

Index of Suspicion in the Nursery

1 A Newborn with Absence of Right Forearm, Preauricular Pit, and an Infantile Hemangioma

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CASE PRESENTATION

AUTHOR DISCLOSURE Drs Reddy Mandadi, Castillo, Mendez, and Rajegowda have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

A female infant is born at 35 weeks' gestation to a 19-year-old Hispanic woman and a 21-year-old Hispanic man. The infant has a birthweight of 2,710 g (10th–25th percentile), length of 46.5 cm (10th–25th percentile), and head circumference of 34.1 cm (10th–25th percentile). Apgar scores at 1 and 5 minutes are 9 and 9, respectively. Her physical examination is remarkable for bilateral ear pits, absence of distal two-thirds of the right forearm and hand, and a stump with rudimentary fingers (Fig 1). Good range of motion was observed at the right elbow and shoulder. The left upper extremity and both lower extremities are normal. All her limbs have a good range of motion. No other dysmorphic features are present and the rest of her physical examination findings are unremarkable. A right extremity radiograph shows congenital absence of the right hand, with hypoplastic right forearm bones and a normal right humerus (Fig 2). Her nursery stay is uneventful and the patient is discharged with her mother.

The antenatal period had been uncomplicated and all maternal laboratory test results are unremarkable. Besides polycystic ovarian disease and a missed abortion 1 year before this pregnancy, the mother denies radiation exposure, trauma, medications, or chorionic villous sampling. The family history is negative for congenital anomalies but the father has bilateral ear pits as well. Prenatal ultrasonography at 7, 21, and 33 weeks did not identify any fetal abnormalities. The placental pathology did not show any evidence of amniotic bands.

During the fourth month health supervision visit, a grade II/VI systolic ejection murmur is identified and echocardiography does not show any congenital abnormalities, pointing toward a functional heart murmur. A hemangioma measuring 1×1 cm of the left labia majora is present (Fig 1), with normal external genitalia and anal opening. No genitourinary abnormalities are found on renal and bladder ultrasonography.

A comprehensive metabolic panel and complete blood cell count are within normal limits. Her karyotype is 46,XX. Microarray testing shows absence of heterozygosity, which can be indicative of uniparental disomy. These genomic findings are considered to be of uncertain clinical significance.

At 18 months of age, the patient is growing and developing well and her multidisciplinary care includes genetics, cardiology, rehabilitation medicine, and general pediatrics.



Figure 1. Physical findings seen in our patient. A. Hypoplastic right arm with absence of distal two-thirds of the right forearm and hand, with rudimentary fingers. B. Bilateral preauricular pits that were also present in the patient's father. C. A superficial hemangioma in the vaginal area.

DISCUSSION

Transverse limb defects (TLDs) are rare congenital abnormalities seen in approximately 3.5 to 6.9 per 100,000 births. (1) Most cases are sporadic and not associated with other abnormalities. Skeletal changes are commonly associated with vascular malformations while they are rarely seen in conjunction with hemangiomas. (2) To our knowledge, there has been no report to date of an association of TLD with perineal hemangioma and preauricular pits.

TLD is defined as a partial or complete absence of 1 or more fetal limbs beyond a certain point across the long axis. It is caused by disruption in the apical ectodermal ridge due to insults such as ischemia, bleeding, or chromosomal mutations, during the fourth to eighth week of gestation. One large study showed that the causes include vascular disruption in 35%, genetic factors in 24% of cases, aneuploidy in 6%, and teratogens in 4%, with 32% of cases being sporadic. (1) Other causes include chorionic villus sampling performed before the 10th week of gestation, maternal diabetes, and amniotic bands. Limb defects are not identified on prenatal ultrasonography in 45% of the cases. When multiple malformations are present, cardiovascular and urinary tract anomalies are common in combination with congenital limb defects (37% and 25% of cases), but digestive tract anomalies are significantly associated with congenital limb defects. Rare minor anomalies associated with TLDs include hemangiomas (<1% of cases) and ear malformation (<0.7% of cases). (3) Hemangiomas usually present in the neonate in the first 2 weeks and most commonly involve the head and neck area. Perineal hemangiomas are rare, and their presence should raise the suspicion of an underlying major anomaly. (4)

Multiple anomalies in this patient may be sporadic, vascular, or chromosomal in origin. As previously discussed, the presence of the 3 anomalies seen in our patient is extremely rare, raising the suspicion of a common etiology. Currently,

well-known syndromes such as posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye abnormalities (PHACE); spinal dysraphism, anogenital, cutaneous, renal and urologic anomalies, associated with an angioma of lumbosacral localization (SACRAL); and familial angiomas were reported initially as incidental findings in patients. This enhances the importance of further evaluation and close monitoring of our patient to identify other probable underlying abnormalities. Besides finding a cause, it is also important to address the consequences of an upper limb defect, including the psychological and physical effect in a developing child.

CONCLUSIONS

TLDs, ear pits, and perineal hemangiomas are commonly known to occur as isolated sporadic anomalies. The presence



Figure 2. A right arm radiograph shows congenital absence of the right hand, with hypoplastic right forearm bones and a normal right humerus. The presence of radii in this patient can rule out other syndromes that present with limb defects.

of major and minor anomalies, should always raise the suspicion of other unidentified abnormalities

Lessons for the Clinician

The differential diagnosis of TLD can be multiple and often includes syndromes with multisystem involvement as follows:

- Thrombocytopenia absent radius syndrome: It is an inherited autosomal recessive disorder characterized by bilateral absence of radii with the presence of thumbs and thrombocytopenia. Hematologic findings may be absent and present within the first few weeks to months after birth.
- Adams-Oliver syndrome: The cardinal features are limb defects and aplasia cutis congenita.
- Fanconi anemia: Most of the cases are inherited in an autosomal recessive pattern. Laboratory findings include thrombocytopenia, macrocytosis, and anemia, but these findings can be absent in one-third of the cases. Absence of radii and hypoplastic thumbs are the most common physical findings.
- Cornelia de Lange syndrome: Despite having upper limb defects such as phalangeal abnormalities or oligodactyly, Cornelia de Lange syndrome is characterized by distinctive phenotypical features and growth restriction.

American Board of Pediatrics Neonatal-Perinatal Content Specification

- Recognize the clinical features and know how to diagnose and manage congenital anomalies of the upper extremities, such as syndactyly, polydactyly, absent clavicles, absent radius, Sprengel deformity, limb reduction.

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