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UNUSUAL SKELETAL GROWTH OF AN ADULT PATIENT WITH ACRONEGANALY: A 12 YEAR FOLLOW-UP AFTER ORTHOGNATHIC SURGERY

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Acromegaly is an uncommon endocrinological disorder, which is rarely seen in patients presenting for orthodontic treatment. Herein, we report a patient who underwent orthognathic surgery and was diagnosed with acromegaly during the retention phase. During disease progression and treatment, gradual changes in the mandible and facial soft tissue were detected. General information and management of acromegaly are reviewed, and the role of orthodontists in the treatment of patients with acromegaly is discussed. (Taiwanese Journal of Orthodontics. 31(3): 166-177, 2019)

Keywords: Class III Orthognathic surgery; growth evaluation; craniofacial anomalies; acromegaly; sella turcica.

INTRODUCTION

Orthodontists, along with family dentists, provide long-term care to growing children and adult patients. Long-term follow-up records provide information on facial skeletal and accompanying occlusion changes. Adult patients with unusual skeletal growth are rare, and may only be detected by orthodontists on observation of changes through serial X-rays and photo comparisons.

Pituitary adenomas (PAs) are benign tumors situated in the hypophyseal fossa of the sella turcica, with a prevalence of 17% based on epidemiologic and radiographic imaging studies. 1 PAs arise from various specialized cells in the pituitary gland. Growth hormone hypersecretion adenomas in non-growing adults, or acromegaly, is the third most common subtype of PAs with 0.006% prevalence. 2 A review article reported the prevalence rate to be 39–82 per million in the Taiwanese population. 3

The clinical manifestations of acromegaly include exaggerated growth of hands and feet, soft tissue hypertrophy such as macroglossia, worsening mandibular...
prognathism, frontal bossing, and widening of the nasal base. In female patients, ovulatory disorders and amenorrhea may be present.

Herein, we present a patient who underwent mandibular setback surgery and was later diagnosed with acromegaly during the retention stage.

**DIAGNOSIS AND ETIOLOGY**

A 25-year-old woman presented to our clinic with protruding lower jaw, facial asymmetry, and anterior cross-bite. Past dental and medical history was unremarkable. Clinical examination revealed 5.5 mm right deviation of mandible on pogonion point, and a Class III molar relationship with concave profile (Figure 1). Cephalometric analysis revealed a Class III skeletal relationship (ANB –2°) due to mandibular prognathism. Postero-anterior cephalometric analysis also indicated menton point shifted to right side by 5.0 mm and different morphology in left and right side of mandible body. Yet there was no obvious occlusal plane canting noted (Figure 2). Proclined upper incisors and retroclined lower incisors were also noted.

![Figure 1. Initial intra- and extra-oral photographs (year 2004, Age 24).](image1)

![Figure 2. Pre-treatment lateral and postero-anterior cephalometric radiographs.](image2)
TREATMENT OBJECTIVES AND PLAN

The preliminary treatment goals were to correct the asymmetric skeletal relationship, improve the facial profile, and achieve a better occlusion with normal overjet and overbite.

Two treatment options were provided. The first option was one-jaw mandible rotational setback surgery combined with extraction upper bicuspids. Another option was a pure orthodontic treatment by extraction four bicuspids to retract the lower anterior teeth. As for the asymmetric facial profile, an additional genioplasty side shifting surgery was required.

In both treatment options, we suggested the patient a plastic surgery to recontour lower mandible body morphology in order to achieve a more symmetric profile.

After explaining the pros and cons to the patient, the definitive plan was one-jaw surgical orthodontic treatment. Yet the patient hesitated about the later plastic surgery part.

TREATMENT PROGRESS

The patient started the treatment in 2004 with 0.022x0.028 slot pre-adjusted bracket system. After leveling and alignment, maxillary first premolars were extracted, and maximum anchorage was prepared for decompensation of the proclined maxillary incisors. In the lower arch, the full-size main archwire was used to regain torque of mandibular incisors. Transversely, arch form coordination and decompensation for asymmetric torque expression were performed.

When the extraction space closed and dental decompensation was achieved, the patient was sent to the oral surgeon. After surgery, the detailing of occlusion took another 6 months. The patient was debonded in 2006. The clear and Hawley retainers were delivered. The total treatment duration was 24 months.

TREATMENT RESULTS

After the treatment, the patient had a harmonious profile due to the asymmetric and protrusive mandible were corrected. Bilateral Class I canine and Class II molar relationship were achieved. Upper and lower incisors also regained normal inclination. From the initial and post-treatment lateral cephalometric superimposition, there was average 6.0 mm and 4.5 mm setback measured at the skeletal and soft tissue pogonion point (Figure 3). Although from the frontal view, there was still asymmetry between bilateral lower jaw morphology, yet the patient refused advanced plastic recontouring surgery. Finally the patient was satisfied with profile and occlusal alignment (Figure 4). The clear retainer and Hawley retainers were given to the patient.

Figure 3. Lateral cephalometric superimposition between initial (pink line) and debonding (black line).

FOLLOW-UP

At the one-year follow-up appointment, minimal overbite, overjet, and deviated lower dental midline were found. On the lateral cephalometric superimposition between debonding and one-year follow-up, her mandible showed forward and downward growth, which was unusual in a 27-year-old adult (Figure 5). Regional mandible superimposition revealed 1.5 mm posterior deposition over the ramus area. During subsequent follow-up appointments, further mandibular changes, worsened occlusion, and lateral profile changes were noted. The negative overjet, deviated dentition and protruded lower jaw eventually could not be ignored (Figure 6).

Figure 5. Lateral cephalometric superimposition between debond (black line) and one-year post-treatment follow-up (blue line).

On review of recent medical history, the patient indicated that she had developed irregular menses,
Figure 3. Lateral cephalometric superimposition between initial (pink line) and debonding (black line).

Figure 4. Intraoral and extraoral photos when debonding (year 2006, Age 26).
Figure 5. Lateral cephalometric superimposition between debond (black line) and one-year post-treatment follow-up (blue line).

Figure 6. Serial intraoral photos from debonding, 1 year, 3-year post-treatment follow-up (from top to bottom).
which was poorly controlled even though she had been undergoing gynecological treatment. She also reported unexplained gain weight and increasing swelling of her bilateral extremities. Follow-up extra-oral photos revealed notable deviation of the facial midline and facial soft tissue hypertrophy (Figure 7).

Because of these findings, we referred the patient to the Endocrinology and Metabolism division for thorough systemic examination. On serology testing, unusual elevation of GH (221.0 ng/ml [normal range: <2.0 ng/ml]) and insulin-like growth factor 1 (IGF-1) levels (793.0 ng/ml [normal range: 114.0–492.0 ng/ml]) were detected. Brain magnetic resonance imaging (MRI) examination showed enlargement of the pituitary gland over the sella region. According to the serology tests, radiographic examination, and indicative changes of physical traits, the patient was diagnosed with a GH hypersecretion-type PA, which in 2012 was known as acromegaly (patient was 32 y/o at then). The patient was referred to neurosurgery and underwent trans-sphenoidal adenomectomy in the same year.

Clinical photos at 1- and 6-years follow-up post-brain surgery still showed mild progressive changes in overjet, deviated dentition, and soft tissue midline (Figure 8). Serial lateral cephalometric superimposition revealed ongoing vertical growth of maxillofacial structures and forward growth of mandible (Figure 9). However, the growth rate decreased significantly after the adenomectomy. Routine postoperative follow-up in the neurosurgery department showed that IGF-1 levels
Figure 8. Intraoral photographs in 1 year after brain surgery and 6-year follow-up after debond.

Figure 9. Serial lateral cephalometric superimposition from debonding in 2006 (black line), post-debonding 1 year in 2007 (blue line), 2 year in 2008 (green line), 5 year in 2011 (purple line) to 11.5 year in 2018 (red line).
gradually increased while the GH level maintained stable although still above the normal range (Figure 10). On yearly brain MRI examination, the sella turcica was reduced in size after adenomectomy and remained stable since then. Thus, no further pharmacotherapy and radiation therapy were suggested. Long-term follow-up is mandatory. The serial profile photographs from pre-orthodontic to 11.5 years post-orthodontic treatment recorded the disease process (Figure 11). Currently, the patient is monitored by neurosurgery in cooperation with our orthodontic department.

**Figure 10.** Hormone level change from diagnosed of acromegaly in 2011 to 2018 follow-up. IGF-1 level still gradually increased after brain surgery. Yet a dramatic decrease of growth hormone level can be seen (from 215ng/ml to 12.94 ng/ml).

**Figure 11.** Serial lateral extra-oral photographs comparison from initial to 11.5-year post-debonding follow-up (from left to right).
DISCUSSION

Acromegaly progresses slowly, and the initial symptoms and signs are diverse, nonspecific, and easily neglected. Proper diagnosis may take years. Abnormal changes in facial appearance and extremities are the most common symptoms prompting a patient to seek help. When Acromegaly diagnosis is established according to clinical signs, laboratory data, and radiographic examination. Serologic examination primarily reveals elevated circulating GH and IGF-1 levels. MRI is the best diagnostic imaging tool, and helps to identify the extent of sella turcica enlargement. However, two-dimensional morphological changes of the hypophyseal fossa of the sella turcica can also be observed on serial lateral cephalometry; thus, orthodontists may play a role in early detection of acromegaly.

The sella turcica is the intracranial aspect of the sphenoid bone. The saddle-shape fossa is encircled from the top by the anterior and posterior clinoid processes. The anterior wall develops in a straight cranial-caudal direction. Nagaraj et al. studied the size of the sella turcica in an Indian population by measuring it on lateral cephalometric radiographs of relatively healthy patients aged 8 to 30 years. Their results showed a mean anteroposterior dimension of 11.83 mm (range 8–16 mm) and a mean depth of 8.21 mm (range 5–13 mm). In our patient, the pre-surgical MRI revealed a sella turcica of 16 mm in anteroposterior dimension and 14 mm in depth. With respect to normal growth of the cranial base, the anterior sella turcica stops growing at approximately 7 years of age, while posterior part continues growing until 16 or 17 years of age. Therefore, abnormal increase in the dimension or a change in the direction of growth of the anterior wall warrants evaluation for the presence of pituitary gland abnormality.

Our patient developed irregular menses after orthodontic treatment. According to Kaltsas et al. (1999), menstrual irregularity is common in 50–75% of female patients with acromegaly. On the basis of this clinical symptom, along with exaggerated growth of facial soft tissue and extremities, abnormal enlargement and changes of sella turcica morphology, gradually protruding lower jaw, and thorough serology examinations, the patient was diagnosed with acromegaly.

The goal of acromegaly management is to remove the origin of abnormal GH secretion or suppress its secretion, thus alleviating the clinical symptoms and maintaining the pituitary gland function; this is accomplished with surgery, irradiation, and pharmacotherapy. Recent information indicates that GH should be 2.5 ng/ml or less after surgery, and the circulating IGF-1 level should be within the normal range. The vast majority of these tumors are a localized mass seated in the sella turcica; therefore, surgical debulking and decompressing under endoscopy remains the gold standard. For patients in whom surgery is contraindicated or failed, radiotherapy including X-irradiation or proton beam therapy is indicated. Drug therapy is another adjunctive treatment when either surgery or radiotherapy is unsuccessful, or when surgery is contraindicated. In those cases, dopaminergic analogs (bromocriptine) and somatostatin analogs (octreotide) are the two most commonly used agents to inhibit the secretion of GH.

Mandibular body length was dramatically shortened in the present patient after the bilateral sagittal split osteotomy (Figure 12). However, due to excessive secretion of GH caused by the PA, the mandibular length increased by 1.64 mm over the next four years. After the trans-sphenoidal adenomectomy, the rate of increase of mandibular length and ramus height dropped significantly from +0.33 to 0 mm/ and +3.57 to +0.32 mm/year, respectively (Table 1).

The upper anterior facial height increased 1 mm as a result of the orthognathic surgery (Figure 12). However, the upper anterior facial height increased a further 3.03 mm within 5 years (0.61 mm/year) as the acromegaly
Figure 12. The change of mandible body length (Gn-Go), mandible ramus height (Co-Go), upper anterior facial height (UAFH, N-ANS), and lower anterior facial height (LAFH, ANS-Me) from pretreatment to post treatment 12-year follow-up (timeline shown in years).
progressed. After the brain surgery, there was only a slight increase in anterior facial height at a rate of 0.17 mm/year. The same phenomenon was observed in the lower anterior facial height (Table 1, Figure 12).

Herrmann et al. observed that acromegaly-associated craniofacial morphological changes in the maxilla are different from those in the mandible.12 Their study demonstrated that the midface bony structure will increase in vertical dimension instead of anterior-posterior dimension. This finding is consistent with the increase in upper anterior facial height as the disease progressed in our patient. However, Herrmann et al. further indicated that apart from the mandible height, the mandibular length is the most affected by the disease, which is in contrast to the findings in our patient. In our case, the morphological change in mandibular length was less than that in the vertical direction (Table 1).

Cosmetic changes associated with acromegaly are usually of great concern to the patients. However, after the disease is cleared medically, plastic surgery and orthognathic surgery may be performed. In our case, if the disease is under control, a second orthodontic combined orthognathic surgery treatment could be considered. However, at present, our patient does not intend to undergo another orthognathic treatment or plastic surgery.

### Table 1. The linear change of mandible length, ramus height and anterior facial height after debonding, brain surgery (5 years after orthodontic treatment) and 7 years after the brain surgery.

<table>
<thead>
<tr>
<th>Linear measurement (mm)</th>
<th>Debonding (2006)</th>
<th>5-year F/U (2011)</th>
<th>12-year F/U (2018)</th>
<th>Increase rate* (mm/year)</th>
<th>Increase rate** (mm/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramus Height</td>
<td>61.0</td>
<td>78.9</td>
<td>81.1</td>
<td>3.57</td>
<td>0.32</td>
</tr>
<tr>
<td>Body Length</td>
<td>84.0</td>
<td>85.6</td>
<td>85.6</td>
<td>0.33</td>
<td>0</td>
</tr>
<tr>
<td>UAFH#</td>
<td>59.5</td>
<td>62.5</td>
<td>63.75</td>
<td>0.61</td>
<td>0.17</td>
</tr>
<tr>
<td>LAFH##</td>
<td>73.0</td>
<td>76.7</td>
<td>79.2</td>
<td>0.74</td>
<td>0.35</td>
</tr>
</tbody>
</table>

# Upper Anterior Facial Height (UAFH)
## Lower anterior facial height (LAFH)
*Rate of increase from debonding to post-treatment 5-year follow-up
**Rate of increase from post-treatment 5 year to 12-year follow-up
CONCLUSION

By presenting this rare case, we hope to provide some insight into diseases seldom encountered during daily orthodontic practice. Frequently, clinical practitioners may focus on details, thus missing the overall clinical picture; this may increase the risk of overlooking critical information. Routine lateral cephalometry analysis, extra- and intra-oral examination during treatment process, including the retention phase, are crucial. These examinations are not only important to gauge the result of treatment, but are also helpful to detect abnormalities over time. If signs and symptoms first appear during orthodontic treatment, it is essential to communicate these findings with the patient and postpone orthodontic tooth movement. Timely referral to specialists including neurosurgeons and endocrinologists is extremely important. It is better to proceed with orthodontic treatment or revise the orthodontic treatment plan after the disease is under control.

REFERENCES