Imiquimod: A potential weapon against Dupuytren contracture

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Summary Dupuytren disease is a proliferative fibroplasia of the subcutaneous palmar tissue, occurring in the form of nodular and cords. Evidence is certainly accumulating for raised levels in Dupuytren’s tissue of growth factors known to stimulate fibroblasts, Interleukin-1, basic fibroblast growth factor, transforming growth factor-beta, prostaglandin-F2, prostaglandin-E2, platelet derived growth factor and connective tissue growth factor have been suggested to have a role.

Imune modification of profibrotic cytokines would provide a novel means to treat dupuytren contracture. Imiquimod cream 5% (Aldara) is an immune modifier, that downregulates transforming growth factor-beta and fibroblast growth factor-2 (the two most important cytokine in producing fibrosis).

Based on previous mentioned evidence we suggest: imiquimod as a potential drug for dupuytren contracture treatment.

A major challenge of contemporary medicine is to break the traditional compartmentalization that frequently separates various fields. Unexpected linkages between various areas of medicine are indeed of particular interest.

In this paper, the aim is to enlighten the hand surgeon colleagues about the recently discovered immunomodulatory effect of imiquimod in order to encourage research on the use of this safe agent in the treatment of Dupuytren contracture.

Dupuytren’s disease is a condition of the hand characterized by the development of new fibrotic tissue in the form of nodules and cords [1].

The site of onset is the fibrofatty layer between the skin and deep structures of the palmar surface of the hand, which had a precisely ordered system of subcutaneous ligamentous fibers. Transforming growth factor-beta (TGF-b), Platelet derived growth factor (PDGF), Epidermal growth factor (EGF), Interleukin-1 (IL-1), Interleukin-4 (IL4), Interleukin-6 (IL-6), Oncostatin M (Osm) and Tumor necrosing factor (TNF), have been demonstrated to regulate fibroblast proliferation and deposition of extracellular matrix in vivo and in vitro [2].

Transforming growth factor-beta (TGF-b) is a key fibrogenic cytokine that has been shown to stimulate fibroblast proliferation and extracellular matrix deposition [3,4].
Evidence is certainly accumulating for raised levels in Dupuytren’s tissue of growth factor known to stimulate fibroblasts. IL-1, FGF, TGF-b, PG-F2, PG-E2, PDGF and CTGF have been suggested to have a role [5–8].

Alioto et al. [9] in an experimental research exposed cells of both the normal palmar fascia and Dupuytren fascia to FGF, TGF-b, PDGF, there were quantitative and qualitative differences between the cell types, with Dupuytren contracture being more metabolically active and more sensitive to the growth factors tested.

Immune modification of profibrotic cytokines would provide a novel means to the Dupuytren contracture.

Imiquimod is a low molecular weight imidazoquinoline that has been approved under the registered name ‘Aldara’ for the topical treatment of Human papilloma virus induced warts. Its capacity to boost immune responses via the induction of cytokines in the treated lesions encouraged several authors to use the drug for the treatment of skin cancers [10].

Imiquimod cream 5% (Aldara) is an immune response modifiers that has demonstrated antiviral as well as antitumor activity both in vivo and in vitro. It induces the cytokine IFNα, IFNγ, TNFα, IL-1, IL-6, IL-8, IL-10, IL-12 and it stimulate cell-mediated immunity (TH1 Pathway).

IFN-γ is a TH1 cytokine that downregulates expression of TGF-b. In addition, it possesses an ability to suppress the TH2 pathway including profibrotic IL4 [2,11].

In an experimental research Hesling et al. [10] measured FGF-2 level in skin biopsy before and after imiquimod application. This study reveals that FGF-2 level decreased from 100% to 24% after imiquimod application.

Based on previously mentioned data we suggest, imiquimod as a potential drug for dupuytren contracture treatment. It is believed that the attempt to enlighten the hand surgeon colleagues about the recently discovered immunomodulatory effects of imiquimod stimulates a multiplicity of investigations on the utility of these agents in Dupuytren contracture, leading to provision of better treatment to patients suffering from this conundrum.

References