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Unveiling a Rare Case of Neonatal Terminal Limb Anomalies with Bilateral Toenail Agenesis and Clubfoot: A Potential Variant of Adams-Oliver Syndrome

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ABSTRACT

Congenital anomalies involving terminal limb defects and nail hypoplasia are uncommon and may signify an underlying syndromic etiology. We report the case of a term female neonate born with absent great toenails bilaterally, congenital talipes equinovarus (CTEV), and radiologically absent talus on one side, along with distal phalanx deficiency. Antenatal ultrasound had indicated fetal growth restriction (FGR), two-vessel umbilical cord, and mild irregular bubble. Postnatal clinical examination, radiological evaluation, and pending genetic studies suggest a provisional diagnosis of Adams-Oliver Syndrome (AOS), a rare genetic disorder known for scalp and limb anomalies. The absence of scalp lesions, however, highlights a broader phenotypic variation. This case underlines the importance of a multidisciplinary approach, early imaging, genetic counseling, and the need to consider AOS even in the absence of classical findings.

Keywords: *Adams-Oliver Syndrome, Limb anomalies, Congenital nail agenesis, Clubfoot, Terminal transverse limb defects, Congenital talus absence*

1. INTRODUCTION

Congenital anomalies affecting the limbs and nails raise immediate suspicion for underlying genetic syndromes. One such rare condition is Adams-Oliver Syndrome (AOS), a genetically heterogeneous disorder primarily presenting with aplasia cutis congenita (scalp skin defects) and transverse limb defects. In recent years, phenotypic variability has broadened the diagnostic spectrum, particularly in cases without classic scalp involvement. Early recognition is essential for comprehensive management, including orthopedic, genetic, and developmental interventions.(1,2,4)

Adams-Oliver Syndrome (AOS) is a rare congenital disorder with an estimated prevalence of **1 in 225,000 live births**, characterized classically by a combination of **scalp defects** (aplasia cutis congenita) and **limb anomalies**, primarily involving terminal transverse limb defects. The syndrome was first described by **Drs. Forrest H. Adams and Clarence Paul Oliver** in 1945 after observing a familial pattern of these distinct abnormalities, hence the eponym "Adams-Oliver."

The hallmark diagnostic criteria for AOS include(11,12):

1. Aplasia cutis congenita of the scalp
2. Terminal transverse limb defects
3. Nail hypoplasia or agenesis
4. Cardiovascular anomalies (in some variants)
5. Cutis marmorata telangiectatica congenita (CMTC)

In this report, we present a case from a tertiary care center in North India of a neonate born with bilateral absent great toenails, unilateral talus aplasia, and bilateral clubfoot deformity. The constellation of findings, alongside suggestive prenatal indicators, directed us toward a diagnosis of AOS. The case underscores the significance of recognizing subtle phenotypic variations and the evolving understanding of this syndrome.

2. CASE REPORT

A female neonate was delivered vaginally at term at N.C. Medical College & Hospital, Panipat, on June 1, 2025, at 12:40 am. The baby weighed 2.3 kg at birth and cried immediately after delivery. There were no perinatal complications. The mother, a 32-year-old multigravida, had received regular antenatal care. Third-trimester obstetric ultrasound performed at 35 weeks revealed fetal growth restriction (abdominal circumference and estimated fetal weight <3rd percentile), single umbilical artery, and a mildly irregular bladder bubble. No gross structural anomalies were reported.

Table 1 : Gestational Assessment

Assessment Type	Gestational Age	Estimated Due Date (EDD)
By Previous USG	38 weeks 5 days	08.06.2025
By Current USG	35 weeks 1 day ± 1 week	03.07.2025

Note: EDD is most accurate by 1st–2nd trimester scans.

Table 2 : Observations

Parameter	Findings
Fetal Heart Action	Present – 131 bpm
Physical Activity	Present
Presentation	Cephalic
Cervical Length	Adequate
Internal Os	Closed
Cord Around Neck	Single loop present
Cord Description	Two-vessel cord (single umbilical artery)
Umbilical Flow	Forward diastolic flow
Placenta	Fundoposterior, away from os
Amniotic Fluid Index (AFI)	Adequate (11–12 cm)
Fetal Bladder	Mildly irregular bubble (communicates with urethra)
HUN Seen?	No

Table 3 : Fetal Biometry

Parameter	Measurement (cm)	Gest Age (wks+days)	Percentile
BPD (Biparietal Diameter)	8.74 cm	35w 2d	4.55%
HC (Head Circumference)	31.78 cm	35w 5d	<3%
AC (Abdominal Circumference)	30.68 cm	34w 5d	<3%
FL (Femur Length)	6.83 cm	35w 1d	<3%
EFW (Estimated Fetal Weight)	**2547 grams ± 377g**		**<3%**

Table 4 : Color Doppler Studies

Doppler Parameter	Value	Percentile
MCA PI (Middle Cerebral Artery)	2.1	98%
UA PI (Umbilical Artery)	0.72	26%
CPR (Cerebroplacental Ratio)	2.92	99%
Right Uterine Artery PI	0.7	—
Left Uterine Artery PI	0.6	—
Mean Uterine PI	0.64	45%

Postnatal examination revealed:

- Bilateral absence of toenails of the great toes
- Right-sided congenital talipes equinovarus (CTEV)
- Left clubfoot deformity
- No scalp defects or skin lesions
- No facial dysmorphism or cardiovascular abnormalities on clinical examination
- Normal external female genitalia

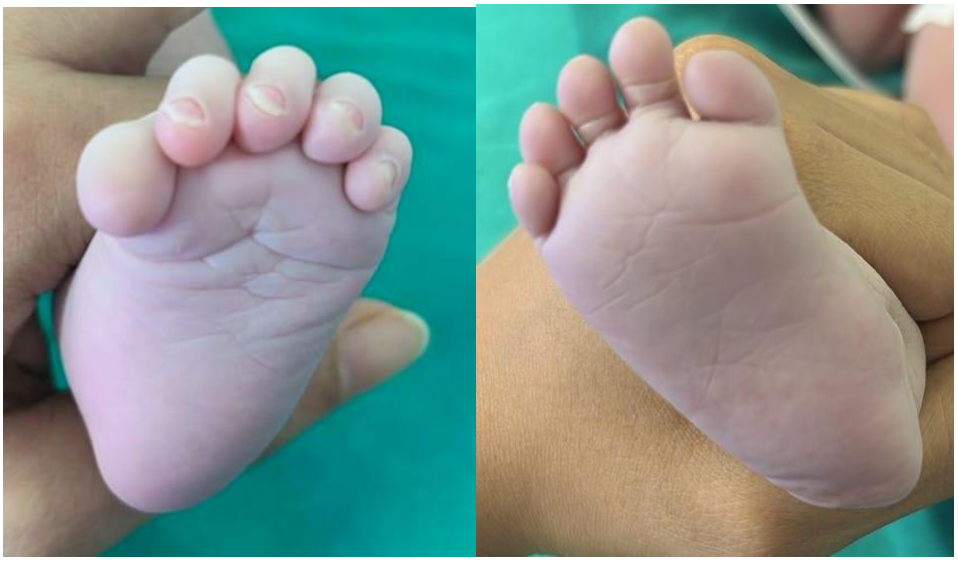

Figure 1 : Postnatal findings

X-rays showed:

- Absence of the talus in one foot
- Missing distal phalanx (likely of the great toe)
- No limb shortening or bony fusions otherwise

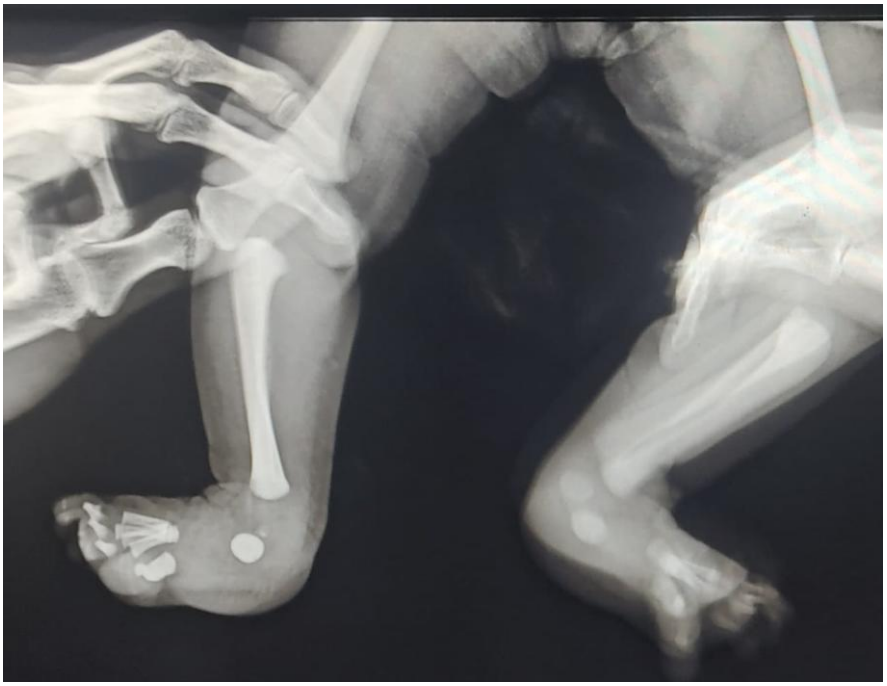

Figure 2 : Xray findings

Further imaging and evaluations initiated:

- Karyotyping and chromosomal microarray (CMA) testing
- MRI of the spine (to rule out occult dysraphism)
- Skeletal survey
- Brain ultrasound
- Ophthalmologic and ENT assessments (pending)

The parents were counseled and consented for genetic evaluation. There was no family history of similar anomalies, spontaneous abortions, or known genetic syndromes. No drug intake, infections, or radiation exposure was reported during pregnancy.

In the present case, the **absence of scalp defects** makes it an **incomplete or variant presentation** of AOS. However, the combination of **bilateral toenail agenesis**, **absence of distal phalanges**, **clubfoot (CTEV)**, and **hypoplastic/missing talus** aligns with the **limb phenotype spectrum** of Adams-Oliver Syndrome. The lack of facial dysmorphism or cardiac involvement further supports a **mild or atypical variant**. Genetic confirmation (e.g., mutations in ARHGAP31, RBPJ, or NOTCH1) would strengthen the diagnosis but was unavailable at the time of this report.

This case thus adds to the growing spectrum of phenotypic variability observed in AOS, highlighting the importance of **clinical suspicion even in the absence of scalp findings**, especially when **multiple terminal limb anomalies** and **nail hypoplasia** coexist.

3. DISCUSSION

Adams-Oliver Syndrome (AOS) was first described in 1945 and is typically characterized by aplasia cutis congenita of the scalp and terminal transverse limb defects. However, emerging literature points to phenotypic variability, including isolated limb anomalies without scalp involvement. Genetic mutations implicated in AOS include DOCK6, ARHGAP31, NOTCH1, EOGT, and RBPJ, among others.

Our case presented a diagnostic challenge due to the absence of the scalp component. However, the presence of bilateral terminal toe anomalies, talar agenesis, and clubfoot raised high suspicion of a syndromic cause. Differential diagnoses such as amniotic band sequence were considered but ruled out due to bilateral and symmetrical involvement. Limb-Mammary Syndrome, another TP63-related condition, was considered but lacked associated mammary or ectodermal anomalies.

A similar phenotypic variant of AOS without scalp involvement was described by Sukalo et al. (2015), who reported EOGT mutations in such patients. Another large-scale review by Stittrich et al. (2014) noted wide genotypic and phenotypic

variation in AOS, further supporting the plausibility of our diagnosis.(1,4)

Adams-Oliver Syndrome has no significant gender predilection. Life expectancy is typically normal in patients without major organ involvement. Our case, presenting with isolated limb and nail anomalies, aligns with a favorable prognosis. Long-term concerns may include developmental delay due to foot deformities and potential need for orthopedic correction.

This case reinforces the evolving clinical picture of AOS and the need for heightened clinical suspicion, even in atypical presentations. Genetic confirmation will guide prognosis, recurrence risk estimation, and tailored multidisciplinary follow-up, including orthopedic, genetic, and developmental support.

4. CONCLUSION

We present a neonate with congenital clubfoot, absent great toenails, and talus agenesis—an atypical yet compelling presentation of Adams-Oliver Syndrome. While genetic testing results are awaited, the clinical constellation supports a syndromic diagnosis. Early recognition and comprehensive workup are critical for management and family counseling. This case highlights the expanding phenotype of AOS and the importance of individualized diagnostic approaches in congenital anomaly syndromes.

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