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Dupuytren's contracture: Is it Originally from Deep Dermis or Palmer Fascia?

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Dupuytren's contracture: Is it Originally from Deep Dermis or Palmer Fascia

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Abstract

Background: Fibroproliferative disorders include Dupuytren's contracture, which involves the palm of the hand, causing flexion contracture deformity of the fingers and functional limitations. The exact pathogenesis of this disorder remains questionable; past studies claimed that myofibroblasts are the cells responsible for Dupuytren's contracture. Despite having no complete cure for Dupuytren's contracture, different treatments are available.

Objective: To determine the histopathological origin of Dupuytren's cord, either from the deep dermis or from the palmar fascia.

Patients and Methodology: This prospective clinical study included twenty patients. We operated on fingers starting from 30 degrees of contracture, with the median preoperative flexion contracture degree being 67.1 (range 30.8-164.1). They all underwent dermo fasciectomy and pathological analysis of diseased tissue by H&E and immunostaining.

Results: The results of this study were based on an H&E stain examination, where we found all dermal slides (100%) stained positive. Eight dermal slides (40%) were positive stains. Also, 15 subcutaneous slides (75%) were positive. By immune stain examination, we found that all fascial slides (100%) were stained positively. Seventeen subcutaneous slides (85%) were positive stains. Also, 12 dermal slides (60%) were positive, ranging in severity from five upper dermis slides (41.66%) to seven lower dermis slides (58.33%).

Conclusion: Abnormal alpha-smooth muscle actin positive in both the palmar fascia and dermis, even the upper dermis. It is undeniable that the skin plays a part in etiology and recurrence.

Keywords: Dupuytren's contracture; myofibroblasts; alpha smooth muscle actin

1. Introduction

Our hands are the upper limb's most crucial component, responsible for grasping and handling motor power and even sensory function. ¹

Fibroproliferative disorders include Dupuytren's contracture, which involves the hand's palm and leads to ongoing persistent flexion contracture deformity of the digits, which restricts hand movements and affects the lifestyle.² Patients complain of contracted fingers, including difficulties while wearing gloves, inserting hands in pockets, and interfering with social connections like shaking or squeezing hands. It also points to difficulties while washing faces or shaving. ³

Dupuytren's contracture leads to transformation in the healthy connective tissue of the hand into fibrous tissue; this evolves into pathological cords or nodules and leads to

flexion contracture. ⁴

Treatment selection is based on the disease's severity, deformity level, and functional restrictions. A variety of non-surgical and surgical options is available for management, such as corticosteroid injection, collagenase injection, Radiotherapy, percutaneous needle fasciotomy, surgical fasciectomy, and dermo fasciectomy. ⁵

There is insufficient histopathological information on the extent of dermal association in Dupuytren's disease. In addition, there is controversy about the involvement of skin in the evolution of the disease. It has been suggested that skin might have a larger role than originally understood. ⁶

Therefore, this study aims to determine the histopathological origin of Dupuytren's cord, either from the deep dermis or from the palmar fascia.

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2. Patients and methods

The research was carried out after approval in April 2021 from the research ethics committee of Al-Azhar University's Faculty of Medicine for Girls.

This diagnostic cross-sectional study included twenty patients with Dupuytren's contracture, all of whom were treated with dermo fasciectomy from June 2021 to October 2022.

We included patients with Dupuytren's contracture at any age and any gender,

a flexion contracture of at least 30° in the MCP, PIP, or DIP joints, and a distinct pathological chord within the palmar fascia. Exclusion criteria: General contraindication to operation re, refusal to participate in the trial, or having a specific treatment preference.

Preoperative evaluation of the patient (general and local): All cases were subjected to the following items: History and physical examination, preoperative investigations, patient consent, preoperative medical photography, and preoperative marking.

Operative technique: Dermofasciectomy was done with excision of visible Dupuytren's diseased tissue with excision of (10mm×3mm) length from skin overlying cord for histopathological examination.

Post-operative care: Following the operation, major issues demand consideration: one-week splinting, wound care management, hand physiotherapy, and nighttime splinting for six months for all patients.

Histopathology: The specimen was preserved in 10% formalin and was sent to a histopathological laboratory for examination.

Haematoxylin- Eosin (H&E): fixed the excised tissues in formol. The 5 µm-thick cross-sections from the paraffin blocks were placed on slides after deparaffinization; one cross-section was conducted for Hematoxylin and eosin (H&E) staining to reassess the diagnosis by light microscope.

Immunohistochemistry: Another section from each paraffin block was mounted on positively charged slides to be submitted for automated immunostaining for alpha-smooth muscle actin, primary antibody (α-SMA)(MM1, Cod: 28330030). Following deparaffinization, the cross-sections were heated in citrate buffer with a pH of 6 to extract the antigen. Then, tissue sections were exposed to antigen retrieval solution with PH 9 at 90 C. Tissue endogenous peroxidases and autoantibodies were blocked by Hydrogen peroxide 3% to avoid producing non-specific binding sites and reduction of the background by bovine serum. A secondary antibody (labeled Streptavidin-Biotin2 System-Horseradish Peroxidase (LSAB2 System-HRP) was used.

The chromogen Diaminobenzidine (DAB) chromogen (Dako (USA) was applied to develop a colored precipitate at the site of antigen expression in the tissue. Mayer's Hematoxylin was utilized for contrast staining. Mounting material from Zymed was applied to seal the slide. The sections were examined using an Olympus BX50 light microscope from Olympus America, Inc., NY, USA.

Control sections were included in each run as negative staining controls. They were processed in phosphate buffer solution as an alternative to the primary antibody taken from adjacent areas of the non-diseased (Dupuytren's) part of the tissue.

Evaluation of Immunostaining: Positive staining was identified by the presence of a brown tint in the nucleus and cytoplasm of the normal or tumor cells. α-SMA staining was assessed based on two parameters: the intensity of nuclear staining and the extent (% of positive cells). The nuclear staining intensity was classified as follows: no staining (0), faint (1+), moderate (2+), or strong (3+). The extent was measured using a semi-quantitative scale ranging from 0% to 100%. The α-SMA staining intensity was categorized into three groups: mild (+), moderate (++), and intense (+++).

The percentage was determined by counting a minimum of 50 nuclei and then computing the ratio of immune-reactive nuclei to the total number of nuclei, multiplied by 100. The percentages were rounded to the nearest 10%: (0): <10% staining (1+): 11- 30% epithelial cell positivity (2+): 31-60% epithelial cell positivity (3+): >60 % positive epithelial cells. Cases with no staining or faint staining covering less than 10% of the area were classified as negative.

Follow-up: All cases were followed for six months at the outpatient clinic to evaluate possible recurrence.

Data analysis using statistics: The data were input into the computer and analyzed using IBM SPSS software version 20.0 (Armonk, NY: IBM Corp). Qualitative data were represented by numerical values plus percentages. Quantitative data were summarized using range, mean, standard deviation, median, and interquartile range (IQR). The significances of the outcomes were assessed based on a P value of $p < 0.05$.

3. Results

Recurrence: Appearance of a new lesion or lesions within the operated area is considered as recurrence. In our study, no recurrence was observed through 6 months follow up of all cases. The present results showed that right hand affection was detected in 45%, both right and left hands in 55%, while left hand alone has not been detected in any of all the studied cases [Table 1](#).

Table 1. Distribution of the cases under the study regarding hand and fingers (n = 20)

<u>PATIENT HANDS</u>	<u>NUMBER OF CASES</u>	<u>PERCENTAGE</u>
AFFECTED HAND		
RIGHT ONLY	9	45%
LEFT ONLY	0	0%
BOTH	11	55%
OPERATED HAND		
RIGHT	15	75%
LEFT	5	25%
FINGERS		
LITTLE ONLY	6	30%
RING ONLY	7	35%
LITTLE AND RING	5	25%
THUMB ONLY	2	10%

Degree of contracture, It was markedly improved post-surgery Table 2.

Table 2. Comparison of the degree of contracture before and after surgery (n = 20)

<u>DEGREE OF CONTRACTURE</u>	<u>PRE-</u>	<u>POST-</u>	<u>Z</u>	<u>P</u>
MIN. - MAX.	30.80 164.1	- 0.0 -30.0	3.920*	<0.001*
MEAN ± SD.	75.67 39.60	± 7.73 ±10.57		
MEDIAN (IQR)	67.10 (40.10 -99.6)	0.0 (0.0 -15.70)		

IQR: inter quartile range.

P: p value for comparing between pre and post-operative

*: statistically significant at $p \leq 0.05$

H&E staining ; presence of fibrosis was distributed in the excised tissues as follows; fascia showed fibrosis in 100% , subcutaneous layer showed in 60% while dermis has been detected in 50% of the studied cases 30% of upper dermis and 20% of lower dermis Table 3 and the following Figure 1, Figure 2 and Figure 3.

Table 1. Distribution of fibrosis in the cases under the study according to H&E stain (n = 20)

<u>H&E STAIN</u>	<u>PRESENCE OF FIBROSIS</u>	
	<u>No. of cases</u>	<u>Percentage</u>
FASCIA	20	100%
SUBCUTANEOUS	12	60%
SKIN	10	50%
	cases	
LOWER DERMIS	6 cases	30%
UPPER DERMIS	4 cases	20%

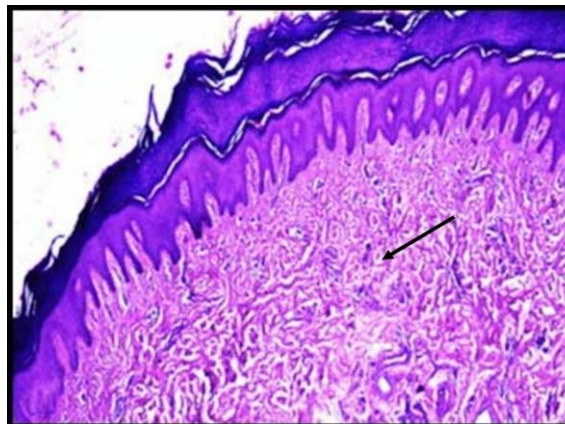


Figure 1. H&E Stain showed a dermal fibrosis of a case of Dupuytren's contracture.

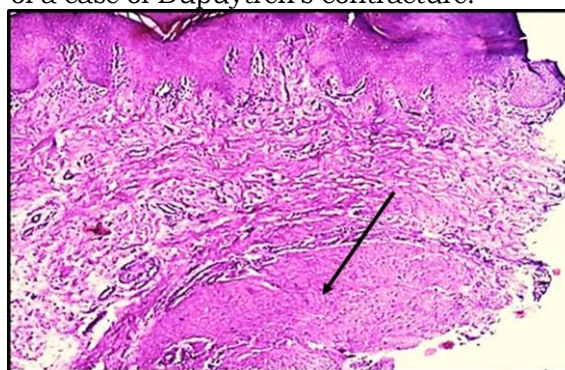


Figure 2. H&E stain showing a Part of skin with underlying part of Dupuytren's contracture (arrow) (x100)

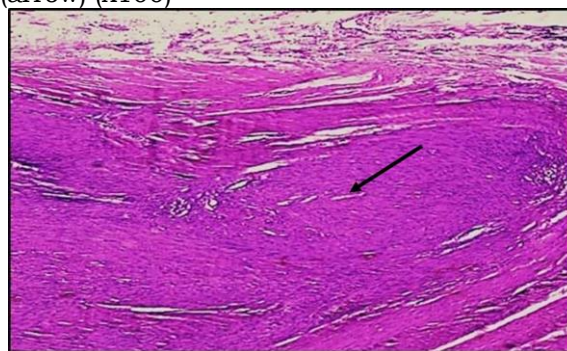


Figure 3. H&E stain show large nodule of immature fibroblasts and myfibroblasts with pushing and focally infiltrating Borders (200x)

Regarding to α -SMA immunostaining; it has been detected positive in different areas of the excised tissues in different patterns. The fascia showed a marked positivity for α -SMA in 100% of the cases. Subcutaneous region showed 80%, while dermis reflected α -SMA positivity in 60% of the studied cases Table 4 and Figure 4,5,6 and 7). The severity and extent of Dermal immunostaining is illustrated in Table 5

Table 2. Distribution of the cases under the study according to α -SMA immunostain (n = 20)

IMMUNOSTAIN	POSITIVEA-SMA	
	No. of cases	Percentage
FASCIA	20 cases	100%
SUBCUTANEOUS SKIN	16/20	80%
LOWER DERMIS	8/12	66%
UPPER DERMIS	4/12	34%

Table 3. Dermal immunostaining severity and the extent (percentage of positive cells)

POSITIVE DERMAL IMMUNOSTAIN OF (A-SMA)		No. of cases	Percentage
NUMBER OF POSITIVE IMMUNOSTAIN	OF	12	60%
MILD		6	50%
MODERATE		4	33.3%
SEVERE		2	16.6%

* The intensity of nuclear staining was graded as: no staining (0), weak (1+), moderate (2+), or strong (3+). The extent was semi-quantitatively estimated with a range of 0% to 100%. α -SMA staining intensity was divided into 3 groups as mild (+), moderate (++), and severe (+++).

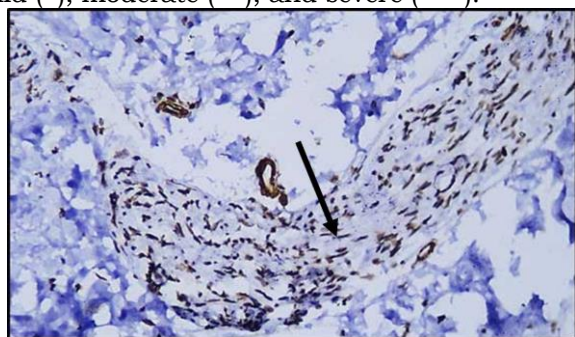


Figure 4. Immune stain of Dupuytren's contraction showed positively stained by α -smooth muscle actin (arrow) (200x)

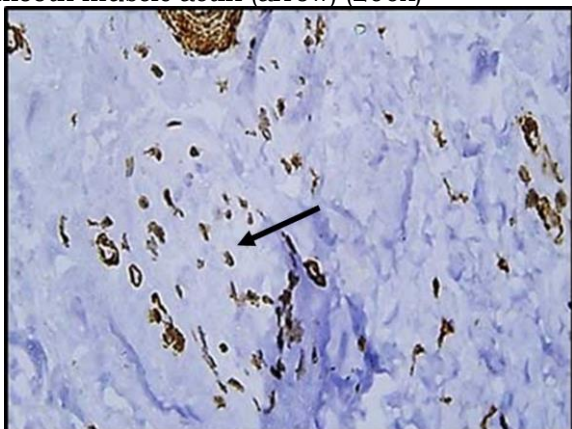


Figure 5. Immune stain show scattered myofibroblast immunostained cells in lower dermis (arrow) (x200)

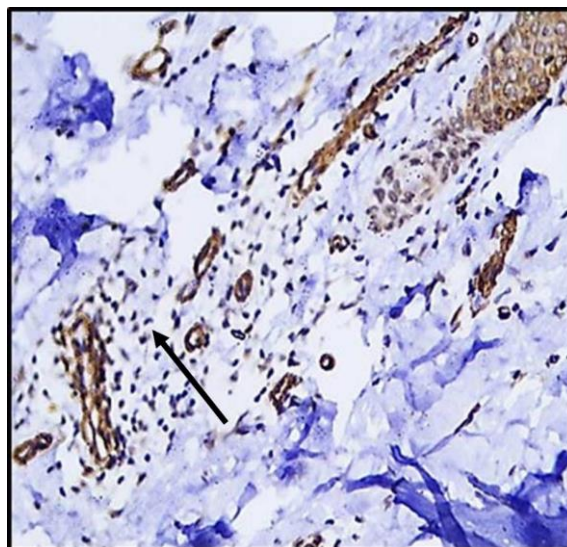


Figure 6. Immune stain by α -SMA show scattered myofibroblast immunostained cells in upper dermis (arrow) (x200)

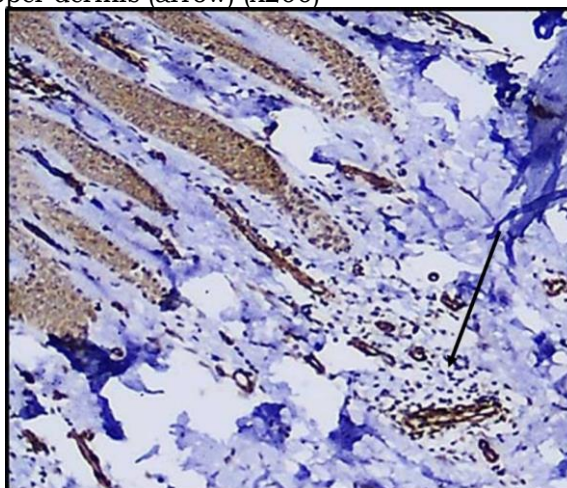


Figure 7. Immune stain by α -SMA show scattered myofibroblastic Cells in upper dermis (arrow) (x200)

A REPRESENTATIVE CASE: A 59 years old male patient complain of decrease function of both hands, irrelevant family history, the patient is ex-smoker; his past medical history is significant for rupture bullous emphysema treated by chest tube, the patient is manual worker (farmer). The condition started ten years ago with nodule in skin of right hand, then cords development gradual over years in ring finger & thumb of the right hand. Right hand dermofasciectomy with skin biopsy from palm over cord have been done. Lt hand show cord less than 30 degree of contracture [Figure 8](#).



Figure 8. Tubiana stage (2), A) preoperative right ring finger contracture angle 60.5° lateral view B) preoperative marking “palmar view” C) intra-op skin dissection and visualization of pretendinous cord D) part of excised cord E) exposure of tendons and palmar vessels and nerves F) 2 weeks postoperative follow up G) 1 month post-operative follow up “palmar view”.

4. Discussion

The French surgeon and pathologist "Guillaume Baron Dupuytren presented a meticulous pathological description and Surgeries for Dupuytren's contracture.³

The etiology and pathogenesis of Dupuytren's contracture are not evidently explained; however, some theories reveal that Dupuytren's disease starts in the palmar aponeurosis and then spreads up to penetrate fascial bands surrounding deep tissues and the skin above.⁶

In our cases, involvement of the right hand was only in 9 cases (45%), and 11 cases involved both hands affection (55%). We did not find any cases in which the left hand was alone affected. Unlike Loos et al., where the right hand was affected by Dupuytren's disease in 28.9% of cases, in 25.3%, only the left hand was affected, and in 45.8%, both hands were affected.⁷

The right hand was more common as it is the dominant hand and is severely affected in most studied populations. According to Bainbridge et al., 2012 of all patients, 3,249 (97%) were operated on only one hand at the rate of 15 cases (75%) in the right hand and five cases (25%) in the left hand.⁸

Regarding Calculate the frequency of contracted digits by dividing the number of affected hands by the total number of hands, the ring finger was involved in seven cases (35%), the little finger was involved in six cases (30%), both little and ring fingers together involved in five cases (25%), while Thumb finger was involved in two cases (1%); with most involved digits ring and little finger. These results are aligned with Lanting et al. 2013 who found that the ring and little fingers are the most common digits involved.⁹

Previous research has shown that myofibroblasts, which are essential cells in Dupuytren's contracture, first appeared during the proliferative phase and eventually made up nearly all of the cells in the highly cellular nodule. Myofibroblasts are smaller and more oriented toward one another during the involutinal phase.¹⁰

Wade et al. detected cutaneous fibromatosis in patients without any visible signs of skin involvement; their results showed an overall rate of dermal fibromatosis (61%) only by an H&E examination.⁶ These data came in a higher percentage than what we have got in the present study, where only (50%) of the cases showed dermal fibromatosis by immature fibroblasts and myofibroblasts detection.

In our studied group we found Alpha-smooth muscle actin (α -SMA) stain positive in 12 cases (60%) in upper and lower dermis of skin ranging from mild infiltration to highly infiltrated, all fascial (100%) were found positive, and also (80%) were found positive in subcutaneous tissue; this finding was close to that of Chen et al. 2009 study where they divided forty-three patients (68 hands) into two groups according to treatment methods: group 1 (dermofasciectomy and full-thickness skin graft) and group 2 (partial fasciectomy).¹¹ In group 1, they found that myofibroblasts were found in the dermis (63.2%) and subcutaneous tissue (55.9%) in group 2; in subgroup 1, of the 13 hands that recurred postoperatively, myofibroblasts were found in the dermis of almost 85% of hands; but in subgroup 2, of the 15 hands in which no recurrence developed, myofibroblasts were found in the dermis positive in 40% of the cases. The last finding is close to our dermal results, with 12 cases (60%) being positive. Also, Myofibroblast-like cells expressing α -SMA have been detected in the subcutaneous tissue and dermis of individuals with Dupuytren's contracture.¹²

The precise cause of the condition remains unidentified, with many theories and studies have assumed that the disease starts from the palmar fascia and extends to infiltrate the overlying skin through facial bands.^{11, 12, 13, 14, 15, 16, 17}

Nonetheless, some authors assumed that the skin, especially the dermis, is involved in the pathogenesis of Dupuytren's contracture^{12,14,17,18} pointing to the recurrence of disease^{14, 15, 18, 17} even from subcutaneous tissue.¹⁹

This study population is rather small as the disease is relatively rare in our region. In addition, we did not include any cases during the onset of the illness; all our cases had an angle of contracture of more than 30 degrees.

4. Conclusion

According to the histopathological study, the presence of alpha-smooth muscle actin in the palmar fascia and the dermis confirms that the dermis may play a role in the pathogenesis and recurrence of Dupuytren's contracture. Dermofasciectomy ensures the excision of the remaining myofibroblasts in the affected dermis, which provides a source for new lesions and recurrence of Dupuytren's contracture.

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There are no conflicts of interest.

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