A multidisciplinary approach to the treatment of oral manifestations associated with Beckwith-Wiedemann syndrome

A long-term case report

Beckwith and Wiedemann provided the first reports of Beckwith-Wiedemann syndrome (BWS) in 1963 and 1964, respectively. Beckwith described three postmortem cases involving extreme cytomegaly of the adrenal fetal cortex, omphalocele, hyperplasia of kidneys and pancreas, and Leydig cell hyperplasia. Wiedemann subsequently reported his findings in three brothers with similar symptoms, as well as umbilical hernia and macroglossia. The prevalence of BWS is estimated to be one in 14,000 births. The use of assisted reproduction techniques can increase the chances of BWS by four or five times, which means an approximate prevalence of one in 3,000 in assisted reproduction births.

BWS is a congenital disorder that involves a somatic overgrowth during the patient's first years of life. Exomphalos, macroglossia and gigantism are the main clinical symptoms. The prevalence of BWS is estimated to be one in 14,000 births. The use of assisted reproduction techniques can increase the chances of BWS by four or five times, which means an approximate prevalence of one in 3,000 in assisted reproduction births.

Clinical Implications. To obtain long-term positive and stable results, an appropriate treatment plan for patients with BWS and dentoskeletal alterations, including macroglossia, requires surgical tongue reduction when the patient is young, combined with physiotherapeutic phases and orthopedic and orthodontic treatment.

Key Words. Beckwith-Wiedemann syndrome; macroglossia; tongue reduction; physiotherapeutic treatment; orthopedic treatment.

ABSTRACT

Background. Beckwith-Wiedemann syndrome (BWS) is a congenital disorder that involves a somatic overgrowth during the patient's first years of life. Exomphalos, macroglossia and gigantism are the main clinical symptoms.

Case Description. The authors describe a 15-year follow-up in a patient with BWS. They focus on a multidisciplinary approach to treating the patient's oral manifestations from age 9 months. The approach included an initial physiotherapy treatment, a partial glossectomy, a first phase of orthopedic treatment with a tongue crib and chin cap, and a second phase of orthodontic treatment with an edgewise appliance.

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JADA 2011;142(12):1357-1364.
growth suppressor cyclin-dependent kinase inhibitor 1C and the increased expression of the paternally expressed growth promoter insulinlike growth factor type 2. These alterations can result from multiple genetic and epigenetic mechanisms, including paternal uniparental disomy of chromosome 11p15.5. Genetic testing should be conducted in the diagnosis of BWS whenever possible and should include karyotype analysis, DNA methylation and genomic analysis of chromosome 11p15.5.

Several investigators have described findings associated clinically with BWS. The most common extraoral clinical findings are unusual earlobe creases, omphalocele, umbilical hernia, somatic overgrowth during infancy, nephromegaly, hepatosplenomegaly, hemihypertrophy and hypoglycemia. Adrenocortical cytomegaly, polyhydramnios, advanced skeletal age, prematurity and capillary malformation also are frequent findings. In rare cases of BWS, patients also can have diastasis recti, clubfoot, nystagmus and strabismus, and low attention span with hyperactivity. Anatomical brain malformations, convulsions, slight mental impairment, scoliosis, congenital cardiopathy and diabetes also have occurred. A patient with BWS is more susceptible to developing cancer than are people in the general population, particularly during the first decade of life (average age, 2 years). Between 7.5 and 10.0 percent of patients with BWS develop a malignancy. This risk increases if the patient has hemihypertrophy or nephromegaly. The tumors usually are embryonic and sensitive to biochemical markers, ultrasonography or both. In 95 percent of patients with BWS, the tumor appears in the abdomen, and most commonly are hepatoblastoma and Wilms tumor. Because clinical findings of BWS are variable, there are no absolute criteria for making a diagnosis, but several of the associated findings should be present to support the diagnosis. Choufani and colleagues recommended that all children with a confirmed diagnosis of BWS or who are suspected of having BWS undergo an α-fetoprotein assay every three months to the age of 8 years, regardless of the molecular etiology.

The infant mortality rate associated with BWS is approximately 21 percent; congestive heart failure or severe malformations are the most common causes. However, once the infant has survived any possible postpartum adaptive difficulties, the prognosis usually is good, although the increased tumor risk in patients with BWS has to be considered.

The typical intraoral finding associated with BWS is macroglossia, which is a major criterion in diagnosing BWS. BWS occasionally has been referred to as “EMG syndrome” because its three main clinical symptoms are exomphalos, macroglossia and gigantism. The occurrence of hypotonia, including in the orofacial muscles, followed by early tooth eruption and cleft palate, also is a frequent clinical characteristic of BWS. Investigators in previous articles have explained that early diagnosis and treatment of oral manifestations of BWS can reduce the development of dentoskeletal alterations and lead to a better quality of life for patients with BWS. In this article, we report a case involving the 15-year follow-up of a patient with BWS. We focus on the multidisciplinary approach we used to treat oral manifestations in the patient. Treatments included physiotherapy, surgical intervention, and orthopedic and orthodontic treatment.

**CASE REPORT**

During the physical examination at birth, physicians observed macrostomia, muscular hypotonia, omphalocele, bilateral cryptorchism, alterations of both earlobes and macroglossia in a boy born in the 37th week of gestation to a 25-year-old primiparous woman who did not have any relevant personal or family history. At 9 months of age, the boy was admitted to the School of Dentistry at the University of Santiago de Compostela, Spain, to be evaluated for oral health status. The most significant findings of the complementary tests (blood test, chest radiograph, chromosomal study) that were conducted at the dental school when the boy was 9 months old were hypoglycemia, which went away in 23 hours; symmetric myocardial hypertrophy; and a normal karyotype. We diagnosed the patient’s BWS.

During our oral examination of the patient, we observed hypotony of the perioral muscles, a prominent tongue that hung over the lower lip (true macroglossia) and severe drooling. Despite the size of the patient's tongue, he did not have severe difficulty in sucking and swallowing. Therefore, we decided to have the patient start oral physiotherapy by using the Castillo-Morales technique, which is a method combining massage exercises for activation and stimulation and a palatal plate. We attached a button to the posterior part of the plate so the
patient could stimulate his tongue, as well as ground in channels so the patient could stimulate his lip muscles. We also included a rotating pearl on the posterior edge to enhance stimulation to a greater degree (Figure 1A). Taking into account that the plate uses the gum profile and tongue to keep the plate in the correct position, we used dental floss to tie the plate to the patient’s shirt to prevent aspiration of the plate.17,26,27 Once we placed the plate on the palate, the patient had an immediate reaction (Weiffenbach reflex) because of the introduction of a foreign body in the mouth. When the tongue presses on the palatal cylinder, it generates a backward and upward force that counteracts the forward and downward position caused by the muscular hypotonia, which keeps the tongue in the oral cavity. The boy’s parents placed the plate in position twice each day, starting for five minutes and then increasing the time progressively until it was 15 minutes per session.

After one month of treatment, we observed that the patient drooled substantially less. The patient underwent physiotherapy and used the plate until he was aged 3 years. We replaced the plate three times between eruption of the anterior and posterior primary teeth (approximately every nine-10 months), according to his maxillary growth and dental eruption.

At this time, the resting position and function of the tongue had improved, although the patient still had some difficulty in swallowing (Figure 1B). When he was age 4 years, we decided to perform a partial glossectomy by using the Egyedi and Obwegeser28 technique (Figures 1C and 1D), because he had developed a progressive anterior open bite secondary to a prolapsed tongue. The results of an oral function evaluation we performed four months later showed that surgical reduction of the tongue’s volume had improved the patient’s swallowing and made speech more intelligible. We recommended that the patient do stimulation exercises while his parents observed him. He was to continue these exercises at home until his permanent first molars had erupted completely.

When the patient was aged 7.5 years, we decided to start the first phase of orthopedic and orthodontic treatment. At that time, the patient had a severe vertical mandibular growth with an anterior open bite, a skeletal Class III malocclusion apical base relationship with a normal-sized maxilla and a long mandible, and a Class I malocclusion molar relationship with a slight tendency to transverse discrepancy and retardation of permanent incisor eruption (Figure 2). Our objectives in this treatment phase were...
inhibition of tongue protrusion, expansion of the maxillary dental arch and control of mandibular vertical growth.

First, the patient used consecutive maxillary active plates with a tongue crib and a plastic stimulating ball for about two years. The patient used two removable plates during this period, approximately one per year, to adapt the appliance to his maxillary growth changes and to improve plate retention.

When the patient’s maxillary and mandibular permanent incisors had erupted, we expanded his maxilla by means of a fixed appliance, instead of removable plates, owing to the patient’s poor cooperation with the previously used removable plates. The patient used a Haas appliance for four months (Figure 3A).

To avoid transverse relapse when no other intraoral devices were being used, we placed a low palatal bar on the maxillary permanent first molars as a temporary retainer with an acrylic central button for vertical control and a plastic ball for tongue control. The patient wore a vertical chin cap 10 to 12 hours per day to redirect mandibular growth until we began the next phase of the treatment (Figure 3B).

When the patient was aged 12.5 years, we started the second phase of orthopedic and orthodontic treatment by having him wear an edgewise appliance with intermaxillary elastic bands to achieve good alignment and occlusion of permanent teeth (Figure 3C). We also continued to manage the mandibular vertical control by having the patient wear a vertical chin cap seven to nine hours per day until the end of this phase (the period of main mandibular growth). When the patient was aged 15.5 years, we placed the retention appliances: fixed lingual retainers on the maxillary and mandibular dentition and a Hawley retainer on the maxillary dental arch. We also performed an esthetic restoration in the maxillary left lateral incisor to make its shape equal to that of the contralateral incisor. This multidisciplinary approach allowed us to achieve an improvement to skeletal Class I malocclusion in the maxillomandibular relationship, with a counterclockwise rotation of the occlusal plane. We also maintained molar Class I malocclusion at the end of active treatment. Eight months after we placed the retention appliances, the patient had an acceptable occlusion and facial profile. He did not need to undergo a second surgical intervention on the tongue or orthognathic treatment (Figure 3D).

We analyzed cephalometric superimpositions across eight years, from the beginning to the end of orthodontic treatment,29,30 and we...
observed that the standard deviation change (1.5˚) in the facial axis was normal for this period (Figure 5A), despite the vertical growth of all of the components of the patient’s craniofacial complex. This finding suggests that the patient’s mandibular vertical growth was controlled because an excessive clockwise growth did not take place. Figures 5B, 5C and 5D show maxillary and mandibular growth, as well as maxillary and mandibular tooth changes, all in the midsagittal plane. Vertical skeletal growth and its dentoalveolar compensations are visible, especially in the maxillary and mandibular anterior teeth.

DISCUSSION
Results of previous studies have shown that macroglossia can lead to three types of complications: dentoskeletal problems, such as mandibular prognathism with an increase in mandibular length, anterior open bite, higher gonial angle and anterior facial height and excessive proclination of the mandibular incisors31-33; functional deficits such as difficulty in swallowing, drooling, alterations in speech and obstruction of the upper airway35,34-38; and psychological consequences derived from the patient’s appearance.39,40 Taking into account these repercussions, several patients with BWS, including the one in our case report, were treated surgically, orthopedically, orthodontically or by means of a combination of all three approaches, depending on the clinic and the age of the patient.3

A logical approach to preventing or correcting the effects of macroglossia is performing tongue reduction surgery, preferably before problems in speech development occur, but not before the patient is aged at least 6 months.23 In less severe cases of BWS, however, Müssig and Zschiesche25 recommended an earlier orthopedic and physiotherapeutic intervention, based on the use of a pacifier and stimulation plates to try to obviate the need for surgery while providing adequate results. In the case we presented, early use of oral physiotherapy did not obviate the need for the patient to undergo a partial glossectomy.

There are several successful tongue reduction techniques. The main philosophy of these techniques involves reducing the central tongue bulk and the tongue’s length, while avoiding damaging the neurovascular bundles that run inferolaterally.40,41 Among the various patients for whom clinicians have used partial glossectomy to treat BWS, different tongue reduction techniques have been used: the Becker method,14 the keyhole technique,41-44 a wedge-
Figure 4. The patient’s appearance with Beckwith-Wiedemann syndrome at age 15.5 years. A. Cephalogram showing the main dental and skeletal structures (black lines) and the final functional occlusal plane (red line) between the maxillary and mandibular posterior teeth. B. The patient’s facial profile. C. Photograph showing occlusion.

Figure 5. Cephalometric superimpositions in the midsagittal plane of the patient with Beckwith-Wiedemann syndrome. Black indicates the pretreatment position, and red indicates the posttreatment position. A. Chin positional changes in the facial axis. B. Maxillary growth. C. Mandibular growth and mandibular tooth changes. D. Maxillary tooth changes.
shaped technique, the Butlin-Handley technique, the rhomboid technique and the central W-shaped technique. The keyhole technique has been used most frequently. The tongue reduction technique we used was described originally by Egyedi and Obwegeser. This technique involved a block excision of the middle and tip of the tongue for adequate width and length reduction. The basic advantages of this technique are the uniform reduction of the tongue and the preservation of the neurovascular bundle and the papillae at the sides and the base of the tongue. Several short-term complications arising from partial glossectomy may occur, regardless of the tongue reduction technique used. The most common complications are decreased articulation, less intelligible speech or a permanently large tongue. The patient whose case we report experienced none of these complications.

Among the cases we mentioned earlier, those limited to preoperative and surgical treatment had no long-term follow-up after the partial glossectomy. In only one case we mentioned previously, investigators reported a follow-up across nine years after partial glossectomy involving the use of a keyhole technique. They found that besides the already existent speech complications, some dentoalveolar problems—such as Class III malocclusion, anterior open bite, diastema and overangulation of the mandibular incisors—occurred. The patient in our case had some of these dentoalveolar and skeletal problems.

It seems appropriate to combine the tongue reduction surgery with subsequent physiotherapeutic, orthopedic or orthodontic treatment, because if the treatment plan is limited only to glossectomy performed when the patient is young, the most probable result is the correction or avoidance of anteroposterior problems such as mandibular prognathism. Vertical problems such as increased gonial angle and open bite, however, might not be corrected.

The patients with BWS in the reported cases who received orthodontic treatment—particularly two phases of treatment—that better and more stable final results for dental occlusion and oral function than did those who did not receive orthodontic treatment. In the first phase of the treatment plan, which usually involves placing active plates with a tongue guard and the use of a vertical chin cap, the patients had an improvement in mandibular protrusion and anterior open bite. In isolated patients, clinicians used three types of orthodontic treatment during the second phase of the treatment plan. As an alternative to the use of multibracket fixed appliances, they used other treatments such as a gnathologic positioner or stability oriented appliances such as a bite block with a Nance holding arch or lingual arch.

Miyawaki and colleagues designed a treatment plan similar to ours that was based on early orthodontic treatment with the use of a tongue crib and a chin cap and a second phase involving fixed orthodontic treatment. Their implementation of their treatment plan resulted in positive and stable results after a 12-year follow-up. In the case we report, after a 15-year follow-up (the longest, to our knowledge), our treatment plan of surgical, physiotherapeutic, orthopedic and orthodontic treatment effectively improved an abnormal dentoskeletal pattern, did not relapse and did not have any unexpected complications.

CONCLUSIONS

To obtain long-term positive and stable results in patients with BWS who have dentoskeletal alterations, including macroglossia, an appropriate treatment plan should involve surgical tongue reduction performed when the patient is young combined with different physiotherapeutic phases and orthopedic and orthodontic treatments. We recommend having a multidisciplinary dental and medical team create the clinical guidelines for patients with BWS. Orthodontists, in particular, play an essential role, as they can evaluate and manage maxillary and mandibular growth to help establish the final dental occlusion and oral function.

Disclosure. None of the authors reported any disclosures.