Radial polydactyly-revisiting its embryological, anatomical and etiological aspects

ANSARI, R. M.1* and KADIR, F. A.2

1Anatomy Discipline, Division of Basic Medical Sciences, Faculty of Medicine, Cyberjaya University College of Medical Sciences, Jalan Teknokrat 3, Cyber 4, 63000 Cyberjaya, Selangor, Malaysia
2Division of Human Biology, School of Medicine, International Medical University, No.126, Jalan Jalil Perkasa 19, 57000 Bukit Jalil, Federal Territory of Kuala Lumpur, Malaysia
*E-mail: reshmaansari77@gmail.com

Abstract

Introduction: Radial polydactyly is a frequently encountered congenital anomaly. What is known less about this anomaly is its diverse etiology. In this situation, this article sheds more light on the embryology of the upper limb, the presentation, classification and a discussion on the varied etiology of radial polydactyly. Methodology: Review of various published literature from Scopus, PubMed central and Wiley’s online library. Results: Latest research proves that the various expressions of Sonic hedgehog (SHH) is responsible for this condition in addition to its varied etiology ranging from environmental factors, maternal diabetes and thalidomide embryopathy to chromosomal mutations. Pediatric surgeons have classified radial polydactyly into various subtypes in respect to its presentation and surgical outcomes. Conclusion: this paper is a concise review of radial polydactyly, exploring its anatomical, embryological and etiological aspects. It can be concluded that both genetic and environmental factors are culprits in the pathogenesis of radial polydactyly, but strong evidence pointing out the causal relationship between the environmental factors and Sonic Hedgehog expression is yet to be explored.

Keywords: radial polydactyly, sonic hedgehog, chromosome 7q26.3 mutation.

1 Introduction

In addition to the face, the only other part of the body that draws attention is the hand. Our upper extremities are responsible for daily life activities such as washing, dressing, feeding as well as for practicing hobbies such as sewing, playing musical instruments and drawing. Hence, congenital anomalies of the upper extremity are of high aesthetic and functional importance (WATT and KEVIN, 2009). A good functioning hand is essential for independent living (GRAINNE, 2010). Congenital anomalies affect 1% to 2% of newborns, and approximately 10% of those children have severe congenital abnormalities (COZIN, 2003). Though worldwide prevalence is still not available, isolated researchers show that the prevalence of polydactyly was of 1.73 x 1,000 in alive newborns, where upper limb polydactyly exceeds that of the lower limb (PÉREZ-MOLINA, ALFARO-ALFARO, LOPEZ-ZERMEÑO et al., 1993). The Polish registry noted the prevalence of polydactyly was of 92.8% of which the hands had a strong predilection of 94.8% (MATERNA-KIRYLUK, JAMSHEER, WISNIEWSKA et al., 2013).

2 Embryology of the Upper Limb with Respect to the Development of the Thumb

Sonic hedgehog (SHH), a diffusible morphogen, expressed by the notochord initiates the development of the limb bud composed of lateral plate mesoderm and somatic mesoderm into the overlying ectoderm (AL-QATTAN and KOZIN, 2013). As a result of this, the ectoderm bulges called as the apical ectodermal ridge (AER) approximately 26 days after fertilization. Out of the four zones (stylopod, zeugopod, mesopod and autopod) that develop in to the future upper limb, the zone which gives rise to the hand is the autopod. There is an undifferentiated progress zone (PZ) immediately under the AER. The autopod cells are the last to leave this PZ as the limb grows distally. As soon as the zones are established, the cartilage precursor cells and connective tissue precursor cells differentiate into the bones and muscles and tendons respectively. Initially the digital rays are fused (Day 41 of intrauterine life). Later apoptosis (programmed cell death) occurs in a distal to proximal fashion (Days 50-54 of intrauterine life) (AL-QATTAN and KOZIN, 2013). Specifically speaking, the thumb detaches from the other fingers as a sequence to division of all the other fingers at the eighth week of intrauterine life (SIQUEIRA, STERODIMAS, BORIANI et al., 2008).

Many transcription factors are involved in the patterning of the limbs in three direction, namely, proximodistal, anteroposterior and dorsoventral axes (AL-QATTAN and KOZIN, 2013). The development of the fingers is principally involved in the development of the anteroposterior axis. SHH in the ZPA is responsible for the symmetrical and structural identity of the hand, wrist and forearm. The area around SHH is divided into three zones (stylopod, zeugopod, mesopod and autopod) that develop in to the future upper limb. There is an undifferentiated progress zone (PZ) immediately under the AER. The autopod cells are the last to leave this PZ as the limb grows distally. As soon as the zones are established, the cartilage precursor cells and connective tissue precursor cells differentiate into the bones and muscles and tendons respectively. Initially the digital rays are fused (Day 41 of intrauterine life). Later apoptosis (programmed cell death) occurs in a distal to proximal fashion (Days 50-54 of intrauterine life) (AL-QATTAN and KOZIN, 2013). Specifically speaking, the thumb detaches from the other fingers as a sequence to division of all the other fingers at the eighth week of intrauterine life (SIQUEIRA, STERODIMAS, BORIANI et al., 2008).

The structures developing form these three zones are shown in the following Table 1 (summarised from AL-QATTAN and KOZIN, 2013).

Thus, the thumb develops from Zone III which, in contrary to other zones develops only in the absence of SHH. Apart from the absence of SHH, the development of Zone III occurs under the influence of other factors such as mesodermal
Structures that develop from the zone
Radial part of the middle finger and the index finger
Radius, the radial column of the carpal bones, and the thumb

Factors involved
Descendants of SHH-expressing cells
Influence of long-range SHH signalling
Absence of SHH activity and influence of other factors such as mesodermal SALL4 and HOXA13 and ectodermal FGF8

It often presents as an isolated abnormality more commonly in Caucasians (GRAINNE, 2010). It ranges from complete duplication of the thumb to various degrees of splitting. More so in many cases, a small vestigial skin tag may be present of the radial side of the thumb (WATT and KEVIN, 2009). Many cases of radial polydactyly which present as skin tag or bifid thumb may be unilateral and sporadic whereas triphalangeal thumb is usually inherited in autosomal dominant pattern (WATT and KEVIN, 2009).

4 Anatomy of Radial Polydactyly and its Classification

Most of radial polydactyly cases have an abnormal osseous anatomy which can be appreciated as bony hypoplasia and abnormally widened and angulated articular surfaces (WATT and KEVIN, 2009). As for the muscular changes, an abnormal connection exists in between the flexor and extensor tendons with the accessory bone (WATT and KEVIN, 2009). In a case of thumb duplication, the abductor pollicis brevis and flexor pollicis brevis insert into the proximal phalanx of the accessory thumb whereas opponens pollicis inserts into the metacarpal. Most of the duplicates have an adequate arterial supply through single digital arteries which may be on the radial or ulnar side or both (WATT and KEVIN, 2009).

Wassel classified polydactyly into seven types based on the anatomic level of duplication and distal to proximal variations as shown in Figure 2. Though it is widely accepted, it has its own limitations in describing the concrete morphology of the duplication (SIQUEIRA, STERODIMAS, BORIANI et al., 2008). Among the different types of Wassel, Type IV is the commonest and type II the least expressed (ANI, 2010).

Hence, Chung, AEK, GONG et al. (2013) have suggested a new classification system based on the anatomic pattern of duplication to facilitate surgical correction of the deformity and to evaluate the outcome (Table 2).

5 Etiology of Radial Polydactyly

Scientists have uncovered that majority of congenital anomalies involving the upper limbs occur between the fourth and eighth week of gestation (WATT and KEVIN, 2009). The pathogenesis of radial polydactyly is multifactorial namely, genetic, teratogenic or environmental (KOZIN, 2003). Materna-Kiryluk, Jamsheer, Wisniewska et al. (2013) have confirmed that non-genetic factors play a crucial role in the etiology of non-familial radial polydactyly. A detailed review of the embryology of the upper limb reveals that a case of radial polydactyly is due to ectopic SHH in the anterior mesoderm. Of various types of expressions, a radial polydactyly due to duplication of a biphalangeal thumb is commonly encountered.
Taking more serious cases of radial polydactyly such as thumb polydactyly with triphalangism, isolated triphalangeal thumb and thumb triplication into account shows us that they require moderate increase in anterior SHH expression and are usually related to point mutations in the ZRS leading to moderate gain of function of SHH expression (AL-QATTAN and KOZIN, 2013). Triphalangeal thumb which requires a higher level of SHH is linked to chromosome 7q36 mutation and occurs due to autosomal dominant inheritance (ZUIDAM, ANANTA and HOVIUS, 2008).

6 Conclusion

Congenital anomalies are not always familial and are not always related to genetic abnormalities. Radial polydactyly is one such anomaly, whose etiology has an equal share of environmental and genetic factors. This defect is due to the high expression of Sonic hedgehog (SHH) which is normally absent in the radial side of the hand. Though familial cases are reported due to chromosome 7q36 mutation and occurs due to autosomal dominant inheritance, isolated sporadic cases have a strong environmental influence in the fetus in utero to produce this defect. Further research pertaining to the causal relationship between these environmental factors to the abnormal or excessive expression of SHH would open up new horizons in morphological development.

References


Received 13 July 2015
Accepted 18 October 2016