent teeth, short roots and taurodontism were observed in the patient, similar to previous reports of ARS [4-6]. Pitx2, a transcription factor known to be associated with ARS, regulates tooth morphogenesis by modulating the expression of various factors such as Lhx6 and Dlx2 [12]. In Pitx2 null mutant embryos, tooth development was arrested at the placode or bud stage [12]. Deficiency in Lhx6, a downstream factor of Pitx2 in odontogenesis, causes a decrease in the size, shape and cusp formation of molars and defects in molar root structures [13]. These reports suggest that Pitx2 mutation in ARS patients is associated with congenital dental anomalies.

In our patient, counterclockwise rotation of the mandible occurred due to intruding maxillary and mandibular molars using miniscrew implants, resulting in a closing of the anterior open bite and improvement of oral esthetics. Importantly, the incisal path during protrusive jaw movement became stable and its length increased during active treatment. These results suggest that the establishment of optimal anterior guidance due to the closing of the anterior open bite resulted in ideal protrusive jaw movement. Moreover, occlusal contact in the incisal region was obtained, and the values of occlusal force and occlusal contact area increased after active treatment. Taking these findings together, it is apparent that the limited orthodontic treatment using sectional archwires with miniscrew anchorage in this ARS patient improved stomatognathic function, as well as occlusion and aesthetics.

EARR is a common side effect of orthodontic treatment; it occurs in most patients who undergo comprehensive orthodontic tooth movement, albeit to a slight degree. However, 16.5% of patients show moderate EARR after orthodontic treatment, defined as resorption of at least 2 mm to one third of the root length [14]. Moreover, 5% of patients show severe EARR after orthodontic treatment, defined as resorption exceeding one-third of the root length [15]. In the present case, moderate EARR occurred in the second premolars, first molars, and second molars in the maxillary dentition. Dressler *et al.* [5] reported that the correction of a skeletal Class III relationship using combined orthodontic-orthognathic therapy in an ARS patient caused EARR on most teeth, including severe resorption of the incisors and first molars in the mandibular dentition. In these two ARS patients, moderate to severe EARR was found. ARS patients may thus be more susceptible to EARR during orthodontic treatment.

Dental morphological anomalies including short-rooted teeth and taurodontism increase the risk of EARR during orthodontic treatment [16, 17]. Patients with Turner syndrome, which is characterized by a partly or completely missing X chromosome, frequently present with dental morphological anomalies, including short-rooted tooth and simple crown morphology, suggesting an increased risk of EARR [18]. ARS patients also frequently display such dental morphological anomalies, as observed in our patient, and these anomalies may be an etiology for EARR in ARS patients.

Intrusion has a significant correlation with EARR [19]. To avoid EARR, intrusion force levels should be carefully managed. In previous studies, 100-300 g of force applied from miniscrew implants was used for molar intrusion and resulted in no significant EARR

[20-22]. In the present case, a light intrusive force of 100 g was applied to a sectional arch for molar intrusion, and moderate EARR was consequently revealed after 12 months of intrusion (Figs. 5B, 6A). A positive anterior overbite was obtained at this point; nevertheless, the amount of overbite was still insufficient and the open bite of the first premolars remained. Continuing intrusion of the molars would have been desirable to obtain sufficient overbite and occlusion in the premolar segment, but the aggravation of EARR by intrusion should be avoided.

Han *et al.* [23] reported that the extrusion of teeth poses one-quarter of the risk of EARR compared to intrusion. We therefore interrupted the intrusion of our patient's molars and instead extruded the maxillary and mandibular premolars for open bite correction by vertical elastic force. Consequently, no aggravation of the EARR by extrusion was observed. These findings suggest that orthodontic mechanics with a lower risk of EARR should be applied for ARS patients.

A recent systematic review showed a high success rate of miniscrew implants, ranging from 79.9% to 86.6% [24]. At our clinic, the success rates of maxillary and mandibular miniscrew implants are 90.7% and 70.7%, respectively [25]. However, miniscrew implants were unstable in all four quadrants in the present case. Some reports indicate that the cortical bone thickness and hardness and the total bone mineral density are related to the stability of miniscrew implants [26, 27]. Foxc1 induces osteoblast differentiation and the alkaline phosphatase activity of mesenchymal cells [28], and Pitx2 stimulates the expression of Lef1, which is an essential inducer of osteogenesis [29, 30]. These findings suggest that mutations in Foxc1 and Pitx2 suppress normal bone formation and metabolism in ARS patients, resulting in the failure of miniscrew implants.

In summary, the present report indicates, for the first time, that orthodontic treatment using miniscrew implants contributes to improvement in the occlusion, esthetics, and stomatognathic function of ARS patients. However, we may need to take the compromised stability of miniscrew implants into account if their use is planned. Moreover, we suggest that ARS patients are at a higher risk of EARR during orthodontic treatment than the general population. Our findings demonstrate that it is critical to carefully design the orthodontic mechanics for ARS patients to eliminate the general risk factors of EARR.

Acknowledgments. This study was supported in part by grants from Japan Science and Technology Agency (D-S).

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