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A Rare Presentation of Adams Oliver Syndrome - A Case Report

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Abstract
We are presenting a case of Adams Oliver Syndrome (AOS) in a newborn. This is rare congenital condition which presents with aplasia cutis congenita with transverse terminal limb defects with or without neurological manifestations. Diagnosis is based on clinical examination. Genetic diagnosis is available .Once the AOS-related pathogenic variants have been identified in an affected family member, molecular genetic prenatal testing for a pregnancy at increased risk and preimplantation genetic diagnosis for AOS are possible.

Keywords- *Adams Oliver Syndrome, Aplasia Cutis Congenita, Cutis Marmorata Telengiectatica Congenita.*

Introduction

Adams–Oliver syndrome (AOS) is a rare variably expressed congenital disorder characterized by the presence of aplasia cutis congenita (ACC) of the scalp and transverse limb defects.[1] AOS is classified as type 2 ACC under Frieden's classification that incorporates both ACC of the scalp and distal limb defects.[2] Other features in the form of neurological manifestations i.e. developmental delay, learning disabilities and structural abnormalities of brain. The first report of AOS was described as an autosomal dominant disorder by Adam and Oliver, however, further case reports suggested that its occurrence is more commonly sporadic.[1],[3]

Synonym- aplasia cutis congenita with terminal transverse limb defects

Case Report

A full term, appropriate for gestational age baby, was born to G3P2L2 mother by normal vaginal delivery with multiple congenital anomalies in the form of aplasia cutis (Fig.1) over the scalp with limb anomalies.

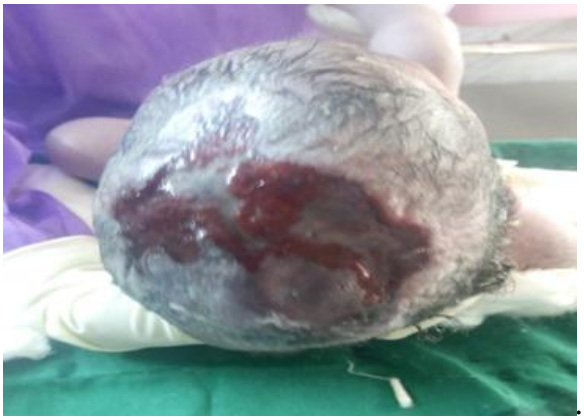

Fig.-1. Aplasia Cutis Congenita

Antenatal scan showed Rt. sided hydronephrosis without hydroureter, likely to be PUJ (pelvi-ureteric junction) obstruction. Baby cried immediately at birth and was admitted in NICU.

X ray of the wrist showed short terminal phalanges of all fingers. X ray of the left foot showed diffuse soft tissue swelling with deformed foot, absent metatarsal with congenital talipes equinovarus of left foot with a projection- tiny punctate calcific densities were noted in the region of metatarsals and phalanges of left foot most likely to be skeletal dysplasia. X ray of the right foot was normal.

Fig.2 Hypoplastic Left Foot

USG-KUB showed left sided gross hydronephrosis likely to be left PUJ obstruction while USG skull showed normal brain parenchyma.

Chest X Ray was normal.

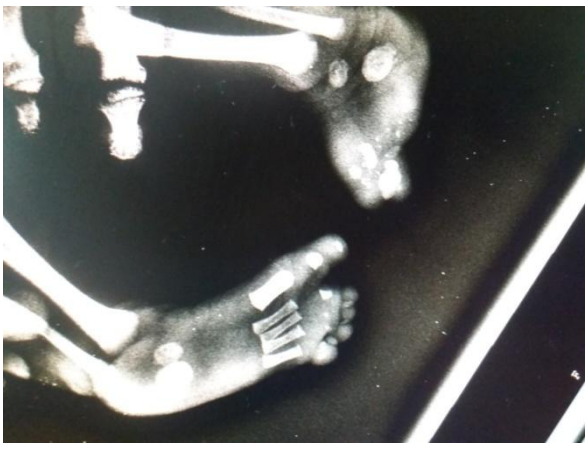

Fig.3 X Ray Foot

Discussion

The pathogenesis of AOS still remains obscure, but few have highlighted various hypothesis. The original description of Adam and Oliver suggested that there is an arrested development or agenesis of certain parts of the skeleton and soft tissue.[1] Later on, intrauterine compression and amniotic band sequelae was suggested as a pathogenic factor.[7] Vascular impairment during embryogenesis has been proposed as a possible mechanism by several authors.[8] Teratogenic factors, intrauterineinfections such as chickenpox, zoster orsimple herpes, fetal exposure to cocaine, heroin, alcohol or antithyroid drugs have all been implicated in the etiopathogenesis also.[9] In our case, the mother gave a history of frequent use of analgesics nature of which was unknown for abdominal pain during the first 3 months of pregnancy. Analgesics like a nonsteroidal anti-inflammatory drug (NSAID), readily cross the placental barrier in the first trimester of pregnancy and accumulate in the fetal tissue. Although there is a lack of evidence of risk of teratogenicity with NSAID during the organogenesis period in humans, one case of possible association of ACC with the use of diclofenac has been reported.[10]

The genetic defects in the bone morphogenic proteins pathway were found to be abnormal in these patients by Baskar et al. who thereby suggested that aberrant morphogenesis rather than vascular anomaly was the underlying pathology.[12]

Clinical Presentations-

AOS is characterized by the presence of variable combinations of ACC of the scalp, transverse limb defects, and cutis marmorata telengiectatica congenita (CMTC). The ACC typically involves the vertex of the scalp and less commonly areas such as the parietal scalp, trunk, and limbs. Scalp ACC may be accompanied with underlying bony defect leading to serious complications such as encephalocoele, meningitis, and hemorrhage.[3]

Probands and Family Members

Finding	Frequency 1
Cutis aplasia	~80%
Transverse terminal limb defects	~85%

Cardiac malformations ~23%
CMTC ~20%
Neurologic abnormalities Uncommon in AD & simplex AOS
~30% in AR kindreds
Ophthalmologic abnormalities <10%
Prenatal complications (intrauterine growth restriction or oligohydramnios) <10%
Renal abnormalities <5%
Adapted from Snape et al [2009] and the literature thereafter
A clinical criterion has been proposed for the diagnosis of AOS as outlined in [Table 1].[14]

Table 1: Proposed clinical criteria for diagnosis of Adams-Oliver syndrome

Criteria	Clinical feature
Major features	
Aplasia cutis congenita	Limited to scalp vertex may involve dura
Terminal transverse limb defects	
Family history of Adams-Oliver syndrome	Wide phenotypic variability
Minor features	
Cutis marmorata telengiectatica congenita	Livedo reticularis and superficial telengectesias
Congenital cardiac defect	Atrial septal defect, ventricular septal defect, tetralogy of Fallot, left sided obstructive lesions
Vascular anomaly	Arterial hypoplasia, hepatoportal sclerosis, broncho-pulmonary hemangioma, arterial aplasia

The presence of two major is sufficient for diagnosis while the combination of one major and one minor is denoted a high likelihood of AOS.

Our patient had limited expression of the disease, which included ACC of scalp and transverse limb defects.

Inheritance Pattern

Phenotypically, there are three types of AOS.[4] Type 1 autosomal dominant form with variable expression caused by heterozygous mutations in the ARHGAP31 gene, a Cdc42/Rac1 GTPase regulator. AOS type 2 is an autosomal recessive form, which can be caused by loss-of-function homozygous or compound heterozygous mutations in the DOCK6 gene, an atypical guanidine exchange factor known to activate Cdc42 and Rac1. AOS type 3 is an autosomal dominant form, which can be caused by heterozygous mutations in the RBPJ gene, a primary transcriptional regulator for the Notch signaling pathway.[4] To establish the extent of disease and needs in an individual diagnosed with Adams-Oliver syndrome (AOS), the following evaluations are recommended.

Summary

Clinical characteristics. Adams-Oliver syndrome (AOS) is characterized by aplasia cutis congenita (ACC) of the scalp and terminal transverse limb defects (TTLD). ACC lesions usually occur in the midline of the parietal or occipital regions, but can also occur on the abdomen or limbs. At birth, an ACC lesion may already have the appearance of a healed scar. ACC lesions less than 5 cm often involve only the skin and almost always heal over a period of months; larger lesions are more likely to involve the skull and possibly the dura, and are at greater risk for complications, which can include infection, hemorrhage, or thrombosis, and can result in death. The limb defects range from mild (unilateral or bilateral short distal phalanges) to severe (complete absence of all toes or fingers, feet or hands, or more, often resembling an amputation). The lower extremities are almost always more severely affected than the upper extremities. Additional major features frequently include cardiovascular malformations/dysfunction (23%), brain anomalies, and less frequently renal, liver, and eye anomalies.
Diagnosis/testing. The diagnosis of AOS can be established in a prob and with one of the following:
Clinical findings of ACC of the scalp and TTLD
ACC or TTLD and a first-degree relative with findings consistent with AOS
ACC or TTLD and either a pathogenic variant in an autosomal dominant AOS-related gene (ARHGAP31, DLL4, NOTCH1, or RBPJ) or two pathogenic variants in an autosomal recessive AOS-related gene (DOCK6 or EOGT)

Management Treatment of manifestations

ACC: Care by a pediatric dermatologist and/or plastic surgeon depending on severity. Goals of non-operative therapy are to prevent infection and

promote healing. Large and/or deep lesions with calvarial involvement require acute care and may eventually also require reconstruction by a neurosurgeon.

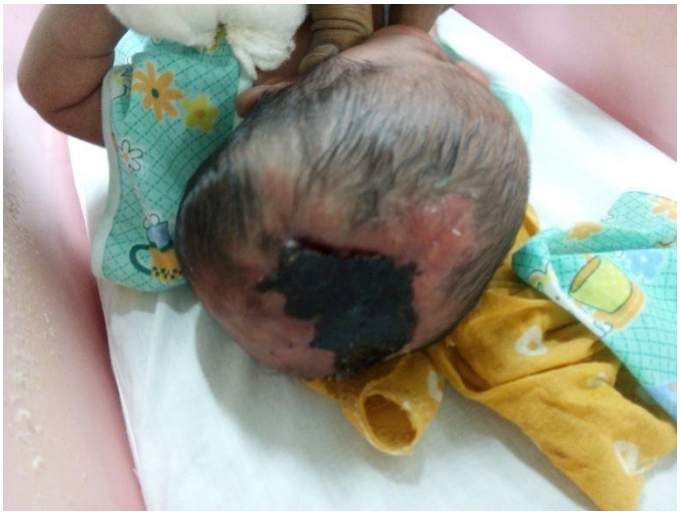

Fig.4-Aplasia Cutis Congenita In Healing Stage

Limb: Many AOS limb anomalies are not severe enough to require surgical or prosthetic intervention. Occupational therapy and/or physical therapy are used as needed to assist with limb functioning. Rarely, surgical intervention for hand malformations is indicated.

Surveillance: Cardiovascular: Echocardiography annually until age three years for signs of pulmonary hypertension.

Neurologic: Annual pediatric care, including neurologic examination and ongoing assessment of psychomotor development.

Ocular: Annual assessment by pediatric ophthalmologist until age three years for evidence of abnormal retinal vascular development.

Differential Diagnosis

Syndromic Aplasia Cutis Congenita (ACC)

Scalp-ear-nipple (SEN) syndrome (Finlay-Marks syndrome; OMIM). Clinical findings include the following:

Treatment of Manifestations Multidisciplinary appr-oach by consultating a plastic surgeon regarding aplasia cutis congenita (ACC), dermatologist for cutis marmorata telangiectatica congenita (CMTC), neurosurgeon in children with a significant calvarial defect and pediatric cardiologist provides individualized approach.

Limb malformations may warrant consultation with specialists in orthopedics, plastic surgery, and/or rehabilitation medicine. X-rays of limbs are often performed immediately after birth but are most informative, in terms of delineating the extent of involvement, after age one year.

Many AOS limb anomalies are not severe enough to require surgical or prosthetic intervention.

Occupational therapy and/or physical therapy is used as needed to assist with limb functioning, such as to improve walking and running stability in those with abnormal toes.

Early physiotherapy can maximize motor function and range of motion.

Surveillance

Cardiovascular

Echocardiography annually until age three years for signs of pulmonary hypertension

Consideration of abdominal ultrasound examination for signs of portal hypertension in those with failure to thrive, persistent nausea, abdominal swelling, or black stools

Neurologic

Annual pediatric care, including neurologic examination and ongoing assessment of psychomotor development

Ocular-

Annual assessment by pediatric ophthalmologist until age three years to identify those with abnormal retinal vascular development.

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