A Study of the Alar Cartilage in Unilateral Cleft Lip Nasal Deformity

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Content

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List of Abbreviations

Unilateral Cleft lip nasal deformity (UCLND).

Fibroblast Growth Factor 18 (FGF 18).

Fibroblast Growth Factor Receptor (FGFR).

Hyaluronic acid (HA).

Glycosaminoglycans (GAGS).

Alveolar Bone Graft (ABG).

Gingivoperiosteoplasty (GPP).

Presurgical Nasoalveolar Molding (PNAM).

Phosphorylated Buffer solution (PBS).

Antigen Antibody Complex (ABC).

Antigen ntibody (AB).

Introduction

The three dimensional combination of rigid skeleton, firm cartilaginous and elastic skin cover makes the nose a unique part of the face. Volumes were written about the complicated anatomy of the nose, so a radically affected nose by a congenital anomaly has a major impact on both function and appearance of the nose **(Van Beek et al, 2004).**

The unilateral cleft lip nose deformity is one of the most difficult aesthetic and functional deformities to surgically correct. The residual sign of an excellent lip repair is the persistent cleft lip nasal deformity and being unilateral, makes it even more prominent and difficult to camouflage **(Sykes and Senders, 1995).**

Huffman and lierle, 1949 were credited with the earliest detailed description of the observed features of the cleft lip nasal deformity. **Hobar, 1994** summarized the features as follows: In the cleft side, the tip of the nose and the caudal septum are deviated toward the non cleft side, the dome of the alar cartilage is depressed, the lateral crus is caudally displaced and the medial crus is retro displaced. The interior of the cleft side nostril is bowed by a linear contracture (the vestibular web) and there is disproportionate, widened nostril floor. (**Fisher and Mann, 1998).**

The proponents of the intrinsic theory state that during embryogenesis, alteration occurs in the cells originating from the neural crest. The alteration accompanied by disorderly migration, differentiation and proliferation which results in mesenchymal impairment of the nasofrontal process and appearance of the cleft

and nasal deformity, along with the changes in the cellularity and matrix of the alar cartilages **(Modolin et al, 2002).**

Pattern, 1971; Stark and Kaplan, 1973 and **Avery, 1976** formulated the hypothesis that there could be mesodermal hypoplasia in the cartilage forming capacity.

Theories holding the extrinsic factors responsible for the deformity were reported by **Huffman and Lierle, 1949; Stenstrom and Oberg`s, 1961; Novoselov, 1979; Park et al, 1998 and Ai-Qun li et al, 2002.**

A plethora of techniques were done for the repair of the unilateral cleft lip nose deformity. Suture suspension of the affected lower lateral cartilage to the upper lateral cartilage, the septum, contra-lateral lower lateral cartilage, nasal bones and external bolsters **(Madorsky and Wang, 1999)**.

Many creative incisional cartilage relocation techniques have been described by **Humby, 1938; Kazanjian, 1939; Brown and McDowell, 1941; Barsky, 1950; Erich, 1953 and Whitlow and Constable 1973.** Although some are effective, they are considered as a camouflage techniques and do not address the underlying deficiencies of the cleft lip nose **(Madorsky and Wang, 1999).**

Different techniques for cartilage grafting were done as on lay grafts over the dome, lower lateral cartilage or as composite grafts in the lateral vestibule after medial advancement of the lower lateral cartilage with the vestibular skin flap **(Madorsky and Wang, 1999)**.

Matsuo et al, 1989 were the first to introduce the presurgical nasal molding as an adjunctive neonatal management for preoperative correction of the nasal deformities, by utilizing the

malleability of the alar cartilages shortly after birth. **Pai et al, 2005** concluded an improvement in nasal symmetry, which is maintained into early childhood despite some relapse one year after the repair.

Grayson et al, 1999 proposed the combination of presurgical orthodontics and nasal molding for approximating the alveolar cleft and improving the nasal deformities.

Finally, the controversies regarding the etiological factor of cleft lip nasal deformity and the need to use cartilage graft are still subjects of considerable debate, which necessitate further investigations.

Aim of the work

The aim of the work is to measure and compare, the lower lateral cartilages of the cleft and non cleft side in patients with primary unilateral cleft lip nose deformity as regard their morphometric dimensions (length, width and thickness), analyze the histological pattern in the lower lateral cartilage of both cleft and non cleft side, so as to reach the optimum operative intervention to such alar deformity.

Embryology of the Face

The head and neck regions of four week old human embryo, is formed of the pharyngeal apparatus which consist of pharyngeal arches, pouches, grooves and membranes. These embryonic structures greatly contribute to the formation of the head and the neck and most of the congenital anomalies in these regions originate during transformation of the pharyngeal apparatus into its adult derivatives **(Jafee, 1972)**.

The Pharyngeal Arches:

During the third week of embryonic development, the primordial mouth or stomodeum initially appears as a slight depression of the surface ectoderm. It is separated from the cavity of the primordial pharynx by a bilaminar membrane the oropharyngeal membrane.

The pharyngeal arches develop early in the fourth week as the neural crest cells migrate into the future head and neck regions. The first pair of pharyngeal arches, the primordia of the upper and lower jaw appear as surface elevations lateral to the developing pharynx. Soon other arches appear as oblique, rounded ridges on each side of the future head and neck regions, these arches are separated by the pharyngeal grooves (clefts). Like the arches the grooves are numbered in a craniocaudal sequence.

By the end of the fourth week, four well defined pairs of pharyngeal arches are visible externally, while the fifth and the sixth arches are rudimentary and are not visible on the surface of the embryo, see figure (4)

The first pharyngeal arches develop two prominences: The maxillary prominence gives rise to the maxilla, zygomatic and squamous part of temporal bone. The mandibular prominence forms the mandible. Consequently the first pair of the pharyngeal arches plays a major role in facial development **(Jafee, 1972)**.

The Neural Crest Cells Formation, Migration and Differentiation

The ectodermal derived cells that are found in the margins of the bilateral neural folds and the transition zone between the neuroectoderm and epidermis are referred as neural crest cell, see figure (1) **(Hall, 1999).**

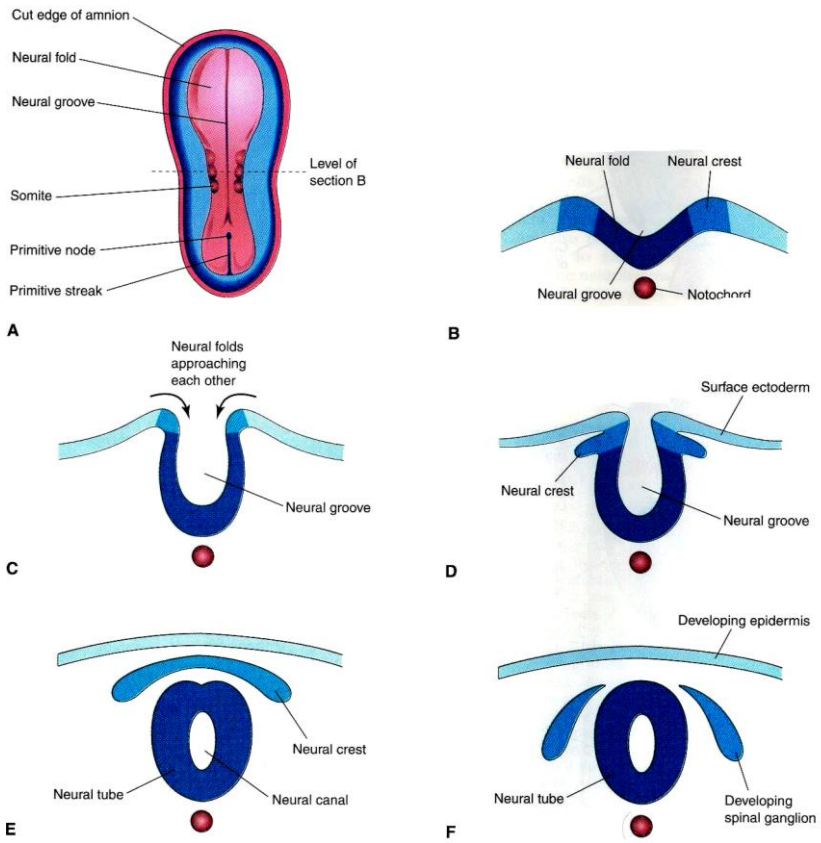

Fig. (1) Diagrammatic transverse section through an embryo illustrating the formation of the neural tube and neural crest cells **(Moore and Persaud, 1998).**

The neural crest cells give rise to a diversity of cell and tissue types (e.g., neural, pigment, skeletal, connective tissue, cardiac, dental and endocrine cells). **Hall, 1999** suggested that the neural crest cells should be considered a fourth germ layer.

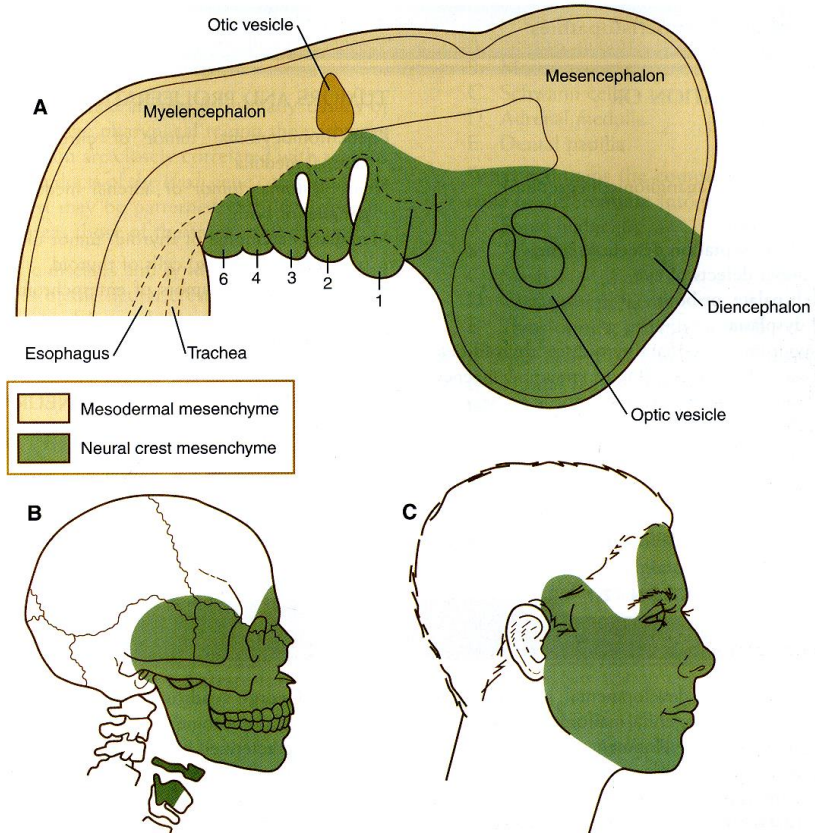

Fig. (2): Shows the neural crest distribution in the head and neck. A. In the early embryo. B and C. in the adult skeleton and dermis **(Carlson, 2004)**.

The neural crest cells migrate into the developing pharyngeal arches and provide the precursors of cartilage, bone, muscle, and connective tissues of the head and neck. The timing and the extent of neural cell migration and differention is dependant on complex pattering of inductive growth factors and genes as [homeobox gene (HOXa-1, HOXa-2), the OTX gene (orthodentical homeobox), the Bone morphogenetic proteins (BMPs 1-7), Epidermal growth factor, Fibroblast growth factors 1-9, etc… **(Sperber, 2002).**

Cranial neural crest cells show remarkable specificity. In the hind brain, it's ultimate destination within the pharyngeal arches.

Neural crest cells associated with rhombomeres 1 and 2 migrate and form bulk of the first pharyngeal arch, those of rhombomeres 4 into the second arch, and those of rhombomeres 6 and 7 into the third arch as three separate streams of cells. The mesenchyme opposite Rhombomeres 3 and 5 exerts a repulsive effect on any neural cell trying to enter this region which is required to maintain the separate streams of neural crest cells that populate the pharyngeal arches, see figure (3) **(Noden, 1991).**

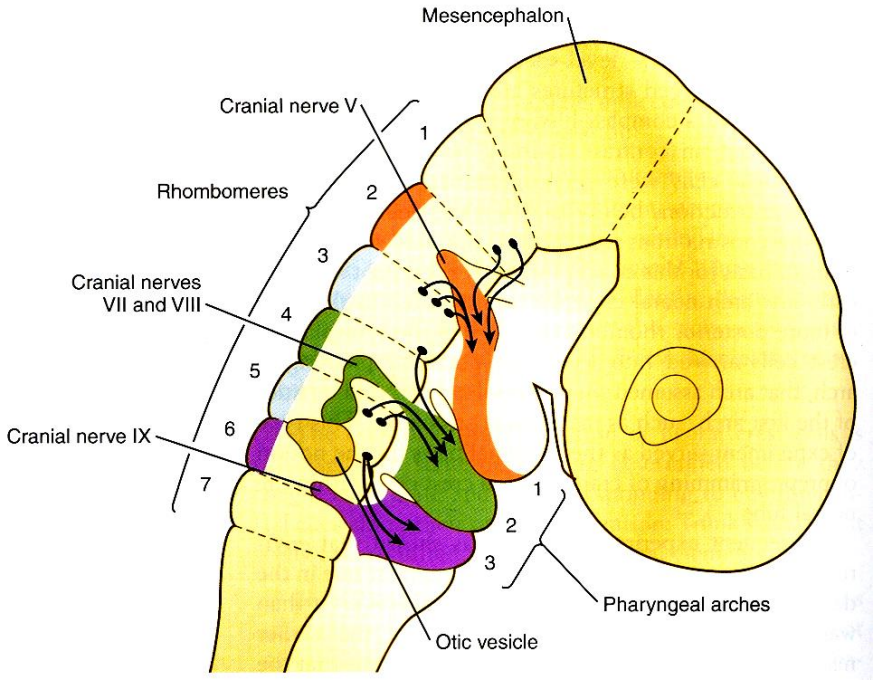

Fig. (3): Migration pathway of the neural crest cells from rhombomeres 2,4 and 6 into the first three pharyngeal arches. Small contribution from rhombomeres 1, 3 and 5 are idicated by arrows **(Carlson, 2004)**.

Pharyngeal arch components

Initially, each pharyngeal arch consists of a core mesenchyme (embryonic connective tissue) and is covered externally by ectoderm and internally by endoderm. The original mesenchyme is derived

from the mesoderm in the third week of intra uterine life **(Jafee, 1972).**

During the fourth week, most of the mesenchyme is derived from the neural crest cells that migrate into the pharyngeal arches. It is the migration of the neural crest cells into the arches and their differentiation into the mesenchyme produces the maxillary and mandibular prominences of the first arch, see table (1)(**Graveson, 1993).**

In the rostral midline is the frontonasal prominence, which populated by mesenchymal cells derived from forebrain and midbrain neural crest cells. On either side of the frontonasal prominence, ectodermal nasal placodes, which arose from the anterior neural ridge, develop into horseshoe-shaped structures, each consisting of nasomedial process, also derived from forebrain neural crest, and a nasolateral process, derived from midbrain neural crest. Farther caudally the stomodeum is bounded by maxillary and mandibular processes **(Noden, 1991).**

Despite the neuroectodermal origin of the neural crest cells they make the major contribution to the mesenchyme of the head and neck as well as to structures in other regions. While skeletal and vascular endothelia however are derived from the original mesenchyme in the pharyngeal arches **(Kirby and Bockman, 1984).**

Fate of the pharyngeal arches