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Original Article

Some vital enzymes in Dupuytren's disease and diabetes mellitus as a risk factor

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Abstract

Dupuytren's disease (DD) is a disease of unknown etiology, when the finger remains in a flexed position due to thickening of the aponeurosis. Our study aimed to investigate a possible relationship between adenosine deiminases 1 and 2 (ADA1, ADA2) and dipeptidyl peptidases 4 and 2 (DPP4, DPP2) with DD. The activity of named enzymes in aponeurosis and blood plasma from patients with DD and with various hand injuries (healthy individuals, HI) were compared. In aponeurosis from DD patients, ADA1 and ADA2 activities were higher by 5.6 and 7.8 times, respectively, compared to aponeurosis from HI. High levels of DPP4 and DPP2 activity were recorded in the DD aponeurosis, whereas they were untestable in the HI aponeurosis. Their activity in blood plasma was ~1.5 times higher in DD than HI subjects. In the aponeurosis, the highest activity of ADA1 was in sever level of DD, while of DPP4 and DPP2 in moderate level. ADA1 and DPP4 activity were significantly higher in DD with diabetes than without it. ADA and DPP can be recommended as targets in the fight against DD using their inhibitors assumed in medicine, which can help to avoid surgical intervention.

Keywords: adenosine deaminase 1, adenosine deaminase 2, aponeurosis, dipeptidyl peptidase 4, dipeptidyl peptidase 2

Introduction

Dupuytren's disease (DD) is a benign myeloproliferative disorder that results in one or more fingers being permanently bent in a flexed position [1]. DD begins with the formation of hard nodules or calluses under the skin. Normally, the palmar flap is composed of type 1 collagen, but in DD predominates more rigid type 3 collagen, which contributes to the formation of thick and coarse nodules [2]. Fibroblasts in the aponeurosis are transformed into myofibroblasts as a result of ischemia (occur at manual mechanical labor, a predominant risk factor of DD) and increased levels of free radicals (occur at any stress in tissue) [3]. At high fibroblast density, type I collagen production was suppressed, which explain the increased type III/I collagen ratio in DD. Fibroblast proliferation and collagen deposition contribute to microvascular constriction and progression of the pathology [2]. In DD collagen undergoes hydroxylation and glycosylation [4]. DD is commonly classified into three levels of severity, depending on the degree of tissue thickening and the extent of finger deformities – mild, moderate and severe [5].

Risk factors for DD are: gender (male), age (40+), heredity (60–70% autosomal dominant type) [6], alcoholism, smoking, manual work, previous hand injury, epilepsy HIV etc. [7]. Diabetes Mellitus (DM) is also among the risk factors for DD. A retrospective study analyzed the prevalence of DD between 2010 and 2020, comparing the type 1 DM (T1DM) and type 2 DM (T2DM) cohorts [8]. DD prevalence was revealed among T2DM patients compared with T1DM, as well as in patients

taking metformin (used in the treatment of T2DM) compared to those using insulin (mainly prescribed for the treatment of T1DM). These observations can be conditioned by elder ages of DD patients, when glycation end products are more pronounced. The relationship between DM and DD is likely based on the similarity of their pathogenesis. In DM, glycation end products are formed, which contribute to increased systemic fibrosis facilitating the DD development. Elevated levels of glycation end products increase fascial stiffness, favoring DD emergence. A diabetic joint mobility syndrome is observed in patients with chronic diabetes [9]. It is diagnosed by painless stiffness of the joints of hands and feet, impaired grip and fine motor skills, a positive "prayer sign". The DD increased prevalence in individuals with DM can be also linked to microvascular distraction and heightened collagen synthesis. The microvascular changes in DD are similar to those in DM [10].

Currently, the DD treatment are surgical or conservative (local injection of steroids from Clostridium Histolyticum [11], anti-inflammatory drugs, colchicine, tamoxifen, interferon, vitamin E, barotherapy and physical therapy or percutaneous needle aponeurotomy). Even with contradictory results and a frequent relapses, patients prefer conservative interventions because of the shorter recovery period. However, surgery remains the most effective treatment for DD despite intraoperative and postoperative complication, and the probability of relapses [12].

Adenosine is an endogenous physiologically active purine nucleoside known as a neurotransmitter, anticonvulsant, modulator of lipolysis, glycogenolysis, blood flow etc. [13]. It is an immunomodulatory and cytoprotective molecule, regulating immune reactions and alleviating inflammation [14]. Adenosine deaminase (ADA, EC 3.5.4.4) is an enzyme converting adenosine to inosine, essential in the development and maintenance of immune system [15]. ADA provides tissue repair and wound healing by promoting cell migration, growth, and differentiation. During inflammation caused by infection or tissue injury, the ADA level increases diminishing adenosine concentration and aggravating inflammation [16]. In humans, ADA is presented by two isoenzymes, ADA1 and ADA2 [17]. These isoenzymes are encoded by different genes, differ in their molecular and catalytic properties, location and physiological function. ADA2 binds to cell surface via proteoglycan receptors and participates in the regulation of cell proliferation and differentiation [18].

Dipeptidyl peptidases are serine proteases removing dipeptide from N terminus of polypeptides and proteins containing proline or alanine in the penultimate position. One of them, DPP4 (EC 3.4.14.5) [19], inactivates incretins hormones, supporting the development of T2DM. DPP4 inhibitors are among the drugs used against T2DM [20]. Non-covalent complex of DPP4 with ADA1 provides an extracellular ADA activity. Together with urokinase, DPP4 participates in the scar formation, stimulating TGFβ1-mediated myofibroblasts differentiation and production of non-physiological extracellular matrix components, precursors of rough scar formation [21]. Topical use of inhibitors of DPP4 and urokinase *in vivo* improved scar quality, suggesting the use of serine protease inhibitors for the treatment of skin fibrosis [22]. Dipeptidyl peptidase 2 (DPP2, EC 3.4.14.2) is a lysosome localized enzyme. It participates in degradation of collagen fragments, myofibril proteins, and neuropeptides, in cell differentiation, pathogenesis of autoimmune diseases [23].

The goal of the present work is to study the activity peculiarities of ADA1, ADA2, DPP4 and DPP2 enzymes in DD, to consider these enzymes as possible factors in the pathogenesis of disease, to identify them as potential therapeutic targets in the DD treatment.

Material and methods

Chemicals

Substrates ADA, adenosine and DPP Gly-Pro p-nitroanilide, Bovine serum albumin (BSA), erythro-9-(2-hydroxy-3-nonly) adenine (EHNA) and Coomassie G-250 dye were purchased from Sigma (USA). Other chemicals used were of the highest available purity.

Objects

Abnormally thickened aponeurosis and blood plasma from patients with DD and patients with various hand injuries (practically healthy individuals (HI, control) were provided by Heratsi Hospital. Samples were taken only from men and grouped by age and severity of the disease. 100 mg aponeuroses tissue was homogenized in 10 ml of 10 mM phosphate buffer pH 7.4 for 15 min in a manual glass homogenizer, centrifuged for 20 min at 17,000 rpm and the supernatant was used in the study.

Enzyme assay

ADA1 and ADA2 activity in the biological samples was assayed by the phenol-hypochlorite colorimetric

Table 1: ADA1 activity (means±SEM) in biological samples of DD and HI persons.

Enzyme	Biomaterial	HI	DD	P-value
ADA1, IU/mg (n)	Aponeurosis	21.05±1.1 (38)	118.3±5.2 (57)	<0.0001
	Blood	26.24±1.52 (25)	39.72±1.96 (28)	<0.001

method described earlier [24]. For two isoenzymes their specific optimal conditions were used: 40 mM K-Na-phosphate buffer, pH 7.8, and pH 6.5, 0.04 mM and 0.25 mM adenosine for ADA1 and ADA2, respectively. In ADA2 assay 1 mM EHNA, a selective inhibitor of ADA1, was included. DPPII and DPPIV activities were assayed in the alike procedures in the presence of 0.24 mM Gly-Pro p-NA using different buffers: 40 mM acetic buffer, pH 5.5, for DPPII and 40 mM K-Na-phosphate buffer, pH 7.4, for DPPIV [25]. All enzymatic activities were expressed in International Units per mg of protein in the assay mixture (IU/mg).

Protein was measured as described by Bradford [26], using BSA as a standard.

Equipment Potter manual glass homogenizer, MPW-352 centrifuge (Poland) and Cary Eclipse spectrophotometer (USA) were used.

Statistical analysis

Statistical analysis was performed using GraphPad prism 8.0 software for Windows, version 8.4.0. (671). One sample t and Wilcoxon analysis was used. The data were expressed as means±SEM.

Results

The activities of ADA1 and ADA2 enzymes

The activity of ADA1 and ADA2 in the homogenates of the aponeurosis of patients with DD was compared with that of conditionally HI. ADA1 activity was also assessed in plasma samples from DD and HI subjects, but ADA2 activity was not measured. The obtained results are presented in Table 1.

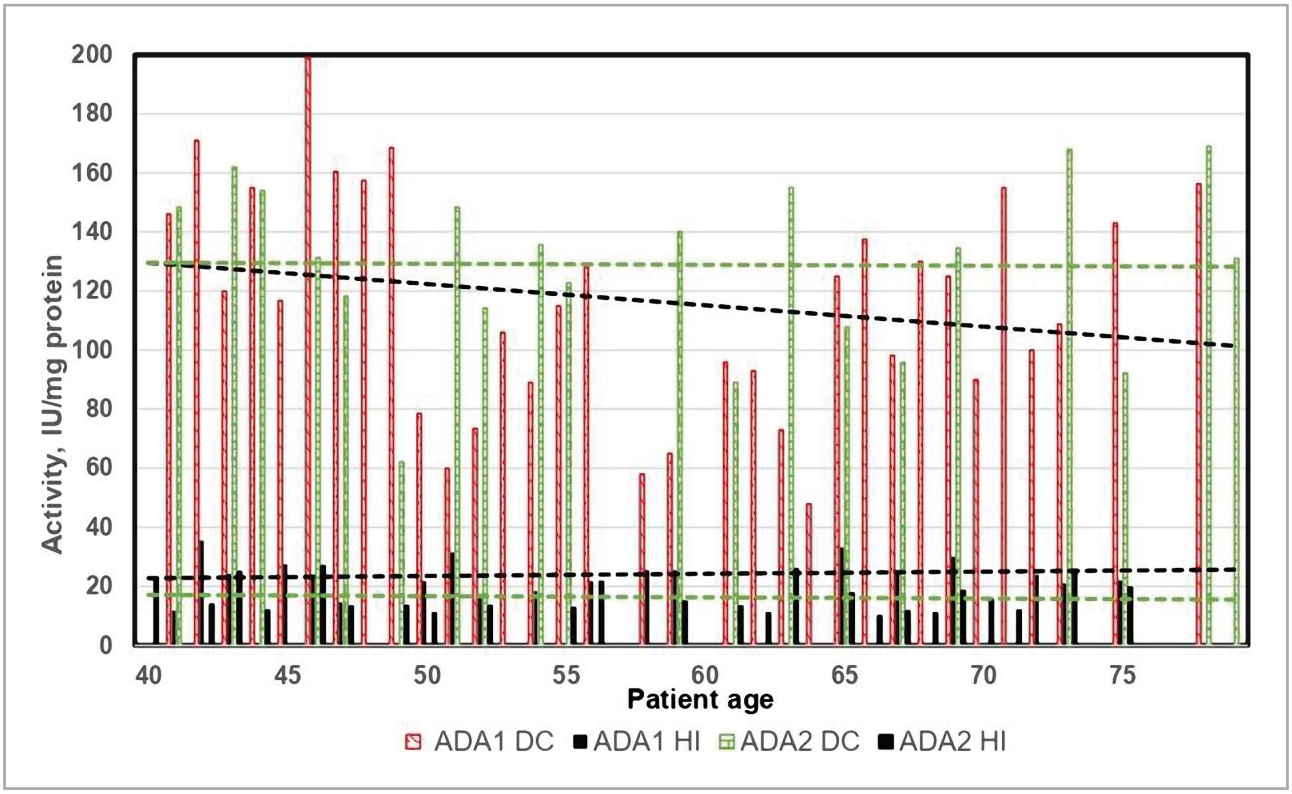

Figure 1: ADA1 and ADA2 activity in homogenates of aponeurosis of from DD and HI subjects in dependence of age; dotted lines are the linear trend lines for data.

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Table 2: DPP4 and DPP2 activities (mean±SEM) in biological samples from DD and HI persons.

Enzyme	Biomaterial	HI	DD	P-value
DPP4, IU/mg (n)	Aponeurosis	NM*	61.52±5.1 (35)	-
	Blood	15.3±0.9 (25)	23.25±0.6 (28)	<0.002
DPP2, IU/mg (n)	Aponeurosis	NM*	48.51±4.5 (28)	-
	Blood	13.7±0.9 (25)	20.34±0.7 (28)	<0.002

Note: * – NM-not measurable.

Table 1 shows that activity of ADA1 in the homogenates of aponeurosis from DD patients is approximately by 5.6 times higher than in the homogenates of aponeurosis from HI persons. The activity of ADA1 in the blood samples from DD aponeurosis is higher than that from HI persons by 1.5 times. The activity of ADA2 in the homogenates of aponeurosis from DD patients (127.9±11.3 IU/mg, n=28) is by 7.8 times higher than in the homogenates of aponeurosis from HI persons (16.3±1.1 IU/mg, n=28), p<0.0001.

The ADA1 and ADA2 activities in homogenates of aponeurosis from DD patients and from HI subjects are demonstrated in Figure 1 in dependence of the person age. A fairly high activity of ADA1 in patients aged 40–50 years (149.3±8.6 IU/mg), is followed by a 1.4-fold lower activity in patients aged 50+ years (105.2±4.5 IU/mg, p=0.001). They were 7.09 and 5 times, respectively, higher than in the samples of HI persons across all the ages (21.05±1.1 IU/mg). ADA2 activity in aponeurosis homogenates in these two age groups differs slightly: in patients aged 40–50 years (129.3±14.9 IU/mg) and 50+ years (125.9±7 IU/mg), and in individuals with HI – 17.23±1.3 IU/mg and 15.96±1.3 IU/mg, respectively.

The activity of DPP2 and DPP4 enzymes

DPP4 and DPP2 activity in tissue homogenates from HI patients was absent or below measurable levels. On the contrary, in homogenates of the aponeurosis of patients with DD, rather high levels of activity of these enzymes were found. Table 2 presents the activities of DPP2 and DPP4 in the blood plasma and homogenates of aponeurosis in DD and HI persons. In blood plasma

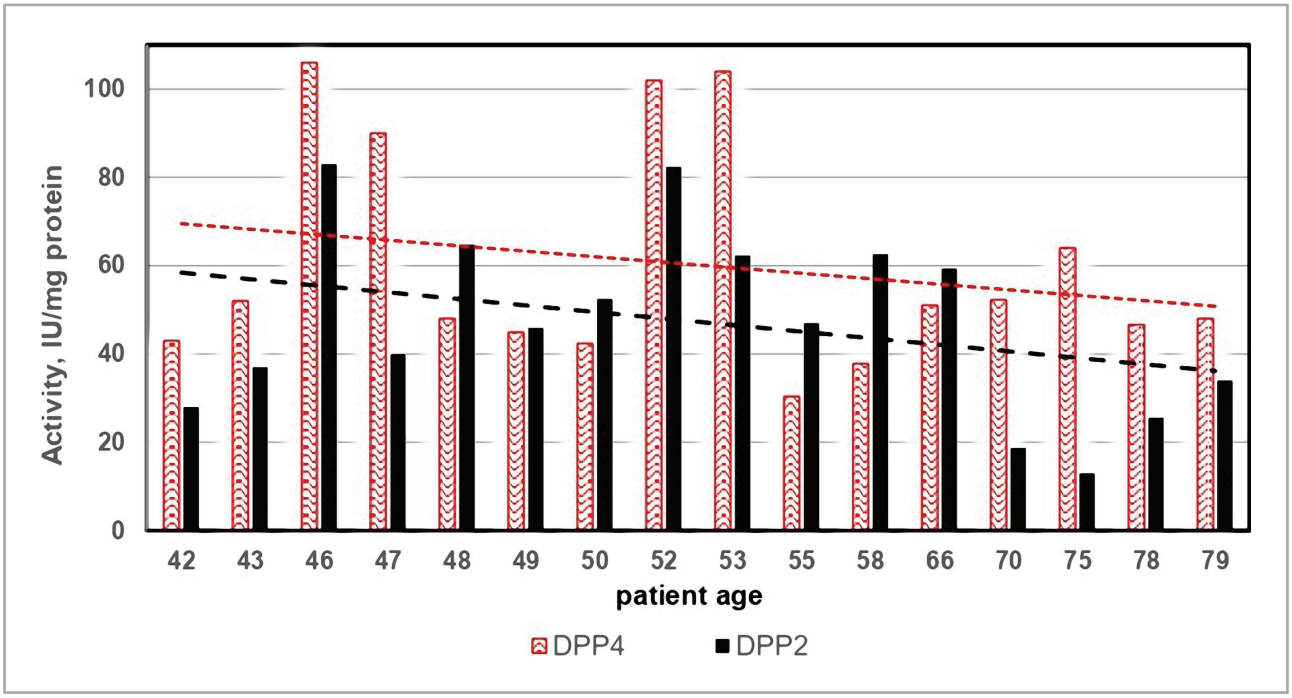

Figure 2: DPP4 and DPP2 activity in homogenates of aponeurosis of DD patients depending on age; dotted lines are the linear trends for data.

of DD patients, the DPP4 and DPP2 activities were close to each other and about 1.5 times higher compared to that in HI.

Figure 2 shows a decrease in DPP4 and DPP2 activity in aponeurosis homogenates from patients with DD with increasing patient age.

Activities of the studied enzymes in dependence of DD severity

ADA1, ADA2, DPP2 and DPP4 activities in homogenates of DD aponeurosis were grouped according to the severity of disease: mild (I), moderate (II) and severe (III) (Figure 3 and Figure 4).

Figure 3 shows the highest ADA activity at highest severity of DD.

Figure 4 shows that both the DPP4 (n=35) and DPP2 (n=28) activities are of the highest level at the moderate DD level (93±10.9 and 79±8.8 IU/mg, respectively), being nearly twice of values at the mild and severe DD levels, at which they differ insignificantly: DPP4 activity is equal to 50±4.2 and 62±7.5 IU/mg, and DPP2 is of 35±6.9 and 38±9.9 IU/mg, respectively. The predominance of the activity of both enzymes in moderate level in relation to the mild and severe levels is statistically significant: p=0.007 and 0.05 for DPP4, and p=0.009 and 0.01 for DPP2, respectively.

Activities of the studied enzymes in DD with and without DM

ADA1, ADA2, DPP4 and DPP2 activity in the aponeurosis homogenates from DD patients with and without DM are presented in Figure 5. Here ADA1 activity is approximately 1.41 times higher in DD patients with DM compared to those without DM (140±10.4 IU/mg and 100±9.6 IU/mg, respectively, p<0.0001).

DPP4 activity is approximately twice as high in the DD+DM compared to DD without DM (81±7 IU/mg and 42±1.5 IU/mg, p=0.02). DPP2 activity in DD with and without DM (47.68±5 IU/mg and 49.34±4.4 IU/mg, respectively), as well as ADA2 (127.0±1.6 IU/mg and 115±1.5 IU/mg, respectively) differ unreliably.

Discussion

Three types of DC were considered in the work [27], from which type 2, "the more normal type of DD, usually found in the palm only" is a subject of the present

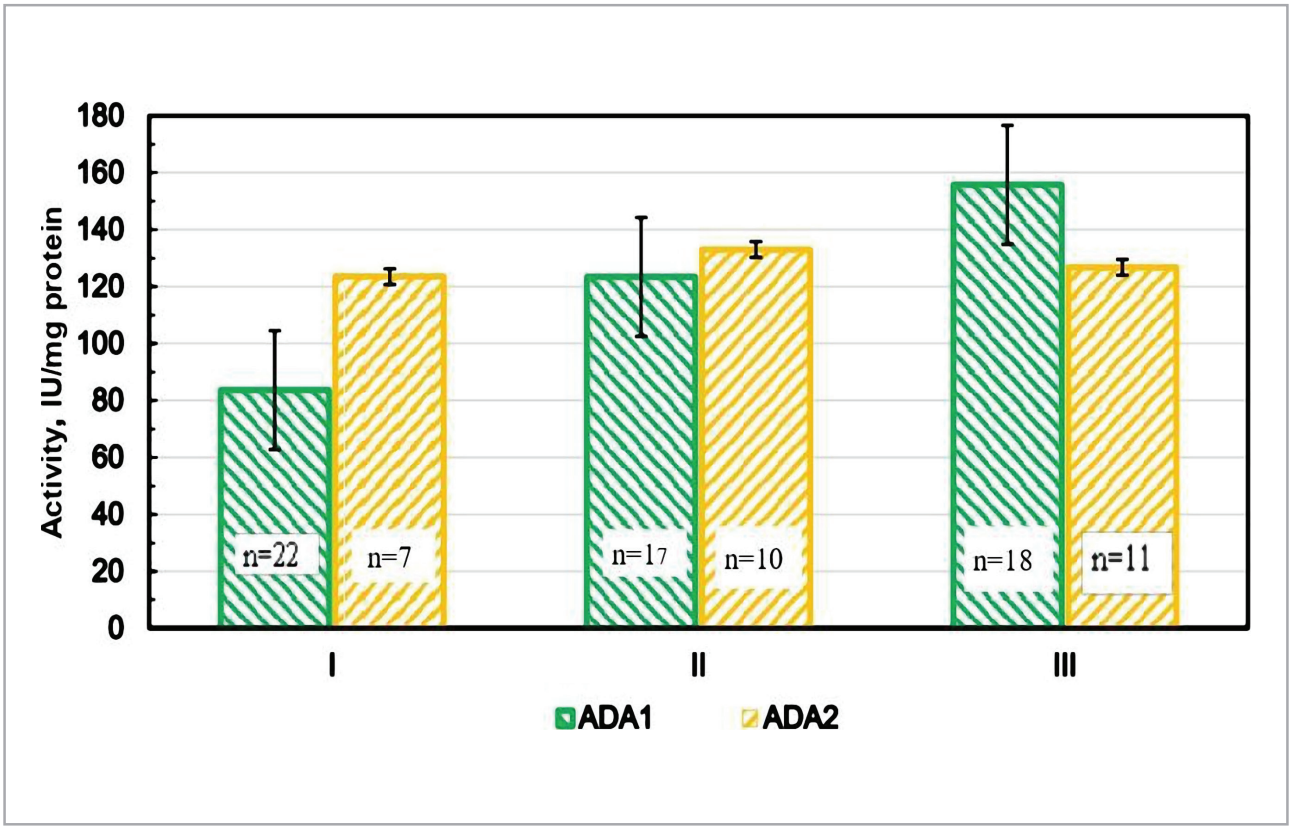

Figure 3: ADA1 and ADA2 activity in aponeurosis homogenates of DD patients in three levels of disease severity.

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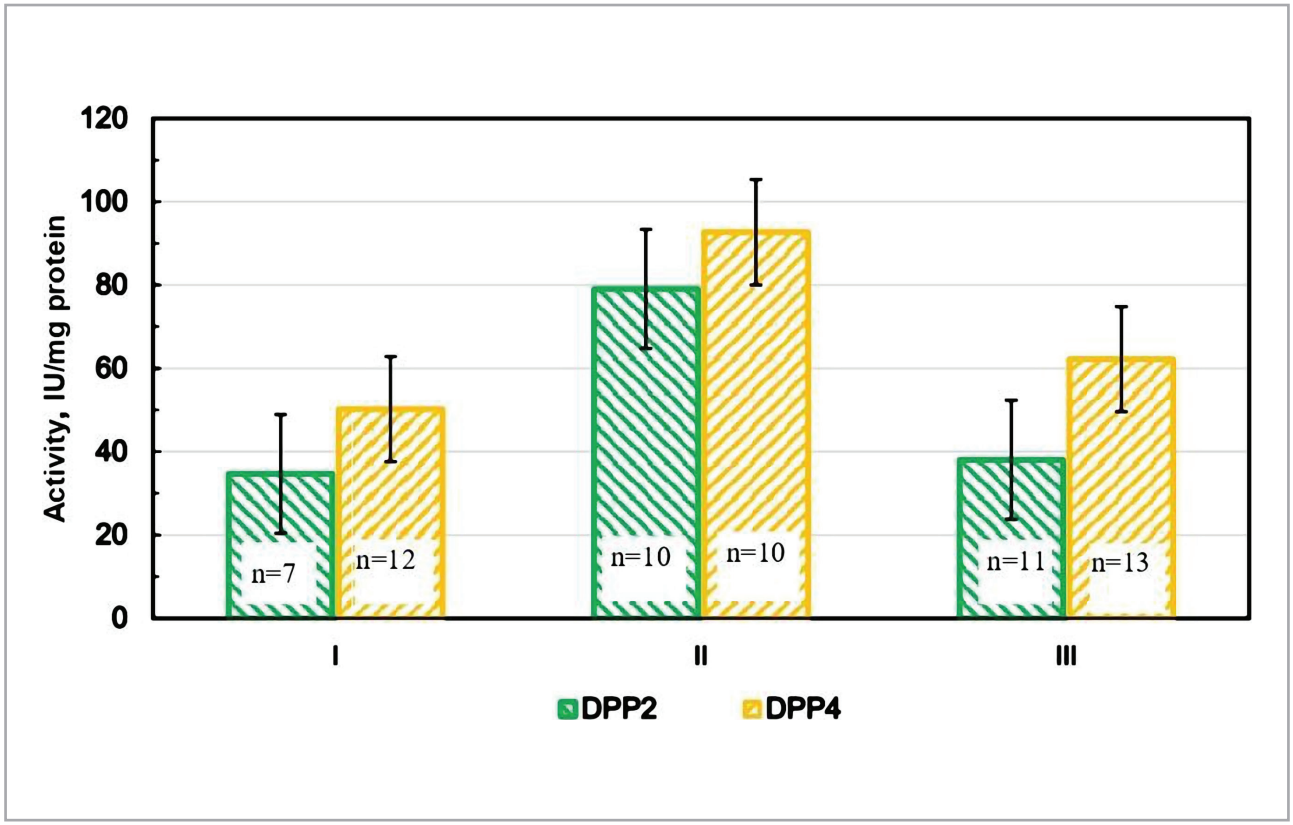

Figure 4: DPP2 and DPP4 activity in homogenates of aponeurosis of DD patients in three levels of disease severity.

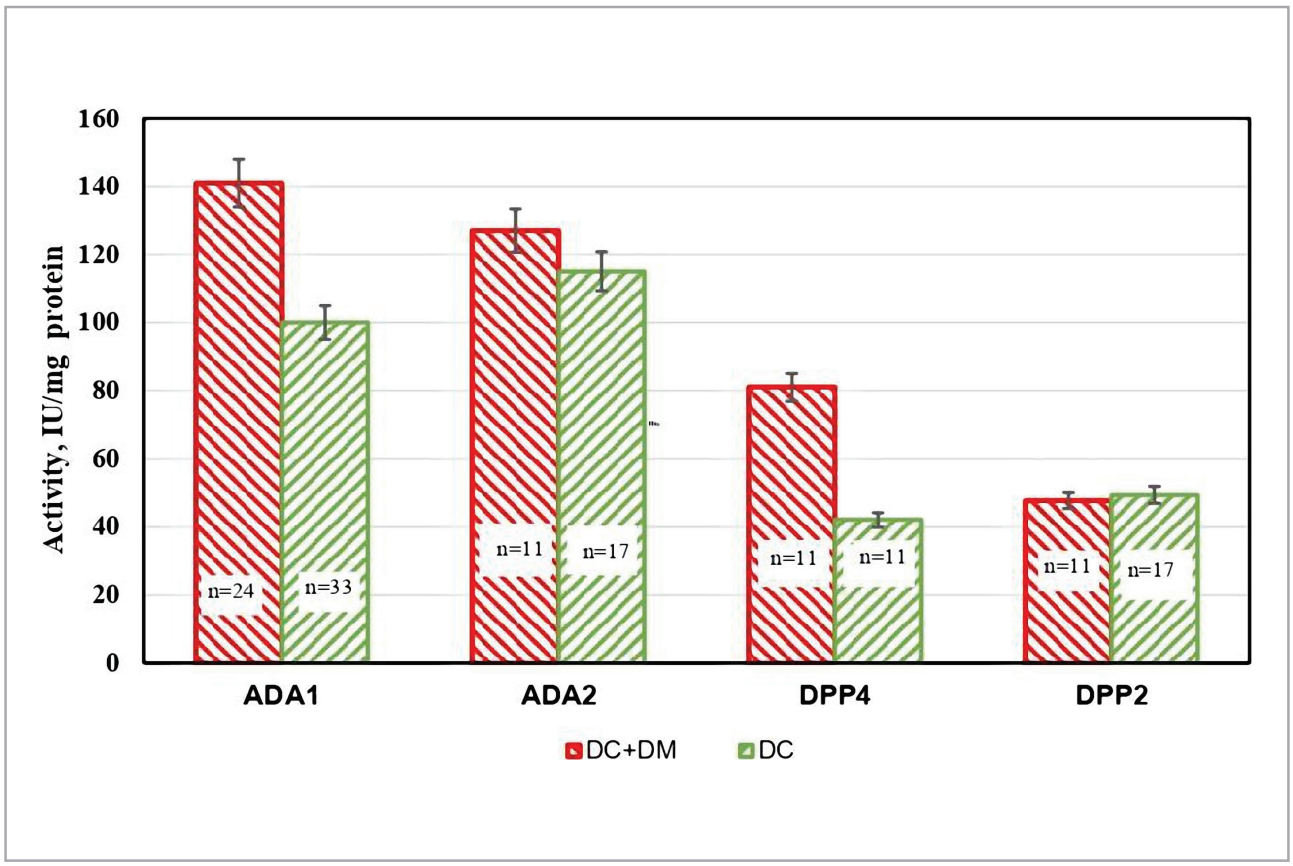

Figure 5: ADA1, DPP4, DPP2 and ADA2 activities in the homogenates of aponeurosis from DD patients with and without DM.

study. The authors noted that "DD is not primarily an inflammatory condition, but inflammation can be a component of the disease". Indeed, there are a few works in which the inflammatory infiltration of palmar tissue from DD has been reported [28]. The increase in dermal dendrocytes and inflammatory cells in DD tissue [29] supports the "extrinsic theory" of DD pathogenesis suggesting changes in the level of inflammatory cytokines in DD tissues, causing migration of Langerhans cells from the epidermis. Immunohistochemistry revealed inflammatory cells in the nodules of DD tissue suggesting the contracture of the fingers as a result of a chronic inflammation, which is supported indirectly by positive results of steroid treatment [30]. The present study documented sharp increase of the ADA activity in aponeurosis tissue homogenate of DD patients (Table 1, Figure 1). Moreover, highest ADA activity was seen at highest severity of DD (Figure 3). Increased ADA activity obviously should result in the exhaustion of its substrate, adenosine, a well-known anti-inflammatory agent in the body, aggravating inflammatory process [16]. This suggests that local inhibition of ADA activity may be useful in combating DD or at least mitigating its exacerbation.

In the introduction, important role of myofibroblasts and collagen in the formation of DD nodules was noted. The scientific publications prove the active participation of CD26/DPP4 in similar processes. It is involved in the pathogenesis of chronic fibrotic diseases: liver cirrhosis, kidney and lung fibrosis etc. Growing evidence suggests that inhibition of DPP4 can modulate the profibrotic tissue microenvironment and reduce fibrotic changes within affected organs [31]. Overexpression of DPP4 promoted fibroblast activation, whereas genetic inactivation or inhibition of DPP4 reduced the proliferation, migration, and expression of contractile proteins and release of collagen, promoted regression and ameliorated fibrosis [32]. Perturbation of fibronectin may result in development of fibrosis. In a model of severe dermal fibrosis, fibroblast cultures showed dysregulated fibronectin deposition with an increase in profibrotic DPP4-positive fibroblasts. DPP4 inhibitors normalized the deposition of fibronectin, fibrillin microfibrils, and collagen I [33]. Topical treatment with inhibitors of DPP4 and urokinase during scar formation *in vivo* improved scar quality, providing antifibrotic activity [21]. Being a lysosome protease, DPP2 participates in degradation of collagen fragments, myofibril proteins etc. Surprisingly, monitoring of DPP2 and DPP4 peptidase activities in homogenates of aponeurosis tissue from 40 "control" subjects showed that they were below the measurable level. The appearance of high activity of both peptidases in the aponeurosis of DD patients (Table 2, Figure 2) is a signal of a deviation of the metabolism of fibrillar molecules from the norm, more significant in the mild level of DD (Figure 4). Hence the inhibition of DPP family enzymes, probably not only the studied DPP2 and DPP4, should be considered as a positive approach to the treatment of DD.

The association of DD with DM is wide reported. The DD and DM conditions increase with age. The DM morphology may trigger DD: microvascular changes in DM contribute to local hypoxia supporting the development of DD. The microvascular changes observed in DD and DM are similar [10]. Present report demonstrated higher levels of ADA1 and DPP4 activity in the homogenate of aponeurosis tissue from patients with DD, suffering sym from diabetes, compared to those in patients with DD only (Figure 5). It is known, that ADA and DPP4 participate in the pathophysiology of T2DM and its complications: a positive correlation between ADA level and glycemic control proved its importance in glucose and lipid metabolic derangements in T2DM patients [34]. The inhibitors of DPP4 are potential drugs for the treatment of T2DM [35].

Conclusion

The strength of this work is that it contributes to the rare studies of the biochemical processes involved in the pathogenesis of DD. In particular, the observed sharp increase in ADA activity in pathological tissue added a new, albeit indirect, indication of the involvement of inflammation in the development of DD. The demonstrated pronounced activity of the DPP family enzymes with the ability to destroy many structural polypeptides of tissue and cells, confirms previously expressed assumptions about the role of serine proteases in DD. Overall, the described results can serve as bases for recommending the use of ADA and DPP inhibitors in topical external application to alleviate the pathology of DD. Such non-invasive treatment will be more attractive to patients than any other currently used means, in particular, surgical intervention. However, to overcome the main weakness of this work and ensure compliance with such recommendations, larger numbers of patients need to be involved in future study.

Conflict of interest

The authors declare no conflict of interest.

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Ethics approval

Human aponeurosis and blood were obtained from patients with their informed written consent, and their use was approved by the Ethics Committee of the 1st Clinical Hospital, Yerevan State Medical University after M. Heratsi, in accordance with the principles of the Declaration of Helsinki.

References

1. Soreide E, Murad M, Denbigh M, et al. Treatment of Dupuytren's contracture: a systematic review. BONE joint J. 100-B: 1138-45, 2018. DOI: 10.1302/0301-620X.100B9.BJJ-2017-1194.R2
2. Murrell G, An insight into Dupuytren's contracture. Ann R Coll Surg Engl. 74(3): 156-60, 1992.
3. Türker T, Murphy E, Kaufman L, Kutz E, Meister A, Hoying B. Response of Dupuytren Fibroblasts to Different Oxygen Environments. The Journal of Hand Surgery. 38(12): 2365-2369, 2013, DOI: 10.1016/j.jhsa.2013.08.122
4. Bazin S, Lous M, Duance V, et al. Biochemistry and histology of the connective tissue of Dupuytren's disease lesions. Eur J Clin Invest. 10(1): 9-16, 1980. DOI: 10.1111/j.1365-2362.1980.tb00003.x
5. Rehman S, Goodacre R, J Day P, Bayat A, Westerhoff H. Dupuytren's: a systems biology disease. Arthritis Res Ther. 13(5): 238, 2011. DOI: 10.1186/ar3438
6. Mella J, Guo L, Hung V, Dupuytren's Contracture: An Evidence Based Review. Ann plast surg. 6S Suppl 1: S97-S101, 2018. DOI: 10.1097/SAP.0000000000001607
7. Broekstra D, Groen H, Molenkamp S, et al. A. systematic review and meta-analysis on the strength and consistency of the associations between Dupuytren's disease and diabetes mellitus, liver disease, and epilepsy. Plastic Reconstructive Surg. 141: 367e-379e, 2018. DOI: 10.1097/PRS.0000000000004120
8. Ganesan S, Tantone R, Komatsu D, Hurst L. The prevalence of Dupuytren's disease in patients with diabetes mellitus. Commun Med. 3, 96, 2023. DOI: 10.1038/s43856-023-00332-7
9. Gerrits E, Landman G, Nijenhuis-Rosien L, Henk J. Limited joint mobility syndrome in diabetes mellitus: a minireview. World J. Diabetes. 6: 1108–1112, 2015. DOI: 10.4239/wjd.v6.i9.1108
10. Hart M, Hooper G. Clinical associations of Dupuytren's disease. Postgrad Med J. 81(957): 425-8, 2005. DOI:10.1136/pgmj.2004.027425.
11. Watt A, Curtin C, Hentz V. Collagenase injection as nonsurgical treatment of Dupuytren's disease: 8-year follow-up. J Hand Surg Am. 35(4): 534-539, 2010. DOI: 10.1016/j.jhsa.2010.01.003
12. Gil J, Akelman M, Hresko A, Akelman E. Current Concepts in the Management of Dupuytren Disease of the Hand. J Am Acad Orthop Surg. 29(11): 462-469, 2021. DOI: 10.5435/JAAOS-D-20-00190
13. Borowiec A, Lechward K, Tkacz-Stachowska K, Składanowski A. Adenosine as a metabolic regulator of tissue function: production of adenosine by cytoplasmic 5'-nucleotidases. Acta Biochim. 53: 269-278, 2006.
14. Haskó G, Cronstein B. Adenosine: an endogenous regulator of innate immunity. Trends in Immunology. 25: 33-39, 2004. DOI: 10.1016/j.it.2003.11.003
15. Cekic C, Linden J. Purinergic regulation of the immune system. Nat Rev Immunol 16: 177-192, 2016. DOI: 10.1038/nri.2016.4
16. Antonyan A. Adenosine deaminase: A target enzymein different pathologies. World Journal of Pharmaceuti. 3(8): 6-18, 2017.
17. Gakis C. Adenosine deaminase (ADA) isoenzymes ADA1 and ADA2: diagnostic and biological role. Eur Respir J. 9: 632–633, 1996. DOI: 10.1183/09031936.96.09040632.
18. Lee P, Aksentijevich I, Zhou Q. Mechanisms of vascular inflammation in deficiency of adenosine deaminase 2 (DADA2). Semin Immunopathol. 44(3): 269-280, 2022. DOI: 10.1007/s00281-022-00918-8.
19. Gorell M, Gysbers V, Mccaughan G. CD26: Multifunctional integral membrane and secreted protein of activated lymphocytes. Scand J Immunol. 54: 249-264, 2001. DOI: 10.1046/j.1365-3083.2001.00984.x
20. Mulvihill E, Drucker D. Pharmacology, physiology, and mechanisms of action of dipeptidyl peptidase-4 inhibitors. Endocrine Reviews. 35(6): 992-1019, 2014. DOI:10.1210/er.2014-1035
21. Vorstandlechner V, Laggner M, Copic D, et al. The serine proteases dipeptidyl-peptidase 4 and urokinase are key molecules in human and mouse scar formation. Nat Commun. 12: 6242, 2021. DOI: 10.1038/s41467-021-26495-2
22. Li X, Zhang K, Zhang Zh, Wum J, Yuan Zh, Yuan F, Chen J. Inhibiting dipeptidyl peptidase 4 positive fibroblasts using zinc sulfide cellulose nanofiber scaffolds to achieve scarless healing. Int J Biol Macromol. 282(Pt 6): 137525, 2024. DOI: 10.1016/j.ijbiomac.2024.137525
23. Maes M, Scharpé S, De Meester I. Dipeptidyl peptidase II (DPPII), a review. Clin Chim Acta. 380(1-2): 31-49, 2007. DOI: 10.1016/j.cca.2007.01.024;
24. Sharoyan S, Antonyan A, Mardanyan S, Lupidi G, Cristalli G. Influence of dipeptidyl peptidase IV on enzymatic properties of adenosine deaminase. Acta Biochim Pol. 53: 539-546, 2006. DOI: 10.18388/abp.2006_3325.
25. Sharoyan S, Antonyan A, Mardanyan S, Lupidi G, Cuccioloni M, Angeletti M, Cristalli G. Bovine dipeptidyl peptidase II binds adenosine deaminase. Biochemistry (Moscow) 73(8): 1168-1176, 2008.
26. Bradford M. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding Anal. Biochem. 72: 248-254, 1976. DOI: 10.1016/0003-2697(76)90527-3.
27. Al-Qattan M. Factors in the Pathogenesis of Dupuytren's Contracture. The Journal of Hand Surgery. 31(9): 1527–1534, 2006. DOI: 10.1016/j.jhsa.2006.08.012.
28. Schubert T, Weidler C, Borisch N, Schubert C, Hofstädter F, Straub R. Dupuytren's contracture is associated with sprouting of substance P positive nerve fibres and infiltration by mast cells. Ann Rheum Dis. 65(3): 414-415, 2006. DOI:10.1136/ard.2005.044016
29. Qureshi F, Hornigold R, Spencer J, Hall S. Langerhans cells in Dupuytren's contracture. J Hand Surg. 26B(4): 362–367, 2001. DOI: 10.1054/jhsb.2000.0518
30. Meek R, McLellan S, Crossan J. Dupuytren's disease. A model for the mechanism of fibrosis and its modulation by steroids. J Bone Joint Surg. 81-B(4): 732-738, 1999. DOI:10.1302/0301-620X.81B4.0810732
31. Ohm B, Moneke I, Jungraithmayr W. Targeting cluster of differentiation 26/dipeptidyl peptidase 4 (CD26/DPP4) in organ fibrosis. Br J Pharmacol. 180: 2846-2861, 2023. DOI: 10.1111/bph.15967
32. Soare A, Györfi HA, Matei AE, et al. Dipeptidylpeptidase 4 as a Marker of Activated Fibroblasts and a Potential Target for the Treatment of Fibrosis in Systemic Sclerosis. Arthritis Rheumatic. 72: 137-149, 2020. DOI: 10.1002/art.41058.

33. Zeyer KA, Bornert O, Nelea V, et al. Dipeptidyl Peptidase-4-Mediated Fibronectin Processing Evokes a Profibrotic Extracellular Matrix. J Invest Dermatol. 144(11): 2477-2487.e13. 2024. DOI: 10.1016/j.jid.2024.03.020
34. Patel B, Taviad D, Malapati B, Chhatriwala M, Shah R. Serum Adenosine Deaminase in patients with Type-2 Diabetes Mellitus and its Relation with Blood Glucose and Glycated Haemoglobin levels. Intern J Biomed Res. 5(9): 556-558, 2014. DOI: 10.7439/ijbr.v5i9.771
35. Mest H, Mentlein R. Dipeptidyl peptidase inhibitors as new drugs for the treatment of type 2 diabetes. Diabetologia 48(4): 616-20, 2005. DOI: 10.1007/s00125-005-1707-5

 https://doi.org/10.46389/rjd-2025-2063