DIPROSOPUS: A RARE ANOMALY. COLLECTIVE REVIEW AND CASE REPORT

By

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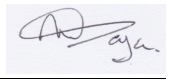
As the candidate's supervisor, I have approved this thesis for submission.

Signed:  Name: Mahendra Daya Date: 16 January 2017

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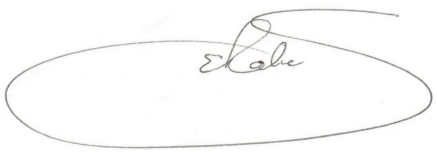
(vii) My contribution to the project is as follows: Sourcing the articles and analysing them for the systematic literature review and the write-up of the case report.

(viii) Dr Mahendra Daya, as supervisor, provided the research materials for the case report, provided academic input, guidance and advice.

(ix) Prof Anil Madaree, as co-supervisor, provided both academic and administrative input in facilitating the completion of the research.

Signed:  Date: 16 January 2017

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OVERVIEW

This research study reports on a descriptive case study of an infant presenting at the age of 2 weeks to our quaternary centre, Inkosi Albert Luthuli Central Hospital, Durban, South Africa with a congenital craniofacial anomaly, diprosopus. The research also includes a collective literature review of the aetiology, classification and management.

Diprosopus is a rare craniofacial anomaly with a prevalence of 1 in 15 million births. It is considered to be one of the subgroups of conjoined twinning. Diprosopus encompasses a broad spectrum of duplications from a single structural craniofacial doubling to two completely formed heads on one neck. The first depiction, in the form of a double-headed Turkish Neolithic shrine statuette, dates back to 6500 years B.C. Jacob van Maerlant's manuscript "The History of Troyes" in 1270 was the first to refer to this condition in the literature.

The rarity of the condition is borne out by the literature featuring only isolated case reports. Therefore, the purpose of the literature review was to consolidate the existing body of knowledge on aetiology, classification and management to improve our understanding of this rare condition.

Our case report is relatively unique in that it represents a complete duplication of the mandible. Other tissues duplicated included the tongue, floor of mouth and the lower lip. In the absence of clear guidelines, it was hypothesised that associated growth abnormalities of the facial skeleton could undergo spontaneous correction if the duplicated mandible and associated tissue were excised early. We, therefore, resolved to excise the duplicated structures at 7 weeks of age. This was later followed by an elective second stage surgery at the age of 15 months to improve the peri-oral aesthetics and lip competence. Patient outcome is presented by retrospectively reviewing all the medical records of the child, which included pre- and post-test photographs and computerised tomography (CT) scans. The outcome achieved answers

the research question “Does early excision of the duplicated mandible and oral tissue produce spontaneous correction of secondary facial deformity?”

To answer the second portion of the research question “What are the controversies surrounding the aetiology of conjoined twinning and diprosopus?” a literature review was performed using online PubMed and Ovid databases search. All articles identified by applying the inclusion and exclusion criteria were reviewed. Key articles referenced in these identified articles were added to the materials for review. A further objective of the study was to explore classifications and management of diprosopus. Pertinent findings are summarised below.

The aetiology of diprosopus remains a controversial topic, and many hypotheses exist. Hypotheses include forking of the notochord, incomplete fission at the end of the twinning period, fusion of adjacent notochords (at susceptible sites), human disorganisation syndrome, genetic causes, ovum abnormalities, uterine environmental changes, abnormal neurocristopathy and teratogen exposure. Stockard alerted us to the role of environmental conditions inducing conjoined twinning by performing experiments on trout embryos. But factors other than the foetal environment are also important. Human cases described, where one twin was normal and the other had diprosopus, lend credence to this. A multifactorial causal relationship in diprosopus is also feasible because of the coexistence of other internal system anomalies of cardiac, gastrointestinal, neurological and respiratory origin.

On review, surgery is the only treatment that can offer functional and aesthetic improvement and, in turn, potentially positively impact the patient’s psychological and social development. Most patients who were offered surgery in the literature had a partial facial duplication. Surgery was usually deferred until the patient was older and more soft tissue had become available to perform the reconstruction. This approach was backed by the postulate that possible growth restriction due to growth centre

manipulation would be less. This finding on the timing of surgery was in direct conflict with our hypothesis.

The outcome of our case study supported our hypothesis in part that early excision of the duplicated mandible and soft tissues resulted in the removal of the deforming forces related to a space-occupying lesion and that correction of the normal portions of the facial skeleton can be anticipated. It was unfortunate that the longitudinal follow-up of this case did not materialise and, therefore, long-term outcome into adulthood is unknown. Despite this, the impact of the study will be of significance in understanding and managing this rare condition.

CHAPTER 1: REVIEW OF THE LITERATURE

1. INTRODUCTION:

Diprosopus is a congenital craniofacial anomaly, generally described as an individual with one body and two faces, and is considered to be the rarest subtype of conjoined twinning.[1,2,3]

This condition is not a new phenomenon. The oldest representation of its existence is a double-headed Turkish Neolithic Shrine statuette dated 6500 B.C.[1,4] It has been noted in other ancient cultures as well. Images of these include the "Pretty Ladies of Tlatilco" which are terracotta figurines estimated to have been sculpted in the period 1200-700 B.C. These were discovered in New Mexico and they include a number of diprosopus and dicephalus statuettes.[5] Another is an effigy crock, belonging to the Chimú culture in Peru (900 - 1470 – 900 A.D.), depicting a diprosopus twin with bilateral cleft lips.[6]

The first literature documentation was in Jacob van Maerlant's manuscript "The History of Troyes, The Miracles of the Far East", in 1270,[7] and, more recently, in the medical literature in 1864.[8] In his "Manual for Midwives", Jacob Rueff, a barber surgeon in the sixteenth century, produced woodcarvings of various types of twinning. Diprosopus was included in his observations.[4]

The diprosopus phenotype encompasses a wide spectrum of duplications,[3,4,8,9,10] ranging from only one craniofacial structure, i.e. *partial* craniofacial duplication [1,5,11,12,13] (involving only a portion of the face, cranial components or a combination thereof), to two complete faces on one neck[1,3,5,11,12] or, in other words, a *complete* duplication of craniofacial structures[5,13] (diprosopus monocephalus).[3,14] The global frequency of conjoined twinning is 1.2 per 100 000 births.[15] The prevalence of diprosopus is 1 per 180 000 to 1 per 15 000 000 births,[3,16] making it the rarest type of conjoined twinning (0.4% of conjoined twins).[3,4,17]

The research question to be answered and the aim of the study was "Does early excision of the duplicated mandible and oral tissue produce spontaneous correction of secondary facial deformity, and what are the controversies surrounding the aetiology of conjoined twinning and diprosopus?"

The objectives of the study were achieved by the following:

- A descriptive outcome-based case study of an infant undergoing early excision of a duplicated mandible and associated structures.
- Reviewing predominantly case report-orientated literature on diprosopus to consolidate our knowledge on its aetiology, clinical presentation, classification and management.

2. CRITICAL LITERATURE REVIEW

2.1 EMBRYOLOGY

The development of a fetus following conception is a complex and ordered process, involving many intricate stages. Fertilization of the female ovum by the male sperm occurs in the ampulla of the Fallopian tube and, thereafter, the ovum undergoes cleavage.[18] At sixteen cells, the mass is known as a morula,[18] resembling a mulberry.[19] An outer layer, known as the trophoblast, surrounds an inner collection of cells called the inner cell mass. Fluid then forms between the inner cell mass and the trophoblast, partially separating the two layers. The morula is now known as a blastocyst.[18,19] This process is regulated, in part, by homeobox genes.[20]

The trophoblast contributes to the development of placental structures to provide nourishment for the embryo. Implantation of the blastocyst into the uterine wall occurs during the 2nd week of pregnancy.[19] During gastrulation, the inner cell mass multiplies to form an embryonic disc with 2 germ layers: the ectoderm and the endoderm.[18,19,20] Later, the mesoderm will form a layer between them. The embryonic disc will be three-

layered or trilaminar.[18,20] On the ectodermal side of the disc, a cavity emerges. This is the amniotic cavity. On the endodermal side, another cavity develops. This is the primary yolk sac.[18]

Close to the margin of the disc, on the endodermal side, the prochordal plate develops. This becomes the central axis of the embryo. The embryonic disc then starts to form an elevation on the ectodermal side, the primitive streak. Proliferating epiblast-derived cells in the primitive streak pass between the ectoderm and endoderm and form the mesoderm. On the cranial aspect, the streak grows to form the primitive knot. Eventually, the notochordal process forms from the primitive knot after cell multiplication and cranial migration of cells to the prochordal plate. During its development, the notochord undergoes various changes.[18,19]

The notochordal process first folds to form a canal and then it develops into a plate, later converting to a shaft-like structure. Most of the notochord will disappear by the end of development. Remnants of the notochord become the nucleus pulposus of the intervertebral disc.[18] In the centre of the primitive knot, a depression develops. This is called the blastopore. The neural plate develops from the thickened ectoderm overlying the notochord. The brain and spinal cord develop from this structure. The plate folds at the cranial and caudal ends to form the neural tube.[18,19] This process is called neurulation, and this leads to the subdivision of the ectoderm into 2: the neural and non-neural (surface) ectoderm. The neural crest cells develop from cells at the junction between these two cell types.[19] A three dimensional foetal structure emerges due to the trilaminar embryonic disc folding. This helps to encompass the endoderm, which will become the mucoepithelial lining of the primitive oral cavity.[20]

Various dedicated tissues, such as the ectoderm, neural crest cells, mesoderm and endoderm, play an essential role in craniofacial development. The pharyngeal arches form on both sides of the foregut, comprising of ectoderm, mesoderm and endoderm. Development of the face and craniofacial complex occurs mainly between 4 to 10

weeks of gestation.[18,19]

The stomatodaeum (which will become the primitive mouth) is a depression between the cranial bulge (produced by the brain) and the caudal bulge (produced by the pericardial cavity). The oral cavity comprises ectodermal elements as well as foregut endoderm. The temporary buccopharyngeal membrane separates these 2 components.[18] The presence of the brain influences further development of the craniofacial structures and is the main component of cephalogenesis.[20,21] By the fourth week, ectoderm has formed around the stomatodaeum and contributes to the face, nasal cavity and oral cavity development.[18]

Neural crest cells contribute to facial bone, cartilage, ligament, odontogenic, adipocytic and connective tissue development. These cells migrate from the cranial crest and are found in the mesenchyme of the pharyngeal arches.[18,19] Any disruption in the migration or the differentiation of the neural crest cells can lead to congenital malformations. In the rest of the body, neural crest cells form neurons and glial cells of the entire peripheral nervous system as well as endocrine cells.[19,21]

There are various theories of how the facial structures develop. The mesodermal penetration theory is most favoured. There are no clear processes but, rather, elevations and depressions with mesodermal penetration between the ectoderm and endoderm to maintain union. The term prominence is used instead of process.[22] Three prominences, derived from neural crest cells, develop around the stomatodaeum.[18,19,20,23] They are the frontonasal process and the right and left mandibular arches (originating from the first pharyngeal arch). The mandibular arch splits into maxillary and mandibular processes. The face, therefore, develops from the interconnection of these 5 processes.[18] The right and left mandibular processes fuse in the midline, forming the lower lip and mandible. The upper lip is formed by fusion of the frontonasal process and the right and left maxillary processes.[18,23] The lateral nasal prominence becomes the ala of the nose. The medial nasal prominence forms the nasal septum. The maxillary prominence forms the

upper cheek region and a portion of the upper lip.[18]

By gestation week 5, the mesenchyme of the mandibular arch has started to fill in across the midline and fusion starts between the medial nasal prominences and the maxillary prominences.[22] At the start of week 6, six auricular hillocks form. These will develop into the ear pinnae.[18,22] By the end of the 7th week, the face has humanoid features.[24] The pace of facial development then slows until birth. Anthropometric changes occur during this time.[24]

Neural crest cells provide data regarding the axial orientation and species-specific morphology of the head and face.[19] The final result is based on the intricate balance between signals acquired by the neural crest cells in the neuroepithelium and the signals from the tissues that come into contact with the neural crest cells during migration.[20,24] A number of molecules have been identified that play a role in these interactions.[20] The migratory route of the neural crest cells is similar in mammals and avians.[19] Hall suggests that neural crest cells should be considered a fourth germ layer.[19,20]

The tongue starts to develop at 4 weeks of gestation. The right and left lingual swellings and the central tuberculum impar develop in the floor of the mouth and correspond to the first pharyngeal arch. These structures will form the anterior two-thirds of the tongue. At 5 weeks, another bulge develops in the median plane, corresponding to the third and fourth arches. This is the hypobranchial eminence. The rostral part of this eminence becomes the posterior third of the tongue. The caudal portion becomes the epiglottis.[18]

The Sonic hedgehog (SHH) gene regulates the inductive activities of the prosencephalic and rhombencephalic organizing centres during development of the head.[20,21] It defines the medio-lateral axis of the embryo.[19] "Fate maps" are then created, predetermining the details of the differentiation of cells to form specific facial

structures.[21] Bone morphogenetic protein family (BMP) molecules are expressed by cells at the junction between neural and non-neural ectoderm. These regulate lateral plate patterning and play a vital role in early head development.[19] Other morphogens also contribute to facial development regulation. They are endothelin (ET1), fibroblast growth factors (FGFs), the wingless family (WNT) and the transforming growth factor beta (TGF-b) family.[20,21]

Facial anomalies can be induced by gene mutations or signal pathway irregularities. Other causes would be teratogenic disruption and mechanical deformation.[20,21] Also, neural crest tissue migration or proliferation variations may lead to conditions known as neurocristopathies. A few examples would include: von Recklinghausen neurofibromatosis, hemifacial microsomia and Treacher-Collins Syndrome.[20] These neural crest cell derangements may be caused by impaired cell migration or unsuccessful induction of structure-formation,[25,26,27,28,29] particularly in the development of craniofacial cartilage and bone.[30] Most craniofacial defects seem to arise from impaired embryonic process fusion or inadequate neural tube closure.[14,15,31] Up to 50% of abnormal embryos are aborted in early pregnancy, some even before the mother is aware of the pregnancy.[18]

Twinning can occur in one of 2 ways:

1. Two ova may be released simultaneously and each is fertilized by a different male gamete. These twins are described as dizygotic twins. They are not identical and may be different sexes. They also have separate chorions and amniotic sacs.[18]
2. Twins can stem from one fertilized ovum. These are known as monozygotic twins. They are identical and the same sex.[18] Various events can lead to the development of monozygotic twins:
    a. Two cells formed after the first division post-conception may split and develop separately. Each of these cells is considered totipotent and is able, theoretically, to become a complete embryo.[18] Stockard challenges this hypothesis by stating that during the first division, an unequal

distribution of genes could occur. This would then lead to the partial formation of an embryo instead of a complete embryo.[32]

b. A single embryo may develop until the sixteen-cell (or morula) stage. During the development of the blastocyst, 2 inner cell masses form and each of them becomes an embryo.[18]
c. Thirdly, the inner cell mass may divide into 2, also developing into 2 embryos.[18]

Conjoined twinning occurs when there is incomplete separation or abnormal merging of the embryos.[18] Kaufmann et al, however, do not regard fusion as a possible cause of conjoined twinning.[33] Stockard, in 1969, experimented with trout embryos to ascertain how changes in the foetal environment could affect their development. He postulated that double monsters could result from an arrest or inhibition during their development.[32]

Fusion of twins can occur at different sites. Ventral merging is the most common compared to dorsal unions.[34] Five types of conjoined twins are joined at the head: craniopagus, cephalopagus, parapagus, diprosopus and rachipagus.[35]

2.2 ANATOMY

The anatomy of key facial structures will be elucidated, as they pertain to the case report in chapter 2.

2.2.1 Mandible

The mandible provides a stable framework for the upper airway and assists in speech production, chewing and swallowing. It also influences the lower face outline.[23] It is also the only mobile bone of the face and this helps to facilitate mastication.[36]

The horseshoe-shaped mandibular bone is divided into the ramus, angle and body. The vertical symphysis joins the 2 hemi-mandibles in the midline. This fusion is complete by the age of 2 years. The body of the mandible is horizontal. The ramus extends from the angle of the mandible in a more posterior-vertical direction (at 110 to 120 degrees to the body of the mandible). The ramus contains the condyle and the coronoid process. These processes are separated by the mandibular notch at the superior end of the ramus. The globular condyle is divided into a head and neck portion. The condylar head is covered by cartilage and this articulates with the temporal bone at the mandibular or glenoid fossa (the temporomandibular joint). [36,37,38]

The coronoid is thin and triangular. The temporalis muscle inserts medially and laterally on the coronoid process. The lateral pterygoid muscle inserts on the condylar neck. A notch is present on the anterior aspect of the condylar neck, through which the masseter receives its neurovascular supply. It is anterior to the condylar process.[36,37,38] The angle of the mandible is at the junction where the inferior rim of the body and the posterior rim of the ascending ramus intersect.[36]

The alveolar part of the mandible contains odontogenic tissue, with 2 rows of tooth buds in paediatric patients. These buds develop into non-permanent teeth (the teeth that erupt during infancy and early childhood) and permanent teeth. Each row contains one type of tooth bud and the non-permanent teeth more superficial than the permanent teeth.[19]

The mandibular foramen is on the inner aspect of the ramus of the mandible. The inferior alveolar nerve, from the third branch of the trigeminal nerve, along with some blood vessels, enters the mandible through this foramen and travels inferiorly and, then, anteriorly towards the mental foramen. Several branches of the inferior alveolar nerve extend to each tooth along the path of the nerve. The mental foramen opens in the midportion of the body of the mandible just inferior to the 2nd premolar. The mental nerve travels through it to supply sensation to the mentum and lower lip. The

mandibular bone has a cortex which is 2-4mm thick surrounding a large medullary cavity.[19,36]

2.2.2 Maxilla

The maxilla is described as a 3-dimensional hexagonal structure. The roof is the orbital floor, the floor of the hexagon is the hemi-palate and alveolar ridge, and the medial wall is the lateral wall of the nasal passage.[19] The maxillary sinus is situated in the body of the maxilla. It reaches its adult size by the age of fifteen years.[39] There are four major processes in the maxilla. These are the alveolar, the frontal, the zygomatic and the palatine processes.[19]

2.2.3 Oral cavity

The oral cavity is oval-shaped and is divided into the oral vestibule and the oral cavity proper.[40] The anterior boundary of the oral cavity is the lip. The soft palate, oropharynx and base of tongue form its posterior margin. The hard palate forms the roof. The buccal mucosa, the mandibular and maxillary alveolar ridges and the retromolar trigones frame the lateral aspect of the intra-oral space. The anterior two-thirds of the tongue and floor of mouth form its inferior portion. Deep to the buccal mucosal layer of the cheek, the mimetic muscles and fat pads can be found. The bony bases for the oral cavity are the mandibular and maxillary bones. The oral vestibule is framed by the lips and cheek mucosa on the external aspect, and the alveolar processes and teeth, on the internal aspect. During intermaxillary occlusion, the vestibule communicates with the oral cavity proper via the intermaxillary commissure behind the last molar teeth.[19,21,40]

2.3 DEMOGRAPHICS

Diprosopus is more commonly found in animals (cattle, pigs, cats, chickens), compared to humans where it presents only rarely.[11,32] According to Rydnert et al, conjoined twins occur more frequently in India and Africa (6 per 100 000 live births) compared to Europe and the USA (1:250 000 live births).[41]

Diprosopus tends to occur in isolation, but, according to a four-case report by Rai et al,[12] diprosopus can occur in twin pregnancies. In these reports, only one twin had diprosopus.[11,12,42] Interestingly, 6% of conjoined twins are part of triplets.[43]

Stillbirths occur in 50% of all conjoined twins.[44] The prevalence of stillbirths is also high in diprosopus patients.[3] In one-third of those born alive, severe defects are present for which surgical correction is not possible.[44,45] 60% of those born alive, do not survive long-term.[46] However, partial facial duplication is not incompatible with life.[16] The recurrence risk for conjoined twinning is negligible.[46]

In diprosopus, the ratio is higher in females (1.3:1) compared to males.[11,15] The two hypotheses are that abnormal X-chromosome inactivation contributes to formation of conjoined twins, thereby leading to this higher incidence.[15] Or, male foetuses may be at higher risk for spontaneous abortion, as is seen in Trisomy 18.[47]

In patients with partial duplication, the mandible and mouth are most commonly affected.[48]

2.4 AETIOLOGY

There are many hypotheses with regards to the aetiology of diprosopus. Most researchers agree that the notochord, which induces neurulation, is at the heart of the problem.[29] The notochord is duplicated in diprosopus patients, and the two main postulations for this picture are either: incomplete rostral splitting/fission of the

notochord[3,5,8,48,49,50,51,52,53] or fusion of two separate but adjacent notochords at susceptible locations.[2,49] Additional backing for specific sites of fusion comes from the close resemblance of craniopagus and pygopagus twins.[2] These commonly involve joining of structures in the neighbourhood of two neuropores.[2]

Duplication of cells at the anterior termination of the notochordal process may initiate duplication of facial-oral elements.[53] Potential pathogenetic causes are:

- forking of the notochord,
- duplication of the prosencephalon (when there is duplication of eyes and nose)
- duplication of the olfactory placodes,
- duplication of maxillary and/or mandibular growth centres around the stomatodaeum.[54,55]

The phenotype of diprosopus patients can range from mild to severe facial duplication and there does not seem to be a solitary cause but a multifaceted sequence of abnormal events.[53] Likely causes are changes in the foetal environment,[32] uterine aberrations,[33] the condition of the ovum,[56] abnormal placental circulation,[11] maternal exposure to teratogens,[57,58] abnormal neurocristopathy[25,26,27,28,59] and genetic abnormalities.[8,11,60]

Chromosomal analyses performed on diprosopus cases, however, have been noted to be normal.[5,9,48] Amniotic band syndrome has been linked to conditions such as craniofacial clefting and anencephaly,[27,62,63] but it has not been associated with duplication of structures.[54] Stockard experimented with the temperature and oxygen concentrations of trout embryos just prior to gastrulation and induced conjoined twins, including diprosopus-like embryos, in 1 - 2.3%.[32] The foetal environment is not the only factor that seems to play a role as there have been documented twin pregnancies where only one foetus had diprosopus.[12,42,55]

Conjoined twins may also occur after assisted reproduction.[33,64] The condition of the uterus may be affected by the recent use of the oral contraceptive pill, possibly leading to delayed implantation, which is also considered as a contributor to diprosopus development in itself.[32,33]

Mutant disorganisation has been studied in the murine model and is known to be transferred in a semi-dominant manner.[65,66] Winter and Donnai suggest that there is a corresponding human disorganisation syndrome.[66] Petzel and Erickson in 1991 described a patient with a duplication of his left tibia with a partially duplicated foot. He also had duplicated urogenital and gastrointestinal structures and was diagnosed with this syndrome.[65] There is an association with conjoined twinning and duplications. Diprosopus may be a part of this spectrum.[49,50,65]

Anterior neural tube closure seems to be affected during certain maternal teratogen exposure. These are Vitamin A, dimethylsulphoxide and urethan.[57] Other teratogens that may be linked to twinning and neural tube defects are: thalidomide, vincristine sulphate, local and general anaesthetics, colchicine, griseofulvin and phenylzine dihydrogen sulphate.[33,57,67]

Partial duplication should be distinguished from teratoma-formation. A teratoma is a congenital mass originating from a sequestration of totipotent stem cells during early foetal development, comprising various tissue or organ components.[13,68] Interestingly, reduplication at one side of a structure has been noted to produce a bilateral structure.[52]

2.5 CLASSIFICATION

There are a number of classifications in the literature for craniofacial duplication, especially partial duplication. They assist the clinician in determining the extent of the duplication. Two classifications deal with diprosopus of all facial areas and three other classifications focus on the lower face (the structures around the stomatodaeum).

The Rating[69] and Barr[54] classifications describe duplications of all the zones of the face and include complete facial duplication:

Rating, in 1933, classified diprosopus into three groups:[11]

1. "Group I - duplication takes place in the upper half of the face. There are two eyes and a nose to each face with one common mouth.
2. Group II - duplication takes place in the lower half of the face. There is a single face with two mouths (or a spectrum thereof).
3. Group III - duplication is symmetrical and may be parallel. Complete diprosopus would fall into this group."

This classification does not mention the specific structures that are duplicated. In Group II, only the mouth is mentioned and not whether the maxilla or the mandible is duplicated. Intracranial abnormalities are also not included.

The Barr classification, formulated by Costa et al 2013,[5] also subdivides the various types of diprosopus into 3:

1. "Duplication of the eyes and nose with or without maxillary duplication by itself or with mandibular duplication.
2. Duplication of the nose with or without maxillary duplication.
3. Duplication of the maxilla with or without mandible or pituitary duplication".

This classification is deficient, as it does not accommodate patients with duplicated mandibles without duplication of the maxilla.

There are, however, three other classifications that deal specifically with partial facial duplication of the lower and mid-face. Facial duplication can either be symmetric or asymmetric:[5]

The Chen and Noordhoff classification divides the stomatodaeal duplications into 3:

"Type I. Duplicated mouth.

Type II. Duplication of maxilla-upper lip or mandible-lower lip complex

Type III. Centrally located, poorly developed lip-jaw duplication." [10,30]

The Gorlin classification is more detailed and also describes oral structure duplication.[5]

(I) "A single mouth with duplication of the maxillary arch

(II) A supernumerary mouth, laterally-placed with a rudimentary mandible

(III) A single mouth with replication of mandibular segments

(IV) Diprosopus with or without anencephaly"

Sun, et al (2013a) realised the lack of information in the previous classifications and developed a comprehensive classification with regards to the duplicated mandible.[13]

- "Type I - Symmetrically duplicated mandibular arches with deciduous teeth or tooth buds. Duplicated tongue, lip and cleft palate are present (may take the appearance of partially duplicated oral cavity).
- Type II - Duplication of the unilateral mandibular body and ramus. The duplicated mandible may extend from the symphysis to the temporomandibular joint as a separate hemi- mandible.
- Type III - Alveolar type. Characterized by the presence of a localized accessory alveolar bone with supernumerary teeth attached to the normal mandible. The mouth may be partially duplicated to present as macrostomia or completely duplicated to present as a separate mouth in the type II and III deformities. The supernumerary teeth in the duplicated mandible are frequently of regular morphology.
- Type IV - Bilaterally duplicated ramus and its remarkable association with Klippel-Feil syndrome."

Owing to the link between anencephaly and monozygotic twinning, Riccardi et al have a separate classification where they have categorised the spectrum of neural tube defects associated with monozygotic twinning into four groups. [70]

1. Twins or triplets concordant for neural tube defects, including anencephaly.

2. Twins discordant for neural tube defects.
3. Incomplete twins (for example: diprosopus and conjoined twins) with anencephaly.
4. Anencephaly, or neural tube defects in general, in the absence of twinning.

2.6 ASSOCIATED ANOMALIES

There are certain conditions, syndromes and anomalies that occur more frequently with conjoined twinning, and, more specifically, with diprosopus. The more anomalies present, the worse the prognosis for the individual affected.[7] The presence of polyhydramnios suggests that there may be a congenital anomaly and is also associated with diprosopus.[4,8,12,43,51,69,70] 50-76% of conjoined twin pregnancies will have polyhydramnios.[44,45] However, it is not a specific sign.

A high percentage of diprosopus patients will also have a neural tube defect.[14,42,47,48,71] Anencephaly is associated with conjoined twinning and the incidence is 1.67 times higher in monozygotic twins compared to dizygotic twins and singletons.[11,14] Spina bifida occurs at a higher incidence in diprosopus cases.[8,11,15,49,51,70] Other neural tube defects common in diprosopus are holoprosencephaly,[11,49] hydrocephalus,[4,51] pituitary duplication,[4,7,48,58] callosal agenesis[48,72] and vertebral column duplication.[11,48]
They may present with associated facial anomalies like craniofacial clefting,[26,27,54,73,74] cleft lip,[28,54,55,73] cleft palate,[28,48,53,59,75] cleft lip and palate,[4,15,42,76] hypertelorism,[48,55,76] facial asymmetry,[73] and cranial nerve abnormalities.[54]

Not only the head and nervous system are associated with diprosopus.[4,11] There can be associated cardiac abnormalities: VSD,[4,7,11,50] ASD,[42,72] PDA,[4,42] dextrocardia[50] and aortic abnormalities.[50,72] Internal organ anomalies involving the gastrointestinal system,[49] urinary tract, [11] respiratory system[4,12] and the adrenal glands[11] may also be present.

Diaphragmatic hernias, agenesis or hypoplasia can occur as well as ventral wall defects.[4,11,14,43]

Known associated syndromes are Klippel-Feil syndrome,[5,28,53,59,73,77] and orofacial-digital syndrome.[75] Pierre-Robin sequence is also linked to diprosopus but is often in combination with another syndrome.[5,28]

2.7 DIAGNOSIS

Ideally, these cases should be diagnosed early, on detailed antenatal ultrasound, where specific signs can be highly suggestive of diprosopus.[8,41] The diagnosis of conjoined twins is possible as early as 12 weeks.[19] These include increased nuchal translucency, lymphangiectasia, neural tube defects, ventral wall defects, renal agenesis, a widened vertebral column, a heart-shaped cranium or bifid cranial vault and duplication of face or facial components.[48,64] In conjoined twinning, a fixed position of the twin bodies on follow-up scans and no separating membrane between the twins are suggestive signs. There should be regular follow-ups with investigations such as ultrasounds, magnetic resonance imaging (MRI) and echocardiography to determine the degree of fusion as well as which organs are involved as well as any complications.[19]

2.8 MANAGEMENT

By diagnosing the condition earlier, a more thorough management strategy can be constructed, which would include delivery options, counselling, involvement of other disciplines and the decision to continue with the pregnancy if the parents desire.[16,41,44] The parents should be counselled compassionately that there is a poorer prognosis with complete facial duplication[50] and that separation is impossible.[45] In an article by Thornton, the parents of a diprosopus baby opted to continue with the pregnancy and felt that, with the support of the treatment team and comprehensive counselling, they were prepared to deal with the death of their baby very soon after delivery. It was much more peaceful than expected and they were able to cope with their loss.[72]

Isolated duplication, however, is not incompatible with life and often can be managed surgically.[5,16] If the parents decide to continue with the pregnancy, they must be made

aware that a caesarean section will most likely be required due to cephalopelvic disproportion.[8]

Once the baby is born, a detailed management plan should be communicated and deliberated with the parents.[30] There are growth, functional and psychological considerations to weigh up when timing surgery.[7,10] Surgery is the only treatment that can offer functional and aesthetic correction and will always be an improvement on the original, especially in severe deformities.[10,78]

Surgery has had varying success. The parents of an affected child should be made aware that there will be visible scarring.[30,48,50,52,55,67] Obwegeser was very critical of his scars post-operatively despite multiple revisions.[30,78] However, Price is of the opinion that good results can be expected and that surgery is mostly straightforward.[79]

Surgery is usually deferred until the patient is older and more soft tissue is available to perform the reconstruction. Obwegeser waited until the patient was 10 years old before he performed surgery but still found that the midface had growth retardation over time.[30]

The literature does not clearly delineate an ideal age at which diprosopus patients should be treated. Owing to the rarity of this condition, it is difficult to formulate the correct treatment plan. Also, the age at which the patients present varies significantly in the literature and, therefore, they could be managed later than deemed appropriate. The aetiology of diprosopus is a controversial subject and further research is required to ascertain the most likely initiating trigger.

3. RESEARCH QUESTION

"Does early excision of the duplicated mandible and oral tissue produce spontaneous correction of secondary facial deformity, and what are the controversies surrounding the aetiology of conjoined twinning and diprosopus?"

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CHAPTER 2: DIPROSOPUS: EARLY EXCISION OF A DUPLICATED MANDIBLE IN A SEVEN WEEK OLD INFANT AND A REVIEW OF THE AETIOLOGY

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Abstract

Diprosopus is a rare craniofacial anomaly and is considered a subgroup of conjoined twinning. It encompasses a broad spectrum of duplications from single structure doubling to two completely formed heads on one neck.

The purpose of this literature review was to consolidate the existing body of knowledge on the aetiology and management of diprosopus in order to improve our understanding of this rare condition.

Our case report is relatively unique in that it represents a complete duplication of the mandible. Other tissues that were duplicated include the tongue, floor of mouth and the lower lip. It was hypothesised that associated growth abnormalities of the facial skeleton could undergo spontaneous correction if the duplicated mandible and associated tissues were excised early.

The aetiology of diprosopus remains a controversial topic, and many hypotheses exist. A multifactorial causal relationship is also feasible because of the coexistence of other internal system anomalies of cardiac, gastrointestinal, neurological and respiratory origin.

On review, surgery is the only treatment that can offer functional, aesthetic and psychological improvement. Most patients who were offered surgery in the literature had a partial facial duplication. Surgery is usually deferred until the patient is older when more soft tissue is available to perform the reconstruction and when there possibly would be less growth restriction due to growth centre manipulation. This finding on the timing of surgery was in direct conflict with our hypothesis.

Keywords

Diprosopus, duplicated mandible, aetiology, management, craniofacial duplication

Background

Diprosopus is a form of conjoined twinning, resulting in a congenital craniofacial anomaly, in which any degree of duplication of the face occurs. The most severe end of the spectrum is an individual with one body and two faces.[1,2]

The word diprosopus comes from the Greek words di, meaning "two" and prosopon, meaning "face".[3,4] The global frequency of conjoined twinning is 1.2 per 100 000 births.[5] The prevalence of diprosopus is 1 in 15 000 000 births,[6,7] making it the rarest type of conjoined twinning (0.4% of conjoined twins) .[6,8] In an epidemiological study by Martínez-Frías et al, raw data obtained from Castilla et al was analysed and the incidence was calculated to be 0.06 per 100 000 births.[5] In diprosopus, the female to male sex ratio is considered to be 1.3:1.[9] This number has been challenged by Martinez-Frias et al, who state that there actually may be more males than females affected. They recommend further studies due to the small sample size.[5] In conjoined twins, the incidence is higher in females. Two hypotheses have been suggested for this. One is that of abnormal X-chromosome inactivation contributing to the formation of conjoined twins.[10] The other is that male foetuses may be at higher risk for spontaneous abortion, as is seen in Trisomy 18.[10] Stillbirths occur in 50% of all conjoined twins.[11] In one-third of those born alive, severe abnormalities are present for which surgical intervention is not possible.[11,12] Sixty-percent of those born alive do not survive long-term.[11,13] However, partial facial duplication can be compatible with life, and the surgical treatment is dependent on the nature of the deformity.[3]

The diprosopus phenotype encompasses a wide spectrum of duplications,[7,8,14,15,16] ranging from duplication of one craniofacial structure, i.e. *partial* craniofacial duplication[1,4,9,17,18] (involving only the face, cranial components or a combination thereof), to two complete faces on one neck[1,4,7,9,17,19] or, in other words, a *complete* duplication of craniofacial structures[4,20] (diprosopus monocephalus).[21] The diprosopus spectrum can be associated with a variety of other anomalies, especially complete diprosopus.[22] According to Wu et al, in patients with partial duplication, the mandible and mouth are most commonly affected.[23] It is difficult to determine accurately the ratio between mandibular vs. maxillary duplication. It is important to mention that Shaikh et

al[24] has been misquoted in a number of articles as saying that maxillary or midface duplication occurs more commonly than mandibular duplication.[4,25,26,27]

The purpose of this article is to report a case of a seven-week-old infant with a duplicated mandible and associated oral anomalies that underwent a two-stage surgical correction in early infancy. The literature is also reviewed with an emphasis on the aetiology of diprosopus.

Method

Ovid and PubMed databases were searched for articles reporting on human studies only. The type of article and the time period for the search was not specified. The key words used were: "diprosopus", "craniofacial duplication" and "duplicated mandible". The identified literature and key referenced articles therein were examined to prepare a collective review of the aetiology.

Aetiology

The pathogenesis of diprosopus is controversial and is yet to be understood fully.[1,28] Many hypotheses exist to explain the initiating event, but most researchers agree that the notochord, which induces neurulation, is at the heart of the problem.[2,15] Each human embryo (and vertebrate) must have its own notochord.[2] As diprosopus is regarded as a form of conjoined twinning,[16] the events that lead up to twinning are also considered as possible contributors to the condition.[17] Between days 13-25 of gestation, as the primitive streak and axial structures start to form, the normal development of the notochord is disturbed and diprosopus may ensue.[29,30] The notochord is duplicated in these patients and the two main postulations for this condition are either incomplete rostral splitting/fission of the notochord[4,7,14,22,23,30,31,32,33] or fusion of two separate but adjacent notochords at susceptible locations.[2,30] The theory of fusion is conceptually supported by the similarities demonstrated by the specific site of fusion in craniopagus and pygopagus twins.[2] Fusion commonly involves structures in the vicinity of two neuropores.[2] Also, Logrono et al, quoted by Kaufman, performed DNA typing on parasitic conjoined twins and found dizygosity instead of monozygosity.[34]

Duplication of cells at the anterior termination of the notochordal process may initiate duplication of facial-oral elements.[32]

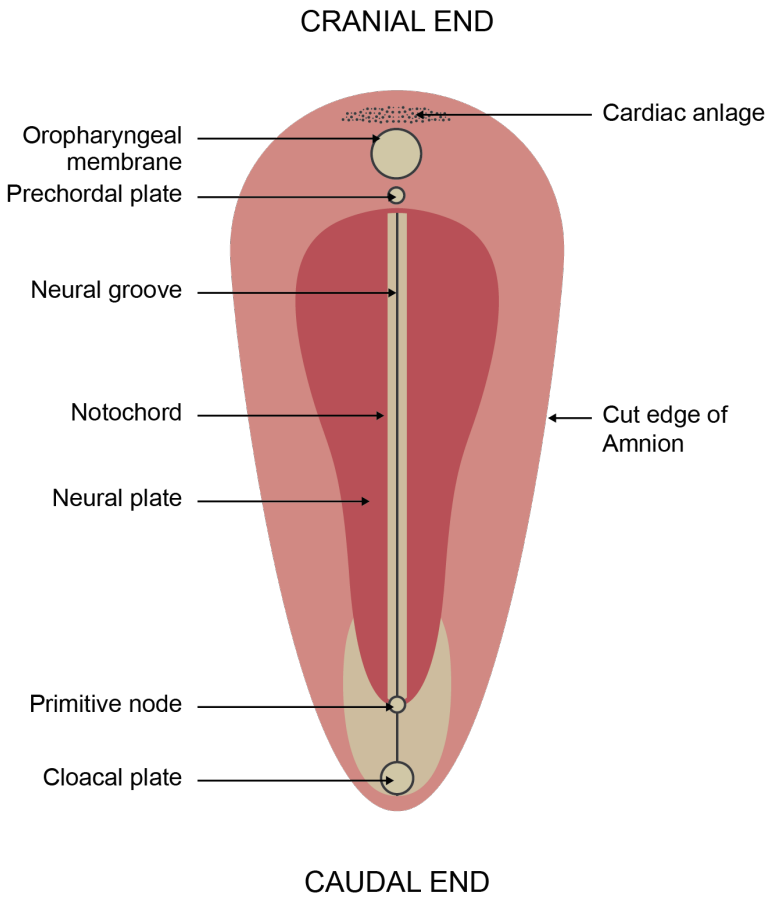


Figure 1: Normal longitudinal schematic image of a human embryo with a single notochord

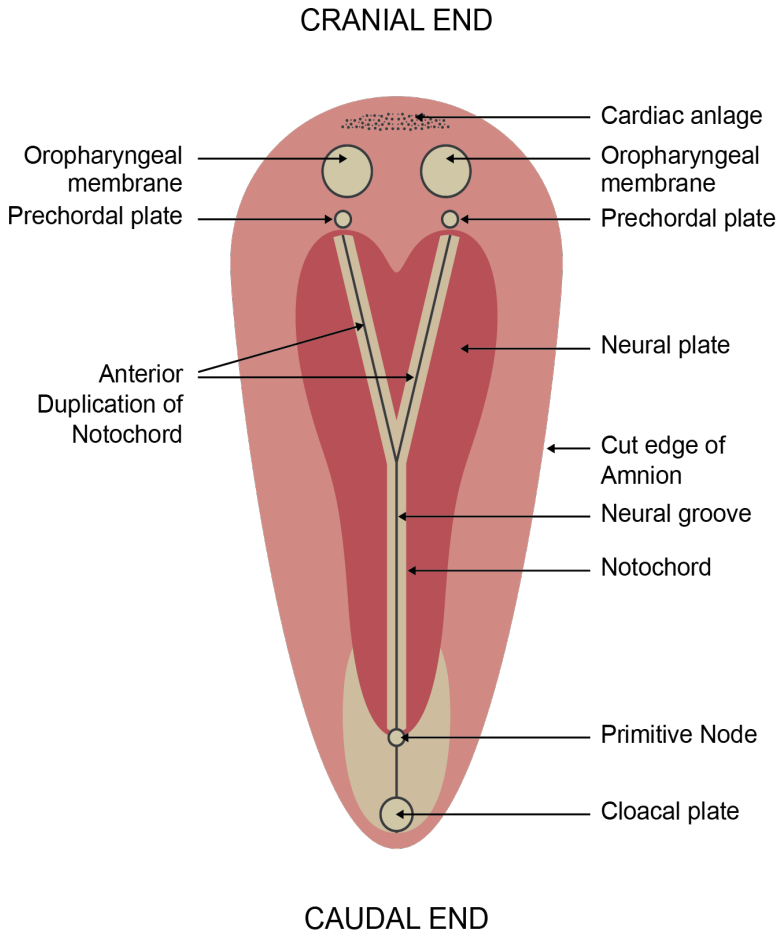


Figure 2: Longitudinal schematic image of a human embryo showing bifurcation of the cranial portion of the notochord

Kaufmann does not regard fusion as a possible cause of conjoined twinning.[21,34,35] Machin suggests that diprosopus is the only condition where there is true rostral notochord bifurcation, compared to other conjoined twins where there are 2 independent notochordal axes.[36] He also puts forward "interaction aplasia" as a possible explanation for why some tissues or organs fail to develop in these cases. This could be due to conflicting cell movement routes or aberrant foci of morphogens.[36]

In partial diprosopus, only certain craniofacial elements or components of the first branchial arch are duplicated.[4,16,20,33,37]

Possible regions of duplication are:

- The prosencephalon (when there is duplication of the eyes and nose),
- The olfactory placodes,
- The maxillary and/or mandibular growth centres around the stomatodaeum.[35,38]

Although pathogenetically unusual, bilateral components may occur in a unilaterally positioned duplicated structure around the stomatodaeum.[33]

There does not seem to be a single cause, but a multifaceted series of events that leads to the recognisable phenotypical spectrum of diprosopus.[32] Potential causes are related to the foetal environment,[39] the uterus,[34] the condition of the ovum,[40] abnormal placental circulation,[9] teratogen exposure,[41,42] abnormal neurocristopathy[27,43,44,45,46] and genetics.[9,14,47] Amniotic band syndrome (ABS), which has been associated with clefting and other anomalies (like anencephaly),[26,48] has also been implicated as a cause.[45] However, documented cases of craniofacial duplication with ABS have not been reported.[35]

Stockard experimented with the temperature and oxygen concentrations of trout embryos just prior to gastrulation and induced conjoined twins, including diprosopus-like embryos, in 1 - 2.3%.[39] The foetal environment is not the only factor that seems to play a role as there have been documented twin pregnancies where only one foetus had diprosopus.[17,38,49]

Irregular or extended menstrual cycles in young or perimenopausal females may lead to late ovulation with over-ripening of the ovum, increasing the risk of duplication of the blastomere.[40] Maternal protein and riboflavin deficiencies may cause multiple ovulation or polyovular follicles, or, otherwise, cause delayed implantation in the endometrium.[40] Conjoined twins may also occur after assisted reproduction.[34,50] The condition of the uterus may be affected by the recent use of the oral contraceptive pill, possibly leading to delayed implantation, which is also considered as a contributor to diprosopus development in itself.[34,39] It has been noted that there is an increase in the incidence of monozygotic twinning in patients where pregnancies followed within six months of cessation of the oral contraceptive pill, and a significant increase in congenital abnormalities when conception occurred within 3 months of stopping it.[34]

It has been observed that there is a high frequency of monozygotic twins born to women with double monster offspring,[51] creating the notion that there is a genetic component to conjoined twinning.[9,51] There have also been familial examples of monozygotic twinning documented.[34] However, chromosomal analyses performed on diprosopus cases have been noted to be normal.[23,52]

The inappropriate expression or deletion of homeotic genes (more precisely Dlx 5 and 6 homeobox genes) can lead to a large spectrum of anomalies across all germ cell layers.[4,17,53,54] These genes are responsible for the spatial organisation of developing structures.[17] Mutant disorganisation has been studied in the murine model and is known to be transferred in a semi-dominant manner.[55,56] Winter and Donnai suggest that there is a corresponding human disorganisation syndrome.[56] This syndrome has been linked to other cases of conjoined twinning and duplication of structures.[30,55] Diprosopus may be a part of this spectrum.

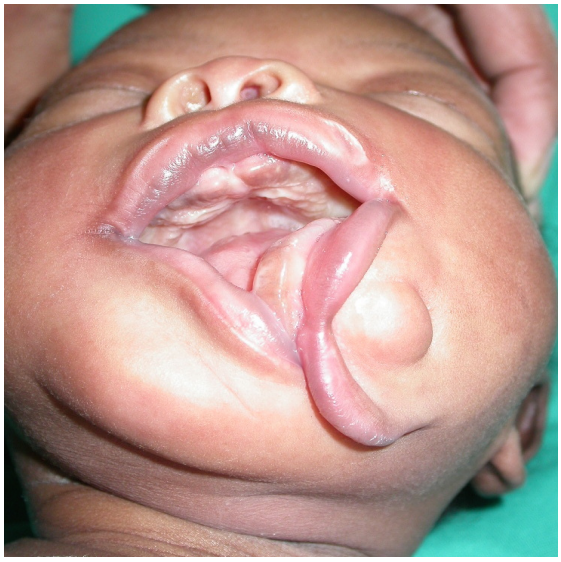
The most common teratogen is ethanol.[34] In a hamster study, various other teratogens (vitamin A, dimethylsulfoxide, and urethan) induced twinning. All these twins also had some degree of failure of anterior neural tube closure.[41] Other teratogens that are implicated in twinning or neural tube anomalies are thalidomide, vincristine sulphate in mice, general and local anaesthetics, colchicine, griseofulvin, and phenylzine dihydrogen sulphate.[34,41,57] A case of dicephalus has been associated with maternal exposure to Chernobyl in 1986.[13] Other factors include viral and parasitic infections.[58]

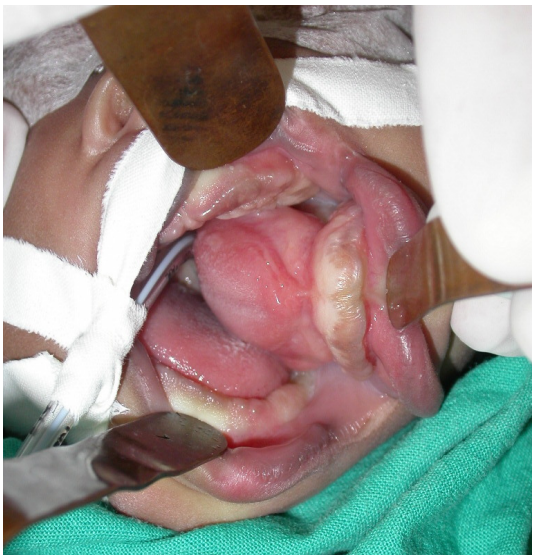
Neural crest cells are a fleeting population of multipotent precursor cells which then migrate and induce formation of diverse cell lineages.[48] Abnormal neurocristopathy may be caused impaired cell migration or unsuccessful induction of structure-formation,[43,44,45,59] particularly craniofacial cartilage and bone formation.[60] Most defects seem to arise from failure of fusion of embryonic processes or failure of neural tube closure.[5,44]

Teratoma formation (sequestration of totipotent stem cells during early development with various tissue or organ components) should be distinguished from partial duplication.[20,37]

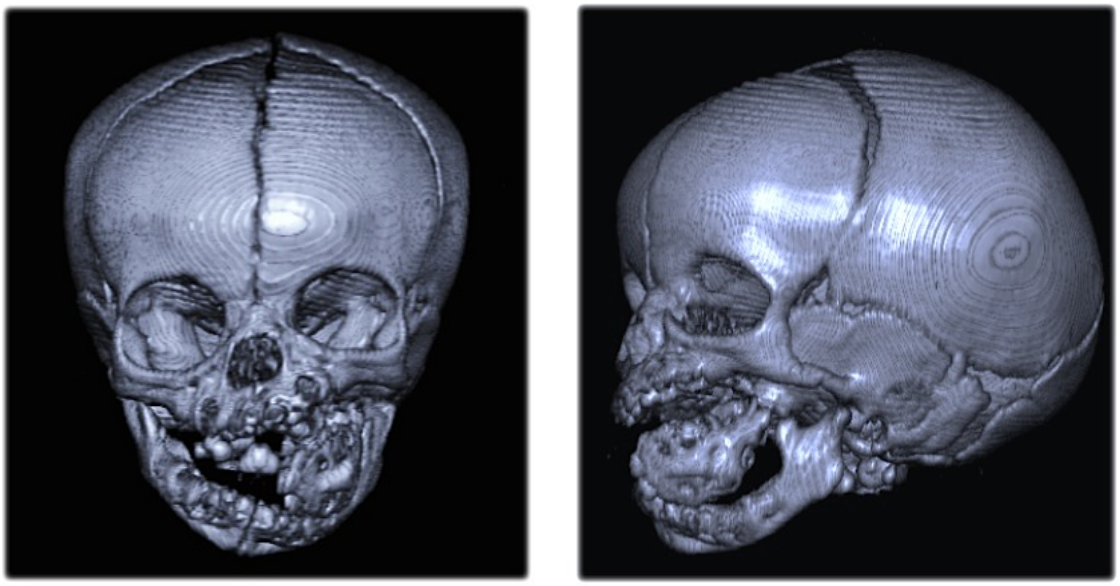
Case Report

A twelve-day-old female neonate, born with duplicated congenital orofacial anatomy, presented to our quaternary centre, Inkosi Albert Luthuli Central Hospital (IALCH), in Kwazulu-Natal. Respiratory and feeding difficulties were not present. The antenatal history was unremarkable and no other congenital abnormalities were clinically obvious. To plan the surgical intervention, a computerised tomography (CT) scan with three-dimensional (3D) reconstruction of the head was performed. This was followed by an examination-under-anaesthetic to assess the abnormal duplicated oral structures. The duplicated structures included the mandible, tongue and floor of mouth, external soft tissues of the mentum and lower lip on the left. A cleft of the soft palate was also present.





Figures 3a and 3b: A duplicated mandible is shown on the left-hand-side of the oral cavity. The duplicated mandible is seen lying vertically and features its own floor of mouth, duplicated tongue and lower lip (on the right of the figure).



Figures 4a and 4b: CT scan and 3D-facial-bone-reconstruction showing a left-sided deformation of the maxilla and primary mandible with an associated open bite, resulting from an unattached space-occupying duplicated mandible in the oral cavity. The left orbit is positioned higher than the right and the temporo-mandibular joint on the left appears to be normal. The duplicated mandible shows numerous unerupted teeth.

At the age of 7 weeks, surgical removal of the duplicated structures was accomplished. The hypothesis, that further deformation of the normal skeletal structures could be prevented and that growth correction of the maxilla, mandible as well as orbital position may occur with growth of the face, was applied. Using an intra-oral approach, the duplicated mandible and tongue were excised from the vertically-orientated duplicated floor of mouth. Soft tissues peripheral to the duplicated mandibular arch were retained. After the excision, the soft-palate cleft was better visualised and it was noted to be unusual as it was not central and the defect was on the left-hand side of the soft palate. A standard repair, therefore, was not possible.

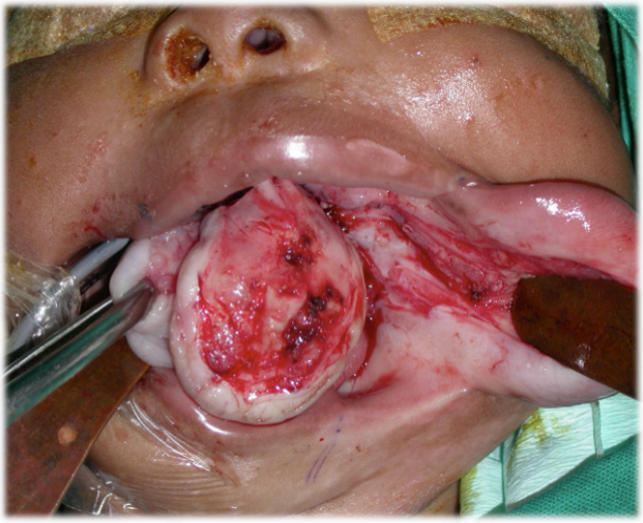
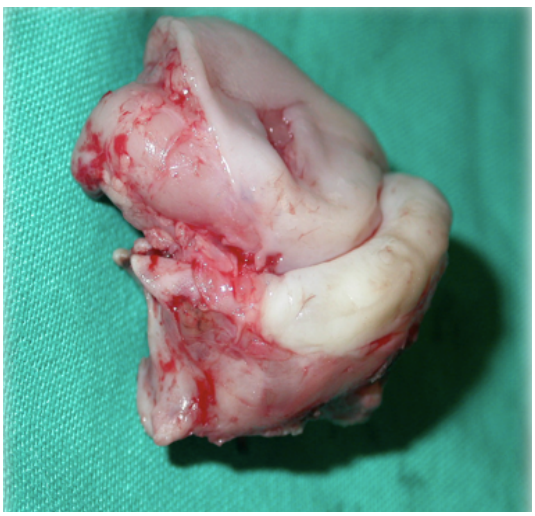
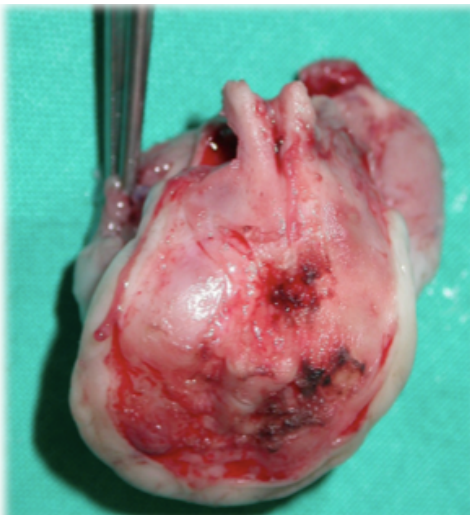


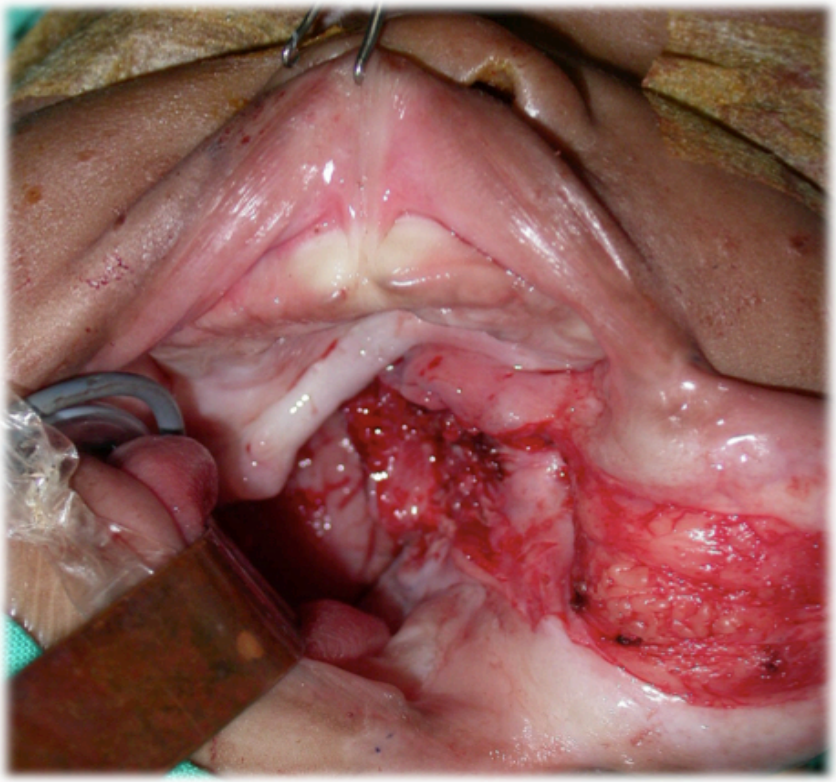
Figure 5: An intra-oral view of a near-total removal of the duplicated mandible and tongue is shown, leaving behind some of the peripheral soft tissue floor.

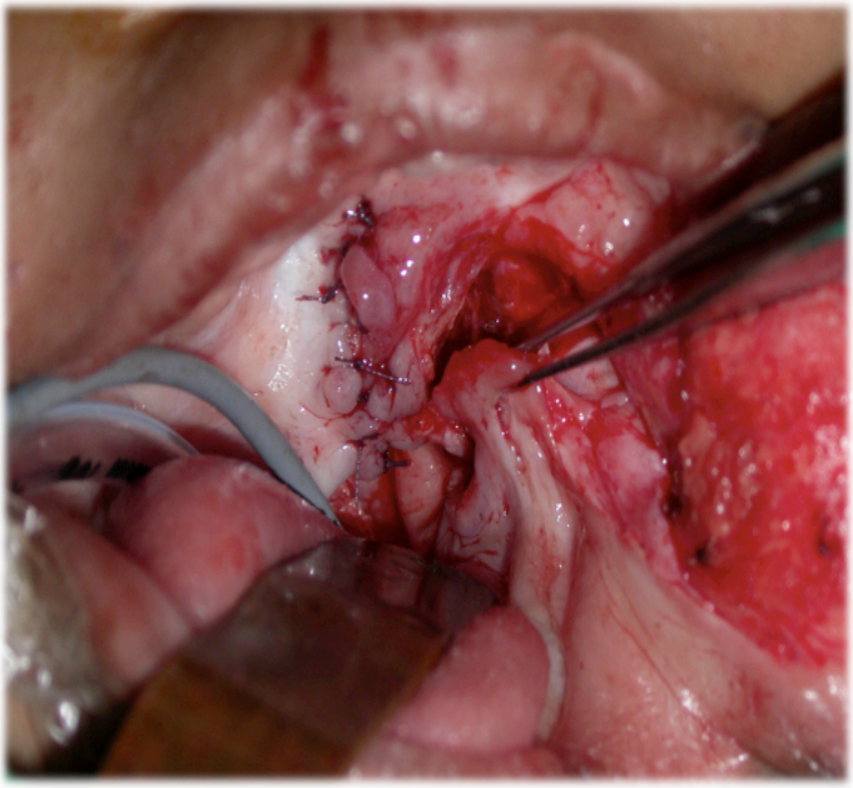


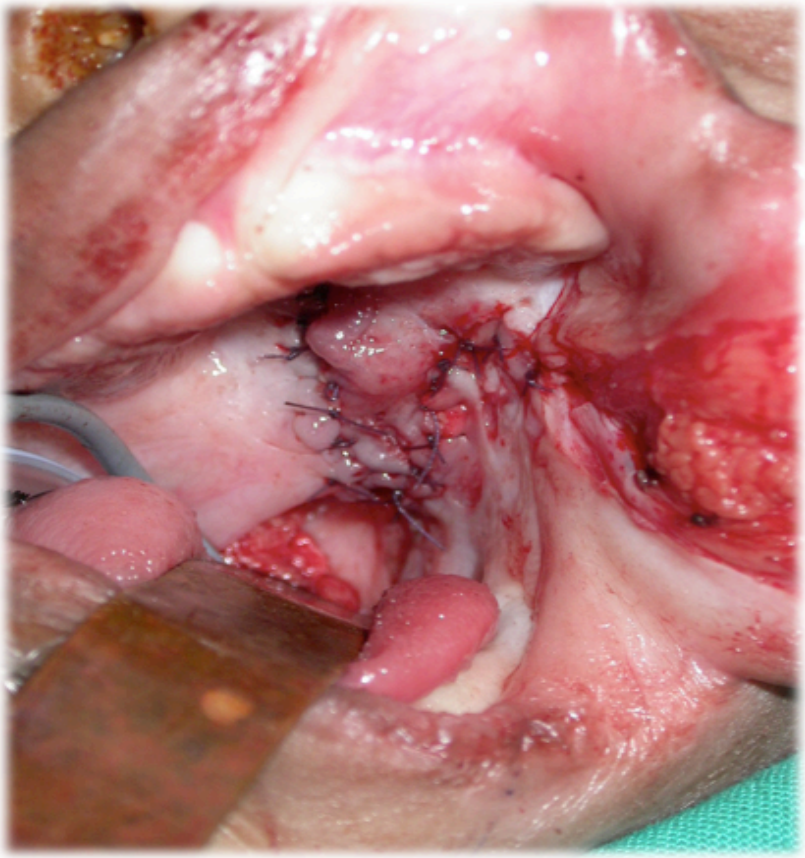


Figures 6a and 6b: The superior surface of the excised duplicated mandible, floor of the mouth and tongue is shown (left). A posterior view of the duplicated mandible, the rami with its condyles abutting each other i.e. posteriorly, the arch of the mandible is not open (right).

Instead, the residual soft-palate edge medial to the defect was pared. A left palatopharyngeus musculo-mucosal flap, lateral to the defect, and mucosal tissue from the residual duplicated floor of mouth were then rearranged to close the oral side of the defect in a dual layer. Flaps were laid parallel to each other.







Figures 7a – c: The palatal defect is shown on the left-hand side of the soft palate after the medial edge is pared (top). A superiorly-based palatopharyngeous flap is visualised, sutured to the medial side of the defect. The residual tissue of the duplicated floor is seen mobilised to close the lateral side of the defect (middle). The soft palate defect is shown, sutured closed with the use of both flaps (bottom).

Following intraoral defect closure, the external perioral tissues were addressed. To preserve a normal looking left commissure, the commissure between the normal upper lip and the duplicated lower lip was retained. The duplicated lower lip, 1cm medial to this commissure with its associated soft tissues of the mentum, was removed. The duplicated lower lip, connected to the normal lower lip, resembled a Tessier's No. 7 craniofacial cleft, similar to macrostromia. The normal lower lip, inferior to the No. 7 cleft, was detached from the cleft, shortened, released and advanced to the cut edge of the duplicated lip near the left commissure and repaired. Excision of all soft tissues was performed as planned, closing the low-lying lateral oral cleft. Correction of lip aesthetics

and oral competence was not our aim at this stage. Lip revision was to be considered once the hypothesised maxillary and mandibular deformity correction occurred in response to the removal of the duplicated structures.

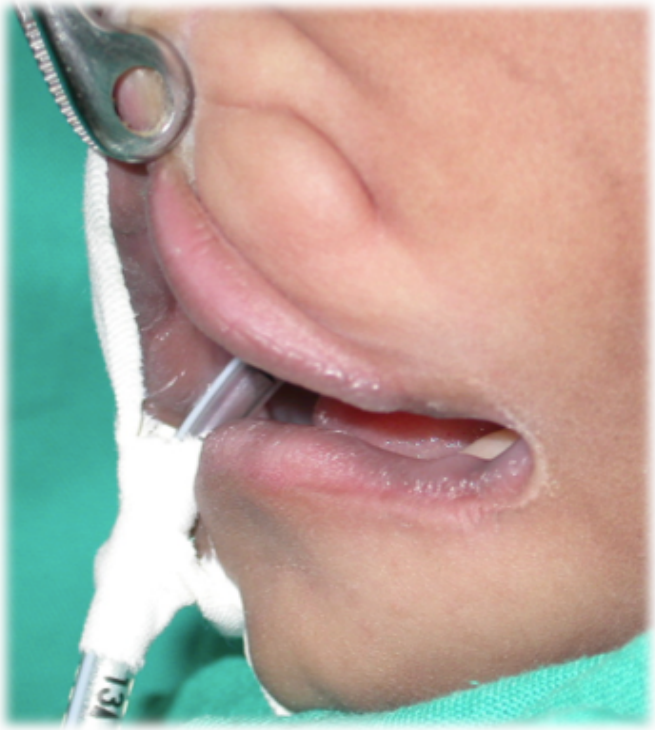
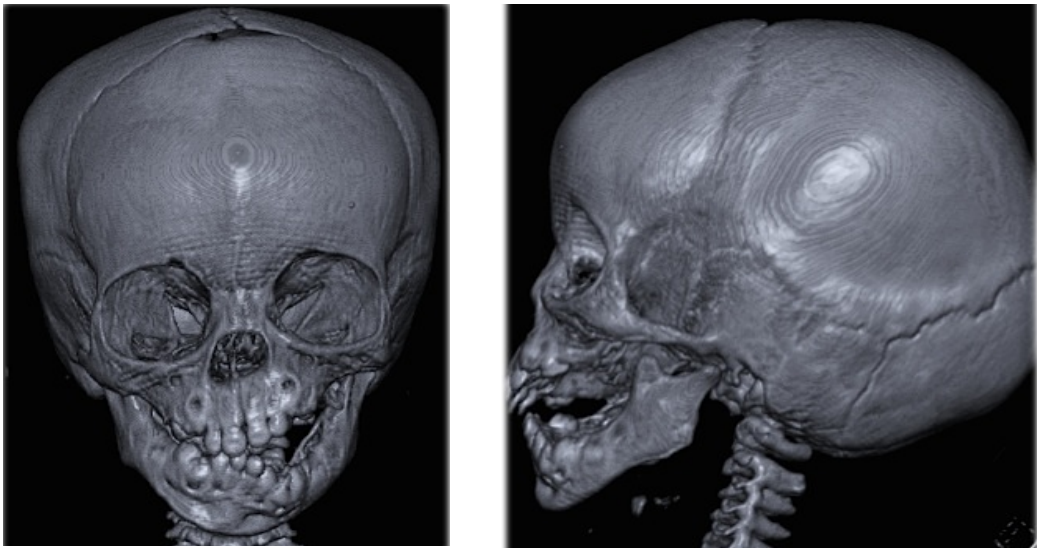


Figure 8: The junction between the duplicated lower lip (above) and the normal lower lip (below), simulating macrostomia of a Tessier No. 7 cleft

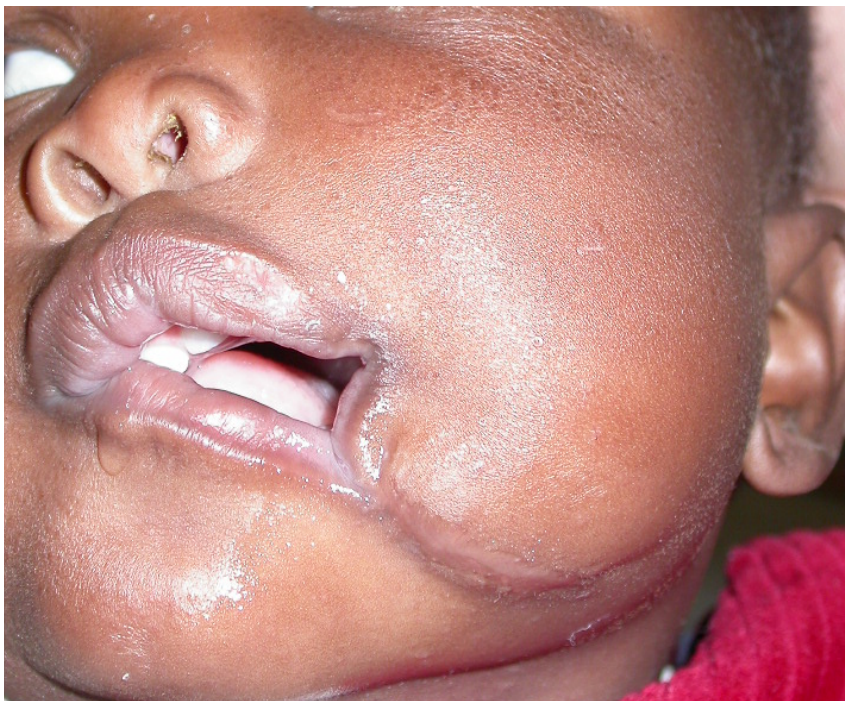
A minor complication of dehiscence of the palate repair was encountered post-operatively. This was allowed to heal spontaneously. The excised duplicated structures were analysed histologically. There were no tissue abnormalities noted. The duplicated mandible had representation of stratified squamous epithelium, odontogenic epithelium, bone, bone marrow elements and developing teeth (in keeping with a duplicated mandible).

Over the ensuing year, the mandible and maxillary deformities and their corresponding occlusion improved.



Figures 9a and 9b: The follow-up CT scan at 17 months of age shows compensatory growth of the affected maxilla and mandible, partially correcting the original deformity and dental occlusion present at birth. Orbital dystopia also has improved.

At 17 months of age, the lip was revised with a wedge excision of the horizontally-elongated lower lip, advancing it to the previously preserved left commissure. Lip competence and lip aesthetics were achieved. The patient was lost to follow up at 1 month after the second-stage surgery.



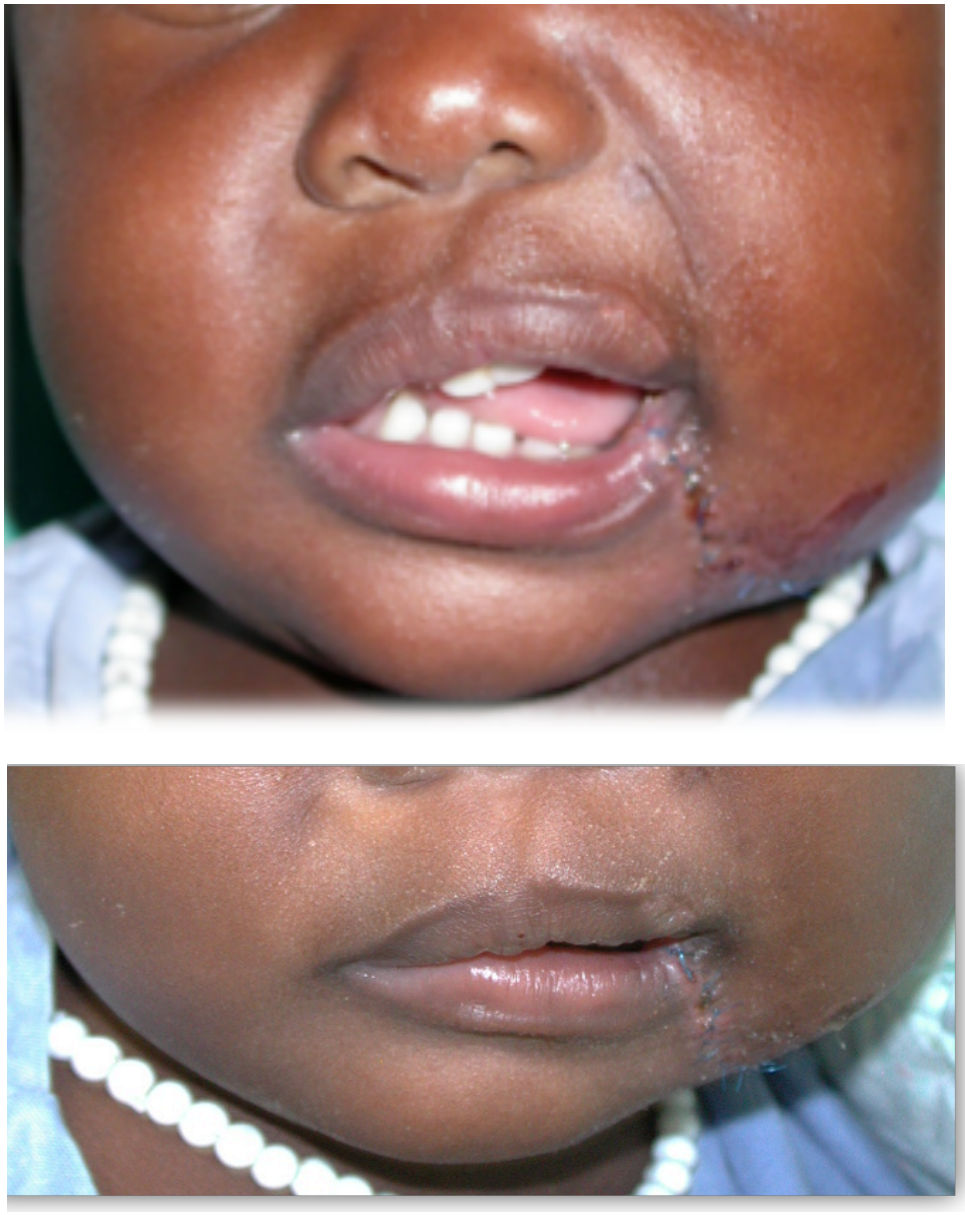


Figure 10 a to c: Repair of the lip is shown at 6 months following the first stage operation (Left). Repair of the lip is shown at the one-week follow-up after the second stage operation at 17 months of age. An improvement in the open bite is also noted. (Bottom right). The lips are shown apposed, demonstrating lip competence

Discussion

Diprosopus cases are challenging to manage and demand extensive interdisciplinary co-operation.[21,61] The management approach is largely dependent on the nature of the duplication with only some partial duplications rendering themselves to appropriate surgical correction.

It is the ideal that this condition be diagnosed early on a detailed antenatal ultrasound. On ultrasound, specific findings can be highly suggestive of diprosopus.[14,62] These include increased nuchal translucency, lymphangiectasia, neural tube defects, ventral wall defects, renal agenesis, a widened vertebral column, a heart-shaped cranium or bifid cranial vault and duplication of the face or facial components.[23,50]

By diagnosing the condition earlier, a more thorough management strategy can be constructed, which would include delivery options, counselling, involvement of other disciplines and the decision to continue with the pregnancy if the parents so desire.[3,11,62] The parents should be counselled compassionately that there is a poorer prognosis with complete facial duplication[22] and that separation is impossible.[12] In an article by Thornton, the parents of a diprosopus baby opted to continue with the pregnancy and felt that with the support of the treatment team and comprehensive counselling, they were prepared to deal with the death of their baby very soon after delivery. It was much more peaceful than expected and they were able to cope with their loss.[61]

Isolated duplication, however, is not necessarily incompatible with life and some can often be managed surgically.[34] If the parents decide to continue with the pregnancy, they must be made aware that a caesarean section will most likely be required due to cephalopelvic disproportion.[14] Once the baby is born, a detailed management plan should be communicated and deliberated with the parents.[60] There are growth, functional and psychological considerations to weigh up when timing surgery.[16,64] Surgery is the only treatment that can offer functional and aesthetic correction and will always be an improvement on the original, especially in severe deformities.[16,24]

Surgery has had varying success, and the parents should be made aware that there will be visible scarring.[29,23,33,38,57,60] Obwegeser was very critical of his scars post operatively despite multiple revisions.[24,60] However, Price is of the opinion that good results can be expected and that surgery is mostly straightforward.[65] Surgery is usually deferred until the patient is older and more soft tissue is available to perform the reconstruction. Obwegeser waited until the patient was 10 years old but still found that the midface had growth retardation.[60]

In our case, we opted to operate as early as 7 weeks of age on the supposition that removing the intraoral duplicated mandible and tongue would eradicate the forces of deformation, produced by their on-going growth, on the rest of the non-duplicated craniofacial skeleton. Although there were no feeding and no airway problems at presentation, they may have developed as the child grew were these duplicated structures not removed. Also, asymmetry of the face would have worsened, sacrificing the psychological wellbeing of the growing child and parents. The interval between the first stage and the second stage operations clinically and radiographically demonstrated a partial correction in the bony deformity of the facial skeleton. It was unfortunate that the patient did not return for further follow-up and that all means of contact failed. A longitudinal follow-up would have been invaluable.

Definitive surgical treatment of the perioral tissues was deferred to a later stage. As the skeletal deformity began to correct over time, it laid the foundation for an improved soft tissue lip positioning and scar contracture correction of the repaired Tessier No. 7 cleft. Maisels noted that when macrostomia was repaired, especially very early, there was a tendency for the commissure to drag as the child grew.[25,33] We performed the surgical revision at the age of 17 months, but there could have been value in an even further delay, anticipating further correction of the jaws.

The soft palate cleft was atypical, presenting with a left-sided defect. The standard techniques of repair were not feasible. The cleft palate repair is generally deferred to 9 months of age or older. We purposely repaired the cleft of the soft palate during the

excision surgery to enable the use of some of the redundant tissues of the duplication. If this opportunity had been missed, then a higher degree of surgical complexity, using local pedicled flaps or even free flaps, would have been required.[66] Duplicated mucosa excision and salivary apparatus removal was not performed, despite being recommended in the literature as there is a higher chance of developing retention cysts.[15,33,37] In our case, no cysts had developed up to the final review but, owing to the loss to follow-up, the risk could not be assessed thoroughly.

Long-term follow-up is important to address any residual deformities not corrected by on-going growth of the craniofacial skeleton. Potentially, orthodontic therapy, orthognathic and further lip revision surgeries are back-up strategies to achieve an ultimately good result.

Conclusion

Diprosopus is very rare. Its pathogenesis is multifactorial but abnormalities in the formation of the notochord may be central to its development. Mainly partial facial duplications are amenable to surgical correction. The type of surgery is dependent on the nature of the duplication. Early excision of the duplicated structures potentially interrupts deformational growth of the normal craniofacial skeleton and may even provide, to some degree, auto-correction. The surgical approach should include use of spare-parts as well as strategic planning in the use of available soft tissues for the best possible functional and aesthetic outcome.

Conflict of Interest

There are no conflicts of interest.

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