



Variant Type of Midline Nevus Flammeus in Cleft Patients: Is it a Physiological or Pathological Sign?

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Introduction

- Midline nevus flammeus (medial telangiectatic nevus) is a congenital capillary malformation of the newborn occurring in the midline of the face and nape¹.
- These lesions are presumed physiological due to their transient nature of existence and usually fade within the first year of life².
- However, some of these capillary malformations have been seen associated with other congenital anomalies and some of these vascular lesions persist till later life³.
- It is uncertain if the persistence or residual vascular lesions in the cleft patients represent a prognostic marker for dysmorphogenesis.
- The incidence of midline nevus in non-syndromic cleft infants is not known.
- We present a variant type of midline nevus flammeus in the non-syndromic cleft infants admitted to Chang Gung Craniofacial Center.

Material and Methods

- Medical records of cleft infants presenting with various types of cutaneous vascular lesions managed at Chang Gung Craniofacial Center, Chang Gung Memorial Hospital, Taiwan were retrospectively reviewed.
- Fifty six cleft infants born with capillary malformation in the head and neck region were identified from the period of May 1998 until March 2006.
- All their clinical records, drawings and photographic documentations from their first visits to subsequent follow-up were reviewed and analyzed.
- The information extracted from these records includes sex, gestational period, birth weight, ethnicity and diagnosis during their first visit.
- The information on the site, size, distribution pattern, extent and color of vascular lesions were obtained from the clinical notes, drawings and photographs.
- The follow-up period ranged from 18 months to 108 months (mean follow-up period:56.1 months)
- Excluded infants were those diagnosed with craniofacial syndromes or multiple congenital anomalies, without clinical documentations or photographs of the vascular lesions.
- Of these 56 infants, 20 cleft infants have complete clinical documentations, drawings and photographs for evaluation.
- All these 20 cleft infants have distinct vascular lesions in the midline of forehead, described as midline nevus flammeus.
- There were 2 groups of cleft patients identified: non-syndromic cleft lip and palate, and non-syndromic cleft palate only.

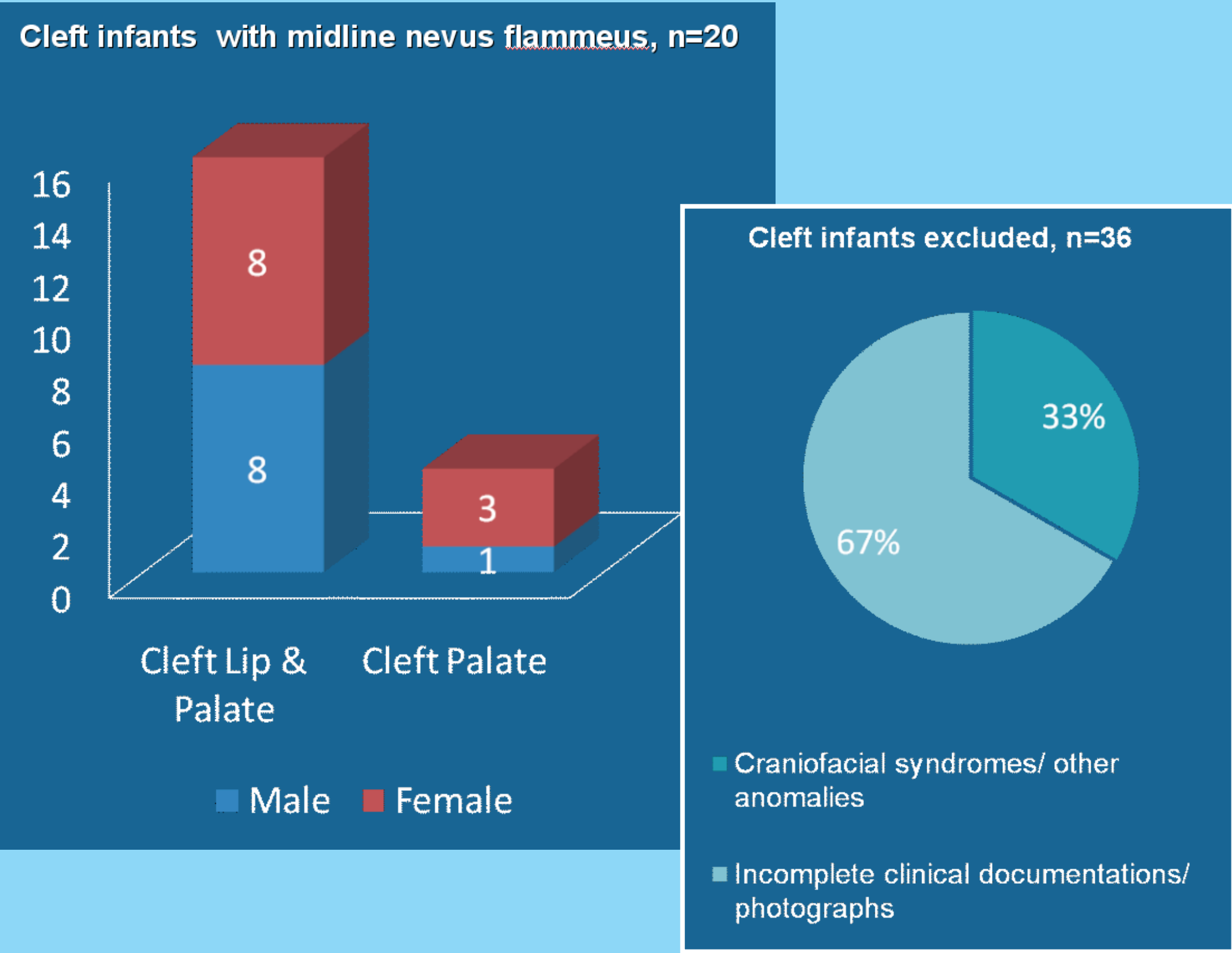
Discussions

- The embryological basis for the distribution pattern of midline nevus flammeus is so far an enigma.
- The underlying histopathogenesis is unclear because of its benign and short-live course.
- In this study we have observed a unique pattern of midline nevus flammeus confined within specific embryonic fusion sites in the cleft infants.
- The pattern of distribution of midline nevus flammeus is V-shaped, usually arising from glabella and the limbs of the ‘V’ spread out symmetrically in a linear fashion to the hairline region.
- Some of these lesions are small and localized, whereas others displayed a linear distribution, covering a wider anatomic region.
- Waner *et al* proposed that the patterns of facial infantile hemangioma corresponded with embryologic facial prominences⁴.
- Likewise, the midline nevus flammeus are also located within the boundaries of facial prominences similar to the segmental patterns described by Haggstrom *et al*⁵.
- These capillary malformations are usually confined within the junction of frontonasal and frontotemporal segments which represent a specific anatomical pattern of distribution and predilection for these regions.
- However, we can postulate that the distinct pattern of midline nevus flammeus in cleft infants may have resulted from errors in the common pathway of the developmental process.
- The formation of facial primordium is derived from mesenchymal cells resulting from migration of neural crest cells^{6,7}.
- It can be postulated that the quantitative and qualitative abnormalities in the neural crest-derived tissue might predisposed to formation of craniofacial cleft as well as cutaneous vascular malformation.
- Ultimately, this would affect the pattern of growth and subsequent integration of the facial primordia and all their constituents including skeletal, muscular, nervous and vascular components.
- In unilateral cleft lip & palate, one limb of the V-shaped nevus is often less demarcated or shorter on the cleft side. In contrasts to the other limb of nevus on the non-cleft side which is more prominent, extensive and intense in color.
- This could possibly due to specific inhibitors that suppressed the angiogenic mechanism on specific areas in the frontonasal and maxillary primordial during facial development resulting in cleft formation.
- Infants with bilateral cleft lip and palate or complete cleft of hard and soft palate or cleft of soft palate, the pattern of V-shaped nevi are symmetrical.
- Most of these lesions are only confined within a small area in the glabella with poorly defined borders, size and color intensity.
- These conditions are perhaps due to over expression of inhibitory signals at both sides of the primordia. It could also be hypothesized that the cleft formation suppressed the angiogenesis on the adjacent primordia on the same side.
- Therefore, we believe that the occurrence of midline nevus flammeus in the cleft infants cannot totally be regarded as physiological phenomenon.
- Instead, it may represent a tell-tale sign of dysmorphogenesis at early stage of embryogenesis.
- These hypotheses warrant further investigations and confirmation.

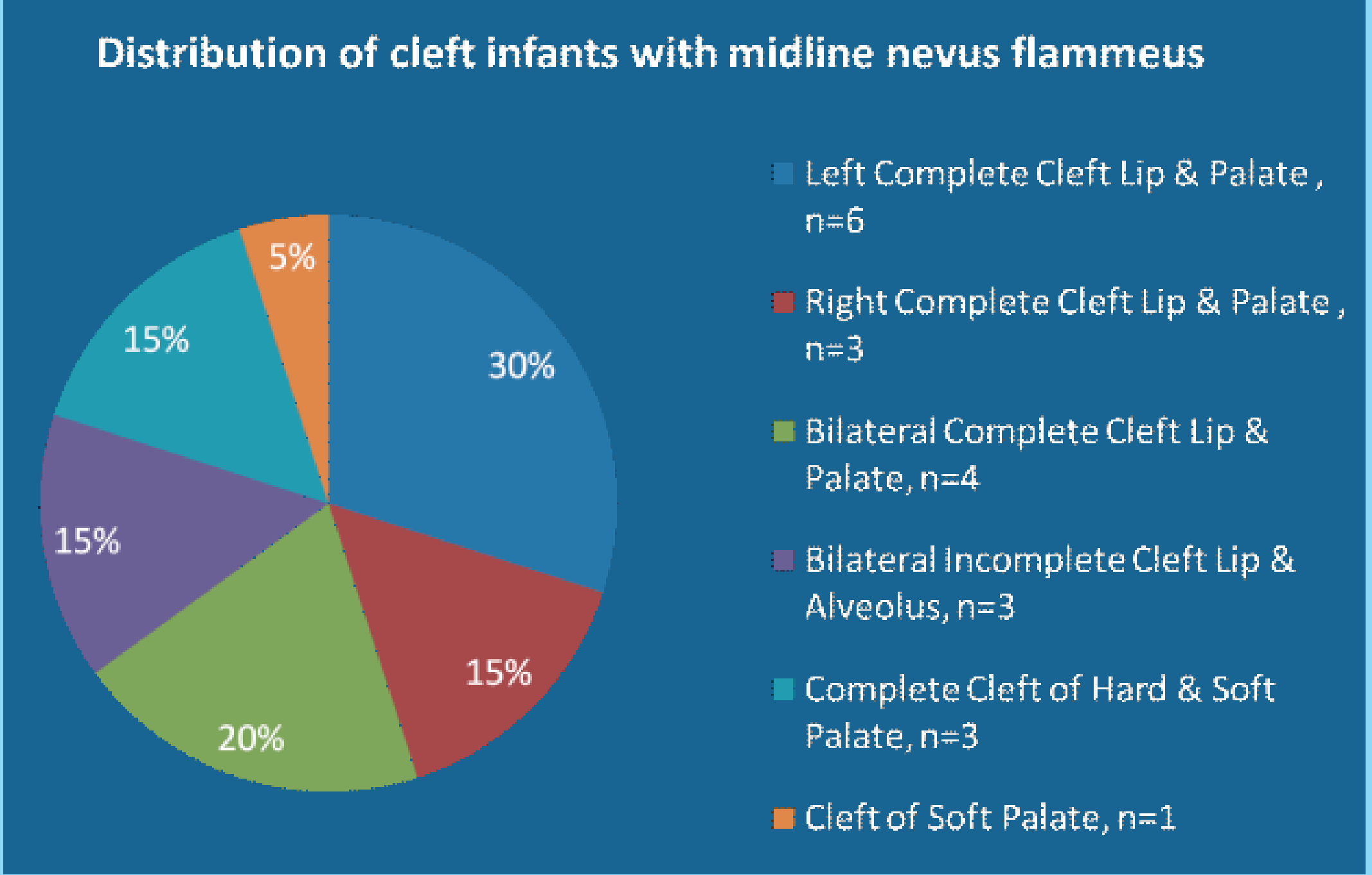
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RESULTS



- 18 cleft infants were born full term & 2 infants were born preterm.
- Birth weight ranged from 0.84 to 4.2 kg (mean birth weight: 3.2 kg).
- All 20 cleft infants with midline nevus flammeus were native Taiwanese.



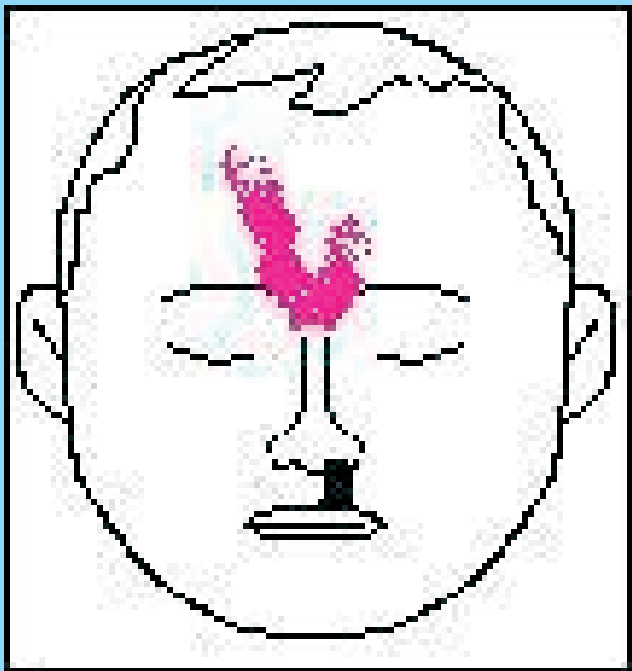
Description of the midline nevus flammeus in cleft infants:

- These vascular lesions have diffused borders with variable color intensities ranging from either pink to purplish red.
- They are all originated from either the upper eyelid or nasion or glabella regions and distributed in a V-shaped pattern.
- Each limb of the V-shaped nevus spreads out across the forehead and faintly disappears at the hairline region.
- The size, pattern, extent and color of nevus flammeus differ accordingly to the type, site of cleft lip and/or palate formation and age of the patients.

(1) Unilateral cleft lip & palate; (45%):

(Left complete cleft lip & palate, n=6 and right complete cleft lip & palate, n=3)

- The pattern of V-shaped nevus flammeus is asymmetrical
- The limb of the V-shaped nevus is usually less demarcated on the same side of the cleft lip and palate.
- For examples: If the complete cleft lip and palate is on the left side, the limb of V-shaped nevus on the right side of the glabella & forehead is longer, more prominent and intense in color as compared to the left side (Figure 1).



(2) Bilateral complete cleft lip & palate, and bilateral incomplete cleft lip & alveolus; (35%) :

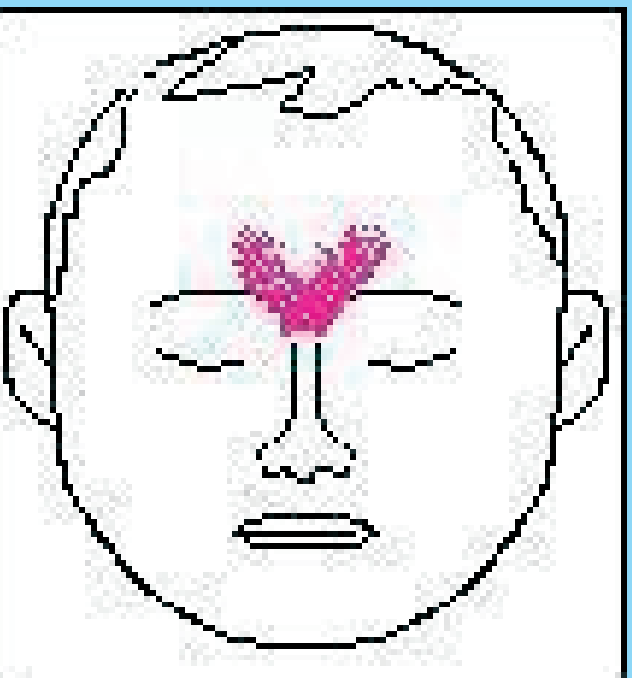
(Bilateral complete cleft lip & palate, n=4 and bilateral incomplete cleft lip & alveolus, n=3)

- The characteristic of nevus flammeus in this group of cleft infants is often less demarcated but symmetrical in pattern, size and color intensity.
- Most of the cases, these nevi are confined to the glabella and nasion region (Figure 2).

(3) Cleft of hard & soft palate, and cleft of soft palate; (20%) :

(Complete cleft of hard & soft palate, n=3 and cleft of soft palate, n=1)

- The appearance of nevus flammeus is symmetrical but the size and color intensity is not well defined (Figure 3).



- Follow-up of all 12 cleft infants with midline nevus flammeus fade spontaneously from cephalad to caudal lesions.
- Some of these lesions remain persistent as much lighter color and smaller sized lesions in later life.