Craniofacial and Dental Manifestations of Proteus Syndrome: A Case Report

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The Proteus syndrome is a rare congenital hamartomatous condition that is characterized by a wide range of malformations, sometimes involving the face. Common manifestations include partial gigantism, congenital lipomas, and plantar hyperplasia. In this report we describe the craniofacial clinicopathological development in a girl with Proteus syndrome from age 6 to 20 years. The patient had pronounced hemifacial hypertrophy, exostoses in the left parietal region, and enlargement of the inferior alveolar nerve and mandibular canal in the affected region. The dental development of the affected left mandible and maxilla was characterized by extremely premature development and eruption of the primary and permanent teeth and by pronounced idiopathic root resorptions. The multidisciplinary management of the patient and the treatment outcome is reported. A review of the Proteus patients in the literature who exhibited manifestation in the craniofacial region is presented.

KEY WORDS: *hemifacial hypertrophy, precocious dental development and eruption, Proteus syndrome*

Proteus syndrome is a complex hamartomatous condition characterized by partial gigantism of the hands, feet, or both; plantar hyperplasia; hemangiomas; lipomas; lymphangiomas; varicosities; verrucous epidermal nevi; macrocephaly; cranial exostosis; and asymmetry of the limbs because of long bone overgrowth. The first description of Proteus syndrome is attributed to Cohen and Hayden (1979), who reported two cases. Unaware of the earlier report, Wiedemann et al. (1983) described four children with similar findings. The syndrome was given the name Proteus, which refers to the mythical Greek god who was capable of changing his bodily shape.

This report describes a female patient with a localized form of Proteus syndrome and compares her with other patients with Proteus syndrome and with patients with hemifacial hypertrophy.

Etiology

The cause of Proteus syndrome is unclear. Its progressive nature and multisystem involvement suggest a genetic cause. Long thought to be sporadic in occurrence, it may be due to a lethal mutation that survives only in a mosaic form. It has been postulated that an acquired somatic mutation may affect receptors of tissue growth factors or fibroblast growth factors in specific parts of the body in this condition (Hall, 1988; Rizzo et al., 1993; Tattelbaum and Dufresne, 1995). The extent of involvement is variable, but diffuse involvement of the entire body or an entire organ system is not characteristic. There is no statistical difference in sex predilection (Gorlin, 1984). The criteria for the diagnosis of Proteus syndrome are divided into general and specific by Biesecker et al. (1999).

Patient History

The patient was seen for consultation and treatment at the Mayo Clinic at age 13 years.

Previous Investigations and Treatment

The propositus was a Caucasian girl, the third child of healthy parents. One male and one female sibling were healthy. She was born at term weighing 7 pounds 4 ounces after a normal pregnancy. In the neonatal period, the maternal grandmother noted mild facial asymmetry, but it was not apparent to other family members. At age 6 months, progressive enlargement of the left cheek, lower lip and tongue was observed (Fig. 1). The lower lip enlarged rapidly, and at age 4 years she had a lip reduction procedure performed by a local surgeon. The histopathology revealed angioma in association with fibroadipose hamartoma. A skin biopsy was taken from a hy-

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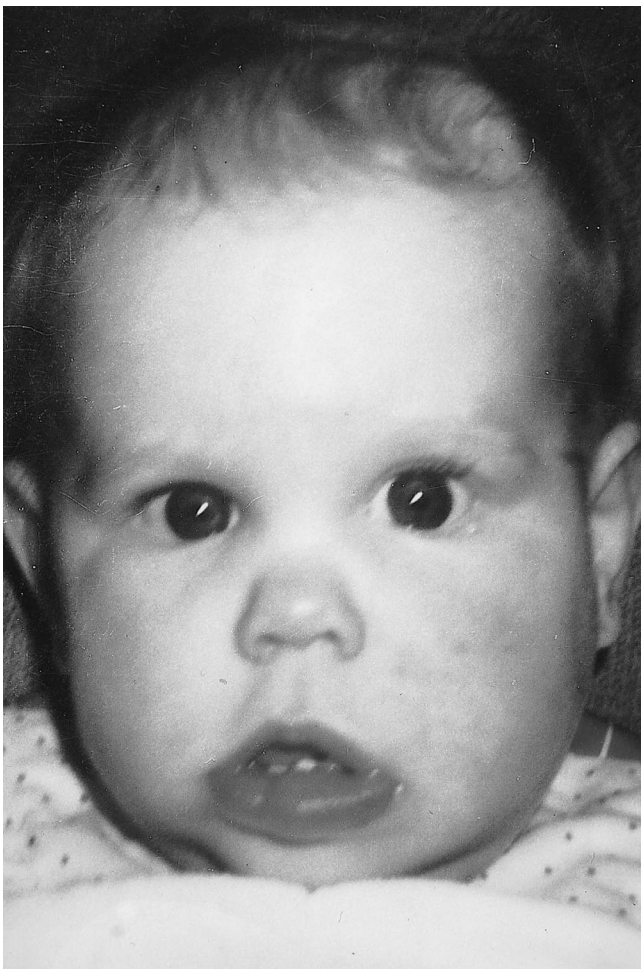

FIGURE 1 Patient at approximately 6 months of age, showing slight enlargement of left cheek and left lower lip.

perpigmented area of the left temporal region. The histopathology revealed an epidermal nevus. Another skin biopsy over an exostosis involving the left parietal bone was undertaken, and the histopathology revealed fibrocollagenous and fibroadipose tissue. Figure 2 shows the patient at 7 years of age.

At age 10 years, she had a partial (30%) glossectomy by a local surgeon. The exostosis involving the left parietal bone was removed, but no histopathology report was available.

The patient's dental development and eruption was unusual, with the first primary tooth erupting at 3 months and all the left maxillary and mandibular teeth developing and erupting significantly ahead of the teeth on the right side. Exfoliation of the deciduous teeth on the left side began at 18 months. Figure 3 and Table 1 document the differential growth and development of the right and left dentition, which was as much as 5 to 5½ years in the first bicuspid teeth. The differential advanced dental development on the left side varied significantly from tooth to tooth.

From age 13 to 15 years, the patient was treated with an activatorlike orthodontic appliance by a local orthodontist, apparently to encourage symmetrical growth and minimize tongue function on tooth and jaw formation. She had a total of seven minor craniofacial surgical procedures prior to referral to Mayo Clinic.

Physical Examination

A comprehensive examination of the patient, aged 13 years, was undertaken by the Craniofacial Team at the Mayo Clinic including oral and maxillofacial surgery, plastic surgery, genetics, ophthalmology, otolaryngology, psychology, speech pathology, and orthodontics.

Craniofacial Appearance

The examination revealed enlargement of the left facial osseous and soft tissue, compared with the right (Fig. 4). The left ear was slightly posteriorly positioned. In the left parietal region, exostoses were palpable and there was overlying partial alopecia. A reddened, rough, well-demarcated hyperpigmented area was observed in the left temporal region extending to the left brow. Overgrowth of coarse, stiff hair was observed in the left preauricular and left chin area.

Oral Examination

All permanent teeth were erupted except both maxillary second molars, the upper right canine, the mandibular right second molar, and the second premolar. There was secondary retention of the left first and second permanent molar in the mandible. Normal dental anatomy (size, shape, and mineralization) including gingival tissue was noted (Fig. 5). The left side of the tongue was symmetrically enlarged.

Speech Examination

There were mild articulatory distortions associated with lingual hypertrophy and malocclusion.

Audiology

The examination suggested that there was a mild left-sided conductive hearing loss.

Genetics

The karyotype from a skin biopsy from the hypertrophied cheek region revealed a normal 46,XX karyotype in 20 of 20 cells at the 450-band stage.

Other Examinations

Aside from the above-described left craniofacial findings, the remainder of physical examination was normal. Intelligence was found to be above normal on psychometric testing.

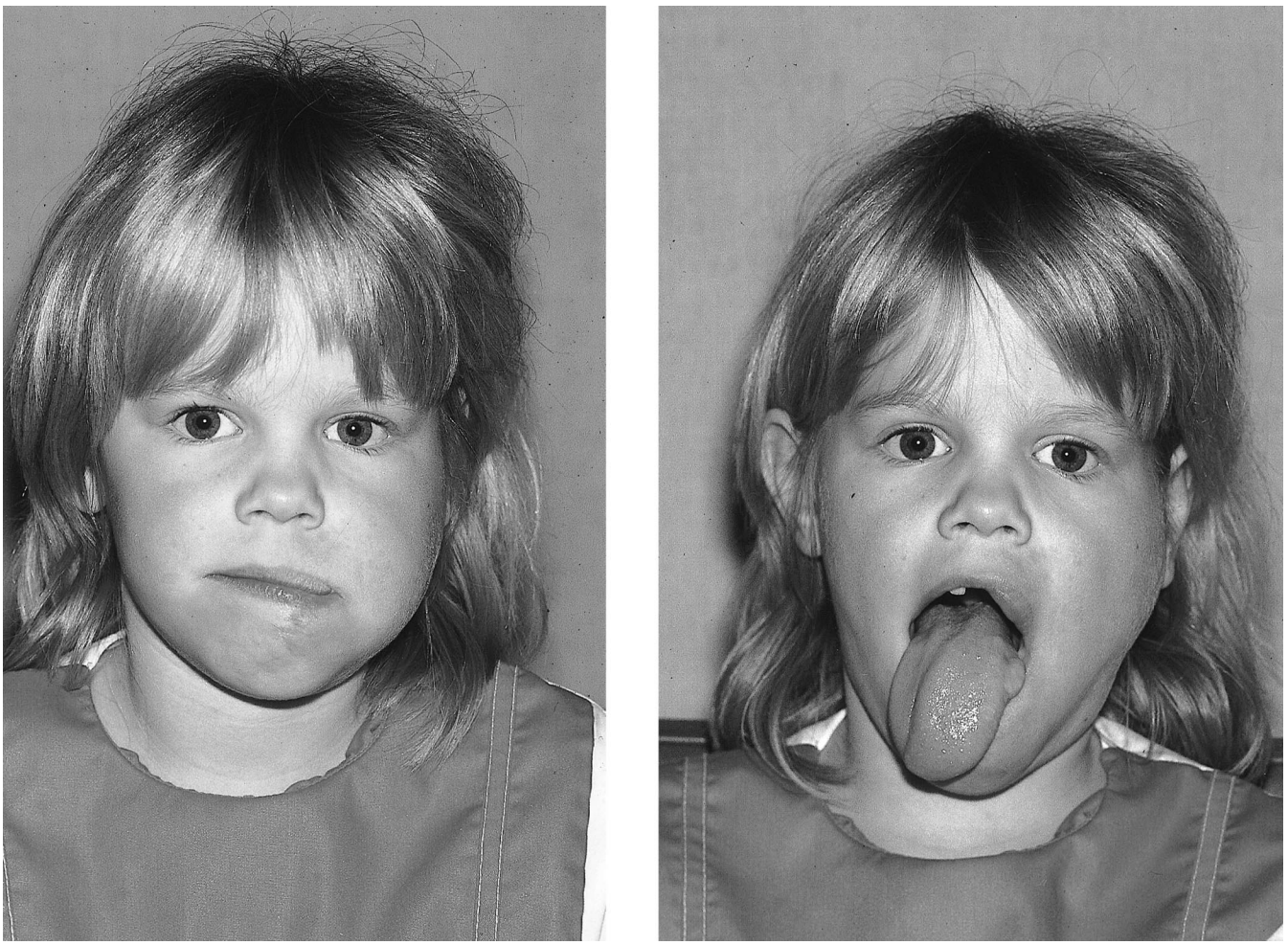

FIGURE 2 At age 6 years 10 months, the left cheek and left side of the tongue shows progressive enlargement. (Surgical reduction of the lower lip had been previously performed.)

Radiological Investigation

Panoramic Radiographs

The dental growth and maturation between the left and right side were significantly different (Tables 1 and 2); development was slightly retarded on the right and advanced in several teeth on the left side. This discrepancy was more pronounced in the mandible (Table 1). Eruption of the left maxillary canine and first premolar and all the permanent teeth on the left side of the mandible was significantly precocious (Figs. 3A and 6).

Dental agenesis (left lower third molar), ectopic eruption, idiopathic root resorption, and various anatomic malformations were recorded (Tables 1 and 2).

Enhanced maxillary and mandibular vertical growth of the left alveolar processes were present. The left condyle, ramus, and body and the left mandibular canal and mental foramen were significantly enlarged (Fig. 6).

Lateral Cephalometric Radiographs

The cephalometric analysis showed prognathism of the maxilla (SNA 85.2 degrees) and the mandible (SNB 82.4 degrees; Table 3). The growth analysis from age 6 years 10 months to age 16 years revealed a normal forward and downward growth pattern of the maxilla and the mandible (Fig. 7). There was a slight enlargement of the exostosis of the parietal bone over the years.

Frontal Cephalometric Radiographs

The analysis of the posterior-anterior cephalometric radiograph (Svanholt and Solow, 1977) at age 6 years 10 months showed that both the maxilla and the mandible were displaced 3.5 degrees to the right, compared with the frontal midline. At age 16 years, the displacement to the right was increased to 4.0 degrees.

Computed Tomography Scan

Computed tomography (CT) of the head showed normal intracranial contents. There was a slight flattening in the high left parietal region, possibly related to a localized sutural abnormality.

There were exostoses of the vertex of the calvarium along

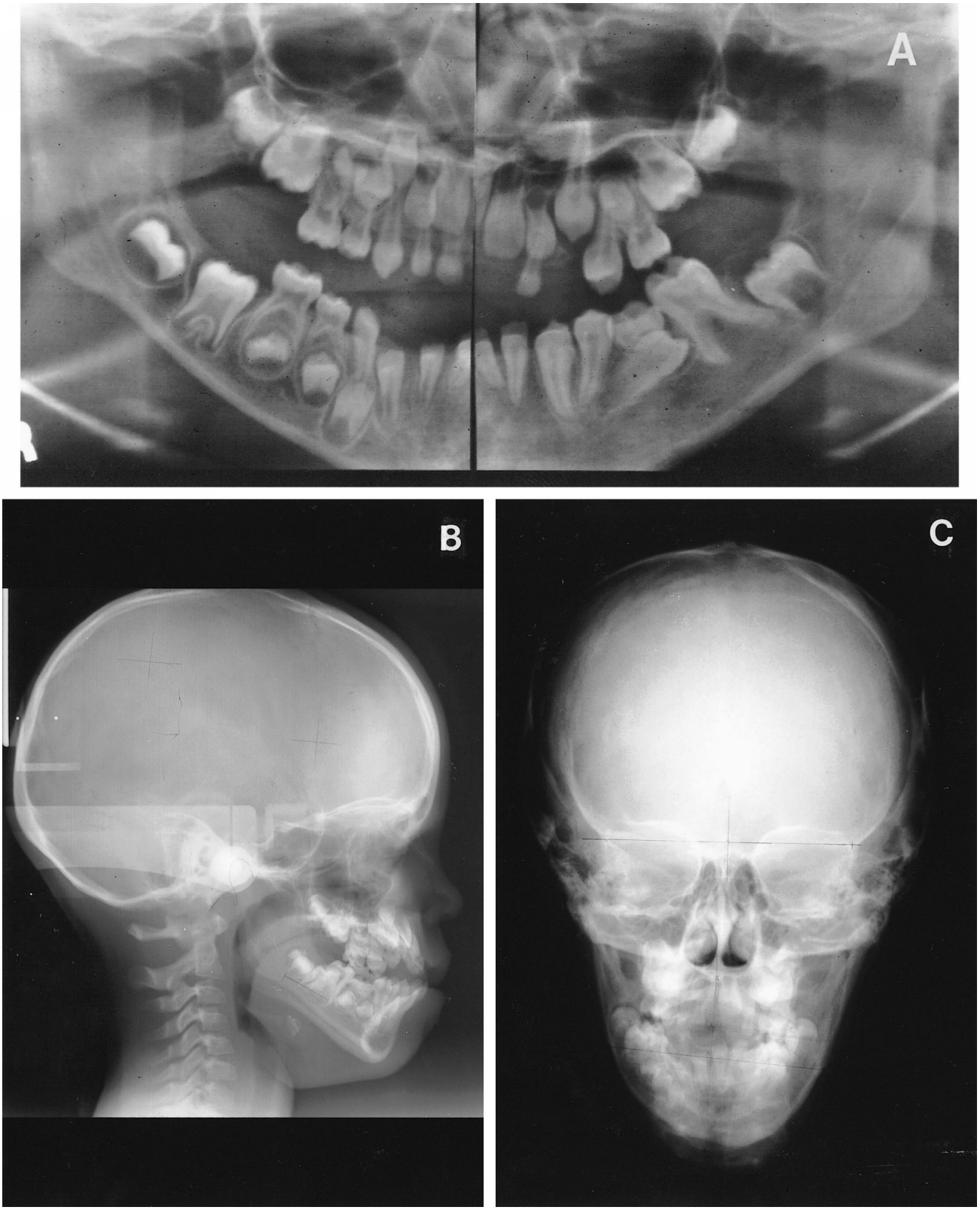

FIGURE 3 Orthopantomogram (A), lateral (B), and frontal (C) cephalometric radiographs at age 6 years 10 months. Note the precocious development and eruption of the dentition on the left side. The difference in dental maturity between the right and left first bicuspids was as great as 5½ years. Note also the effect of tongue enlargement on the lower incisors and mandibular asymmetry.

TABLE 1 Dental Development at Age 6 Years 10 Months*

	Dental Developmental Stage		*Difference From Mean (Δ in Months)*		*Difference Between Sides (Months)*	*Root Resorption*		*Malformations*		*Eruption/Emergence*	
Tooth	*Right (y^{mo})*	*Left (y^{mo})*	*Right*	*Left*		*Right*	*Left*	*Right*	*Left*	*Right*	*Left*
Upper											
M_2	$Cr_{3/4}$ (5^6)	$Cr_{3/4}$ (5^6)	−16	−16	0	No	No	No	No		
M_1	$R_{1/2}$ (5^3)	$R_{1/2}$ (5^3)	−19	−19	0	No	No	No	No		
Pm_2	Cr_c (6^0)	Cr_c (6^0)	−10	−10	0	No	No	No	No		
Pm_1	R_i (5^0)	R_c (10^0)	−22	+38	60	No	No	No	No	Late	Early
C	$R_{1/4}$ (5^3)	R_c (10^0)	−19	+38	57	No	No	No	No		Early
I_2	$R_{1/4}$ (6^6)	$R_{1/4}$ (6^6)	−4	−4	0	No	No	No	No		
I_1	$R_{1/4}$ (6^0)	$R_{1/2}$ (6^6)	−10	−4	6	No	No	No	No		
Lower											
M_2	Cr_c (6^6)	$R_{1/4}$ (9^3)	−4	+29	33	No	No	No	No		Early
M_1	$R_{1/2}$ (5^6)	A_c (9^0)	−16	+26	42	No	No	No	Divergent roots		Early
Pm_2	Cr_c (6^0)	$R_{1/2}$ (8^9)	−10	+25	35	No	No	No	No		Ectopic early
Pm_1	R_i (5^9)	$A_{1/2}$ (11^3)	−13	+53	66	No	No	No	No		Early
C	$R_{1/4}$ (5^9)	$A_{1/2}$ (10^0)	−13	+38	51	No	No	No	No		Early
I_2	$R_{1/2}$ (6^0)	R_c (8^6)	−10	+20	30	No	No	No	Short root		Early
I_1	$R_{1/2}$ (5^9)	R_c (7^9)	−13	+11	24	No	No	No	Short root		

* According to Moorrees et al. (1963). + = advanced dental development; − = retarded dental development.

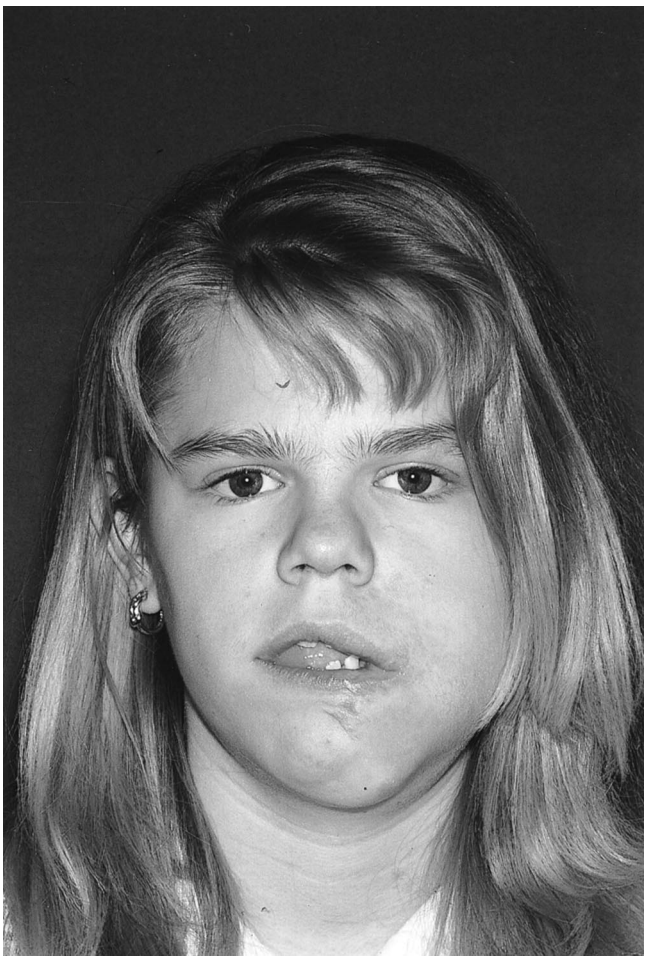

FIGURE 4 Patient at age 13 years with differential enlargement of left facial osseous and soft tissue with slight lowering of the medial and lateral left canthi. The left malar region was slightly more prominent than the right. The soft tissue of the left cheek and upper lip region was significantly thickened. The left oral commissure was reduced by 3 mm, and significant scar tissue was present in the lower lip secondary to previous surgical reduction. Note that the nasal and ocular structures are normal.

the sagittal suture, greater on the left side as well as along the left coronal suture. There was asymmetric increased soft tissue along the left side of the face and upper neck; this included subcutaneous, parapharyngeal, lingual space fat, and submandibular and parotid glands. Because of the soft tissue enlargements there was a mild deformity of the pharyngeal airway. The radiologist suggested lipoma or lymphangioma based on the density and water content of the enlarged soft tissue.

Treatment Objectives at the Mayo Clinic

Presurgical orthodontic treatment was planned. The first-stage surgical reconstruction was planned when skeletal growth was completed.

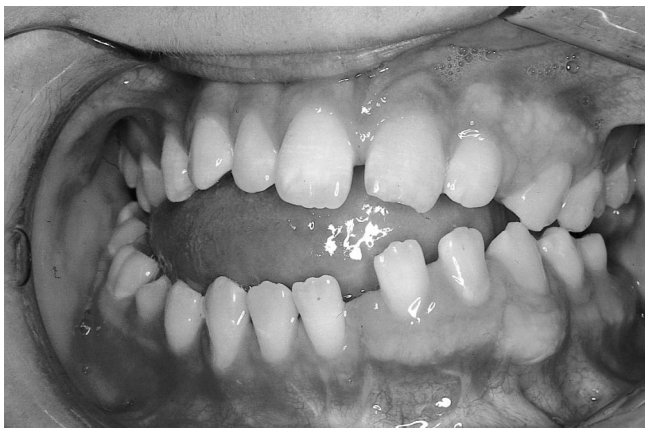

FIGURE 5 Occlusion at age 13 years. Anteriorly 2 mm of horizontal overjet, the molar occlusion was Class I on the right and Class III on the left. Four millimeters of open bite was recorded on the left laterally. The left maxillary and mandibular alveolar processes are showing increased growth in the vertical dimension, leading to a 7-mm open bite on the right side from the midline to the second molar. Both the maxillary and mandibular midlines were displaced 5 mm to the right. Dental spacings were present on the left side of both maxilla and mandible.

TABLE 2 Dental Development at Age 13 Years 5 Months*

	Dental Developmental Stage		*Difference From Mean (Δ in Months)*		*Difference Between Sides (Months)*	*Root Resorption*		*Malformations*		*Eruption*	
Tooth	*Right (y^mo)*	*Left (y^mo)*	*Right*	*Left*		*Right*	*Left*	*Right*	*Left*	*Right*	*Left*
Upper											
M_2	R_c (11^3)	R_c (11^3)	−26	−26	0	No	No	No	Taurodont		Secondary retention
M_1	Completed	Completed	—	—	—	No	No	Taurodont	Taurodont		
Pm_2	$R_{3/4}$ (10^0)	Completed	−41	—	—	No	No	No	No		
Pm_1	R_c (10^0)	Completed	−41	—	—	No	No	No	No		
C	$A_{1/2}$	Completed	−41	—	—	No	+++	No	No		
I_2	Completed	Completed	—	—	—	No	No	Invagination	Invagination		
I_1	Completed	Completed	—	—	—	No	No	No	No		
Lower											
M_2	R_c (11^3)	Completed	−26	—	—	No	++	Taurodont	Taurodont		Secondary retention
M_1	Completed	Completed	—	—	—	No	++	No	No		Secondary retention
Pm_2	$R_{3/4}$ (10^0)	Completed	−41	—	—	No	+	No	No		
Pm_1	R_c (10^0)	Completed	−41	—	—	No	++	No	No		
C	Completed	Completed	—	—	—	No	No	No	No		
I_2	Completed	Completed	—	—	—	No	+	No	No		
I_1	Completed	Completed	—	—	—	No	+	No	No		

* According to Moorrees et al., (1963). − = designates retarded dental development.

Orthodontic Management

From age 13 to 15 years, the patient wore a removable oral tongue crib appliance to attempt to reduce the effect of macroglossia on the erupting dentition.

Comprehensive orthodontic treatment was initiated at age 16 years. Three permanent teeth were removed because of advanced root resorption, secondary retention, or both. The orthodontic treatment was performed on right- and left-side segmental arches in the mandible (Fig. 8A through 8E).

Postorthognathic surgery anterior nocturnal vertical elastic were terminated at age 17 years, and a maxillary Hawley retainer and a mandibular overlay retainer with posterior tongue restraining loops was initiated.

Progressive root resorption in connection with the orthodontic treatment was observed on the maxillary left canine and incisors and premolars in the left side of the mandible (Fig. 8C).

Surgical Management at Mayo Clinic

Liposuction of the left cheek was performed at age 14 years. At age 17 years, skeletal growth was complete and orthognathic surgery was performed under general anesthesia.

Mandible

A right ramus sagittal osteotomy was performed to advance and rotate the right mandible. The symphysis was exposed by degloving from right to left first molar. The mental nerve was transpositioned and preserved bilaterally utilizing burr technique. A horizontal osteotomy was placed 20 mm superior to the mandibular inferior border in the anterior region and 10 mm above the mandibular inferior border in the region of the first molars. The tooth-bearing segment of the mandible was osteotomized at the midline in 5 mm of interdental space that had been created by orthodontic treatment. The osteotomy was followed by removal of the 5-mm interdental bone to allow rotation of the right segment of the mandible anteriorly and medially. The left segment was rotated inferiorly. The two tooth-bearing segments were repositioned and secured with a prefabricated interocclusal-lingual splint. The inferior border segment of the mandible was then advanced 8 mm. The left side of the posterior inferior border was reduced vertically 5 mm. The inferior border segment was then secured by transosseous wires. The mental nerves were repositioned.

Maxilla

A Le Fort I osteotomy was accomplished at the level of the floor of the nose from the pyriform aperture to the pterygoid plates.

Intermaxillary fixation was accomplished. Two blocks, 10 by 20 by 20 mm, of corticocancellous bone were obtained from the superior medial iliac crest. The bone blocks were fashioned and fit on the right side to accomplish a downward movement of 6 mm in the molar region and 5 mm at the pyriform aperture. On the left side, there was no vertical movement in the posterior region. The maxilla was secured in this position by miniplates and titanium screws.

Soft Tissue

A wedge of the interfering buccal mucosa on the left side, 30 mm in length and 20 mm in width, was removed. The fat pad of Bichat of the left cheek was also removed, through the same buccal incision, after blunt dissection exposure through the buccinator muscle posteriorly.

Postoperative Management

Anterior intermaxillary elastics were applied to control occlusion postoperatively. The postoperative period was unevent-

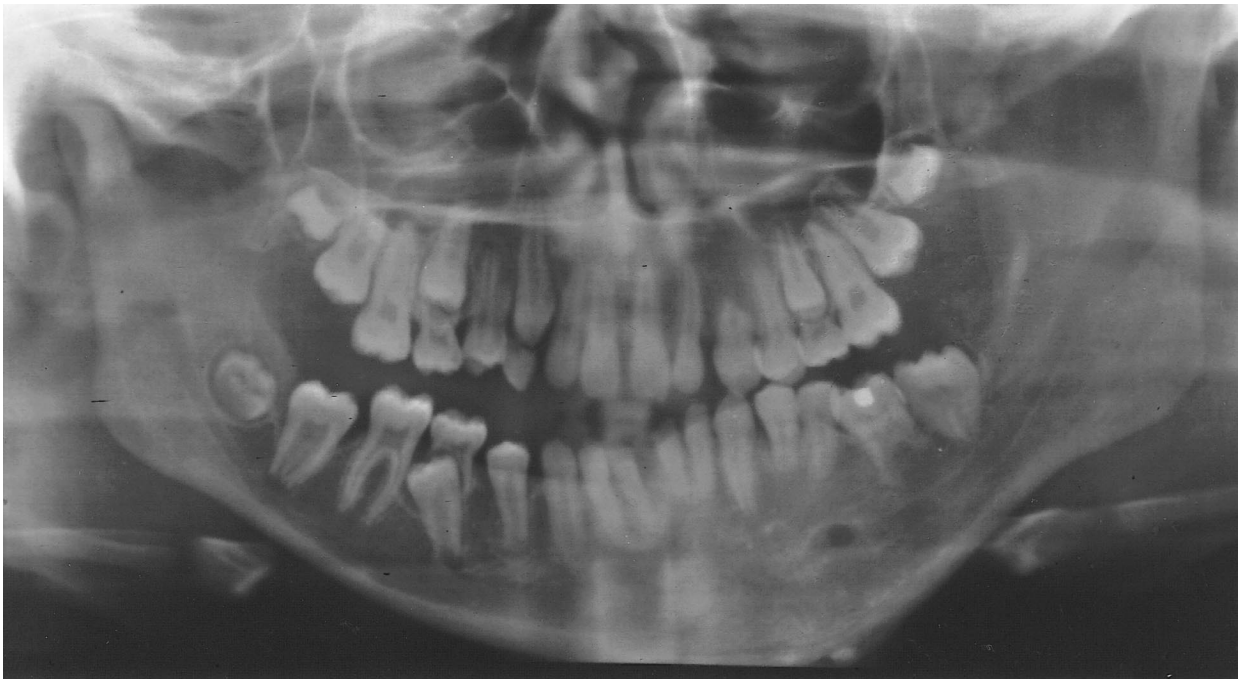

FIGURE 6 Panoramic radiograph at age 13 years. Note the enlargement of the left mandibular canal and mental foramen. Pronounced idiopathic root resorption is observed on the maxillary left canine and mandibular left dentition.

ful. Decreased sensation in the distribution of the right mental nerve was noted.

At age 20 years, the patient was seen for follow-up. There was a widened scar on the lower left lip and some numbness and paresthesia in the right lower lip (Fig. 9). Ophthalmologic investigation showed no ocular problems.

Limited continued root resorption was seen on the upper left canine and lower left premolars. Additional bone growth was observed on the left posterior lower alveolar crest (Fig. 10A through 10C).

There was a tendency to 1-mm vertical opening of the occlusion on the right side (Fig. 11).

Superimposition of a lateral cephalometric radiograph (taken at this appointment) with earlier lateral cephalometric radiographs revealed that the parietal exostoses were unchanged.

Ongoing Surveillance

Yearly eye examination by an ophthalmologist was recommended; in addition, a CT scan of the head should be obtained if any headaches or other neurological symptoms should occur.

TABLE 3 Cephalometric Morphology

Angle	*Degrees (Age 13 y)*	*SU**	*Degrees (Age 16 y)*	*SU**
SNA	85.2	1.1	87.6	1.7
SNB	82.4	1.4	84.2	1.9
ANB	2.8	−0.4	3.4	−0.1
SN-GoGn	35.9	0.4	36.6	0.5
Palatal plane	8.4	2.1	5.8	1.3
U1 to SN	113.6	1.2	114.8	2.4
Lower 1 to MP	92.1	−0.7	93.1	−0.5

* $x - \bar{x}/SD = SU$, where x is the observation and $\bar{x}$ is the mean.

A second-stage soft tissue surgery could include rhytidectomy, liposuction, and a subperiosteal facelift.

Discussion

Proteus Syndrome

Proteus syndrome may be difficult to recognize because of its variable phenotype. The variable distribution of lesions and

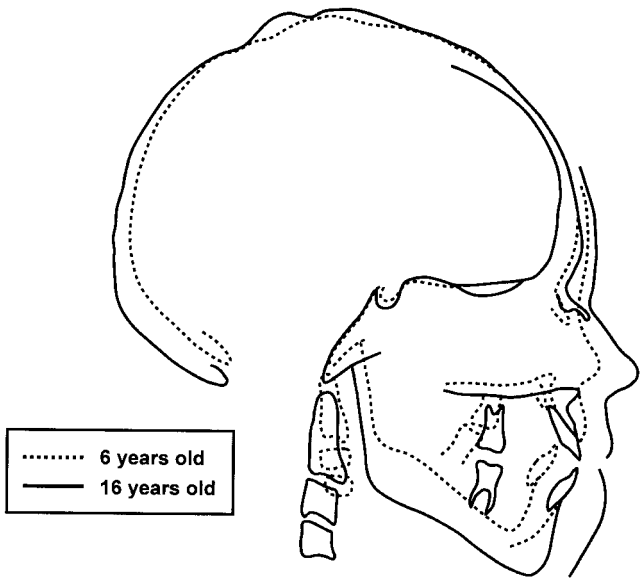

FIGURE 7 Growth tracing from age 6 years 10 months to 16 years. There is normal forward and downward growth of the maxilla and mandible. The parietal exostosis is showing slight enlargement.

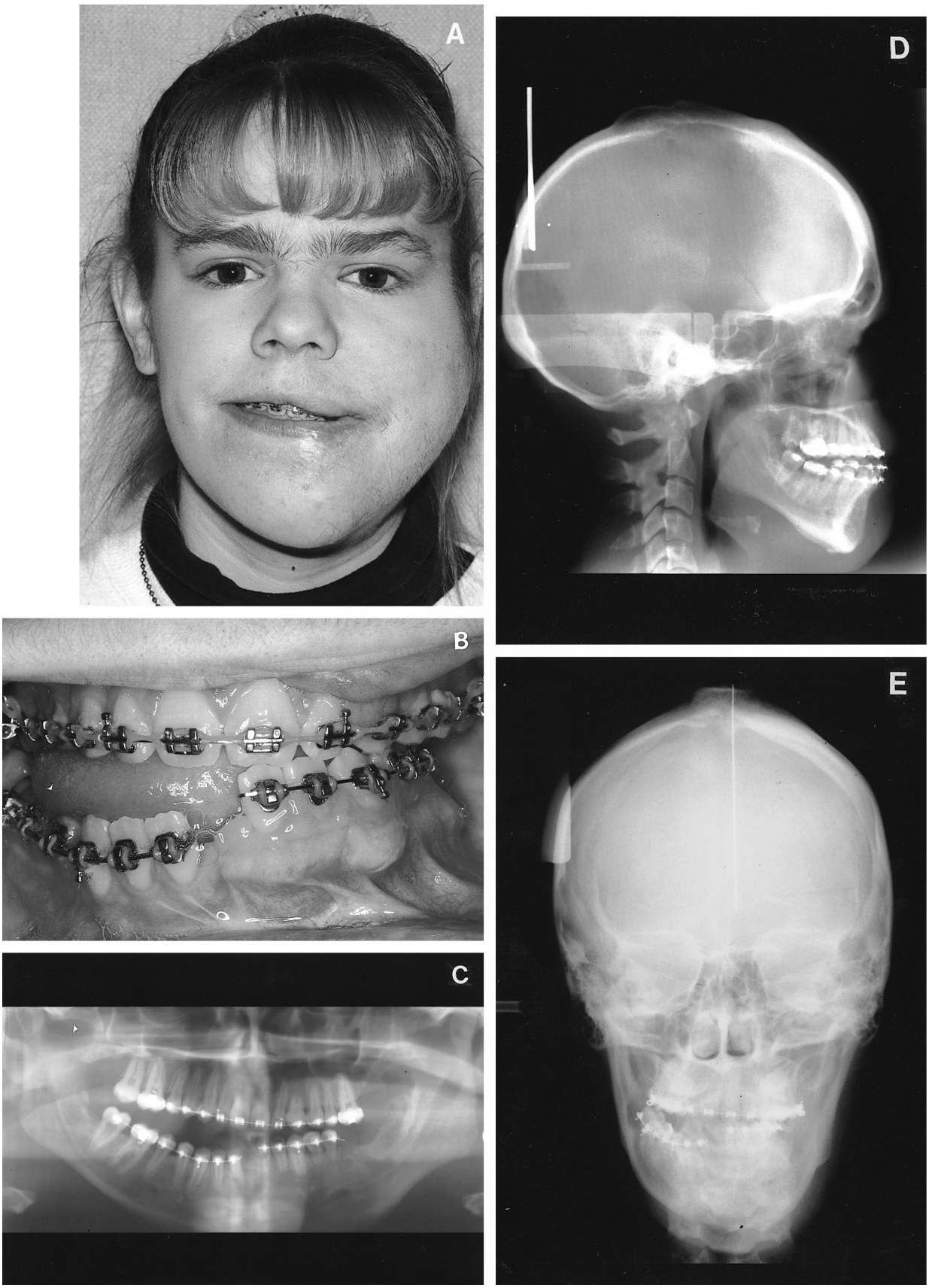

FIGURE 8 Patient at age 17 years. A. Patient prior to orthognathic surgery. Note hair overgrowth in the left preauricular and left chin area. B. Occlusion before orthognathic surgery. C. Progressive root resorption can be observed on the mandibular left incisors and premolars. Also note increased alveolar bone formation in the left molar and retromolar pad area. Lateral (D) and frontal (E) cephalometric radiographs at age 16 years. Continued open bite growth pattern and canted maxillary occlusal plane are evident.

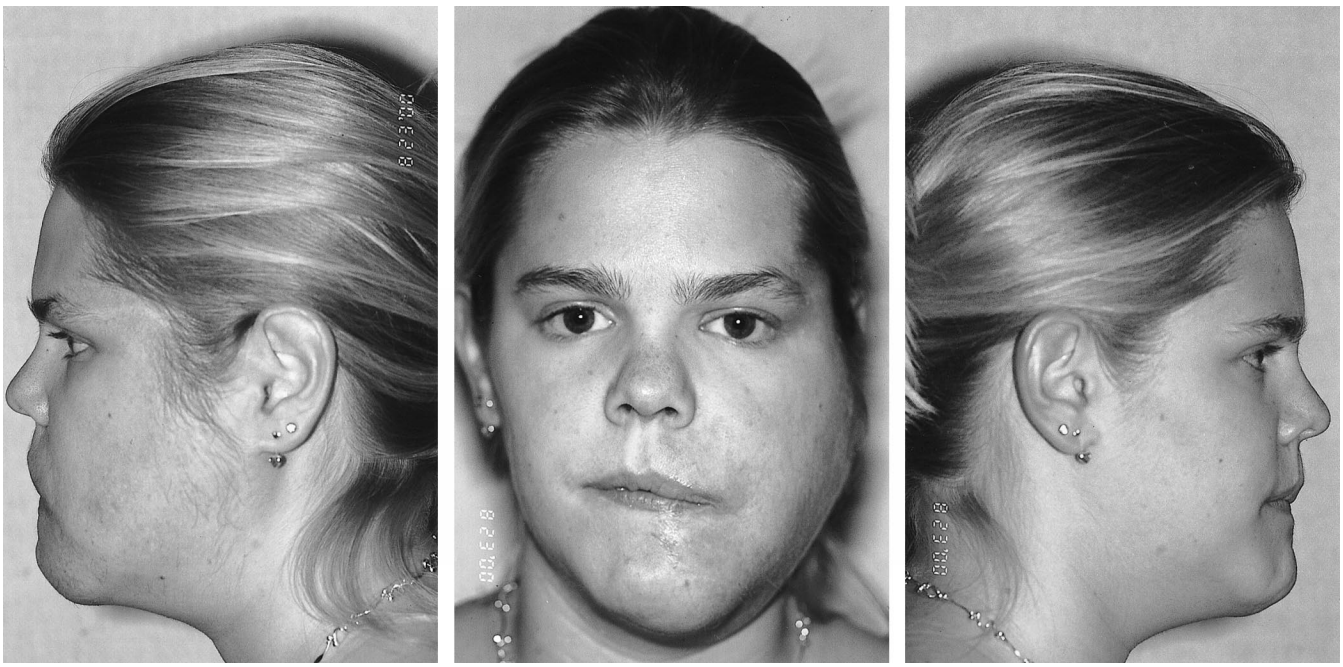

FIGURE 9 Patient at age 20 years. Note the apparent continued soft tissue hypertrophy.

variable extent of involvement are characteristic of patients with Proteus syndrome. It was suggested by Cohen (1993) and Rizzo et al. (1993) that the criteria for the diagnosis of Proteus syndrome should be liberal rather than overly rigid.

In 1983, Weidemann et al.'s description of the syndrome included seven major physical features (Table 4). Diagnostic criteria for Proteus syndrome have also been described by Biesecker et al. (1999). With increased recognition of the syndrome, a wide variety of other manifestations have been documented (Table 5).

The subject in this study had a mosaic distribution of the lesions, a progressive course, and sporadic occurrence. These are the mandatory general criteria of Proteus syndrome described by Biesecker et al. (1999).

Furthermore the following specific criteria were observed: (1) exostoses of the skull, (2) epidermal nevus, (3) unilateral mandibular and maxillary hypertrophy, (4) unilateral precocious dental development, (5) soft tissue hypertrophy, (6) alopecia, and (7) abundant hair growth, all in the affected region.

The tissue overgrowth in Proteus syndrome is progressive in nature and appears to plateau after adolescence (Cohen, 1993); this was also observed in our patient. We are aware of other Proteus patients who have exhibited continued but episodic growth of exostoses and other lesions.

The diagnosis of Proteus syndrome was made in our patient. The major craniofacial and dental manifestations described in patients with Proteus syndrome are shown in Table 5.

Two different modes of abnormal bone growth are characteristic of Proteus syndrome (Kreiborg et al., 1991). One type involves focal overgrowth of intramembranous bone (appositional) producing exostoses; the second type involves excessive generalized growth of the mandibular condyle, body, and ramus. Both types of excessive bone growth were demonstrated in our patient. The enhanced eruption of the dentition on the left side has led to increased height of both the left maxillary and mandibular alveolar processes.

Increased apposition on the left coronoid process and angulus mandibularis can also be observed. The enlargement of the mandibular canal is interesting and implies that the left inferior alveolar nerve also was enlarged (Figs. 6 and 8C).

The patient in this study had abundant hair growth in the hypertrophied area (Fig. 8A). This has been observed earlier in a patient who had abundant hair growth over a hypertrophied leg (Malamitsi-Puchner et al., 1987); hypertrichosis has also been described in other overgrowth syndromes (Prasad et al., 1995).

Dental and intraoral findings associated with Proteus syndrome have rarely been described. The most frequent feature described is a high arched palate (Table 5); this was not observed in the present patient.

Precocious dental development (growth, maturation, and eruption) along with idiopathic root resorption has to our knowledge not been previously described in Proteus syndrome.

Somatic mutation of receptors of tissue growth factors or fibroblast growth factors in specific parts of the body has been suggested in Proteus syndrome (Hall, 1988; Rizzo et al., 1993; Tattelbaum and Dufresne, 1995).

In the early 1960s, Cohen (1962) showed that epidermal growth factor could cause precocious incisor eruption in mice. The dental follicle, which is responsible for intraosseous eruption, has been demonstrated to bind epidermal growth factor in human premolars (Thesleff et al., 1987). It seems reasonable to suggest that this type of tissue growth factor or receptor could be affected in our patient.

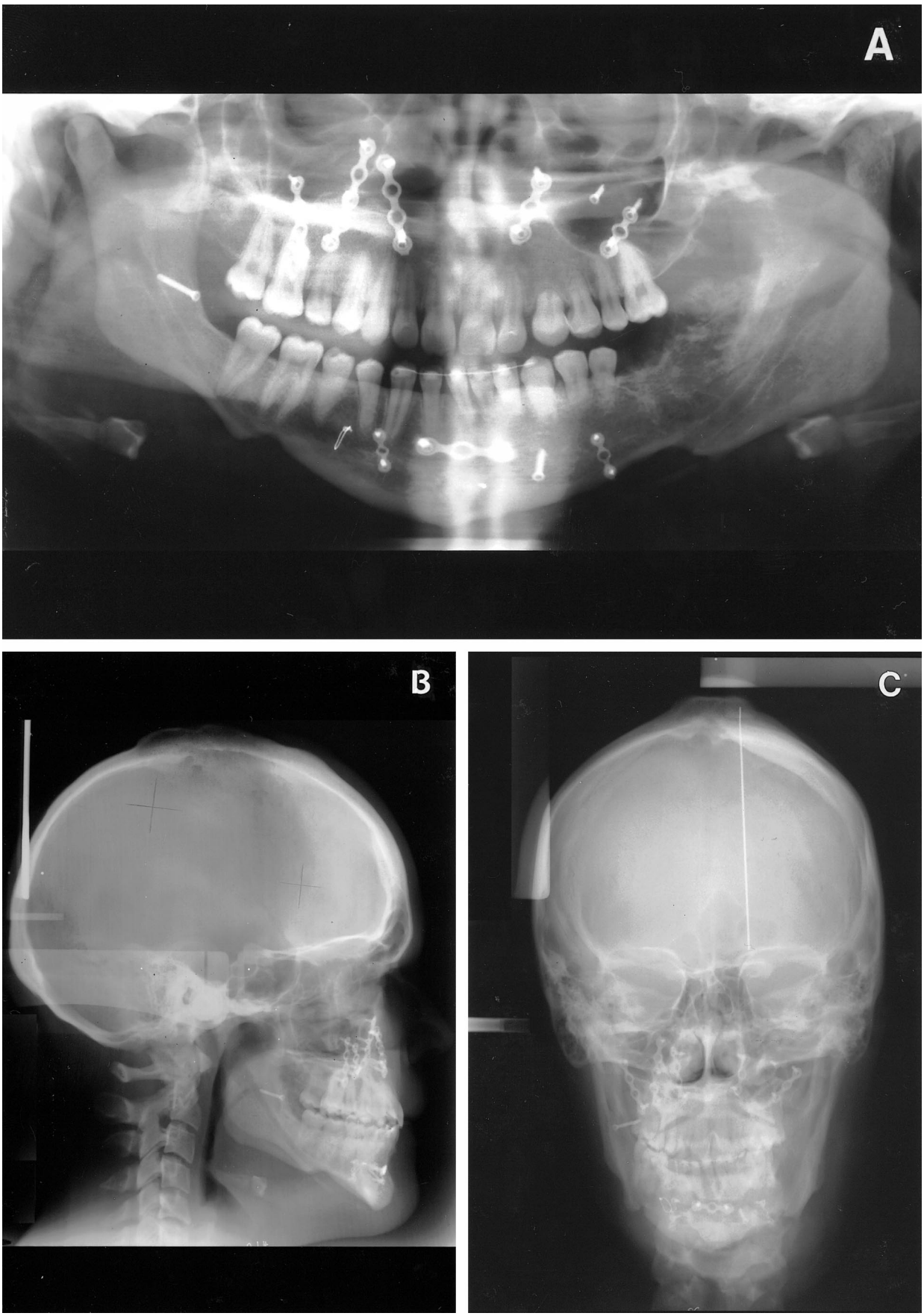

FIGURE 10 Panoramic (A), lateral (B), and frontal (C) cephalometric radiographs at age 20 years. Continued increased bone overgrowth can be observed on the posterior part of the left mandibular alveolar process. Note the relative osseous symmetry and leveled maxillary occlusal plane. This is in contrast to the obvious facial asymmetry from soft tissue hypertrophy (see Fig. 9).

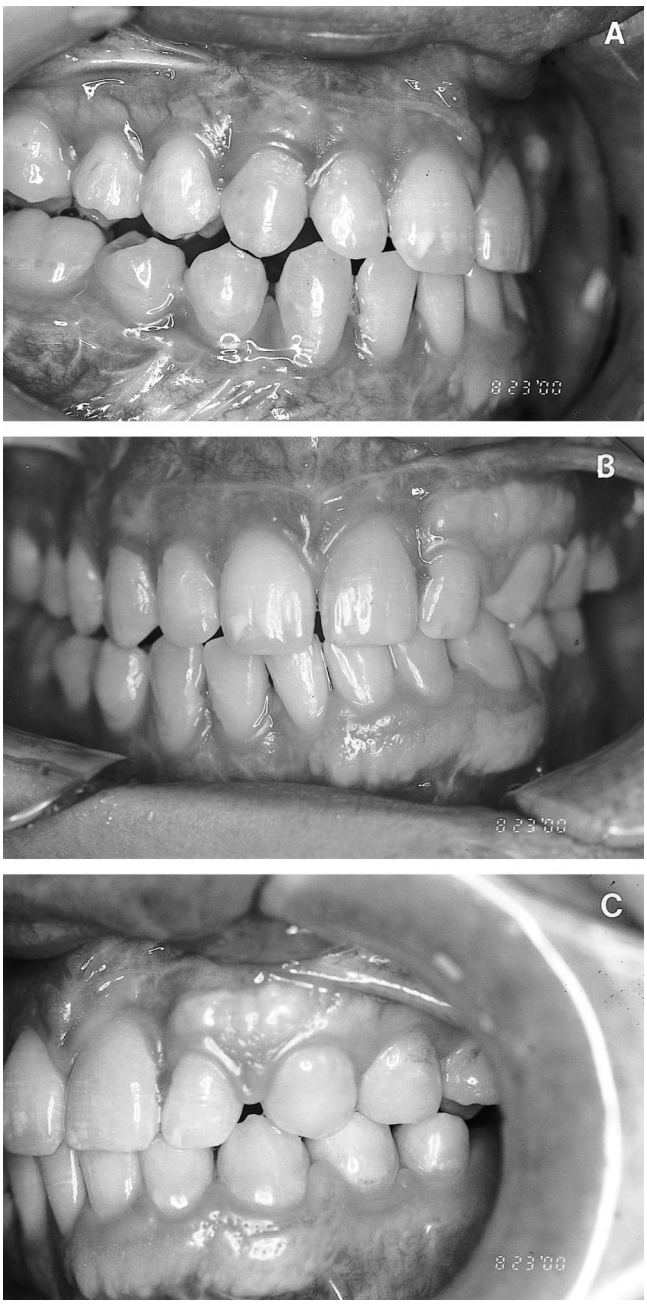

FIGURE 11 Occlusion at 20 years. There is a tendency to a slight bite opening on the right side.

Differential Diagnosis

The disorder must be distinguished from the following conditions.

Encephalocraniocutaneous lipomatosis (ECCL)

ECCL, long thought to be a separate entity, is now classified as a more circumscript form of Proteus syndrome (Wiedemann and Burgio, 1986). Some case reports of ECCL described hyperostoses of the skull and visceral lipomas, suggesting overlap.

TABLE 4 Major Manifestations of Proteus Syndrome*

Partial gigantism of the hands or feet or both
Pigmented nevi
Hemihypertrophy
Subcutaneous tumors, especially congenital lipomas
Accelerated growth (at least in the first years of life)
Viceral abnormalities

* Described by Wiedemann et al. (1983).

Hemifacial Hypertrophy

Some patients have exhibited a condition known as hemifacial hypertrophy (Kogon et al., 1984; Pytlik, 1987; Lawoyin et al., 1989; Yoshimoto et al., 1998); these patients were compared with our patient. Similarities in dental development with earlier dental maturity on the affected side, early eruption, and idiopathic root resorption were found. The patients from the literature also had soft tissue involvement and hypertrophy of the mandible and maxilla.

Patients with hemifacial hypertrophy often have macrodontia, which was not seen in our patient. To our knowledge exostoses have not been described in patients with hemifacial hypertrophy. In a recent study of a patient with hemifacial hypertrophy (Yoshimoto et al., 1998), proliferative activity in bone fragments from the affected side of the mandible was reported. Osteoblast DNA synthesis and cultured osteoblast proliferation was markedly increased in the hypertrophied bone, suggesting that a fibroblast growth factor or its receptor signal transduction pathway may be altered in affected osteoblasts (Yoshimoto et al., 1998). Khanna and Andrade (1989) reported a patient with hemifacial hypertrophy, macrodactyly, polydactyly, syndactyly, scoliosis, and clubfoot. Many of these features resemble the characteristics of Proteus syndrome, and from a clinical standpoint hemifacial hypertrophy and Proteus syndrome exhibit some clinical overlap.

Facial Infiltrating Lipomatosis

Facial infiltrating lipomatosis is a rare but well-known disease and is characterized by proliferation of mature unencapsulated adipose tissue that infiltrates surrounding soft tissue; the presence of fibrous tissue with various nerve bundles and thickened wall vessels; the absence of signs of malignancy; hypertrophy of subjacent bone; and congenital origin (Slavin et al., 1983).

Neurofibromatosis I

Neurofibromatosis I can be ruled out in this patient on the basis of the presence of epidermal connective tissue nevi, the presence of exostoses, and failure to meet the diagnostic criteria for neurofibromatosis I (National Institutes of Health, 1988).

TABLE 5 Findings Reported in Proteus Syndrome

Growth	Craniofacial
Digital hypertrophy[1,2,3,4,5,6,7,8,9,10,11]	Broad and bossed forehead[6,11,14,18]
Hemitrophy of upper limbs[1,2,4,5,6,8,11]	Hemimegalocephaly[8,12,20]
Hemitrophy of toes and feet[1,2,4,5,6,7,10,11,12,13,14]	Macrocephaly[1,2,11,20]
Hemitrophy of lower limbs[2,4,5,6,7,8,10,11,13,15]	Craniosynostosis (metopic, coronal)[17]
	Asymmetry of the cranium[2,11]
Skin	Hemifacial hypertrophy[1,2,4,9,11,12,21]
Abundant hair growth[3]	Ptosis, nystagmus[17]
Hyperkeratotic epidermal nevi[1,2,4,5,7,8,10,11,13,14,15,16,17,18]	Alopecia[20]
Café au lait spots[2]	Depressed nasal bridge[8,18]
Pigmented linear nevi[11,16]	Prominent exostosis of the skull[4,5,6,8,11,15,20]
Gyriform hypertrophy feet, palmar[2,4,7,9,10,11,12,13,14]	Exostosis of the parietal bone[20]
	Exostosis of the frontal bone[12,14,17,22]
Skeletal	Exostosis of the occipital bone[15,17,22]
Scoliosis[1,4,7,9,10,12,13,14]	Exostosis of the temporal bone[14,15]
Dystrophic intervertebral disk[10,19]	Exostosis of the orbital rim[22]
Spinal anomalities[14,18]	Exostosis of the zygoma[15]
Pelvic asymmetry[2]	Exostosis of the nasal bone[12,15,17,22,23]
Vertebral abnormalities[4,7,10,13,19,20]	Exostosis of the anterior clinoid process[22]
Hip subluxation[4,10,13]	Exostosis of the chin[17,23]
Spatulated ribs, rib prominence[4,6,18]	Exostosis of the angle of the mandible[22]
	Exostosis of the auditory canal[4,7,8,12,15,22]
Psychosocial	Condylar overgrowth[12,23]
Seizures[1,8,17,21]	Mandibular prognathism[12]
Normal (well in school)[4,10,13,15,20,22]	Midline asymmetry[12,23]
Mental retardation[2,5,8,12,17]	Hyperpigmented skin[10,11,21]
	Lipoma orbital area[20]
Tumors	Submandibular lymphangioma[1]
Fibrocystic disease[12]	
Lipoma[4,5,12,20]	Oral
Angioma[14]	Primary dentition abnormal[11]
Epibulbar dermoid[5,17]	Yellow teeth[8,12]
Subcutaneous lipoma[11]	Gingival hypertrophy[1,17]
Lymphangioma[11,12,14,20]	High arched palate[8,14,15,16,17]
Hamratomas[11]	Class III Malocclusion[15]
Sclera tumor (eyeanomalia)[4,8,12,14,22]	Crossbite[15]
Angiolipomatous tumor[10,18]	Crowding[17]
Hemangioma[4,10,12,14]	Malocclusion[12]
Inguinal hernia[4,8]	Multiple frenulae in the mandible[22]
	Hypertrophied tonsilla[8,12]

[1] (Alavi et al., 1993).
[2] (Baron-Mazurera et al., 1997).
[3] (Bialer et al., 1988).
[4] (Clark et al., 1987).
[5] (Costa et al., 1985).
[6] (Hauer et al., 1998).
[7] (Hornstein et al., 1987).
[8] (Malamitsi-Puchner et al., 1987).
[9] (Pinto et al., 1998).
[10] (Skovby et al., 1993).
[11] (Viljoen et al., 1987).
[12] (Cohen, 1988).
[13] (Stricker, 1992).
[14] (Wiedemann et al., 1983).
[15] (Tattelbaum and Dufresne, 1995).
[16] (Arendorf and Hansolo, 1995).
[17] (Cohen, 1993).
[18] (Ring and Snyder, 1997).
[19] (Biesecker et al., 1999).
[20] (Rizzo et al., 1993).
[21] (McMullin et al., 1993).
[22] (Smeets et al., 1994).
[23] (Kreiborg et al., 1991).

Bannayan-Riley-Rulvacava

Bannayan-Riley-Rulvacava syndrome is distinct from Proteus syndrome and is due to mutations in the PTEN gene (Cohen, 1998). This syndrome is characterized by macrocephaly, lipomas, capillary malformations, polyposis of the colon and rectum, pigmented macules of the penis, and Hashimoto thyroiditis (Gorlin et al., 1992).

Conclusion

The protean manifestation of this unusual syndrome gives credence to its name. Localized Proteus syndrome involving only the head and neck has been described previously (Rizzo et al., 1993; Smeets et al., 1994). The dental manifestations and dental development has to our knowledge not been described before. Some of the dental manifestations observed in this patient have been described in patients with hemifacial hypertrophy. The similarities and the fact that all three germ lines (ectoderm, endoderm, and mesoderm) are involved in both entities suggest that these two conditions may be due to aberrant growth factors, growth factor receptors, or a growth factor signal transduction pathway.

Care providers involved with these rare patients must be aware of other potential musculoskeletal manifestations. Teams of medical and dental specialties need to be involved in the treatment of patients with craniofacial manifestations of Proteus syndrome.

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