Case Report

A case report on Adam oliver symdrome

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Abstract

Adam Oliver Syndrome (AOS) is a rare congenital disorder which follows autosomal dominant inheritance. However, autosomal recessive inheritance cases have also been reported too. The genes involved are ARHGAP31 or RBPJ gene. When inherited in an autosomal recessive manner, the gene that is mutated are DOCK6 or EOGT gene[1]. This syndrome causes scalp, skull and limb abnormalities in association with heart, eyes, skin abnormalities. It is believed to occur due to interrupted blood flow in certain blood vessels during the fetal developmental stage. Some cases may be very mild while others may be severe. In AOS, scalp defects are present with or without multiple hairless scarred areas that may have abnormally dilated blood vessels under the affected skin. It may also include underlying defects of the bones of the skull, hypoplasia of the hands, arms, feet or legs, glaucoma, cataract, ventricular or atrial septal defects, etc. Cutis Marmorata Telangiectatica Congenita (CMTC), Trisomy 13, Bart Syndrome also has similar features. However, the diagnosis may be confirmed by a detailed patient history, clinical examination and a variety of specialized tests, such as CT Brain, MRI Brain, Ultrasonic B scan. This case reports discusses a 2 day old, male baby with aplasia cutis, hypoplasia of bilateral toes and fingers, atrial septal defect, both eyes microphthalmos and micro cornea, right eye sclerocornea with left eye albinotic fundus.

Key Words: Adam oliver symdrome.

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INTRODUCTION

Adam Oliver Syndrome (AOS) has been described first by F. Adams and C.P. Oliver in 1945 in 8 members of the same family[2]. Stittrich *et al*[3] (2014) stated that the incidence of AOS is approximately 1 in 225,000 individuals. It is a very rare congenital disorder that causes scalp, skull, and limb abnormalities. According to National Organization for Rare Disorders (NORD)[4], this genetic disorder has been reported to be running in multiple members of same families for more than one generation. When one or both parent(s) have Adams-Oliver Syndrome, the risk of a child being born with this disorder is 25-50% which increases if the parents have a consanguineous marriage. There is also no racial or ethnical preference noticed. Hoyme *et al*[5] found that the placentas from patients with AOS contained multiple organized thrombi throughout large fetal main stem villous vessels. They hypothesized that an in-utero vascular thrombotic accident led to interruption of blood supply to developing structures. Others suggested that AOS is the result of the thrombotic interruption of embryonic blood supply in the subclavian or vertebral arteries or interruption of the early embyonic blood supply[6]. Swartz *et al*[7] suggested that the abnormalities in AOS develop because of a generalized abnormality in small vessels causing disruption of blood flow. These small vessel irregularities would account for the aplasia cutis congenita (characterized by the lack of skin and hair in certain areas, mostly scalp), terminal transverse limb defects, as well as the cardiac, hepatic, and pulmonary vascular lesions. The vascular anomaly in AOS could be the result of a gene defect causing decreased stability of embryonic blood vessels toward tensile forces during the period of 6 to 8th week of embryonic life. The other features include[7,4,1]:

- Growth deficiency
- Alopecia
- Ascitis, Cirrhosis, Congenital hepatic fibrosis

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- Esophageal variz
- Bradydactyly syndrome
- Absense of fingernails, Syndactyly
- Various intracranial abnormalities have been described such as encephalocele, microcephaly, hypoplasia of the left arteria cerebri, medial and right spastic hemiplegia, cortical dysplasia, pachygyria, hypoplastic corpus callosum, parenchymal calcifications, abnormal cerebral vasculature, ventriculomegaly and dysplasia of the cerebral cortex. As a consequence, secondary symptoms, such as epilepsy and mental retardation are frequently found in AOS patients[8]
- Complete or partial absence of an arm and/or leg (transverse limb defects)
- Hypoplasia of the fingers, toes, hands, and/or feet which causes abnormally short fingers and/or toes due to underdevelopment or absence of metacarpals and/or terminal phalanges.
- Ventricular septal defect (VSD), Atrial septal defects (ASD) and tetralogy of Fallot
- Intellectual disabilities
- Pulmonary hypertension, pulmonary artery atresia
- Ocular manifestation - strabismus, glaucoma, cataract, prominent iris vessels, microphthalmos, microcornea, leucoma, sclerocornea, optic disc drusens, retinal folds, bilateral retinal detachment, rod dystrophy, posterior retinal arterial narrowing and venous dilatation with combined (arterial and venous) blood column segmentation (boxcarring appearance), incomplete retinal vascularization with gliosis, and intravitreal neovascularization.[9,10]

The clinical diagnosis of Adams-Oliver Syndrome is made when one condition from major and one from minor criterion is present[1]:

Major Criteria

- Limb defects
- Aplasia cutis congenital (absence of skin)
- Family history of Adams Oliver Syndrome

Minor Criteria

- Cutis marmorata (skin has marbled appearance in cold temperatures)
- Congenital heart defect
- Vascular problems

CASE REPORT

A 2 day old, full term male baby, was referred to the Department of Ophthalmology in view of congenital anomaly screening. The informant was the mother. The baby was born of a non consanguineous marriage, at 36 weeks of gestation by a Lower Segment Caesarean section, indication being breech presentation. Postoperatively, there were no complications. The mother is 26 years old, $G_3L_3A_0$. The first and the second child do not have any such anomalies. No history of smoking, drinking or intake of any drugs during pregnancy. No history of any systemic illness or exposure to radiation during pregnancy. No family history of AOS, mental retardation, or central nervous system abnormalities. The baby's general condition was stable. Baby was afebrile and irritable. There was no evidence of any cyanosis, pallor, icterus, oedema or any evident lymphadenopathy on palpation of pre auricular and submandibular lymph nodes. Systemic examination was normal. Birth weight was 2.50kgs with head circumference of 34cm. The baby had hyoplasia of left hand (Figure 1), hypoplasia of bilateral toes (Figure 2), wide open anterior fontanelle (6x4cm), anti mongoloid slant, short neck, scapocephaly, sparse eyebrows, low set ears, setting sun sign, mildly high arched palate, depressed nasal bridge, absent hair patch on scalp over right frontoparietal region (8x2cm) (Figure3) and hypotelorism. Ocular examination on torch light, during vision assessment. Visual axis is misaligned - alternating esotropia (Figure 4). Both eyes seem to be small, suggestive of microphthalmos. Patient had mild conjunctival congestion and sticky discharge in both eyes. There was a whitish opacity on the right eye cornea, suggestive of sclerocornea (Figure 5) which was covering half the pupil temporally due to which temporal margin of pupil was not seen clearly. Cornea of both eyes seemed to be smaller than the normal size (9.5-10.5 mm) suggestive of microcornea (RE>LE). Pupils were irregular in shape, reacting to light. Left eye had a pupillary tag. On distant direct ophthalmoscope, fundus glow was absent in right eye and present in left eye. Examination was performed under sedation. For dilated fundus examination, tropicamide and phenylephrine eye drops were instilled in both the eyes. On dilatation, both pupils appeared irregular in shape. On indirect ophthalmoscope, right eye had dull glow due to the sclerocornea. Therefore, detailed fundus examination could not been done. However, posterior synechiae was noted. On examination of the left eye, fundus appeared to be albinotic. Right eye B-scan was done which showed no obvious posterior segment abnormality. Neurosonography revealed no significant abnormality, no evidence of hydrocephalus, intracranial haemorrhage or any space occupying lesion. 2D ECHO was suggestive of small atrial septal defect (1.5mm) with left to right shunt. Blood investigation and chest x-ray appeared normal. Karyotyping was done which was suggestive of Male 46, XY.

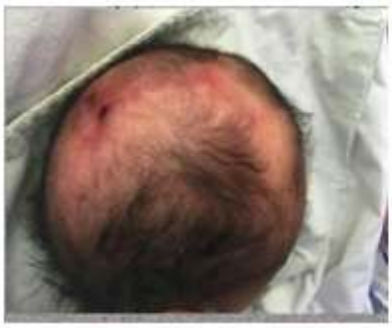

Figure 1

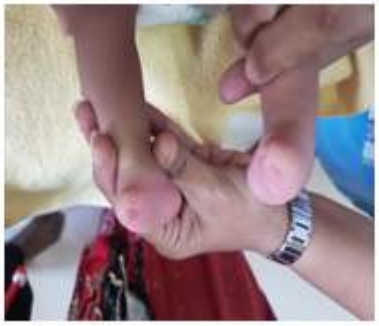

Figure 2

Figure 3

Figure 4

Figure 5

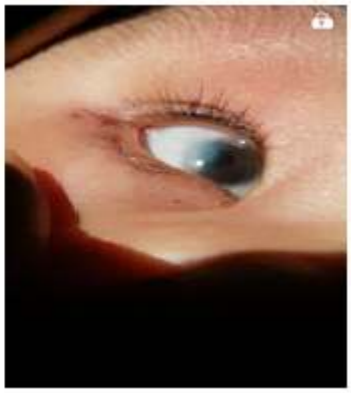

Figure 6

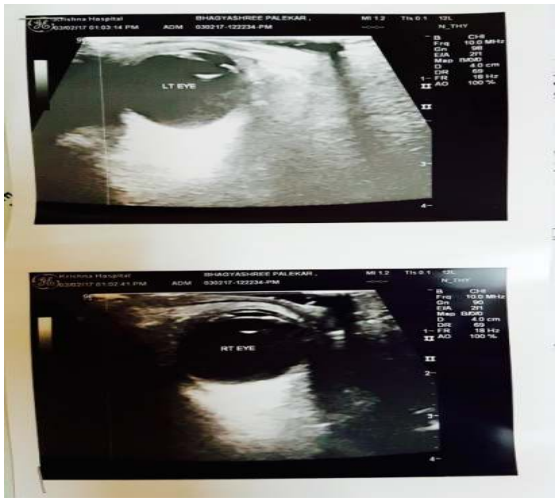

Figure 7

DISCUSSION

Adam Oliver Syndrome (AOS) is a rare congenital disorder which is believed to occur due to interrupted blood flow in certain blood vessels during the fetal developmental stage. It is characterised by multiple congenital anomalies as described above. Autosomal dominant forms of Adams-Oliver syndrome include AOS3, caused by mutation in the RBPJ gene on chromosome 4p15; AOS5, caused by mutation in the NOTCH1 gene on chromosome 9q34; and AOS6, caused by mutation in the DLL4 gene on chromosome 5q32. Autosomal recessive forms of Adams-Oliver syndrome include AOS2, caused by mutation in the DOCK6 gene on chromosome 19p13.2, and AOS4, caused by mutation in the EOGT gene on chromosome 3p14. AOS1 is caused by heterozygous mutation in the ARHGAP31 gene on chromosome 3q13[3]. This syndrome causes multiple congenital anomalies which could lead to multiple

complications. For example, there is high risk of meningitis in these patients as scalp deformities may bleed or may become the entry point for germs, disabilities caused due to the limb defects, heart defects may progress to heart failure, if it is not promptly diagnosed and treated. Management of microphthalmia is mostly supportive. In this cases, the good eye can be patched first to strengthen vision in the microphthalmic eye. A prosthesis can be made to cap the microphthalmic eye to help with cosmetic appearance, while preserving the remaining sight. Prosthesis are sometimes used to stimulate the growth of the socket. Other treatment options for micropthalmia are socket expanders Microphthalmia and sclerocornea may cause visual disturbances and learning disabilities. Baby has high chances of being hypermetropic due to microphthalmia and microcornea. Sclerocornea can be treated by keratoplasty. In patients with albinotic fundus, due to lack of melanin pigments, choroidal vessels become prominent. Treatment is directed toward correcting refractive errors and lessening the photophobia with dark glasses or tinted contact lenses. The treatment of Adams-Oliver syndrome is directed toward the specific symptoms. Skin grafting, cranial surgery, and/or other surgical procedures may be required for affected individuals who exhibit underlying defects of the bones of the skull. This case report highlights the importance of antenatal care, detailed checkup in the antenatal period. Prenatal testing is encouraged, as it allows the healthcare provider to assess the risk of developing the disorder in the child, and provide supportive measures at an early stage. Genetic testing of the expecting parents (and related family members) and prenatal diagnosis (molecular testing of the fetus during pregnancy) may help in understanding the risks better during pregnancy. If the family history is positive, then genetic counselling will help assess risks, before planning for a child.

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