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A CONTRIBUTION TO GENETIC ETIOLOGY OF COMPLEX REGIONAL PAIN SYNDROME TYPE I (ALGODYSTROPY SYNDROME) BASED ON QUANTITATIVE ANALYSIS OF DIGITOPALMAR DERMATOGLYPHICS IN SIXTY MEN

PRILOG GENETIČKOJ ETIOLOGIJI KOMPLEKSNOG REGIONALNOG BOLNOG SINDROMA - TIP I (SYNDROMA ALGODYSTROPHICUM) NA TEMELJU KVANTITATIVNE ANALIZE DIGITOPALMARNIH DERMATOGLIFA U ŠEZDESETORICE MUŠKARACA

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„If I talk (Jehovah), shall it alleviate my pain; If I stop, shall it go away?"
Job 16:6 (DK)

Summary

The patterns of the ridges of the skin of the fingers and palms were determined in sixty men with complex regional pain syndrome (type I) as a measure of disease prevention. The study included 25 dermatoglyphic traits: number of epidermal ridges on all ten fingers; their sum for five and ten fingers; four traits on both palms, i.e. between a-b, b-c and c-d triradii; atd angles: and their bilateral sum. The data obtained were compared with those recorded in a control group of 200 pairs of imprints of phenotipycally healthy male adults from the Zagreb area. Statistically significant difference from control values were found in 12 dermatoglyphic variables, including an increased sum of ridges on nine fingers (except for left second finger pad), and total sum for five and ten fingers. These findings suggested the polygenic system responsible for development of dermatoglyphics to be identical with some polygenic loci for the onset of algodystrophy syndrome, which might prove useful in disease prevention (e.g., taking fingerprints following a trauma and before rehabilitation), and to facilitate identification of risk groups, and thus the treatment for this longterm and yet obscure syndrome.

Key words

dermatoglyphics, algodystrophy syndrome - complex regional pain syndrome type I, male sex, quantitative dermatoglyphics analysis, prevention

Sažetak

U svrhu prevencije, u ovom se genetičkom ispitivanju, istražio broj kožnih grebenova na prstima i dlanovima šezdesetorice muškaraca s kompleksnim regionalnim sindromom Tip I (Syndroma algodystrophicum). Ispitivanje je provedeno u 25 dermatoglifskih značajki: broju epidermalnih grebenova na svih deset prstiju, njihovu sveukupnom zbroju na pet i deset prstiju, četirima svojstvima na oba dlana - između triradijusa a-b, b-c i c-d, te atd kutovima, i njihovom obostranom zbroju. Dobiveni podaci su uspoređeni s kontrolnom skupinom - 200 pari otisaka odraslih i fenotipskih zdravih osoba Zagrebačke regije. U dvanaest dermatoglifskih varijabli pronađene su statistički značajne razlike prema kontroli: u povišenom broju grebenova na devet prstiju (izuzev jagodice drugog prsta lijevo),

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te u ukupnom zbroju na pet i deset prstiju zajedno. Iz toga se može pretpostaviti, kako je poligenetički sustav odgovoran za razvoj dermatoglifa identičan s nekim lokusima za oboljevanje od algodistrofičnog sindroma, a što bi se moglo iskoristiti u preventivne svrhe (uzimanjem otisaka ruku nakon traume, odnosno prije rehabilitacije), te formiranjem rizičnih skupina, a time i usmjeriti liječenje tog dugotrajnog i tajanstvenog poremećaja.

Ključne riječi

dermatoglifi, syndroma algodystrophicum - kompleksni regionalni sindrom tip I, muški spol, kvantitativna dermatoglifska analiza, prevencija

Introduction

Algodystrophy is debilitating syndrome from the group of extra-articular rheumatism, characterized by rapid bone demineralization, burning pain, hyperesthesia, swelling, hyperhidrosis, and trophic lesions of the skin and nails (1,2). The first description of the disorder has been atributed to Hunter, who drew attention to more distal effects of articular trauma as early as 1776 (3). Then, it was reported by Mitchell in 1864, as a complication of gunshot wounds of perifepheral nerves during the American Civil War (4). Now, more than a hundred years later, there is no consensus yet on how to term the disorder, what its cause is and how to treat it best. According to the last classification, there are two groups of disorders: complex regional pain syndrome (type I) and causalgia (type II) (5). As all our 60 patients developed algodystrophy syndrome following extremity fractures, they fell into the type I group.

Although no such study has been conducted to date, a genetic impact has been noted in the syndrome development. In 1983, Albert and Ott reported on hip algodystrophy in three brothers (6). In 1994. Mailis and Wade found a higher frequency of HLA A3, B7 and DR2 antigens in 15 female Caucasians (7). In 1999, Kemler et al. reported on association of HLA DQ1 antigen and reflex symphatetic dystrophy (8). The present study in which a statistically significant difference from controls was found in 12 of 25 variables investigated, shed some more light on the genetic predisposition and thus on the possible prevention of development of this obscure post-traumatic disorder.

Materials and methods

Dermograms of 60 men with post-traumatic algodystrophy were examined by quantitative dermatoglyphic analysis according to Kozin's criteria (9), as suggested by Miličić et al. (10), atlthough considerably more sophisticated criteria have been established in the meantime (3). Results were compared with those obtained in 200 pairs of dermatoglyphic palm and finger imprints of phenotypically healthy men from the Zagreb area, kept at Institute of Anthroplology from Zagreb (11). Student's t-test was used to test the statistically significant differences in the ridge count between the patient and control group.

Patient imprints were taken onto a transparent adhesive tape (Tovarna dokumetnega in kartnega papirja, Radeče, Slovenia) by use of Folien-Vogel fine-granulated silver-grey powder (Magna powder, Cat. No. 57, Austria).

The following 25 traits were examined by quantitative dermatoglyphic analysis: 1) FRD 1 number of ridges on the right hand first finger; 2) FRD 2 number of ridges on the right hand second finger; 3) FRD 3 number of ridges on the the right hand third finger; 4) FRD 4 number of ridges on the rhe right hand fourth finger; 5) FRD 5 number of ridges on the right hand fifth finger; 6) FRD 1-5 pooled number of ridges on all five right hand fingers; 7) PRD 1 number of ridges between c and d triradii on the right palm; 8) PRD 2 number of ridges between b and c triradii on the right palm; 9) PRD 3 number of ridges between a and b triradii on the right palm; 10)

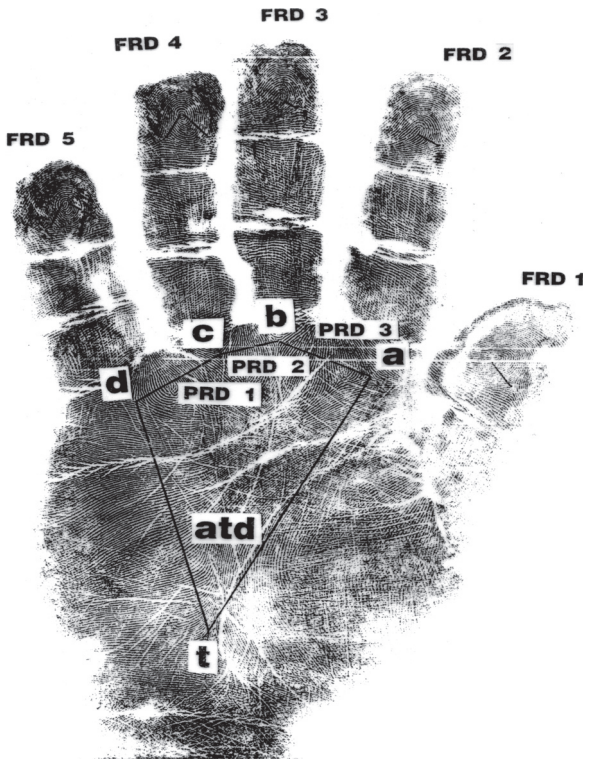

Figure. **Sites of quantitative analysis of digitopalmar dermatoglyphics with characteristic marks, triradii, between which skins ridges were counted**
Slika. **Mjesta kvantitativne analize digitopalmarnih dermatoglifa s karakterističnim oznakama, triradijusima, između kojih su brojani epidermalni grebenovi**

PRD 1-3 pooled number of ridges between d and a triradii on the right palm; 11) ATDD atd angle on the right hand in degrees; 12) FRL 1 number of ridges on the left hand first finger; 13) FRL 2 number of ridges on the left hand second finger; 14) FRL 3 number of ridges on the left hand third finger; 15) FRL 4 number of ridges on the left hand fourth finger; 16) FRL 5 number of ridges on the left hand fifth finger; 17) FRL 1-5 pooled number of ridges on all five left hand fingers, 18) PRL 1 number of ridges between c and d triradii on the left palm; 19) PRL 2 number of ridges between b and c triradii on the left palm; 20) PRL 3 number of ridges between a and b triradii on the left palm; 21) PRL 1-3 pooled number of ridges between d and a triradii on the left palm; 22) ATDL atd angle on the left palm in degrees; 23) PRD 1-3 and PRL 1-3 sum of all ridges between d and a triradii on both palms; 24) ATDT bilateral sum of atd angle degrees on the both palms; 25) FRD 1-5 and FRL 1-5 pooled number of ridges on all ten fingers.

Figure shows the sites of quantitative analysis of digitopalmar dermatoglyphics with characteristic marks, triradii, between skin ridges were counted.

Results

Results are tabularly presented in Tables 1-3. The following 12 of 25 study variables showed a statisically significant difference between patient and control imprints in terms of increase in the former: first (FRD 1), second

Table 1. **Quantitative properties of right hand digitopalmar complex in patients and control subjects**
Tablica 1. **Rezultati analize kvantitativnih svojstava digitopalmarnog kompleksa u bolesnika i kontrole na desnoj ruci**

Variable	Patient group			Control group				Risk level
	n	x	SD	n	x	SD	p	
FRD 1	60	22.63	5.51	200	I9.38	5.63	.000	stat. significantly differ. fr. controls
FRD 2	60	14.03	6.73	200	11.42	7.27	.013	stat. significantly differ. fr. controls
FRD 3	60	14.17	5.65	200	11.99	6.58	.021	stat. significantly differ. fr. controls
FRD 4	60	18.13	5.43	200	16.16	6.15	.026	stat. significantly differ. fr. controls
FRD 5	60	15.25	4.81	200	13.64	5.16	.032	stat. significantly differ. fr. controls
FRD 1-5	60	84.83	21.93	200	72.57	24.65	.001	stat. significantly differ. fr. controls
PRD 1	60	38.65	6.45	200	37.94	6.07	.435	
PRD 2	60	28.87	5.48	200	28.58	5.87	.740	
PRD 3	60	41.85	6.82	200	41.85	6.82	1.000	
PRD 1-3	60	109.20	13.88	200	108.47	13.39	1.000	
ATDD	60	46.15	9.98	200	47.43	8.27	.320	

Table 2. **Quantitative properties of left hand digitopalmar complex in patients and control subjects**
Tablica 2. **Rezultati analize kvantitativnih svojstava digitopalmarnog kompleksa u bolesnika i kontrole na lijevoj ruci**

Variable	Patient group			Control group				Risk level
	n	x	SD	n	x	SD	p	
FRL 1	60	19.52	5.48	200	16.20	6.14	.000	stat. significantly differ. fr. controls
FRL 2	60	12.50	6.56	200	10.76	6.78	.079	
FRL 3	60	15.12	5.58	200	11.78	6.37	.000	stat. significantly differ. fr. controls
FRL 4	60	18.20	5.50	200	16.25	6.17	.028	stat. significantly differ. fr. controls
FRL 5	60	15.80	4.43	200	13.50	4.60	.001	stat. significantly differ. fr. controls
FRL 1-5	60	165.20	40.86	200	141.03	47.44	.000	stat. significantly differ. fr. controls
PRL 1	60	36.35	6.81	200	36.30	7.00	.807	
PRL 2	60	28.82	6.33	200	28.71	5.85	.906	
PRL 3	60	42.32	5.86	200	43.58	7.05	.208	
PRL 1-3	60	107.45	14.18	200	109.02	14.79	.469	
ATDL	60	45.65	9.41	200	47.86	7.70	.066	

Table 3. **Quantitative properties of digitopalmar complex on both hands in patients and control subjects**
Tablica 3. **Rezultati analize kvanitativnih svojstava digitopalmarnog kompleksa u bolesnika i kontrole na obje ruke zajedno**

Variable	Patient group			Control group				Risk level
	n	x	SD	n	x	SD	p	
FRD1-5+FRL1-5	60	165.20	40.86	200	141.03	47.44	.000	stat. significantly differ. fr. controls
PRD1-3+PRL1-3	60	216.65	27.14	200	217.94	27.19	.750	
ATDD+ATDL	60	91.80	18.67	200	95.28	14.30	.126	

(FRD 2), third (FRD 3), fourth (FRD 4) and fifth (FRD 5) finger on the right hand, and all five fingers of the right hand together (FRD 1-5); first (FRL 1), third (FRL 3), fourth (FRL 4) and fifth (FRL 5) finger of the left hand, and all five fingers of the left hand together (FRL 1-5); and all ten fingers of both hands together (FRD 1-5+FRL 1-5).

Discussion

To the best of our knowledge, no similar genetic study has been performed to date, as multiple survey of more than 1200 literature items yielded no such report. While traumatologists would argue that cases of algodystrophy are less frequently encountered since fractures have been ever more commonly manged by ostesynthesis rather than plaster immobilization, clinical experience shows it still to occur and to be highly refractory to treatment, which generally takes one to two years or even longer. It was one of the reasons stimulating us to embark upon this investigation, to hopefully contribute to the prevention and possible avoiding of this mysterious disorder.

In 1983, Albert and Ott noted genetic predisposition for algodystropy. Algodystrophy of the hip occured at intervals, i.e. in December 1978, March 1980 and October 1980, in three brothers born in south-west Italy and living in different parts of Switzerland for more than 10 years. HLA antigens were identical, representing a rare coincidence: A30 or A31, B8-B37, BW4-6, DR7-X and MT3-1,2 (6).

Based on the anlysis performed in three families with two or more members affected with algodystrophy, Greipp and Thomas conclude in their selected abstracts from 1991 that there most be a genetic susceptibility to disorder, unfortunately, providing no additional data (12).

Having employed an appropriate initial approach, Mailis and Wade recorded an increased frequency of A3, B7 and DR2(15) antigens in 15 female Caucasians with the place of birth determined in the probands and their parents, as compared to a homogeneous control group. Five of the six patients with DR2(15) antigen were higly resistant to therapy. Tabular presentation revealed that DQ1 antigen was found in three, and DQW1 antigen (which is almost identical to DQ1) in another nine of the 15 study patients, however, this finding is not discussed in the paper at all (7).

In 1999, Kemler et al, recorded an increased frequency of DQ1 antigen in 36 (69%) of 52 patients as compared with control subjects (n=142, 42%). DQ3 and Cw7 were positive in 30 patients (8). An interesting discussion about the role and value of these findings appeared in two commentaries in 2000 (13,14).

As no similar dermatoglyphic study in algodystrophy has been reported to date, there is no data to compare the present results with, however, an acount can be given of the diseases related to or even associated with this disorder. For example, post-traumatic algodystrophy was observed to precede the occurence of psoriasis and psoriatic arthritis (15), which is by no means a rare phenomenon because both psoriasis and psoriatic arthritis are precipitated by trauma.

A study of psoriasis (140 patients, 70 male and female each) also revealed an elavated number of epidermal ridges on the finger of male patient, i.e. on the first, second, third and fifth finger of the right hand, and their sum; on the first, second and third finger of the left hand, and their sum; and in overall sum of all ten fingers (16). An increased number of epidermal ridges on the third finger of both hands was recorded in ankylosing spondylitis (17); on the first and fifth finger of both hands in rheumatoid arthritis (18); on the first and third finger of both hands, and on the fifth finger of the left hand in Reiter disease (19); and on the first three fingers of the right hand and on all five fingers of the left hand in primary hypertrophic osteoarthropathy, where concurrent algodystrophy has occasionally been reported (20).

Of course, these comparisons refer exclusively to male sex because dermatoglyphics differ according to sex in control group as well, thus have to be analyzed in separate (11).

Conclusion

In conclusion, dermatoglyphic analysis as a genetic method could prove useful on assesing the relative risk for the occurence of post-traumtic algodystrophy. Upon obtaining dermatoglyphic imprints, the potential risk groups could be identified and proper measures taken to prevent the development of this longterm and therapy refractory disorder. Additional studies in a greater number of patients may render the method useful in the differential diagnosis against the above mentioned diseases in the near future.

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