Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate (AEC) Syndrome in Monozygotic Twins: Two Cases Report and Reviews

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Ankyloblepharon-ectodermal defects-cleft lip/palate syndrome or Hay-Wells syndrome is a rare congenital malformation. First described by Hay and Wells in 1976(1), the syndrome is the result of an autosomal dominant inheritance which causes heterozygous missense mutations in the SAM domain of p63 gene(2). This research presents the first summary of the clinical features and results of treatment of AEC syndrome in female monozygotic twins.

Case Report

One-month-old female twins were referred to Srinagarind Hospital for assessment of abnormalities. The patients were born to healthy parents (their second pregnancy) at 37 weeks’ gestation in 2005. The respective birth weights of twin A and B were 2,242 and 2,234 g. The parents did not report any history of congenital abnormalities in the family and the older sibling had no congenital defects. Except for threatened abortion at 12 weeks’ gestation, the pregnancy was negative for maternal exposure to drugs and teratogens.

Clinical features and results of treatment in twin A

The deformities consisted of total scalp hair loss with erosions and hemorrhagic crusts, eyelashes remaining intact, ichthyosiform scaling, syndactyly of right toes 3 and 4, nail dystrophy, helical rim deformities with incomplete bilateral cleft lip and complete bilateral cleft palate (Fig.1-5).

At the time of the first admission, the echocardiography, brain ultrasonography and renal ultrasonography were within normal limits. Purulent otitis media was treated with antibiotics. The defect of the scalp skin was cleaned with normal saline solution, and the skin infection treated with topical antibiotics. Surgical procedures were to follow the protocol of our cleft center following the consensus of a multidisciplinary team; however, cheiloplasty were delayed because of failure to thrive until the child was 5 months of age. The second operation was a two flap palatoplasty at 16 months of age. At the time, she still had chronic otitis media and canal stenosis. She showed...
Clinical features and results of treatment in twin B

Deformities of the scalp skin, hair, helical rim and nails were similar to twin A. She presented complete left unilateral cleft lip and cleft palate (Fig. 6-9). At the time of her first admission, the echocardiography showed left ventricular enlargement, while the renal ultrasonography revealed caliectasia of the left kidney and minimal localized caliectasis at the upper pole of the right kidney. The brain ultrasonography was normal. Like her sister, twin B had purulent otitis media which was treated with antibiotics. The defect of the scalp skin was cleaned with normal saline solution and the skin infection treated with topical antibiotics. Surgery such as cheiloplasty, palatoplasty and cleft lip/nose correction and myringotomy were performed at the same schedule as for twin A.

Discussion

Hay-Wells syndrome is a complicated,
combined developmental embryonic disorder, including: ankyloblepharon filiforme adnatum, ectodermal tissues and cleft lip/palate. Ankyloblepharon is adhesion of the fibrous band at the ciliary edges of the upper and lower eyelids to each other. Ectodermal defects present as sparse or absent scalp hair, eyebrows and eyelashes. The hair is of uncombable quality. The patients have several degrees of nail anomalies, e.g., partial or totally absent nail plates, thickening of nail plates, loss of cuticle(s), pseudopterygium formation and subungual hyperkeratosis. The skin fails to develop a mature epidermis which causes scalp erosion, hypohydrosis, pigmentation changes, palmar and plantar changes. This syndrome is associated with cleft lip and palate, but more commonly cleft palate than cleft lip. In addition, other anomalies include maxillary hypoplasia, small mandible, hypoplastic alar nasi, hypospadias and syndactyly.

The more common condition of non-syndromic cleft lip/palate has a better quality of life prognosis due to fewer deformities. The incidence of cleft lip/palate in twins is almost the same as in general population although the severity may be worse among twins. Laatikainen et al found that the craniofacial morphology of the twins group compared with the non-twins group was a more retrusive mandible and a more obtuse cranial base angle. Other congenital malformations are about four times more likely in twins than singletons. Syndromic cleft in twins varies between 8 and 14%.

Facial cleft occurs with syndromes like Van der Woude, Goldenhar, Hay-Wells, first and second branchial arch (Table 1).

The association between the AEC syndrome and twins is rare: we found only one report. Caswell and McNulty reported on a case of affected dizygotic twins (male and female). In the current study, we describe monozygotic, female twins concordant for ankyloblepharon, ectodermal defects and helical rim deformities, but discordant for cleft, syndactyly of toes, heart and urinary tract abnormalities. Twin A had a syndactyly of the right third and forth toes with an incomplete bilateral cleft lip and a complete bilateral cleft palate. Twin B had left ventricular enlargement, caliectasia of both kidneys with left unilateral cleft lip and cleft palate.

The p63 gene is required for both the proliferative and differentiation potential of developmentally mature keratinocytes. The role of p63 may also initiate the process of re-epithelialization, migration and muscle repair that affect wound healing. For these reasons, we were cautious about doing surgery because of potentially poor wound healing.

The protocol of our cleft center is to start with cheiloplasty at three months of age but in this case we delayed until five months of age due to the child’s failure to thrive and because of a scalp infection in both twins. The next procedure is palatoplasty at 12-18 month of age then cleft lip nose correction at pre-school age. All of these procedures were performed on the twins successfully, without complications of either wound dehiscence, wound infection, oronasal fistula or hypertrophic scarring, which accorded with other reports of no complications after surgery. Oral hygiene is reportedly similar to that expected in the general population of the same ages.

Our experience, confirmed by the literature,
Table 1. Syndromic cleft with twins

<table>
<thead>
<tr>
<th>References</th>
<th>Year published</th>
<th>No. of Patients</th>
<th>Zygote development</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervenka(11)</td>
<td>1967</td>
<td>2</td>
<td>monozygotic</td>
<td>Van der Woude</td>
</tr>
<tr>
<td>Hersh(12)</td>
<td>1992</td>
<td>2</td>
<td>monozygotic</td>
<td>Van der Woude</td>
</tr>
<tr>
<td>Tokat(13)</td>
<td>2005</td>
<td>2</td>
<td>monozygotic</td>
<td>Van der Woude</td>
</tr>
<tr>
<td>Ryan(14)</td>
<td>1988</td>
<td>2</td>
<td>monozygotic</td>
<td>Goldenhar</td>
</tr>
<tr>
<td>Kokavec(15)</td>
<td>2006</td>
<td>2</td>
<td>monozygotic</td>
<td>Goldenhar</td>
</tr>
<tr>
<td>Satoh(16)</td>
<td>1995</td>
<td>2</td>
<td>monozygotic</td>
<td>First and second branchial arch</td>
</tr>
<tr>
<td>Caswell(17)</td>
<td>2008</td>
<td>2</td>
<td>diazygotic</td>
<td>AEC</td>
</tr>
<tr>
<td>Jenwitheesuk</td>
<td>2010</td>
<td>2</td>
<td>monozygotic</td>
<td>AEC</td>
</tr>
</tbody>
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Fig. 10  Happier after treatments

demonstrates the safety of the surgical procedures used to correct this syndrome. Notwithstanding, our patients needed more intensive care with multidisciplinary teams for a suite of problems particularly regarding the alveolar cleft, maxillary hypoplasia, delayed speech, conductive hearing loss, otitis media, and frequent scalp infections. In addition, from a psychosocial perspective, the twins had to adapt themselves to the non-hospital world for acceptance and understanding—this is an ongoing process (Fig. 10).

Acknowledgements

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References

11. Cervenka J, Gorlin RJ, Anderson VE. The syndrome...