A Case of Adams-Oliver Syndrome

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Case Presentation

A one-month-old female presented to the dermatology clinic for evaluation of scalp aplasia cutis congenita (ACC) and terminal transverse limb defects (TTLD). She was born at 38 weeks by an uncomplicated vaginal delivery and was found to have a 5x3 cm, stellate area of ACC on the vertex scalp (Images 1-2), hypoplastic toenails, pan-brachydactyly of her toes, and mild syndactyly of her second and third bilateral toes (Images 6-7). An echocardiogram prior to hospital discharge was unremarkable. She was discharged home with bacitracin for wound care of her scalp ACC.

Her family history was remarkable for similar scalp ACC in her mother which was repaired at 3 years of age as well has brachydactyly of her toes and a small atrial septal defect. Her maternal uncle was born with a small patch of alopecia and a septal defect. The patient met the three major criteria for the diagnosis of Adams-Oliver Syndrome (AOS): large stellate aplasia cutis congenita of the scalp, terminal transverse limb defects, and a positive family history. The diagnosis of AOS prompted further workup with abdominal ultrasound and ophthalmologic exam which were normal, and referrals to cardiology, plastic surgery, orthopedics, and genetics.

Genetic workup revealed a heterozygous mutation in NOTCH1 at c.1441 G>A, variant p.Gly481Ser.

The patient's course was complicated by repetitive bleeding from a superficial scalp vein which required admission and transfusion. A CT head showed a large calvarial defect of absent to demineralized and thinned bone along the midline parietal bones measuring 5.5x3.9cm (Images 3-4). Brain MRI, MRA, and MRV were normal, but superficial serpentine scalp veins were noted in the region of the defects prompting protective skin grafting by plastic surgery.

The skin grafting was successful and the patient had no further complications (Image 5). She was fitted for a protective helmet at 3 months of age, and has otherwise been healthy and meeting normal developmental milestones.

Table 1

AOS Genes	Inheritance Pattern	AOS Features	Unique Reported Features
ARHGAP31	AD	ACC & TTLD	No reported systemic anomalies
NOTCH1	AD		Skull defects, Congenital heart defects, brain anomalies, portal HTN and GI varices, lymphedema
DLL4	AD		Skull defects, Congenital heart defects-pulmonary artery stenosis, brain anomalies
RBPJ	AD		Congenital heart defects
EOGT	AR		Skull defects, brain anomalies
DOCK6	AR		Brain and eye anomalies, intrauterine growth restriction

Clinical Presentation

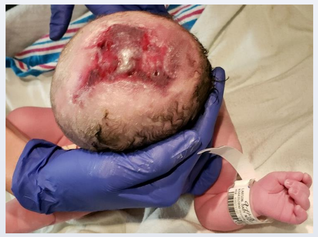

Image 1: ACC at birth

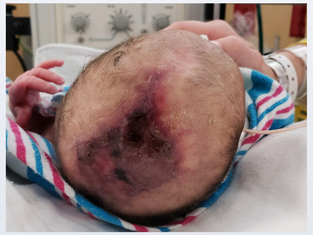

Image 2: ACC at 1 week old

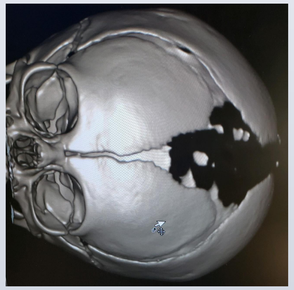

Image 3: Frontal view of calvarial defect

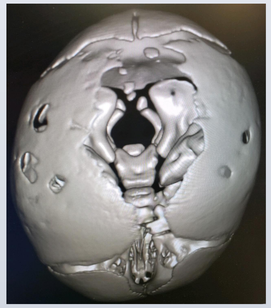

Image 4: Axial view of calvarial defect

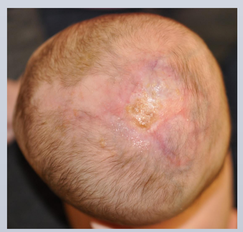

Image 5: ACC s/p skin graft

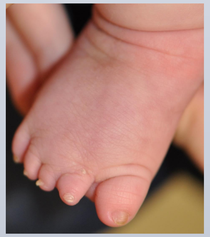

Image 6: Right brachysyndactyly

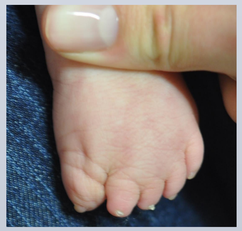

Image 7: Left brachysyndactyly

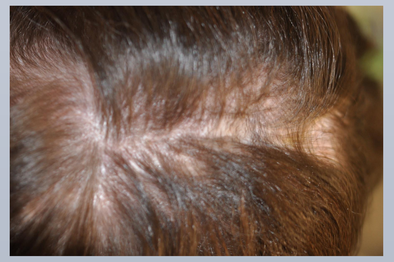

Image 8: Maternal ACC s/p tissue expander and cranioplasty

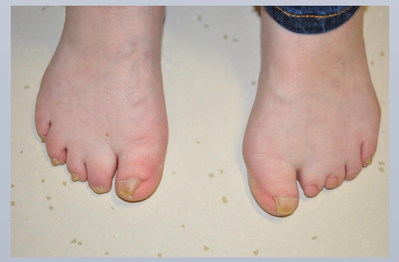

Image 9: Maternal brachysyndactyly

Discussion

Adams-Oliver Syndrome was first described in 1945. It is a rare condition which is characterized by stellate aplasia cutis congenita of the scalp and terminal transverse limb defects. Six causative genes have been identified to date: ARHGAP31, DOCK6, EOGT, RBPJ, NOTCH1, and DLL4.

Our case demonstrates a previously un-reported type of NOTCH 1 mutation of the c.1441 G>A, p.Gly481Ser variant. Our patient and her mother both demonstrated large, stellate ACC with underlying skull defects in addition to brachysyndactyly of the toes. NOTCH1 mutations in AOS have reported associations with higher risk for underlying skull involvement, hemorrhage from scalp veins and the dural sinus, congenital heart defects such as pulmonary artery stenosis and septal defects, brain anomalies, portal hypertension, and lymphedema when compared to other variants. Genetic testing is important for AOS patients as the six reported genes each have different reported systemic associations that can guide screening (Table 1).

Given the variety of systemic associations, regular screening is important for AOS patients. An annual echocardiogram and annual ophthalmologic exam is recommended for AOS patients until the age of 3 to monitor for possible pulmonary artery stenosis, septal or valvar defects, and retinal vascular anomalies. An abdominal ultrasound should be considered, especially in NOTCH1 variants, given reports of portal hypertension and GI varices. Skull and brain imaging is necessary in patients with larger lesions and in those with mutations associated with increased reports of underlying skull or brain involvement. Orthopedic, PT, and OT involvement may be necessary for patients with severe TTLDs.

Careful wound management is important in AOS patients. Standard wound care involves silver coated, non-adherents with overlying silicone or hydrocolloid dressing. It is important to avoid a dry wound as this can lead to traumatic separation of an overlying eschar or crust and cause bleeding or trauma to the sagittal sinus or vein. In cases with underlying skull involvement, such as in our patient, a helmet should be worn, usually around 3 months when mobility increases. Cranioplasty can be considered around age 3 to 4 years of age.

References

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