

Cases Report

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 (AEC) syndrome (or Hay-Wells syndrome) is a rare congenital malformation. Our first cases were a pair of female monozygotic twins with AEC syndrome at Srinagarind Hospital. In this study, we describe monozygotic female twins concordant for ankyloblepharon, ectodermal dysplasia and helical rim deformities, but discordant for cleft, syndactyly of toes, heart and urinary tract abnormalities. Twin A had syndactyly of the right third and fourth toes with incomplete bilateral cleft lip and complete bilateral cleft palate. Twin B had left ventricular enlargement, caliectasia of both kidneys with complete left unilateral cleft lip and cleft palate. The twins were treated by multidisciplinary teams with satisfactory results.

Keywords: Ankyloblepharon-ectodermal defects-cleft lip/palate syndrome, AEC syndrome, Hay-Wells syndrome, Monozygotic twins

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Ankyloblepharon-ectodermal defects-cleft lip/palate (AEC) 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

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Fig. 1 Pre-operative pictures of twin A: incomplete bilateral cleft lip, erosions and hemorrhagic crusts of her scalp with helical rim deformities



Fig. 4 Twin A: syndactyly of right third and fourth toes

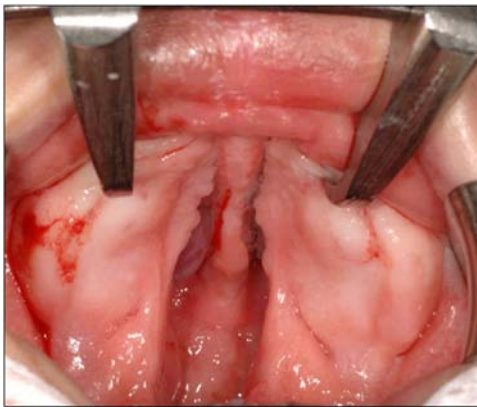


Fig. 2 Pre-operative pictures of twin A: complete bilateral cleft palate



Fig. 5 Twin A: at age five with maxillary hypoplasia and sparse hair



Fig. 3 Twin A: erosion of her palms and loss of the fingertips and cuticles



Fig. 6 Pre-operative pictures of twin B: complete left unilateral cleft lip, erosions and hemorrhagic crusts of her scalp with helical rim deformities

bilateral conductive hearing loss and bilateral myringotomy was performed. At two and half years of age, correction of lip and nose deformities was performed. At the time of this writing, she was 5 years of age and a speech pathologist and her family were taking care of her speech problems.

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 caliectasia 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,

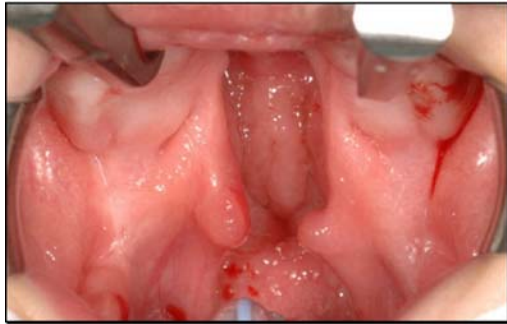


Fig. 7 Pre-operative pictures of twin B: complete left unilateral cleft palate



Fig. 8 Twin B: erosion of her palms and loss of the fingernails and cuticles

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⁽³⁾. 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⁽⁴⁾.

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⁽⁵⁻⁷⁾ 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



Fig. 9 Twin B: at age five with maxillary hypoplasia and sparse hair

and a more obtuse cranial base angle⁽⁸⁾. Other congenital malformations are about four times more likely in twins than singletons⁽⁹⁾. Syndromic cleft in twins varies between 8 and 14%⁽¹⁰⁾. 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)⁽¹⁷⁾. 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 fourth 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⁽¹⁸⁾. The role of p63 may also initiate the process of re-epithelialization⁽¹⁹⁾, migration⁽²⁰⁾ and muscle repair that affect wound healing⁽¹⁹⁾. 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^(21,22). Oral hygiene is reportedly similar to that expected in the general population of the same ages⁽²³⁾.

Our experience, confirmed by the literature,

Table 1. Syndromic cleft with twins

References	Year published	No. of Patients	Zygote development	Syndrome
Cervenka ⁽¹¹⁾	1967	2	monozygotic	Van der Woude
Hersh ⁽¹²⁾	1992	2	monozygotic	Van der Woude
Tokat ⁽¹³⁾	2005	2	monozygotic	Van der Woude
Ryan ⁽¹⁴⁾	1988	2	monozygotic	Goldenhar
Kokavec ⁽¹⁵⁾	2006	2	monozygotic	Goldenhar
Satoh ⁽¹⁶⁾	1995	2	monozygotic	First and second branchial arch
Caswell ⁽¹⁷⁾	2008	2	dizygotic	AEC
Jenwithesuk	2010	2	monozygotic	AEC



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).

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Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate (AEC) Syndrome ในผู้ป่วยแฝดชนิด ไข่ใบเดียว: รายงานผู้ป่วยแฝด 2 รายและทบทวนวรรณกรรม

กมลวรรณ เจนวิถีสุข, พลากร สุรกุลประภา, บวรศิลป์ เซาวนชื่น, จรูญ เจตศรีสุภาพ

Ankyloblepharon-ectodermal defects-cleft lip/palate (AEC) syndrome หรือ Hay-Wells syndrome เป็นความผิดปกติทางพันธุกรรมที่พบบ่อยมาก โดยผู้ป่วยเป็นแฝดเพศหญิงชนิด monozygotic twins ที่มารับการรักษาที่โรงพยาบาลศรีนครินทร์ด้วยกลุ่มอาการ AEC syndrome แผลทั้งคู่มีกลุ่มอาการลักษณะเดียวกันคือ ankyloblepharon, ectodermal dysplasia และกระดูกอ่อนใบหูผิดปกติ แต่มีลักษณะที่แตกต่างกันคือแฝดรายแรกนิ้วเท้าที่ 3 และ 4 ติดกัน และปากแหว่งเพดานโหว่ทั้งสองข้าง ส่วนแฝดรายที่สองเป็นปากแหว่งเพดานโหว่ของข้างซ้าย รวมทั้งมีความผิดปกติของหัวใจและไต ผู้ป่วยทั้งสองรายได้รับการรักษาโดยทีมสหสาขาวิชาชีพของโรงพยาบาลศรีนครินทร์ ซึ่งมีผลการรักษาเป็นที่น่าพอใจ
