



(RESEARCH ARTICLE)



## Continuous phenobarbital treatment and palmoplantar fibromatosis

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### Abstract

Palmoplantar disease is a hyperproliferative disorder with dystrophic nodules in the superficial plantar and palmar fascia. It can be associated with other pathologies such as Lapeyronie's disease, diabetes, alcohol dependence or continuous phenobarbital treatment. We report the rare case of a pathological association made of Ledderhose's disease, Dupuytren's disease and barbiturates in an epileptic patient. Conservative treatment well conducted for more than 6 months is not satisfactory. A complete fasciectomy is performed with good functional results without recurrence. The association between epilepsy and palmoplantar fibromatosis is extremely rare. The role of barbiturates in mediating tissue growth factors would in theory explain this hyperproliferative disorder of the plantar fascia. The association between fibromatosis and cell growth mediators evokes new approaches aimed at modulating these cells for better therapeutic control.

**Keywords:** Ledderhose disease; Palmoplantar fibrosis; Epilepsy

### 1. Introduction

Ledderhose disease is an uncommon hyperproliferative condition. Its etiology is still unknown. It is responsible of dystrophic nodules growing on the superficial plantar aponeurosis [1, 2], It was described for the first time by the German doctor Georg Ledderhose in 1897 [3]. It's a very rare disease with an incidence lesser than 0.23 %. It mainly affects subjects between 30 and 50 years with a clear male predominance (sex ratio at 2:1) [5, 6]. It can affect both feet and can be associated with other disorders such as Dupuytren's, Lapeyronie's, penile fibromatosis, diabetes, frozen shoulder or even alcohol addiction. In this paper we report a rare case associating Ledderhose and Dupuytren disorders (palmoplantar fibromatosis) in an epileptic patient under continuous phenobarbital treatment.

### 2. Material and methods

A 35 years old female, presented with a history of 5 years growing nodules on plantar aponeurosis of both feet and palmar aponeurosis of the right hand. The pain preventing here from standing for a long time. She had a negative medical family history. She was diagnosed for epilepsy at the age of 7 years old and was treated by continuous phenobarbital treatment.

The right foot presented two central firm nodules, the bigger one had a diameter of 2 cm, the left foot presented a unique nodule with a diameter lesser than 1 cm (fig 1, 2). These nodules were firm, painful and adherent to plantar fascia. On the right hand we found a fibrotic thickening of the palmar fascia associated with a central digital cord preventing the extension of the metacarpophalangeal and interphalangeal articulations of the thumb, the 4<sup>th</sup> and the 5<sup>th</sup> fingers (fig 3).

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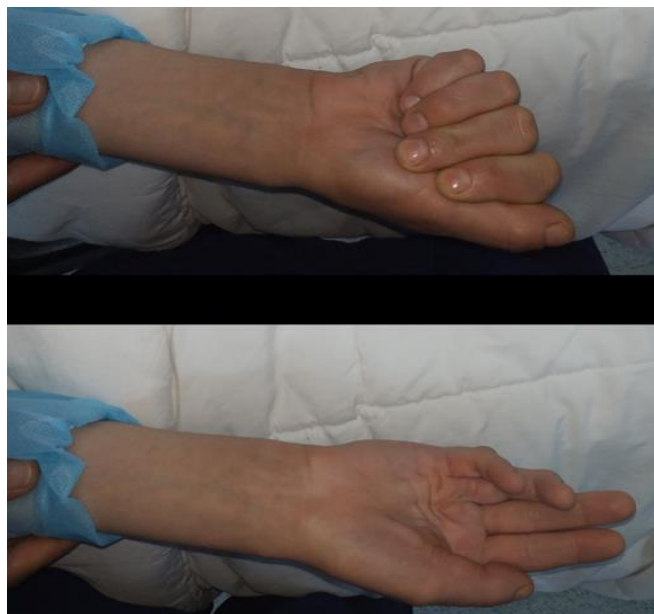
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**Figure 1** Clinical aspect of the feet (frontal view)



**Figure 2** Clinical aspect of the feet (lateral view)



**Figure 3** Clinical aspect of the right hand

### 3. Results

The patient was diagnosed with palmoplantar fibromatosis and after a well conducted conservative treatment (nonsteroidal anti-inflammatory drugs, silicon insole, cryotherapy ...) over 6 months without any improvement, the surgical management was indicated (total plantar fasciectomy). An S-curved shaped incision of the plantar skin was made (fig 4), and careful dissection was performed to avoid undermining the skin and injuring the vascularity of the dermis, then the plantar fascia containing the nodules was isolated and excised (fig 5).



**Figure 4** Aspect of the S-curved incision



**Figure 5** Plantar fascia excised

Finally, the skin was sutured without tension, the procedure was completed by the excision of the central palmar and the first ray cords by a longitudinal zig-zag approach associated with a VY flap (fig 6).



**Figure 7** Excision of the central palmar and first ray cords

Weight bearing wasn't allowed for 3 weeks, until the wound was reevaluated and the sutures were removed. There were no complications. The diagnosis was confirmed through histological examination of the excised tissue. After a follow up of one year there was no complications or recurrences (fig 7).



**Figure 7** Final aspect (after 2 months)

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#### 4. Discussion

Ledderhose disease, or plantar fibromatosis, mainly affects middle-aged people (between 30 and 50 years old). However, some cases have been reported in children under the age of 16 [8]. Its prevalence and etiology are not always specified. It continues to appear on the list of rare diseases [11] affecting quality of life and causing severe functional disability [12]. The characteristic nodule of Ledderhose disease measures between 0.5 and 3.0 cm in diameter, it is most often located in the medial or central plantar fascia [1, 2, 5]. Typically, these are small, painless nodules that barely interfere with footwear or prolonged standing. The evolution, as slow as it is, is characterized by the increase in the diameter of knots which can become very painful and inflammatory in severe forms [1, 13, 14].

The diagnosis of Ledderhose disease is mainly clinical [14]. The presence of one or more well defined nodules along the plantar fascia is pathognomonic of this disease. However, other differential diagnoses should be ruled out: The heel compression test can identify a calcaneal stress fracture; tarsal tunnel syndrome is identified by the presence of

pain and numbness radiating to the plantar heel upon percussion of the posterior tibial nerve into the tarsal tunnel; finally, plantar fasciitis is characterized by excessive sensitivity of the medial border of the calcaneal tuberosity [13, 14].

Additional examinations are requested in cases of uncertain or doubtful diagnosis. In ultrasound we can morphologically visualize the "Comb sign": It is a hyperechoic aspect of the fibrous areas of the nodule on a background of hypoechoic cell matrix [15]. On MRI, these nodules appear as heterogeneous oval lesions included in the plantar fascia [16].

As for management, conservative treatment of Ledderhose disease is indicated for early forms of this pathology [14]. It is based on hygienic-dietary measures of plantar comfort such as orthopedic insoles. Other means of symptomatic treatment are proposed, such as nonsteroidal anti-inflammatory drugs, intra-nodular corticosteroid infiltrations, infiltrations by hyaluronidases and collagenases, localized radiotherapy or even extra-bodily shock waves [6, 14]. Nevertheless, surgery currently remains the only treatment providing satisfactory results. Three techniques have been used in the surgical management of plantar nodules: local excision, partial fasciectomy and total fasciectomy. Numerous studies have shown that local excision of the nodule has a very high recurrence rate (up to 100%) [17 - 19]. The entire removal of the plantar fascia presents the lowest risk of recurrence (50 to 0%) [17 - 19].

As in our patient, Ledderhose disease - rare as it is - often appears concomitantly with other hyperproliferative fibromatous syndromes such as Dupuytren's disease, La Peyronie's disease or the formation of keloids in a generalized way [2, 14, 18]. The association between epilepsy and palmoplantar fibromatosis was first described in 1941 by Lund where he noted an incidence of Dupuytren's disease reaching 50% in 190 men and 25% in 171 women with epilepsy in his series [20]. In 1969, James [21] argued that epilepsy and palmoplantar fibromatosis are both genetically determined and represent dominant linked genes; this has been refuted by other observations [22 - 25].

Finally, another hypothesis which could explain the association between administration of phenobarbital and palmoplantar fibromatosis involves the mediation of tissue growth factors. Indeed, the observation of Ghosh and McCandless [26] suggests that the acceleration of growth is manifest in children with temporal lobe epilepsy by the fact that phenobarbital can affect the release of corticotrophin, gonadotropin and antidiuretic hormone. These hypotheses broaden the therapeutic perspectives of Ledderhose disease. In this regard, treatment with synthetic non-steroidal anti-estrogens such as tamoxifen has been suggested. In-vitro, observations have confirmed that the proliferative activity of fibroblasts exposed to tamoxifen has been reduced by inhibiting the expression of TGF- $\beta$  [27].

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## 5. Conclusion

Ledderhose disease remains an exceptional pathological entity whose etiological mechanisms are not yet fully understood. Surgical excision of the plantar fascia always exposes to the non-negligible risk of recurrence. The association between fibromatosis and cell growth mediators suggests new approaches aimed at modulating the latter for better therapeutic control.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

None.

### *Statement of ethical approval*

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study."



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