MULTIGENERATIONAL TRIPHALANGEAL THUMB: SUSPICION FOR A NEW DOMINANTLY-INHERITED DISORDER OF HAND DEVELOPMENT

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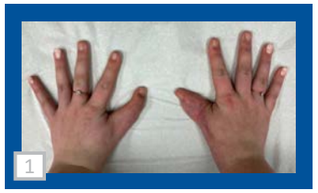
INTRODUCTION

- Triphalangeal thumb (TPT) is a congenital hand anomaly in which the thumb consists of three rather than two phalanges
- Usually inherited as an autosomal dominant trait and, therefore, is commonly seen affecting multiple family members
- Exact genetic transmission patterns and penetrance for this congenital anomaly are unknown or, at best variable, and many are assumed undiscovered
- Various mutations in the zone of polarizing activity-regulatory sequence (ZRS) are implicated in these and similar limb anomalies
- **This case presents a unique combination of triphalangeal thumb and concurrent preaxial polydactyly with a strong familial component**

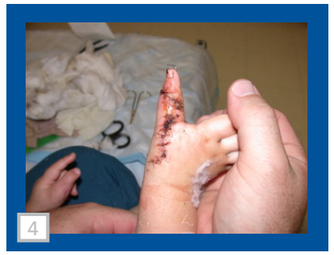
AIMS

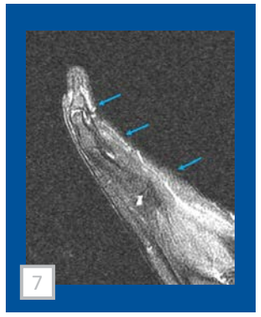
- Identify a potentially new genetic etiology for triphalangeal thumb with ongoing genetic evaluation
- Better characterize phenotypic expression and patterns of transmission for this congenital anomaly

CASE PRESENTATION



- 16-year-old female presented to the plastic surgery hand clinic with history of bilateral preaxial polydactyly and triphalangeal thumbs of maternal inheritance
- Underwent surgical repair of polydactyly at 6 months of age and subsequent arthrodesis of the right PIP joint for correction of the triphalangeal thumb





Figures. **1.** Proband bilateral hands on presentation—dorsal 2. Proband bilateral hands at presentation—volar 3. Proband bilateral hands at birth **4.** Right thumb status-post polydactyly repair **5.** Proband right thumb XR demonstrating triphalangeal thumb with PIP joint ankylosis **6.** Proband right thumb XR status-post arthrodesis **7.** Proband right thumb MRI – arrows demonstrating three joints **8.** Proband's mother with bilateral triphalangeal thumb **9.** Proband's mother demonstrating full thumb flexion at all three joints. **10.** Five-generation family pedigree

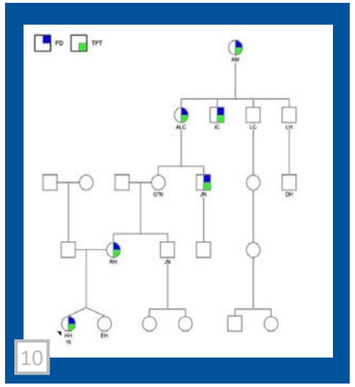
- Right thumb radiograph demonstrated congenital deformity of the thumb with a long proximal phalanx status-post osteotomy, shortening, and interphalangeal joint arthrodesis
- Primary concern was soft tissue bulk and aesthetic appearance, thus subsequently underwent right thumb debulking procedure for improved cosmesis
- Patient's mother also presented with bilateral triphalangeal thumb, and a unique family history of other relatives with this anomaly leading to extensive genetic evaluation

GENETIC ANALYSIS

- **No causative genetic lesion** was discovered on (1) chromosomal microarray, (2) next generation sequencing panel or (3) whole exome sequencing
- **Multi-generation pedigree** was constructed identifying three affected individuals— mother, maternal great uncle and maternal great grandmother
- Notably, the maternal grandmother was unaffected and the proband has an unaffected twin

Genes Commonly Associated with Limb Anomalies

ESCO2, HDAC8, LMBR1, NIPBL, NSDHL, RAD21, SALL1, SALL4, SHH, SMC1A, SMC3, TBX5, TP63, WNT3



CONCLUSIONS

- We suspect that this patient harbors a potentially new and unidentified autosomal dominant gene mutation for triphalangeal thumb
- Ongoing genetic evaluation is needed to better characterize and understand its phenotypic expression and mode of transmission
- Genetic studies remain at the forefront of identifying unknown genetic mutations of congenital hand anomalies
- **This case is another great example of the vast genetic frontier that contains unidentified genetic mutations for congenital hand anomalies!**