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LYMPHSPIRATION

THE IMPORTANCE OF THE STUDY OF DERMATOGLYPHICS FOR LYMPHOLOGISTS

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ABSTRACT

A recent genome-wide association study (GWAS) looking for the genes determining fingerprint and palmar crease patterns disclosed one gene, among many others, which causes lymphedema (CELSR1) while others influencing tissue growth. Since digital fluid influences the height of the volar pads, influences of lymphedema on dermatoglyphics should be sought.

Keywords: dermatoglyphics, dermal ridges, volar pads, lymphedema genes

There has long been an interest in the study of differences in fingerprints among individuals. Although the major interest was for forensic purposes, an early interest in the differences between individuals with some genetic diseases and the normal individuals developed. For instance, the human geneticist, Lionel Penrose (1), reported the differences in average fingerprints (and palmar creases) between individuals which we now know have trisomy 21 from those of the general population. The founder of dysmorphology, the study of genetically inherited patterns of external appearances which has led to the discovery of over a thousand genetic syndromes with altered facial and other body features, David

Smith (2) emphasized the early stages of development during which the differences appeared. He and colleagues pointed out that the height of the finger pad in the fetus influenced the resulting dermatoglyphic patterns. If the pad was domed up, whorls resulted; a normal height pad resulted in the most common loops, opening either to the radius or ulna; and flat, low pads resulted in the less complicated pattern of arches (*Figure*).

Recently a massive Genome Wide Association Study (GWAS) was performed looking for the genetic variation underlying multiple dermatoglyphic parameters in a predominately Han (Chinese) population (3). This study clarified the genetics of dermatoglyphics and

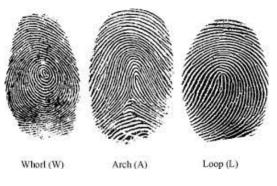


Fig.: Relationship between finger pad height and the resulting digital dermatoglyphics.

the confirmation of the classic (2,3) discriminations of whorl, arch, and loop as the best discriminants. These, of course, reflect the shape of the underlying volar pad, where the major signal found by this GWAS, *EV11*, is expressed and promotes proliferation.

There are other factors which influence the shape of the volar pad, i.e., fluid. Although only one gene identified in this study also is involved in lymphedema (CELSR1; 4,5), the role of the lymphatics in influencing dermatoglyphic patterns deserves more attention. For instance, a number of chromosomal disorders (which, generally are not, investigated by GWAS) have lymphedema and altered dermatoglyphics. While trisomy 21 has altered digital growth and altered dermal ridge patterns, the role of lymphedema may be more primary in 45, X syndrome with its high percentage of whorls. Among the syndromes listed in Table 2 in Li et al (3), the flattening of the face seen in some, such as Robinow's, is very similar to that seen in some lymphatic disorders (compare to Hennekam's syndrome). Perhaps the paucity of overlap is the failure of lymphologists to look at dermal ridges (not necessary for diagnosis) and the early lethality of many severe lymphatic disorders (genes currently identified in lymphatic disorders are mapped in Witte et al [6]).

Many of the genetically inherited lymphedema disorders do not appear until after birth, or later, especially, the teenage period. However, multiple genes, which when mutated, cause fatal fetal hydrops (FFH) have been found. These include AHCY(ahcySadenosylhomocysteine hydrolase (7) and FOXC2-the initial publication identifying FOXC2(8) had 2 cases of FFH in one family and others have found more (9). The importance of modifying genes for this phenotype has been indicated (10,11). Other genes involved in FFH are VEGFR3(9) and EPHB4 (12). These cases of FFH indicated that some of the genetic variants we study are being expressed long before eternal appearances lead to the diagnosis but the dermatoglyphics have not been studies in these cases. Thus, I would recommend that we lymphologists pay attention to dermatoglyphics in all our patients to extend our knowledge of genes affecting the development of the lymphatics.

CONFLICT OF INTEREST AND DISCLOSURE

The author declares no competing financial interests exist.

REFERENCES

- 1. Penrose, LS: Dermatoglyphics. Sci. Amer. 221 (1969), 72-87.
- 2. Mulvihill, JJ, DW Smith: The genesis of dermatoglyphics. J. Ped. 75 (1969), 79-89.
- 3. Li, J, JD Glover, H Zhang, et al: Limb development genes underlie variation in human fingerprint patterns. Cell 185 (2022), 95-112.
- Gonzalez-Garay, ML, MB Aldrich, JC, Rasmussen, et al: A novel mutation in CELSR1 is associated with hereditary lymphedema. Vasc. Cell 8 (2016), 1 https://doi.org/10.1186/s13221-016-0035-5.
- Erickson, RP, L-W Lai, DJ Mustacich, et al: Sex-limited penetrance of lymphedema to females with CELSR1 haploinsufficiency: A second family. Clin. Genet. 96 (2019), 478-482.
- Witte, MH, RP Erickson, L Luy, et al: Human chromosome map of lymphedemalymphangiogenesis genes: Template for current and future discovery. Lymphology 54 (2021), 167-169.
- Grubs, R, O Vugrek, J Deisch, et al: Sadenosylhomocysteine hydrolase deficiency: Two siblings with fetal hydrops and fatal outcomes. J. Inherit. Metabol. Dis. 33 (2010), 705-713.
- Fang, JM, SL Dagenais, RP Erickson, et Mutations in *FOXC2* (MFH-1), a forkhead family transcription factor, are responsible for the hereditary lymphedema-distichiasis syndrome. Am. J. Hum. Genet. 67 (2000), 1382-1388/
- 9. Galamkarpour, AC, E Debauche, E Haan, et al: Sporadic in utero generalized edema caused by mutations in the lymphangiogenic genes *VEGFR3* and *FOXC2*. J. Ped. 155 (2009), 90-93.
- 10. Sargent, C, J Bauer, M Khalil, et al: A five generation family with a novel mutation in *FOXC2* and lymphedema worsening to

hydrops in the youngest generation. Am. J. Med. Genet. A, 164A (2014), 2802-2807.

- 11. Lai, L-W, RP Erickson, M Bernas, MH Witte: From childhood onset lymphedema to fatal fetal hydrops: Possible modifying genes for a *FOXC2* mutation. Lymphology 50 (2018), 85-88.
- 12. Martin-Almedina, SI, R Martinez-Corral, R Holdus, et al: *EPHB4* kinase-inactivating mutations cause autosomal dominant lymphatic-related hydrops fetalis. J. Clin. Invest. 126 (2016), 3080-3086.

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