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Case Report

Familial synpolydactyly with variable expressivity in two siblings: a case report and review of literature

Sri Hari Ram V. S.*, Burhannuddin Chathriwala, Binoti Sheth, Aravind Rathod, Rajath Shetty, Harshil Soni, Abhijit Gedam

Department of Orthopaedics, Lokmanya Tilak Municipal Medical College and General Hospital (Sion Hospital), Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Sri Hari Ram V. S.,
E-mail: 1997srihari@gmail.com

ABSTRACT

Synpolydactyly (SPD), classified as syndactyly type II, is a rare congenital anomaly characterized by central digit syndactyly with associated digital duplication. Most nonsyndromic SPD cases arise from HOXD13 polyalanine repeat expansions, which demonstrate variable expressivity and incomplete penetrance. This case report describes two biological male siblings with congenital limb anomalies. Detailed clinical examination, radiographic analysis, developmental assessment, and family evaluation were conducted. A literature review was performed to contextualize the phenotypic variability of HOXD13-associated SPD. The elder sibling demonstrated complex polysyndactyly of both hands and feet, including postaxial polydactyly and hypoplastic accessory digits. The younger sibling exhibited milder features consisting of syndactyly and polydactyly of the hands and unilateral partial toe syndactyly. Both parents had normal limb examinations, supporting reduced penetrance, a known feature of HOXD13-associated SPD. These cases highlight the considerable intrafamilial phenotypic variability characteristic of HOXD13-related SPD. Recognition of reduced penetrance is essential for accurate counseling and recurrence-risk assessment. Early diagnosis permits timely surgical planning and referral for genetic counseling.

Keywords: Congenital anomaly, HOXD13, Polyalanine repeat, Synpolydactyly, Penetrance, Limb development

INTRODUCTION

Synpolydactyly (SPD) is a congenital limb malformation characterized by syndactyly of the central digits with associated duplication, classically involving both hands and feet.

Classification of congenital hand anomalies was reported in 1976 by Swanson. This classification was widely accepted and adopted by the American Society for Surgery of the Hand and the International Federation of Societies for Surgery of the Hand. The Swanson classification categories are (I) failure of formation of parts, (II) failure of differentiation (separation) of parts, (III) duplication, (IV) overgrowth, (V) undergrowth, (VI) congenital constriction band syndrome, and (VII) generalized skeletal abnormalities. The polydactyly can be preaxial (radial), central, or postaxial (ulnar).[3] Polydactyly is sometimes referred to as mixed, if the condition is both radial and ulnar, or as crossed, when the feet are involved.[1]

Classification of syndactyly can be descriptive, including terms such as incomplete or complete (involvement of the entire length of the digit), simple or complex (presence of bony fusion), and/or complicated (presence of accessory phalanges or abnormal bones).

Another classification commonly cited is the Tentamy and McKusick classification:

Type I

Most common with involvement of the long and ring fingers in the upper extremity or second and third toe in the lower extremity, following an autosomal dominant pattern with incomplete penetrance.

Type II

SPD with the involvement of the long and ring fingers in the upper extremity and/or fourth and fifth toes in the lower extremity with an accessory digit in the syndactyly web.

Type III

Syndactyly involved in the ring and small finger.

Type IV

Complete syndactyly of all fingers.

Type V

Metacarpal or metatarsal fusions of the ring and small finger in the upper extremity and third and fourth toes in the lower extremity.[2]

Of the nine non-syndromic syndactyly known, it is clinically and genetically one of the most hetero-geneous malformations. Three genetically distinct SPD malformations are now known and have been designated as SPD1, SPD2 and SPD3 (Table 1), but a characteristic clinical delineation between these entities has not been appreciated.

Table 1: Clinical features and the known loci/genes for synpolydactylies (SPDs).

Type	Cardinal features	Locus`	Gene
SPD 1	SPD is central in hand and post axial in feet	2q31	HOXS13
SPD 2	SPD is central and post axial in hands, post axial syndactyly in feet	22q13.31	FBLN1
SPD 3	SPD is central in hand and post axial in feet	14q11.2-q12	

Our case is categorized as Syndactyly type II and is strongly associated with mutations in the HOXD13 gene, particularly expansions of its polyalanine tract.[3,5] These expansions disrupt transcriptional regulation during limb development and impair downstream pathways essential for digit patterning.[6]

Despite its autosomal dominant inheritance, SPD demonstrates wide phenotypic variability and incomplete penetrance.[3,4] Families may show marked differences in severity among affected individuals, and asymptomatic carriers are well documented.[5,6] Reported phenotypes range from subtle soft tissue webbing to complex polysyndactyly with metacarpal or metatarsal anomalies.[4]

The study presented two brothers with markedly different expressions of SPD born to unaffected parents, illustrating characteristic variability of HOXD13-related anomalies.

CASE REPORT

This observational case report includes two biological male siblings presenting with congenital hand and foot anomalies. Detailed clinical assessments were performed, including inspection for syndactyly, polydactyly, hypoplastic digits, and limb symmetry. Standard radiographs of both hands and feet were obtained for morphological evaluation. Antenatal history, perinatal events, developmental milestones, and pedigree information were recorded. Both parents underwent complete limb and digit examinations to identify subtle manifestations of SPD. Written informed consent was provided by the parents for publication of anonymized clinical information and images.

Two male siblings from the same family presented with congenital limb anomalies suggestive of familial SPD with variable expressivity. The elder male child, born in 2011, had multiple anomalies involving both the hands and feet since birth. On examination of the left hand, there was complete simple syndactyly of the 4th and 5th digits, associated with postaxial polydactyly involving the 5th digit. A hypoplastic sixth digit composed of three small phalanges was also present, while five normally developed metacarpals were noted. In the right hand, postaxial polydactyly of the 5th finger was observed, along with a hypoplastic accessory digit without syndactyly. Examination of the left foot revealed postaxial polydactyly with partial syndactyly between the 5th toe and the duplicated 6th toe, and a shared metatarsal for the 5th and 6th toes. The right foot showed a rudimentary 4th toe, with complete cutaneous syndactyly involving the 4th toe, rudimentary 5th toe, and the 6th toe. Systemic examination of the child was normal, with no abnormalities detected on assessment of craniofacial features, cognitive development, cardiac evaluation, or renal system.

The younger male sibling, born in 2012, demonstrated milder limb involvement, highlighting the variable expressivity within the same family. Examination of the right hand showed complete simple syndactyly between the 4th and 5th digits, along with postaxial polydactyly of the 5th finger and the presence of a hypoplastic accessory digit. The left hand demonstrated postaxial polydactyly with hypoplastic phalanges. Examination of the feet revealed partial simple syndactyly between the great toe and the second toe on the right foot, extending up to the proximal interphalangeal joint, while the left foot was normal. Overall, the younger sibling showed normal

growth and systemic development, with no associated systemic anomalies identified. A comparison between the clinical features of the 2 siblings is mentioned in Table 2.

Table 2: Comparison between siblings.

Features	Elder sibling	Younger sibling
Limbs affected	4	3
Severity	Severe	Mild
Polydactyly	Hands + Feet	Hands + unilateral foot
Syndactyly	Extensive	Limited
Hypoplastic digits	Present	Present

Figure 1: Clinical image of elder sibling of bilateral hand showing right sided polydactyly and left sided SPD.

Figure 2: Clinical images of b/l foot of elderly child showing bilateral SPD with hypoplastic digits.

Figure 3: Anteroposterior Xray of bilateral hand of elder sibling.

Figure 4: Anteroposterior Xray of bilateral foot of elder sibling.

Figure 5: Clinical image of younger sibling of bilateral hand showing right sided SPD and left sided polydactyly.

Figure 6: Clinical images of b/l foot of younger child showing right foot polydactyly with hypoplastic digits. Left foot was normal.

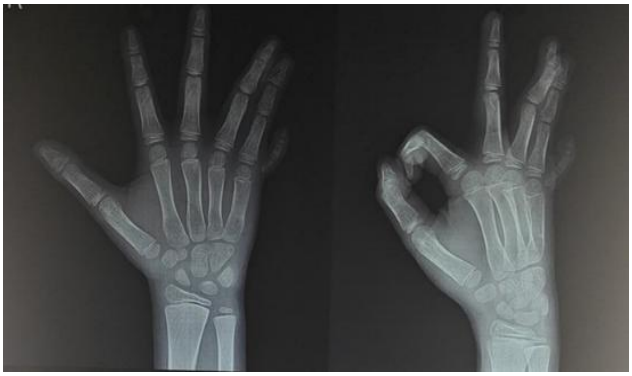

Figure 7: Anteroposterior X-ray of bilateral hand of younger sibling.

Figure 8: Anteroposterior Xray of bilateral foot of younger sibling.

DISCUSSION

These two cases demonstrate the hallmark intrafamilial variability of HOXD13-mediated SPD. Polyalanine expansions in HOXD13 are the most common cause of SPD and demonstrate a predictable but variable genotype-phenotype relationship.[3,5] Larger expansions generally correlate with more severe phenotypes, but expressivity remains inconsistent even among carriers of identical mutations.[3]

The elder sibling's complex polysyndactyly involving both hands and feet aligns with classical SPD type II, while the younger sibling exhibited milder limb involvement. Similar variability has been widely reported in multiple familial studies across populations, including Turkish, Chinese, European, and South Asian cohorts.[4]

Incomplete penetrance is a characteristic feature of HOXD13 expansions.[5] Asymptomatic carriers are well documented, and subtle signs may be overlooked without careful examination. The phenotypically normal parents in this report strengthen the likelihood of reduced penetrance or a minimally manifesting carrier state.

Embryologic studies indicate that HOXD13 plays a critical role in establishing digit identity and boundary formation through regulatory interactions with growth-differentiation pathways.[6] Disruption of these processes results in the observed spectrum of syndactyly, polydactyly and digital hypoplasia. Sequencing of the HOXD13 PCR products revealed that all the affected family members had a 27-bp insertion encoding nine additional alanine resi-dues. No other mutation was identified in the coding region.[7]

Due to the variability of the disease, it can be challenging to make a genetic-based diagnosis, such as carrier testing, and most diagnoses are made after birth. More research is needed to determine the causes and origins of syndromic or nonsyndromic syndactyly. Although our knowledge of syndactyly is improving, treatment still depends on age, functional issues, and severity of the condition. It is crucial to advise expectant mothers to avoid taking herbal and teratogenic medications during pregnancy. Surgeons must take a proper medical history and physical examination before surgery. Performing surgery appropriately and providing good follow-up care can prevent further complications and deformities.[8]

CONCLUSION

Familial SPD demonstrates wide variability, even among siblings sharing the same genetic background. These cases highlight the need for heightened clinical awareness of reduced penetrance in HOXD13-associated limb malformations. Thorough family evaluation and genetic counseling are key to comprehensive management.

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REFERENCES

1. Althobaity AN, Alkabbaa SA, Aljaied SS, AlKahtani MM. Polydactyly MAS Classification. Plast Reconstr Surg Glob Open. 2018;6(12):e2022.
2. Hinkley JR, Fallahi AKM. Syndactyly. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2025.
3. Goodman FR, Mundlos S, Muragaki Y, Donnai D, Giovannucci-Uzielli ML, Lapi E, et al. Synpolydactyly phenotypes correlate with size of expansions in HOXD13 polyalanine tract. Proc Natl Acad Sci USA. 1997.Synpolydactyly phenotypes correlate with size of expansions in HOXD13 polyalanine tract. Proc Natl Acad Sci U S A. 1997;94(14):7458-63.
4. Zaib T, Ahmed I, Tariq M, Xiaoling Z, Pingnan S. Recent advances in syndactyly: genetic basis and emerging concepts. Genes. 2022;13(5):771.
5. Chen X, Li Y, Xu X, Yixuan C, Xiuli Z. New insight into synpolydactyly caused by HOXD13 polyalanine expansion. BMC Med Genomics. 2024;17(1):259.
6. Muragaki Y, Mundlos S, Upton J, Olsen BR. Altered growth and branching patterns in limb cartilage of HOXD13-mutant mice. Science. 1996;272(5261):548-51.

7. Zhou J, Chen Y, Cao K, Zou Y, Zhou H, Hu F, et al. Functional classification and mutation analysis of a synpolydactyly kindred. Exp Ther Med. 2014 Nov;8(5):1569-74.
8. Akbari H, Saraee A, Shafaei Y, Akhoondinasab MR, Akbari P. Syndactyly in
9. Twins: A Case Report. World J Plast Surg. 2025;14(2):126-30.

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