Duplication

Andrew J. Watt, MD[a], Kevin C. Chung, MD[b,*]

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• Congenital • Duplication • Polydactyly
• Thumb duplication • Mirror hand

Congenital anomalies of the upper extremity present a formidable aesthetic and functional challenge for the reconstructive surgeon. Over the past half-century, surgeons and scientists have begun not only to characterize these anatomical aberrations but also to elucidate the underlying embryologic mechanisms responsible for these deformities. Congenital deformities affect 1% to 2% of all newborns, and 10% of these deformities involve the upper extremity.[1,2]

Congenital limb anomalies are classified according to the embryonic failure that underlies their clinical presentations. The most widely accepted classification, proposed by Frantz and O'Rahilly and modified by Swanson, divides these anomalies into seven categories of embryologic failure: failure of formation of parts, failure of differentiation, duplication, overgrowth, undergrowth, congenital constriction band syndrome, and generalized skeletal abnormalities.[3,4] This article addresses Swanson's category of duplication, inclusive of pre- and post-axial polydactyly, central polydactyly, and mirror hand, and provides a review of the relevant embryology, anatomy, surgical approach, and outcomes of intervention.

EMBRYOLOGY AND MOLECULAR MECHANISMS

Upper extremity development begins after 4 weeks of gestation and culminates in a functionally complex, anatomically mature limb by 8 weeks of gestation. The majority of congenital anomalies occur during this 4-week period of rapid limb development. Embryologic development happens in a highly orchestrated temporal and spatial fashion by relying on interactions among three known signaling centers and a host of transcription factors, secreted proteins, and receptors. The three primary signaling centers consist of the apical ectodermal ridge (AER), the zone of polarizing activity (ZPA), and the Wingless-type signaling center (WNT).

The AER is a specialized region of the ectoderm that condenses over the developing limb bud and mediates proximal to distal orientation. The AER specifically expresses a number of signaling molecules in the fibroblast growth factor family (FGF-2, -4, -8) that coordinate growth along the proximal-to-distal axis and is responsible for interdigital apoptosis.[5,6] Although the AER supplies these factors, there is clearly a complex interaction with the underlying mesoderm.

The ZPA exists within the lateral plate mesoderm and its position is determined prior to the formation of the limb bud itself. The ZPA determines the anterior-to-posterior (radio-ulnar) axis via secretion of the sonic hedgehog (SHH) protein.[5,7] In addition to this critical role in determining radio-ulnar growth, SHH is also necessary for the maintenance of proximal-to-distal growth by inducing FGF-4 expression in the AER.[8,9] This interrelationship dictates proportional growth along these two axes. Misplacement of this signaling center or aberrant production of SHH results in duplication of elements along the radio-ulnar axis and provides a plausible pathway in congenital errors of duplication.[6,10]

The WNT signaling center resides in the dorsal ectoderm and secretes WNT-7a, which defines the dorsal differentiation pathway.[7]

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[a] Division of Plastic and Reconstructive Surgery, Department of Surgery, Stanford University Hospitals and Clinics, 770 Welch Road, Suite 400, Palo Alto, CA 94304, USA
[b] Section of Plastic Surgery, Department of Surgery, University of Michigan Medical School, 2130 Taubman Center, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-0340, USA
* Corresponding author.
E-mail address: kecchung@umich.edu (K.C. Chung).

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A complementary protein, engrailed-1, exists in the ventral portion of the limb. As the limb develops along these three axes, a series of Homeobox (HOX) genes are expressed in specific regions of the limb and are responsible for the ultimate differentiation of the highly specialized tissues of the upper extremity.[11–14] At this time, the exact molecular signals that activate these HOX genes remain unclear; however, signaling molecules including SHH have been implicated.

The exact molecular mechanisms that are responsible for congenital duplications of the hand are likely heterogenous; however, several chromosomal loci have shown a clear association with polydactyly. Polydactyly is a clinical characteristic of 119 phenotypic disorders and has been associated with 39 genetic mutations.[15] The most clearly defined are several examples of SHH misregulation resulting in pre-axial polydactyly. Several investigators have defined mutations in a ZPA regulatory sequence (ZRS).[16,17] This sequence has been mapped to the long arm of chromosome 7 and is highly conserved throughout a variety of species. The ZRS appears to act as a CIS-regulatory element controlling the expression of SHH. Single base-pair substitutions have been associated with pre-axial polydactyly, triphalangeal thumb, and triphalangeal thumb-polysyndactyly.[18–20] It is clear that with time, molecular research will continue to define more specific loci and genetic mechanisms responsible for disorders of duplication.

PRE-AXIAL POLYDACTYLY

Pre-axial polydactyly encompasses a range of congenital anomalies of the thumb. Thumb polydactyly or duplication is the second most common congenital hand disorder, and the incidence of pre-axial polydactyly is reported as 1 in every 3,000 live births.[21] Duplication alone is typically unilateral and sporadic; however, duplication in the setting of a triphalangeal thumb is inherited in an autosomal dominant pattern. Polydactyly of the thumb ranges from a vestigial radial skin tag to varying degrees of splitting to complete duplication. Depending on the level of duplication, anatomic variation presents a complexity of challenges.

Classification

Thumb duplications are classified according to the level of duplication. Wassel's classification is the most widely accepted and applied; however, several investigators have proposed a variety of subclasses for Type IV as well as triphalangeal thumbs.[22] Wassel's classification is based distal to proximal. Uneven numbers refer to bifid or incomplete duplications. Even numbers refer to complete duplications and Type VII refers to duplications with triphalangism (**Table 1**). This classification scheme is simple, descriptive, and clinically relevant; however, as several investigators have noted, the Wassel classification does not fully describe the anatomic complexity that is associated with thumb duplication. Type IV thumbs may be subdivided into subtypes A, B, and C, each of which contains a triphalangeal component. Type IV A is characterized by duplication at the level of the proximal phalanx, with two triphlanageal components articulating with a common metacarpal head. Types IV B and C are characterized by duplication at the level of the proximal phalanx with a single triphalangeal component arising on the radial and ulnar sides respectively.[23,24] Wood also further subdivided Wassel's triphalangism designation into four subtypes: *A*, in which the triphalangeal ray originates at the level of the metacarpal on the ulnar side; *B*, in which a radial and an ulnar triphalangeal ray originate at the level of the metacarpal; *C*, in which the triphalangeal ray originates at the level of the metacarpal on the radial side; and *D*, in which a central triphalangeal ray articulates with hypoplastic, nontriphalangeal rays on either side (triplication).[23]

Recently, Zuidam and colleagues[25] have proposed an adjusted nomenclature that allows classification of triphalangeal components and triplication in radial polydactyly. Zuidam's classification assigns roman numerals in a distal-to-proximal system analogous to Wassel's classification. Type VII refers to a bifid trapezium. Type VIII refers to a duplicated trapezium. Abbreviations for triphalangism (Tph), triplication (T), symphalangism (S), deviation (D), and hypoplasia (H) are introduced. The position of the duplicated part is assigned according to the ulnar (u), middle (m), or radial (r) position. Triplication is classified by first assigning the most proximal duplication, followed by the distal duplication. For example, duplication at the level of the proximal phalanx with a triphalangeal component on the ulnar aspect, is classified as Type IV Tph u.

Anatomy

The complexity of classification in pre-axial polydactyly suggests that the pathologic anatomy is both variable and complex. The recognition that none of the anatomic components of either duplicate are normal is paramount. The surgeon must also consider the level of duplication, the degree of hypoplasia of each component, stability of the involved joints, and position of the thumb with respect to the bony axis and first web space.