



Localizador: 17057

# Ledderhose's disease associated with Dupuytren's disease in a patient with acquired immunodeficiency syndrome: first-time report

Doença de Ledderhose associada à doença de Dupuytren em paciente com síndrome da imunodeficiência humana: primeiro relato

Raquel Nardelli de Araujo,\* Renata Marcarini,\* Aaron Alarcon Novillo,‡ Daniela Alves Pereira Antelo§

## Key words:

Plantar fibromatosis, Ledderhose's disease, acquired immunodeficiency syndrome.

## Palavras-chave:

Fibromatose plantar, doença de Ledderhose, síndrome da imunodeficiência adquirida.

\* Resident in Dermatology.

‡ Resident in Radiology.

§ Master's and PhD in Dermatology - Associate Professor of Dermatology Department.

Pedro Ernesto University Hospital, University of the State of Rio de Janeiro, Rio de Janeiro-RJ, Brazil.

Conflict of interest: None.

Received: 01/November/2017.  
Accepted: 11/June/2018.



## ABSTRACT

The plantar fibromatosis (PF), also known as Ledderhose's disease, is characterized by affecting the plantar aponeurosis. In a general way, it is a benign fibrous condition still quite unclear in its various aspects, such as its etiology and treatment. To date, it has not been described in association with AIDS. Our patient presented PF previously hospitalization due to occurrence of many opportunistic infections due to AIDS at an advanced stage. We have described the case of a 45 year-old male patient with acquired immunodeficiency syndrome at a late stage, associated with Dupuytren's disease (DD) and the emergence of bilateral PF. Treatment was conservative as the plantar lesions were asymptomatic and the risk of recurrence with invasive measures is high. About 15% of people affected with PF have concomitant Dupuytren's contracture. HIV patients with advanced disease have DD in combination in up to 36% of cases. To our knowledge, this is the first case in which there is association of these three conditions in a single patient. Despite the evident need for research on PF, we believe that this paper may contribute to further elucidation about the disease.

## RESUMO

A fibromatose plantar (FP), também conhecida como doença de Ledderhose, é uma doença caracterizada por acometer a aponeurose plantar. Trata-se de uma condição fibrosa benigna ainda pouco clara nos seus diversos aspectos, como a etiologia e o tratamento. Descrevemos o caso de um paciente de 45 anos do sexo masculino portador de síndrome da imunodeficiência adquirida em fase avançada, associado à doença de Dupuytren (DD) que evoluiu com o surgimento da FP bilateral. O tratamento foi conservador, pois as lesões plantares eram assintomáticas e o risco de recorrência com medidas invasivas é elevado. Em torno de 15% dos acometidos com FP possuem contratura de Dupuytren concomitante. Pacientes com HIV com doença avançada apresentam associação com DD em até 36% dos casos. Para o nosso conhecimento, esse é o primeiro caso em que se observa a associação dessas três condições em um único paciente. Apesar da notória necessidade de pesquisas voltadas para a FP, acreditamos que este artigo possa corroborar para futuros esclarecimentos sobre a doença.

## INTRODUCTION

Plantar fibromatosis (PF), Ledderhose's disease, is an uncommon benign fibrous disorder involving the plantar aponeurosis, and was first reported in 1894 by Dr. Georg Ledderhose.<sup>1</sup> It is one of the superficial fibromatoses alongside Dupuytren's disease, KnucklePads, the Infantile Digital Fibromatosis and Peyronie's disease.<sup>2</sup> The exacerbated proliferation of connective tissue can form irregular masses or nodules in the plantar of the aponeurosis, especially in the central band.<sup>2,3</sup> Its incidence, as well as its etiology and treatment, are not clearly defined yet due to the

rarity of the disease. The incidence increases with advancing age, although it can occur in childhood. In addition, man are affected twice as often as females.<sup>4</sup>

In this article, we report the case of a male patient of 45 years old, with human immunodeficiency syndrome at an advanced stage, with PF and DD clinical settings. To our knowledge, there is no reported case involving these three conditions in the same patient.

## CASE REPORT

A 45 year-old male patient, born in Rio de Janeiro, has had confluent firm nodules in the

plantar surface of both feet for about 10 years (Figure 1). He reports that the injuries began in his left foot and two years later, similar injuries were also noticed in the right foot. He denies similar family cases, trauma, pain or other manifestations on the lesion's site.

Seven years ago, the patient needed several hospital admissions due to opportunistic infections, when he was diagnosed with acquired human immunodeficiency syndrome. He presented neurotoxoplasmosis, neurosyphilis, pneumocystosis, cytomegalovirus colitis, pseudomembranous colitis, hepatitis B, Kaposi sarcoma, pulmonary tuberculosis and Dupuytren's contracture of the right hand with palpable nodule between the fourth and fifth fingers and retraction of the fifth finger (Figure 2). He used various medications in the period, among them phenytoin to control recurrent tonicoclonic seizures.

He underwent ultrasound examination with a 14 MHz linear transducer on the plantar surface of both feet which revealed massive expansive heterogeneous and solid formation located in the middle of the left plantar aponeurosis without significant vascular flow to the amplitude Doppler, with measurements of 67 x 12 x 35 mm in larger diameters (Figure 3). The radiological aspect was compatible with plantar fibroma. On the right side, hypoechoic thickening of the middle third of the plantar aponeurosis was also observed, which measures 28 x 4 mm in larger diameters, also consistent with fibromatosis. Histopathological analysis showed presence of dense collagen fibers proliferation in the dermis, as seen in the description of PF.



**Figure 1.** Firm nodules and well-defined limits on the plantar surface of both feet.

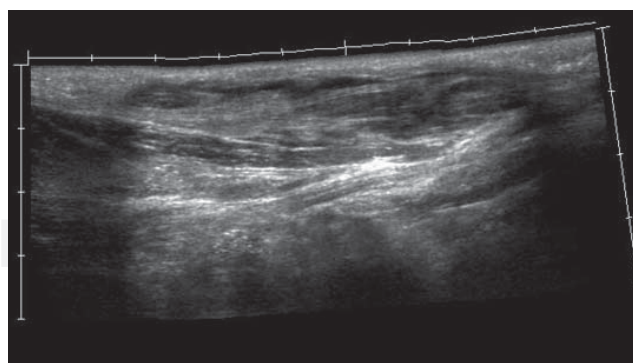
Conservative measures to treat PF were adopted since the patient did not complain of pain on the injuries. He was referred to the orthopedics for surgical treatment of the contracture due to the limitations resulting from this clinical setting.

## DISCUSSION

The fibromatoses represent a group of diseases characterized by fibroblast proliferation with similar histological appearance and are classified as superficial and deep.<sup>2</sup> Superficial fibromatosis include hand injuries (Dupuytren's contractures, knuckle pads, Infantile digital



**Figure 2.** Dupuytren's contracture of the right hand.



**Figure 3.** Presence of firm nodules, well-defined limits with large fibroid and mixed echogenicity located in the plantar aponeurosis.

fibromatosis), feet injuries (plantar fibromatosis), and penis injuries (Peyronie's disease). The palmar fibromatosis is the most common of them, occurring in 1 to 2% of the population with male predominance, usually bilaterally.<sup>2</sup> The plantar fibromatosis (PF) affect a younger age group, affecting men twice as often as women and are bilateral in 20 to 50% of cases.<sup>2,4</sup> The PF are well defined slow-growing lesions and are usually located in the medial surface of the plantar fascia.<sup>4,5</sup> The nodules may be multiple in 33% of cases and are generally asymptomatic. However, they can be locally aggressive and produce pain when the lesion involves the neurovascular bundles, muscles, or tendons. Approximately 15% of patients with PF have Dupuytren's disease in association.<sup>4,6</sup>

There are numerous conditions associated with superficial fibromatoses. Among them, DD is the most studied one, having alleged connections with heredity, alcohol, epilepsy, trauma, diabetes, rheumatoid arthritis, gout and HIV.<sup>7,8</sup>

Concerning epilepsy, it was noted that the actual link would be through anticonvulsants rather than the genetic association. The suggested mechanism is the stimulation of tissue growth factors by anticonvulsants, causing its users to be more prone to other chronic fibrotic conditions as Knuckle Pads or PF.<sup>7,8</sup> One study reported the appearance of PF due to the use of phenobarbital in three patients, but one of them also used phenytoin.<sup>9</sup>

It was described that 36% of patients with HIV were noted to have DD, all of whom had advanced infection. It is assumed that the free radicals act in the DD pathogenesis and at the same time are part of the intermediate mechanism for the development of AIDS.<sup>7,9</sup> The free radicals induce fibroblast proliferation and the production of type III collagen, leading to aponeurosis palmar fibrosis.<sup>9</sup>

To our knowledge, this is the first case described of HIV advanced disease and PF, since we did not find any report at PubMed literature. The appearance of these plantar nodules few years before patient hospitalization at the moment of AIDS diagnosis might suggest an association.

The reported patient was an HIV carrier with advanced disease and had PF and DD. No association was found in the literature of these three conditions in a single patient. The use of phenytoin by this patient occurred years after the rise of fibromatosis, not configuring a concrete causal factor.

PF injury on ultrasound test usually shows hypoechoic, well defined, elongated and with funneled ends image. Posterior acoustic enhancement, cystic components, hypervascularization and heterogeneity are also reported. In general, lesions measure up to 20 mm long and are

located in or on the plantar fascia. Larger dimensions are unusual and tend to move the fascia profoundly. In our case, the patient had 67 mm lesions on the left plantar region and 29 mm on the right one. It was suggested that the development stage of the lesion may influence the physical and sonographic appearance. The superficial location and appearance should strongly suggest the diagnosis, but should not be considered pathognomonic. Although MRI is effective in assessing the infiltration of surrounding tissues, and, thus, is important in the preoperative period, its high cost and low availability restrain its use. The advent of transducers with frequencies over 7.5 MHz with better resolutions, make the ultrasound a suitable method to study PF.<sup>4,10</sup>

Microscopically, there is fibroblast proliferation organized in parallel fascicles, with elongated and hyperchromatic nucleus, dense deposit of collagen fibers and occasional mitoses. The old and well-developed lesions are hypocellular, possessing greater amount of dense collagen and mature fibrous tissue.<sup>11</sup>

Microscopically, there is fibroblast proliferation organized in parallel fascicles but usually in nodules, with elongated and hyperchromatic nucleus, dense deposit of collagen fibers and occasional mitoses. The old and well-developed lesions are hypocellular, possessing greater amount of dense collagen and mature fibrous tissue. The histological characteristics of plantar fibromatosis are non-specific, but immunohistochemistry can be helpful in distinguishing between the differential diagnoses of this condition.<sup>11</sup>

PF treatment varies according to the evolution of the disease. In the early stages, one should be guided on the benignity of the lesions and the importance of controlling possible risk factors.<sup>12</sup> Conservative therapy should be initiated at the onset of symptoms, when the pain acts as the main indication as it is originated from the invasion of adjacent structures. Among the possible measures are physiotherapy, the use of appropriate footwear and specific shoe insoles to relieve pressure on prominent nodes, intralesional injection of corticosteroids and use of non-steroidal anti-inflammatory drugs.<sup>1,12</sup> Radiation therapy may be an option to prevent progression of symptoms in the early stages, reducing the size of the lesion and relieving pain. Despite the fact that the acute side effects of radiation therapy are well-tolerated, there is a concern over long term malignancy in young people. The injection of collagenase has also been described.<sup>12-14</sup>

Surgical intervention is reserved when conservative measures fail or when the symptomatology is exuberant, such as severe pain, walking impairment or difficulties

adapting to shoes.<sup>12</sup> Historically, simple excision of the lesion was performed. However, patients evolved with relapse in up to 100% of cases.<sup>12,13</sup> Risk factors for the recurrence of DD are: male sex, disease onset in those younger than 50 years, bilateral disease, LD, family history, ectopic fibromatosis, first ray involvement, multiple ray involvement (more than 2 digits).<sup>3,14</sup> Studies show that wide resection of the lesion associated with plantar fasciotomy is responsible for lower recurrence rates.<sup>12,13</sup> In 1993, methotrexate was described as an adjuvant therapy, and radiotherapy may also be used.<sup>1,12</sup> The presence of multiple nodules also influences the resurgence of lesions.<sup>12,15</sup>

Despite the need for further studies to elucidate its precise role in the treatment of PF, treatment with high-energy extracorporeal shock waves was able to reduce patients pain without presenting side effects. Further large-scale prospective trials are warranted to elucidate the recurrence and efficacy of high-energy extracorporeal shock waves in PF.<sup>15</sup> Unfortunately, until today's date, there is no consensus regarding PF treatment, and the role of alternative therapies is still undetermined.<sup>13,15</sup>

## CONCLUSIONS

About 15% of people affected with PF have concomitant Dupuytren's contracture. HIV patients with advanced disease have DD in combination in up to 36% of cases. To our knowledge, this is the first case in which there is association of these three conditions in a single patient. Despite the evident need for research on PF, we believe that this paper may contribute to further elucidation about the disease.

This was the first case description of advanced acquired immunodeficiency syndrome, Dupuytren's disease (DD) and PF. We highly recommend requesting HIV serology testing in patients with sudden occurrence of PF.

### Correspondence:

**Raquel Nardelli de Araujo**

Boulevard 28 de Setembro, 77, Vila Isabel,

Rio de Janeiro - RJ, Brazil, Zip code: 20551-030

Phone number: (1) 5521999440704

**E-mail:** raquelnardelli@yahoo.com.br

## BIBLIOGRAPHY

1. Fausto de Souza D, Micaelo L, Cuzzi T, Ramos-E-Silva M. Ledderhose disease: an unusual presentation. *J Clin Aesthet Dermatol.* 2010; 3 (9): 45-47.
2. Montgomery E, Lee JH, Abraham SC, Wu TT. Superficial fibromatoses are genetically distinct from deep fibromatoses. *Mod Pathol.* 2001; 14 (7): 695-701.
3. Souza BG, de Souza Júnior GZ, Rodrigues RM, Dias DS, de Oliveira VM. Surgical treatment of a case of Ledderhose's disease: a safe plantar approach to subtotal fasciectomy. *Case Rep Orthop.* 2015; 2015: 509732.
4. Walker EA, Petscavage JM, Brian PL, Logie CI, Montini KM, Murphey MD. Imaging features of superficial and deep fibromatoses in the adult population. *Sarcoma.* 2012; 2012: 215810.
5. Zgonis T, Jolly GP, Polyzois V, Kanuck DM, Stamatidis ED. Plantar fibromatosis. *Clin Podiatr Med Surg.* 2005; 22 (1): 11-18.
6. Gudmundsson KG, Jónsson T, Arngrímsson R. Association of Morbus Ledderhose with Dupuytren's contracture. *Foot Ankle Int.* 2013; 34 (6): 841-845.
7. Hart MG, Hooper G. Clinical associations of Dupuytren's disease. *Postgrad Med J.* 2005; 81 (957): 425-428.
8. Bower M, Nelson M, Gazzard BG. Dupuytren's contractures in patients infected with HIV. *BMJ.* 1990; 300 (6718): 164-165.
9. Strzelczyk A, Vogt H, Hamer HM, Krämer G. Continuous phenobarbital treatment leads to recurrent plantar fibromatosis. *Epilepsia.* 2008; 49 (11): 1965-1968.
10. Bedi DG, Davidson DM. Plantar fibromatosis: most common sonographic appearance and variations. *J Clin Ultrasound.* 2001; 29 (9): 499-505.
11. Adib O, Noizet E, Croue A, Aubé C. Ledderhose's disease: radiologic/pathologic correlation of superficial plantar fibromatosis. *Diagn Interv Imaging.* 2014; 95 (9): 893-896.
12. Lee TH, Wapner KL, Hecht PJ. Plantar fibromatosis. *J Bone Joint Surg Am.* 1993; 75 (7): 1080-1084.
13. van der Veer WM, Hamburg SM, de Gast A, Niessen FB. Recurrence of plantar fibromatosis after plantar fasciectomy: single-center long-term results. *Plast Reconstr Surg.* 2008; 122 (2): 486-491.
14. Degreef I, De Smet L. Risk factors in Dupuytren's diathesis: is recurrence after surgery predictable? *Acta Orthop Belg.* 2011; 77 (1): 27-32.
15. Knobloch K, Vogt PM. High-energy focussed extracorporeal shockwave therapy reduces pain in plantar fibromatosis (Ledderhose's disease). *BMC Res Notes.* 2012; 5: 542.