Freeman-Sheldon syndrome: dental and orthodontic implications

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The manifestations of the Freeman-Sheldon syndrome (FSS) in four members of a South African family of Xhosa stock have been documented. Orofacial manifestations are a major syndromic component and warrant early, specialized orthodontic intervention. Our protocol for dental management is outlined and suggestions for holistic oro-dental care are provided.
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INTRODUCTION

The Freeman-Sheldon syndrome (FSS) [OMIM 193700] is a rare disorder in which a characteristic facies is associated with abnormalities in the hands and feet.[1,2] The descriptive designation "Whistling Face Syndrome" denotes the typical pursed lips, microstomia and dimpled chin,[3] while an earlier name "carpotarsal dysplasia" pertains to flexion and ulnar deviation of the fingers and a propensity to talipes equinovarus.

The orofacial features of the FSS are a major component of the disorder and warrant specialised orthodontic management.[4] In this context we have documented the manifestations in four affected persons in three generations of a South African family, and drawn up a protocol for the ongoing care. Our observations and proposals are outlined in this article.

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CASE REPORTS

Patient 1

BM a female of South African Xhosa stock, born in 1974, was seen in 2004 at the Red Cross Children's Hospital, Cape Town together with her affected infant daughter. At this time the diagnosis of the FSS was established on a basis of the typical characteristic facial and digital features.

BM had an immobile face with microstomia and mandibular asymmetry. Her lips were incompetent in the midline and the intercommissural distance was 3.8cm (normal adult female = 5.2cm). She had a flat face and both the mandible and the maxilla were protrusive. An indurated midline linear dimple was present on her chin, her nasal bridge was flat and the nares were notched (Figure 1). She had an anterior open bite and bilateral cross-bites with over-eruption of several posterior teeth. There were no significant changes in the temporomandibular joints.

Intra-oral examination revealed evidence of poor oral hygiene with generalized calculus and plaque deposits. Both occlusal and interproximal carious

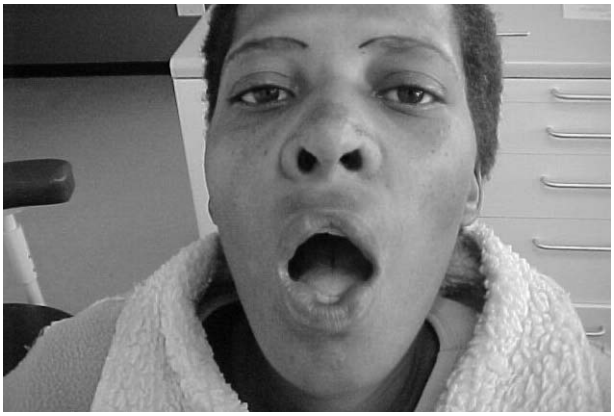

Figure 1. BM. The characteristic "whistling" facies and dimpled chin are evident.

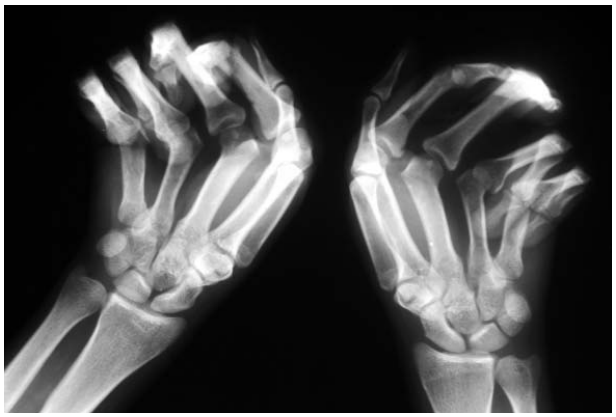

Figure 2. BM. Antero-posterior radiograph of the hands showing digital contractures.

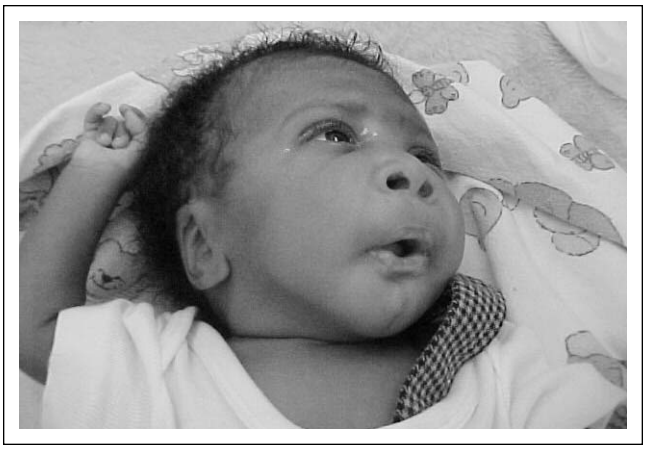

Figure 4. SM. The infant has microstomia, dimpled chin and digital contractures, which are very similar to those of her mother.

lesions were present. Her palate was high but intact, while the teeth were not malaligned. The maxillary and mandibular midline frenular attachments were normal. The tone of her speech was impaired by the restriction in mouth opening and she had difficulty in swallowing. She stated that she was unable to control the discharge of mucous from her mouth and nose when sneezing or vomiting. She did not have habits such as tongue thrusting, lip wedging, digit sucking or bruxing.

The digits of both hands showed flexion contractures and ulnar deviation, involvement being maximal in the index fingers (Figure 2). The feet were normal. Intelligence was unimpaired and there were no abnormalities in any other systems.

A Panorex pantomograph revealed carious teeth and roots, without significant periapical pathology.

Cephalometrical analysis revealed that both upper and lower facial height was proportionate and within the normal range. Bimaxillary prognathism was evident. The SNA (Sella-nasion-A point) was 85º, the SNB (Sella-nasion-B point) was 78º and the ANB (A point-nasion-B point) measured 7º (Figure 3).

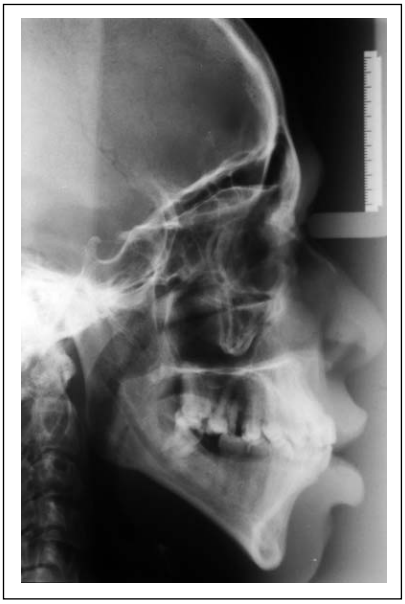

Figure 3. BM. Lateral cephalograms. The upper and lower facial heights are proportionate and in the normal range.

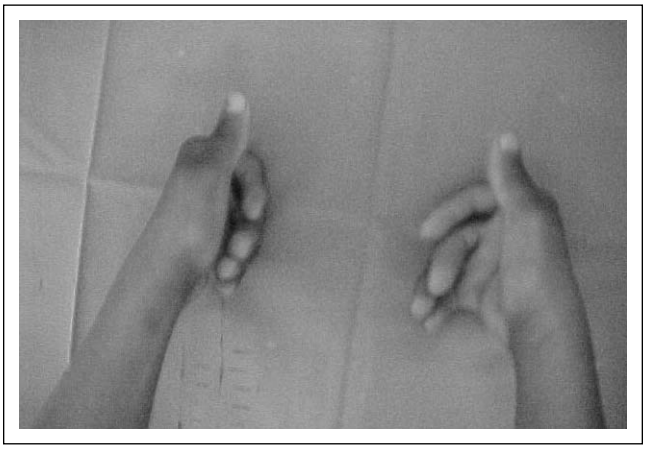

Figure 5. GM. The fingers are contracted in flexion and ulnar deviation.

Patient 2

SM the infant daughter of BM, examined at the age of 6 weeks had facial features and digital malalignments, which were very similar in configuration and severity to those of her mother (Figure 4). Her hand abnormalities had been detected by ultrasound at 22 weeks of pregnancy, but the diagnosis of the FSS was not established at that time. Respiratory problems had occurred during the neonatal period and swallowing had been difficult at breastfeeding and bottle-feeding. Regurgitation of milk through her mouth and nose was frequent.

Patient 3

GM the younger sister of BM born 1989 was examined in 2004 at the Faculty of Dentistry, University of the Western Cape, Cape Town (UWC). She had similar, but less severe facial and digital features of the FSS

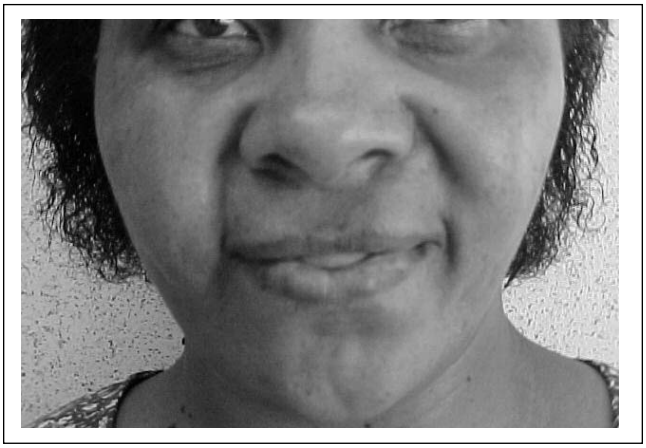

Figure 6. LN. The dimpled chin is the only obvious feature of the syndrome; the width of the mouth is normal.

(Figure 5). In particular, the lack of facial mobility and microstomia was comparatively mild and her facial asymmetry was minimal. Her lips were competent but strained when together, and the upper lip was slightly notched. The intercommissural distance was 4,1cm (normal width for her age and gender = 4.7 cm). Her midface was flat and both the mandible and the maxilla were protrusive. An indurated midline linear dimple was present on her chin, but it was not as pronounced as that of her older sister. There were no significant clinicopathological changes of the temporomandibular joint. Intra-oral examination revealed evidence of relatively good oral hygiene with no obvious supragingival plaque deposits. Her palate was high but intact. Occasional occlusal and interproximal carious lesions were present. There was mild crowding of the anterior mandibular and maxillary central incisors. The upper and lower frenae were normal.

A Panorex pantomograph revealed carious teeth without significant periapical pathology. Unerupted mandibular molar teeth and an impacted mandibular second premolar were evident. In the maxilla, the molars were impacted.

Cephalometrical findings were similar to those of her elder sister, BM.

Patient 4

LN born in 1960, the mother of BM, was examined at UWC in 2004. She had subtle changes in the upper lip and bridge of her nose and an indurated dimple was present on her chin (Figure 6). The intercommisural distance was 5.8cm (normal). Apart from multiple extracted teeth, there were no significant intraoral changes. The fifth finger of her right hand had been fixed in flexion since birth. Her hands were otherwise normal.

PROTOCOL FOR LONG TERM DENTAL MANAGEMENT

General

1. Education regarding oral health maintenance will regularly be reinforced.
2. The family's normal diet is rich in carbohydrates, composed of maize meal, bread and other starches, and alternative suggestions and ideas will be proposed.
3. Conservative management of general oral health and caries is important. This approach would include mechanical removal of the plaque and calculus and well as removal of root remnants.
4. Carious teeth will be restored.

INDIVIDUAL

Patient 1 (BM)

1. A fixed bridge will be considered for replacement of the missing teeth in the right mandible. Removable partial dentures, either acrylic or chrome-based are an option. Integrated osseous implants with crowns would be most effective in replacement of missing single teeth.
2. For aesthetic purposes, her profile and occlusal problems will be assessed for possible correction by orthognathic surgery.

Patient 2 (baby) (SM)

1. Education of the mother regarding oral hygiene specifically for infants, including the prevention of bottle-caries
2. Regular monitoring of oral health of the baby especially during the period of tooth eruption

Patient 3 (sister) (GM)

1. Impacted teeth will be removed surgically
2. For aesthetic purposes, her profile will be assessed for possible correction by orthognathic surgery.

Patient 4 (mother) (LN)

1. Removable partial dentures, either acrylic or chrome-based can be constructed to replace the missing maxillary teeth and posterior mandibular teeth to improve function.
2. A fixed prosthesis will be considered.

DISCUSSION

Ernest A Freeman (1900-1975) was an orthopaedic surgeon at the Royal Wolverhampton hospital, near Birmingham, UK, and his colleague, Joseph H Sheldon was a physician at the same hospital. In 1938 they presented two unrelated dysmorphic children at a meeting

of the Royal Society of Medicine, London, and case details were subsequently published under the title "Cranio-carpal-tarsal dystrophy".[1,2] Twenty-five years later, a British plastic surgeon documented four additional affected children and introduced the term "whistling face".[3] Thereafter case reports accumulated, heterogeneity was proposed and uncertainty arose concerning syndromic boundaries and overlap with the distal arthrogryposes.[4,5]

Although rare, the FSS has a worldwide distribution, and about 100 cases have been reported. The only affected persons previously documented in South Africa were an affected father and daughter together with another girl, all of Tswana stock.[6] The sole report from other regions of sub-Saharan Africa pertains to an affected girl in Tanzania.7

The pathogenesis of the FSS has not been fully elucidated. There is good evidence for autosomal dominant inheritance in some families, but many reported persons have been sporadic. A determinant gene in an atypical form of the condition has been localized to chromosome 11p15-5.[8] The basic defect is probably in the muscles[9,10] and it is likely that the malalignment and flexion contractures in the hands and feet are secondary phenomena. Apart from these deformities, the skeleton is radiographically normal. Stunted stature and kyphoscoliosis are infrequent concomitants, which may be indicative of heterogeneity or diagnostic uncertainty.

The most striking yet variable orofacial features of FSS include a stiff immobile flat mid-face and elongated philtrum with rounded cheeks and a small nose, together with dimpling of the chin. Microstomia is a consistent feature and when excessive, may substantially reduce the intercommissural distance.[11] The upper and lower lips are either tightened or held into a whistling position. The palatal arch may be high and clefting occasionally occurs.[12] There is a propensity for the underdevelopment of the mandible and tongue. Fibrous induration extending from the middle of the lower lip to the chin forms H or V-shaped scar-like dimples, which are present in approximately 30% of affected individuals. Hypertelorism, epicanthal folds, strabismus, downslanting palpebral fissures and ptosis are common minor manifestations.[11,5] Skull radiographs indicate that the facial skeleton is small and that the anteroposterior length of the skull and cranial base is short in comparison with facial height.[13,4]

Cephalometric analysis of the affected adult (BM) revealed an ANB angle of 7º, and bimaxillary prognathism. Despite this facial skeletal disharmony, a soft tissue profile described as a "flat face" has been noted as a characteristic feature of the FSS[1,5]. In this individual, early orthodontic correction would have greatly reduced the lip incompetence and enhanced her image and functional well-being.

There is considerable variation in severity in affected persons, and between affected members of the same family. In particular, the facial features and the characteristic deformities of the hands and feet can all exist in isolation. Upper airway obstruction may occur, and the occasional necessity for tracheostomy has been recorded.[14,15] It is likely that the altered anatomy of the mouth and buccal cavity contributes to the obstruction, and laryngomalacia may also be a component.[16] Recurrent bronchopneumonia represents another potential hazard.[17]

Management in the FSS is essentially orthodontic and orthopaedic. In the former context, the microstomia in our first patient led to difficulty in swallowing, speech impairment, deficient oral hygiene and dental caries. In turn, dental management, including extraction and filling was made difficult by the small dimensions of the oral aperture. Stretching of the mouth by regular use of an expansion prosthesis has been recorded,[18] and this measure may have a place in the management of the affected mother and child.

Complex dental measures, which require general anesthesia, may be complicated by the difficulties in suction and endotubation, due to the microstomia. Muscular rigidity following halothane anaesthesia has been recorded.[19] In view of the myopathic element in FSS, malignant hyperthermia is also a potential hazard which warrants an appropriate anaesthetic approach.[20] The implications for anaesthesia in FSS have been discussed.[21,22] Further complications could arise as a result of the frequent regurgitation most probably a result of the myopathy.

In the differential diagnosis, the Schwartz-Jampel syndrome or chondrodysplasia myotonica is the major potential source of confusion.[23] In this autosomal recessive disorder, affected persons have stunted stature and an immobile facies which resembles that of the FSS. The various forms of Distal Arthrogryposis, especially the trismus-pseudocamptodactyly syndrome has features in common with the FSS.[24] It is relevant that in South Africa, these entities have all been confused with the FSS at one time or another.

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