Connection between Dupuytren’s contracture and plantar aponeurosis

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ABSTRACT

Dupuytren’s disease of the foot is not an uncommon disease that affects the plantar aponeurosis. It is a different clinical entity from Dupuytren’s contracture of hands. It presents clinically with slowly growing painless hard nodules on the medial aspects on the feet. Though the pathophysiological mechanisms remain elusive, hyperproliferation of fibroblasts and excessive synthesis of collagen fibers type III are proposed to be the main pathogenetic processes resulting in nodule development and growing. The most widely accepted theory for disease development is the combination of genetic predisposition and environmental risk factors such as smoking chronic alcohol consumption, diabetes mellitus, and other forms of superficial or deep fibromatosis. This article will discuss the dupuytren’s disease of the foot as regards the epidemiology, the pathophysiology, the clinical presentation, diagnosis, and lines of treatment. It will provide a special focus on the mechanisms of affection of plantar aponeurosis.

Keywords: Dupuytren’s contracture, Ledderhose disease, Plantar aponeurosis

INTRODUCTION

Dupuytren’s contracture is a rare fibrosing disorder that has been known to affect the palmar fascia leading to shortening, thickening of the fascia, and consequently debilitating contracture at the fingers particularly at proximal interphalangeal and metacarpophalangeal joints. This fibromatosis of the palmar fascia has been a subject of concern for many years, and researchers were arguing the rare involvement of the plantar fascia (or plantar aponeurosis) with a similar pathology. They noted that affection of the plantar aponeurosis would rarely symptomatize. However, more recent researches noted that fibromatosis of the plantar aponeurosis is much more common than what was expected, and it should be considered in the differential diagnosis of many foot conditions.1-4

This article will discuss the Dupuytren’s contracture of the foot as regards the epidemiology, the pathophysiology, the clinical presentation, diagnosis, and lines of treatment. It will provide a special focus on the mechanisms of affection of plantar aponeurosis.

DUPUYTREN’S DISEASE OF THE FOOT

Dupuytren’s contracture of the foot is not uncommon hyperproliferative disease that affects the plantar aponeurosis. It was first described in 1894 by Ledderhose as a Dupuytren-like disease affecting the feet.5 Therefore, it is also referred to as “Ledderhose disease”. The disease
is also referred to as “Plantar fibromatosis”, “Dupuytren-like contracture of the foot”, and “Dupuytren’s disease of the foot”. The term ‘contracture’ is less often used, because fibromatosis of the plantar aponeurosis seldomly results in contracture.6,7

Fibromatosis of the plantar aponeurosis is a clinical entity that is distinct from the fibromatosis of the palmar fascia (Dupuytren’s contracture of hand). It has different characteristic, pathophysiology, clinical presentation, and gross and microscopic anatomy. It is characterized by the formation of hard nodules on the plantar surface of the feet in affected individuals.8 It typically progresses very slowly and may affect both feet.

**EPIDEMIOLOGY**

Although Dupuytren’s disease of the foot was thought to be a rare disease, many authors report that it affects up to 25% of middle-aged and elderly individuals.5 In the past, authors reported very low incidence between 1/100,000 and 1.75/100,000.10,11 The notable difference is most probably attributed to better understanding and accurate diagnosis of the disease during the few last decades. It is more common among males, with males affected almost 10 times more than females.5 Dupuytren’s disease of the foot may occur at any age. However, it is most common among middle-aged and elderly individuals. The disease is commonly unilateral, but it can affect both feet in 5% of cases. The disease is sometimes associated with other disorders of fibromatosis e.g. Dupuytren’s contracture of the hands, knuckle pads, or Peyronie’s disease.5,10

**DIAGNOSIS**

Diagnosis of Dupuytren’s disease of the foot is often carried out on clinical basis. Patients with the disease present with slowly growing firm to hard nodules evolving on the medial and central aspects of the plantar surface of their feet, usually at the highest point of foot arch.12 The nodules usually range from 1 to 2 cm in diameter and they are typically painless.13 However, they may become painful later on especially with walking.13 Pain occurs when the nodules rubs the floor or the shoes. The nodules typically affect one foot, but bilateral affection may occur in 25% of patients.14 Contracture of toes is rare and does not occur except in advanced stages of the disease.12 Other less characteristic symptoms include arthralgia, paresthesia, and lack of skin elasticity.15

Patients with Dupuytren’s disease of the foot may have other fibrosing hyperproliferative conditions such as Dupuytren’s contraction of hands (palmar fibromatosis), Peyronie disease (penile fibromatosis), or Knuckle pads. Physical examination reveals painless firm to hard subcutaneous nodules with a freely movable overlying skin.5

Though Dupuytren’s disease is a clinical diagnosis, some authors recommend magnetic resonance imaging of the feet to confirm the diagnosis, exclude differential diagnoses, and assess disease severity.16 Ultrasound is also sometimes used. Confirmation of diagnosis requires excision and histopathological examination.9,17

**TREATMENT**

Many lines of management have been established for treatment of Dupuytren’s disease of the foot. Small painless nodules may be managed conservatively with steroid injection, particularly at early stages of the disease. Large painful or recurrent nodules usually require surgical excision. Surgical excision may be local, wide or total fasciectomy. Local resection are not preferred because they are associated with high relapse rate (up to 100%).18 Wide resection comprises resection with a safety margin between 2-3 cm. The recurrence rate after wide resection is about 78%.19 Total fasciectomy, although associated with the lowest relapse rate (25%), is not preferred because of the resultant foot deformity.18 Radiotherapy is a third line of therapy that is used either early to stop disease progression or late in advanced stages to reduce nodular size.11 Other recent advances include collagenase injection, n-acetyl-L-cysteine, cryotherapy, needle aponeurotomy, and shock waves.5,8

**CONNECTED BETWEEN DUPUYTREN’S CONTRACTURE AND PLANTAR APONEUROSIS (THE PATHOPHYSIOLOGICAL MECHANISMS)**

To date, the exact etiology of the Dupuytren’s disease of the foot remains elusive. However, certain risk factors and pathophysiological mechanisms had been identified. This section will review these factors and mechanisms.

**Pathophysiology**

Dupuytren’s disease of the foot is a hyperproliferative disorder characterized by a locally-infiltrative proliferation of abnormal fibrous tissue at the plantar aponeurosis. The newly formed fibrous tissue (fibromatosis) results from active proliferation of mature fibroblasts and mature collagen formation. Though the fibromatosis represents a locally infiltrative and aggressive process that replaces adjacent normal aponeurosis, no malignant cytological features were detected on histopathological studies.

The pathophysiology of Dupuytren’s plantar fibromatosis include various forms of soft-tissue proliferation. This proliferation is induced either by active fibroblast activity promoting deposition of mature collagen or by active proliferation of myofibroblasts. The exact mechanism for stimulation of fibroblastic proliferation has not been revealed yet. Some authors propose that individuals who develop fibromatosis are initially genetically predisposed since birth, and activation of fibroblasts occur when an inciting life event takes place later in adult life.20 These
inciting events include risk factors that accelerate microvascular damage and ischemia e.g. chronic alcohol consumption, smoking, and diabetes mellitus. The resulting tissue ischemia accelerates free radicals formation (through a cascade of chemical reactions leading at the final pathway to formation of xanthine and uric acid and subsequently free radicals). Free radicals induce fibroblast proliferation and the release of cytokines, particularly transforming growth factor beta (TGF-β), fibroblast-growth factor, and platelet-derived growth factors.\textsuperscript{21} This will lead to further fibroblast proliferation and a vicious circle of hyperproliferative fibrous tissue deposition. The growth factors also activate the differentiation of fibroblasts into myofibroblasts and the production of mature collagen.\textsuperscript{15} Furthermore, platelet-derived growth factors signal myofibroblasts contraction. Via a cascade of events, they increase intracytoplasmic calcium and promote smooth muscle contraction.

Another mechanism for the fibromatosis is the disproportionate increase in collagen type III to collagen type I ratio.\textsuperscript{22} Under normal condition, the plantar aponeurosis is mainly composed of type I collagen fibers. With the hyperproliferation of fibroblasts, collagen type III production increases significantly leading to formation of hard firm fibrous nodules on the surface of the plantar aponeurosis. On the other hand, some authors propose that the formation of fibrous nodules does not begin intrinsically inside the normal aponeurosis, but it results from an extrinsic protein called “periostin” that promote fibroblast hyperproliferation and differentiation.\textsuperscript{21} To date, the exact mechanism remains unclear.

The local fibrous formation leads to the formation of slowly growing nodules on the plantar surface of the foot. The newly formed fibrous tissue is aggressive, it replaces the normal plantar aponeurosis. It often affects the medial and central areas of the plantar aponeurosis. Microscopic examination of these nodules reveals that they are formed of proliferating well-differentiated fibrocytes that arise from the plantar aponeurosis and bulge either towards the deep structures or, more often, towards the subcutaneous tissue of the feet. Plantar fibromatosis has a high recurrence rate. For many years, they were misdiagnosed and treated as fibrosarcoma partly due to the high cellular content on microscopic examination and partly due to the frequent recurrence after excision.\textsuperscript{14,22} However, further extensive research confirmed the benign nature of the lesions.\textsuperscript{5}

Fibromatosis is a wide-spectrum disease, rather than a single entity, that affect many tissues and form multiple clinical diseases. It commonly affects the palmar and plantar aponeuroses. Some of these diseases may occur at young age (such as juvenile fibromatosis), whilst others present at adulthood (such as Dupuytren’s disease of foot and Dupuytren’s contracture of hand). Fibromatosis may less commonly affect the deep structures as in cases of extra-abdominal fibromatosis, abdominal fibromatosis, and visceral fibromatosis. This deep fibromatous if usually less aggressive.

**Genetics**

As previously mentioned, some authors believed Dupuytren’s disease evolves due to a combination of genetic predistortion and environmental inciting factors.\textsuperscript{20} Hindocha et al, in their research studying the hereditability of Dupuytren’s disease, reported a high risk of sibling affection.\textsuperscript{25} Some genes, such as MafB gene, had been identified to be upregulated in Dupuytren’s disease and to be responsible for fibroblast hyperproliferation.\textsuperscript{25,26} Maternal mitochondrial pattern of inheritance was demonstrated in other studies.\textsuperscript{20,27} Authors of these studies argued that the defective mitochondrial metabolism was responsible for the production of free radicals and the absence of normal physiological apoptosis. Autosomal dominant inheritance was also noted, and chromosomal abnormalities resulting in errors of fibroblast growth genes have been proposed.\textsuperscript{12,28,29} The genetic predisposition remains a matter of debate under research.

**Risk factors**

Many factors have been established to increase the risk of Dupuytren’s disease development. The most identified risk factors include repeated foot trauma, smoking, chronic alcohol-consumption, smoking, diabetes mellitus, chronic liver disease, and epilepsy.\textsuperscript{5,8,30} Family history of the disease and the presence of other forms of superficial or deep fibromatosis (e.g. Peyronie’s disease) have also been associated with higher risk to develop the disease.\textsuperscript{8}

Although the mechanisms whereby these factors may lead to development of Dupuytren’s nodules remain unclear, some authors – as mentioned in the previous section – believe that many of these factors promote vascular ischemia and induce production of free radicals which subsequently increase fibroblast proliferation and differentiation.\textsuperscript{15,20,21}

**CONCLUSION**

Dupuytren’s disease of the foot is not an uncommon disease that affects the plantar aponeurosis. It presents clinically with slowly growing painless hard nodules on the medial aspects on the feet. Though the pathophysiological mechanisms remain elusive, hyperproliferation of fibroblasts and excessive synthesis of collagen fibers type III are proposed to be the main pathogenetic processes resulting in nodule development and growing. The most widely accepted theory for disease development is the combination of genetic predisposition and environmental risk factors such as smoking chronic alcohol consumption, diabetes mellitus, and other forms of superficial or deep fibromatosis.
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