CASE REPORT

Proteus Syndrome: A Rare Entity

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ABSTRACT

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 a case of an 18-year-old male patient with Proteus syndrome, who 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 permanent teeth. The proposed multidisciplinary management of the patient and a review of literature of the Proteus patients, who exhibited manifestation in the craniofacial region is discussed in this report.

Keywords: Hemifacial hypertrophy, Precocious dental development and eruption, Proteus syndrome.

INTRODUCTION

Proteus syndrome (also known as Wiedemann's syndrome) is a rare congenital 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 sometimes involving the face.

The first description of Proteus syndrome is attributed to Cohen and Hayden (1979),[1] who reported two cases. The disorder designated as proteus syndrome by Wiedemann et al (1983).[2] The syndrome was given the name Proteus, which refers to the mythical Greek sea-god, who was capable of changing his bodily shape.

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.[3]

CASE REPORT

An 18-year-old male patient, student by occupation and residing in Kuppam district in Andhra Pradesh, came reported the Department of Oral and Maxillofacial Surgery with a chief complaint of swelling on the left half of face since childhood, which was slow in onset and gradually increased in size and developed to present size. It was not associated with any secondary changes like pain, fever or pus discharge.

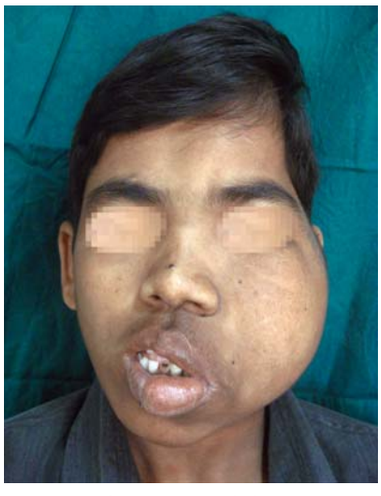


Fig. 1A: Frontal view

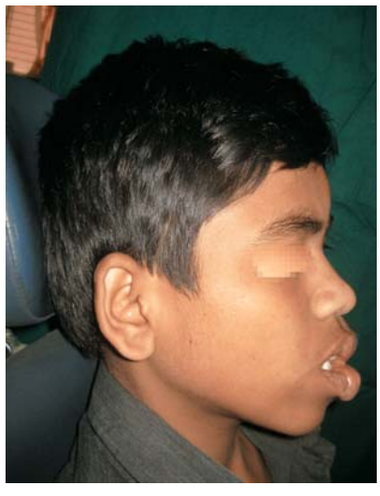


Fig. 1B: Lateral view

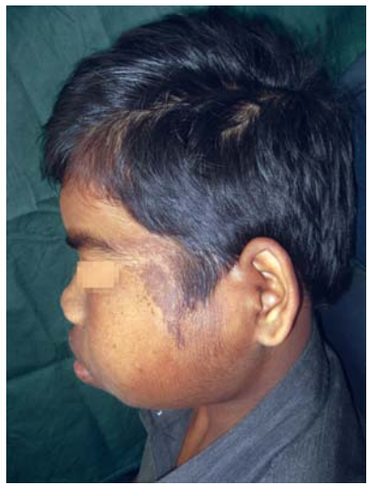


Fig. 1C: Lateral profile

Fig. 2: Showing occlusal cant

Medical history revealed that the patient had no systemic problems, not allergic to any drugs. Patient gives no history of hospitalization. Family history revealed that he is born of normal pregnancy and delivery to nonconsanguineous parents. His milestones of development were normal. He is the second son, his parents and two siblings are normal. Patient was weakly built and nourished, vitals were within normal range. Patient was found to be anemic with appreciable pallor of skin and sclera.

Extraoral inspectory (Figs 1A to C) findings were enlargement of the left facial osseous and soft tissue compared with the right. The left ear was slightly posteriorly positioned. In the left parietal region, exostoses were palpable. A hyperpigmented area was observed in the left zygoma extending to the left brow.

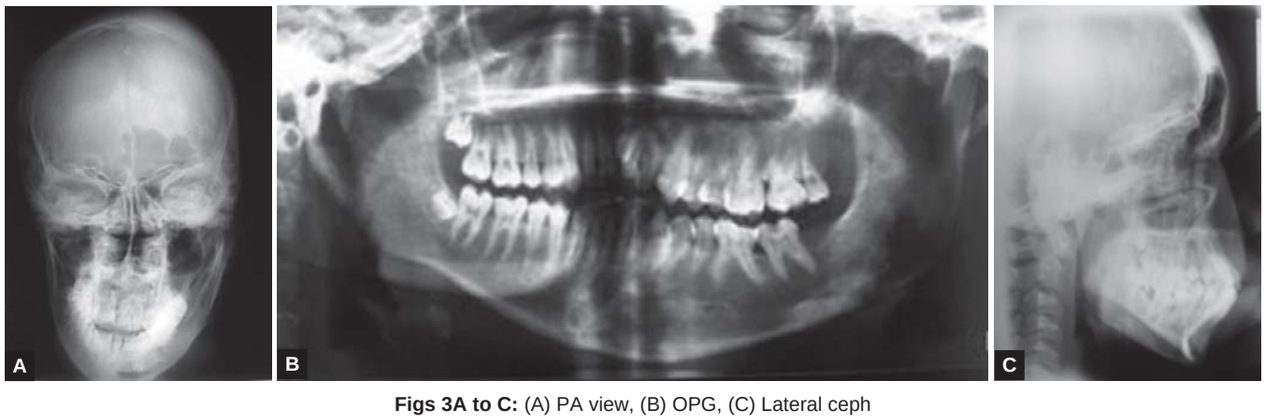
On intraoral examination, it was found that all permanent teeth except 18, 38, 48 were not erupted, generalized crowding of teeth was observed with angles class I occlusion and a occlusal cant (Fig. 2) along with mouth opening of 4 cm. Macrodontia seen on left side starting from the midline till third molar in the maxillary and mandibular arch. Enlargement of the left half of the tongue was observed. 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.

INVESTIGATION

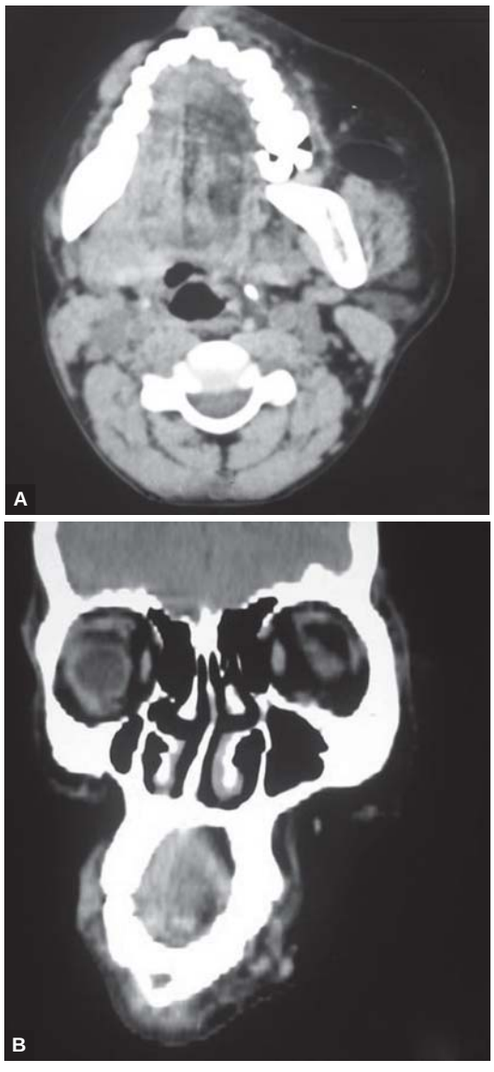
Routine blood and urine investigation was carried out and everything was found to be within normal range except for Hb which was 5 gm%. Growth hormone and FSH and LH estimation was also found to be within normal limits.

Radiographic examination (Figs 3A to C): The dental growth and maturation between the left and right side were significantly different. Development was slightly retarded on the right and advanced in several teeth on the left side. This discrepancy was more pronounced in the mandible dental agenesis (left lower third molar) and various anatomic malformations were recorded. 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.

Computed tomography (CT) (Figs 4A and B) 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 exostosis of the vertex of calvarium along 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 CT suggested lipoma or lymphangioma based on the density and water content of the enlarged soft tissue.



Figs 3A to C: (A) PA view, (B) OPG, (C) Lateral ceph



Figs 4A and B: CT

Table 1: Major manifestations of Proteus syndrome[4]

- 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)[4]

Table 2: Diagnostic criteria for Proteus syndrome[4]

For diagnosis: General criteria (mandatory) *Mosaic distribution of lesions* *Progressive course* *Sporadic occurrence*		*+ Specific criteria (category signs)* *Either one from A or* *Two from B or* *Three from C*
Category signs	*Manifestations*	*Relative frequency*
A.	1. Connective tissue nevus	C
B.	1. Epidermal nevus	C
	2. Disproportionate overgrowth (one or more)	
	Limbs	
	• Arms/legs	C
	• Hands/feet/digits	C
	Skull	
	• Hyperostoses	C
	• External auditory meatus	
	• Hyperostosis	U
	• Vertebrae	
	• Megaspondylodysplasia	C
	• Viscera	
	• Spleen/thymus	U
	3. Specific tumors before end of second decade (either one)	
	• Bilateral ovarian cystadenomas	U
	• Parotid monomorphic adenoma	U
C.	1. Dysregulated adipose tissue (either one)	
	• Lipomas	C
	• Regional absence of fat	C
	2. Vascular malformations (one or more)	
	• Capillary malformation	C
	• Venous malformation	C
	• Lymphatic malformation	C
	3. Facial phenotype	U
	• Dolichocephaly	
	• Long face	
	• Minor downslanting of palpebral fissures and minor ptosis	
	• Low nasal bridge	
	• Wide or anteverted nares	
	• Open mouth at rest	

C—common; U—uncommon.

DISCUSSION

Proteus syndrome is a complex disorder comprising malformations and overgrowth of multiple tissues. The disorder is highly variable and appears to affect patients in a mosaic manner. This intrinsic variability has led to diagnostic confusion associated with a dearth of longitudinal data on the natural history of Proteus syndrome. In 1983, Weidemann et al's[4] description of the syndrome included seven major physical features (Table 1). Diagnostic criteria for Proteus syndrome have also been described by Biesecker et al (1999)[4] (Table 2).

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. 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. The tissue overgrowth in Proteus syndrome is progressive in nature and appears to plateau after adolescence, 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. Two different modes of

Table 3: Differential diagnosis[4]

- Differential diagnosis of proteus syndrome
- Klippel-Trenaunay syndrome
- Parkes-Weber syndrome
- Maffucci syndrome
- Ollier disease
- Neurofibromatosis type 1
- Epidermal nevus syndrome
- Bannayan-Riley-Ruvalcaba syndrome
- Hemihyperplasia—multiple lipomatosis syndrome
- Familial lipomatosis
- Symmetric lipomatosis

abnormal bone growth are characteristics of Proteus syndrome. 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 was also enlarged.

Various syndromes considered in differential diagnosis are listed in Table 3, but not in order of importance. Rather, they are grouped for convenience as vascular syndromes, syndromes with pigmentation and lipomatoses. The two disorders most commonly confused with Proteus syndrome are Klippel-Trenaunay syndrome and hemihyperplasia/lipomatosis syndrome.

- Hemihyperplasia with multiple lipomas is a distinct subset of hemihyperplasia. Cutaneous capillary malformation may occur in some instances. Mild to moderate signs are present at birth. Progressive overgrowth does not occur. Rather, it tends to be commensurate with growth of the child.
- Klippel-Trenaunay syndrome is a "slow flow" vascular malformation involving lower or upper limbs and/or trunk. Overgrowth is also present at birth and commonly severe in contrast to Proteus syndrome in which overgrowth is usually mild or absent at birth.

MANAGEMENT

Proposed treatment plan is surgical soft tissue debulking with lipoma excision of the left cheek along with bimax orthognathic procedures to correct occlusal cant and facial asymmetry. Treatment has been kept on hold due to financial constraints of patient.

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 rarely. 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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