Onychalgia Causes and Mechanisms: The “GIFTED KID” and the “FOMITE”

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Keywords

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Abstract

This article gives an account of the commonest causes of nail pain. The acronyms GIFTED KID and FOMITE will help aid doctors in a busy clinical setting to remember the main causes of onychalgia, respectively, on the fingers and toes. It includes a brief overview of the clinical characteristics and focuses on the type of pain for each condition as well as the mechanisms that cause it.

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Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (International Association for the study of Pain, 2017).

It can be described according to its onset as acute or chronic, according to its duration as intermittent or constant, according to its nature as dull ache, throbbing, burning, shooting, and stinging, and according to its intensity as mild, moderate, and severe.

The causes of onychalgia (Onychas = Greek for nail + algos = Greek for pain) are numerous such as traumatic, infectious, inflammatory, neoplastic (bone and non-bone), iatrogenic, and syndromic.

Many textbooks and articles report nail pain but do not describe the mechanisms of pain. The purpose of this article is to describe the commonest causes of nail pain in the fingers and toes and to explain how pain arises in the nail unit in each described condition.

To understand the mechanisms of pain at the distal digit, some anatomy should be recalled (Fig. 1a).

The pulp is compartmentalized by fibrous septae (between 15 and 20) that run from the periosteum to the skin in a radial fashion and anchor the skin and pulp to the bone. The subcutaneous fat that is very abundant in the tips of the digits, is loculated by the fibrous septae which they create a very tight space with no room for expansion. Therefore, acute increase in pressure from the edema/blood and the subsequent tightness in the area are perceived as very painful.

The *Pacinian corpuscles* (Fig. 1a) are rapidly adapting vibration and pressure mechanoreceptors found in finger pulps [1]. They are large in size and respond to sudden changes in pressure, as the gradual changes get filtered by the connective tissue that covers the nerve endings. They are enclosed in a capsule, are oval or round in shape, and

Fig. 1. The anatomy of the nail unit. **a** Fat: loculated by fibrous septae, Pacinian corpuscles: rapidly adapting mechanoreceptors, respond to sudden changes in vibration/pressure. Ruffini corpuscles: slowly adapting mechanoreceptors, respond to stretch, proprioception, mechanical deformation within joints, located superficially. **b** Schematic demonstration of pain in glomus tumor. **c** The mechanism of bone pain in enchondroma, inclusion cyst, and keratoacanthoma.

have a characteristic onion-like cut surface with single A β -fibers terminating at the center of the inner core [2].

The *Ruffini corpuscles* (Fig. 1a), on the other hand, are slowly adapting mechanoreceptors that respond to stretch and proprioception of the finger as well as mechanical deformation within joints. They are both found in the pulp, the Ruffini are situated more superficially, whereas the Pacinian are found deeper in the dermis. They are present along the digital nerves and appear into the nail bed during fetal vascular development but undergo severe depletion after birth due to mechanical stress from the nail [3, 4].

The digits and nail unit are innervated by the volar and dorsal branches of the digital nerves running along the vascular bundle and the flexor tendons. There are 3 fascicles, the main one running under the nail bed and innervating the bed and the matrix. There is dual sensory innervation dorsally on the thumb, ring, third, and radial half of the ring finger. The median nerve supplies the distal halves of the abovementioned fingers, whereas the radial nerve supplies the proximal halves, respectively. The ulnar half of the ring finger and the entire little finger are innervated by the ulnar nerve both dorsally and ventrally. The palmar aspect of the first three 1/2 fingers is innervated by the median nerve.

Some of the causes of onychalgia are due to bone injury, which has 4 stages responsible for pain [5]:

- 1 The activation and sensitization of mechanosensitive sensory and sympathetic nerve fibers. This stage is re-

inforced by the release of acid from osteoclasts during the process of bone resorption, creating an acidic environment, which is sensed by the ion channels.

- 2 The upregulation of neurotransmitters, receptors, and ion channels that are expressed by sensory neurons. The neurotransmitters are the nerve growth factor, vascular endothelial growth factor, and epidermal growth factor.
- 3 The ectopic sprouting of the sensory and sympathetic nerve fibers induced by the neurotransmitters. The sprouting is not pruned back unless there is complete healing of the bone. Therefore, there is a resultant hyperinnervation of the bone.
- 4 The central sensitization in the brain and spinal cord that amplifies pain. Therapies targeting the nerve growth factor have been successful to relieve pain in bone cancer [6].

The acronyms GIFTED KID (Table 1) and FOMITE (Table 2) were coined by the authors in an attempt to aid doctors in a busy clinical setting to remember the commonest causes of onychalgia, respectively, on the fingers and toes.

The Causes of Pain in Fingernails (Table 1)

Glomus Tumor

A glomus tumor is the hyperplasia of one or many glomus bodies found in areas rich in those such as subun-

Table 1. The causes of pain in fingernails: “GIFTED KID”

G	Glomus tumor
I	Infections (acute paronychia, herpetic whitlow, mould onychomycosis)
F	Foreign body
T	Trauma (hematoma, inclusion cysts)
E	Enchondroma
D	Drugs (retinoids, chemotherapy especially taxanes, and epidermal growth factor receptors inhibitors)
K	Keratoacanthoma
I	Ice/frostbites
D	Droppings (in Latin: gutta → French: goutte → English: gout: gout was believed to be caused by the dropping of diseased matter – urate crystals – from the blood into the joints)

gually, in the hands, feet, wrists, and forearms. Glomus bodies are arteriovenous anastomoses located between a preterminal arteriole and an efferent end vein and are sensitive to temperature. The high concentration of glomus bodies subungually explains the presence of 75–90% of glomus tumors on the hands [7]. The tumor is commoner in women in their forties. When located in the nail bed, it presents as a red/blue spot of under 10 mm in diameter, often visible through the nail plate, which does not blanch with pressure. When submatricial, it manifests with longitudinal erythronychia and distal notching of the nail plate. The following tests are available for the clinical diagnosis of glomus tumor: the *transillumination test* [7], the *Love’s test* (probing with a blunt instrument induces severe pain) [7], the *Hildreth test* (where a cuff is inflated to >300 mm Hg and probing with a blunt instrument does not induce pain) [7], and the *cold sensitivity test* (ice cube induces severe pain) [7]. T2-weighted MRI is the investigation of choice [7].

Mechanism of pain: Glomus tumor (Fig. 1b) is surrounded by a connective tissue capsule that contains myelinated and nonmyelinated nerve fibers that may account for the pain. Additionally, the cytoplasm of that capsule contains myofilaments that contract with the temperature changes, with a subsequent increase in intracapsular pressure that is transmitted to the unmyelinated fibers, hence the sensation of pain [8].

Type of pain: Chronic, intermittent, throbbing, severe: provoked after slight trauma which is worse at night and in the cold (or temperature variation), with the pain radiating up to the ipsilateral shoulder. Glomus tumor should be evoked with the triad of pain, pinpoint tenderness, and hypersensitivity to cold.

Table 2. The causes of pain in the toenails: “FOMITE”

F	Frostbites
O	Onychoclavus (heloma)
M	Mechanical causes/trauma
I	Ingrown nails
T	Tophi (gout)
E	Exostosis

Infections

A. Bacterial Infection: Acute Paronychia

It results from a minor trauma to the cuticle and proximal nail fold enabling bacterial inoculation, mainly staphylococcus, evolving rapidly toward pus collection. This monodactylic infection presents with all the signs of inflammation such as erythema, edema, tenderness, hot digit, and pain. It is an emergency in toddlers, who still have very soft nails and susceptible matrix and on which pus collection causes pressure necrosis and may rapidly induce a permanent dystrophy.

Mechanism of pain: the acute inflammation with its 5 cardinal signs of rubor, calor, tumor, dolor, and function laesa. Cytokines and chemokines (chemotactic cytokines for neutrophils) play an important role in the resolution of the acute staphylococcal infection [9]. However, they are also responsible for the pain on the skin, as in other conditions (joints, breast cancer) [10, 11]. Moreover, the subsequent pus formation causes acute pressure on the nail folds with activation of the Pacinian corpuscles and transmission of pain (Fig. 2a).

Type of pain: Acute, constant, throbbing, moderate to severe.

B. Viral Infection: Herpetic Whitlow

This infection secondary to Herpes simplex viruses (HSV) 1 and 2 [12] presents as single or clustered umbilicated vesicles on an erythematous base affecting usually the thumb and less so the other fingers. The distal digit becomes very painful followed by edema and crusting. The vesicles contain clear or turbid fluid but no pus, a sign seen in distal dactylitis [13]. It occurs commonly in dental workers [14] and children [12]. In children, primary HSV-1 oropharyngeal infection causes auto-inoculation following thumb-sucking and a break in the skin. In the health care workers, it is secondary to unprotected exposure to infected oropharyngeal secretions of patients. The herpetic whitlow in adults is mostly due to contact with HSV-2-infected genitals [15].

Fig. 2. Pain induced by the activation of the Pacinian corpuscles as seen in (a) acute paronychia, (b) foreign body, and (c) trauma/hematoma. Pain induced by the activation of the Ruffini corpuscles as seen in (d) non-dermatophytes, (e) gouty tophi, and (f) retronychia. NET, neutrophil extracellular trap.

Mechanism of the pain: Neuropathic pain. There is invasion and replication in the nervous system during the primary infection, maintenance of the infection in the nerve ganglia during the latent period, and reactivation during reinfection. Primary infection is very severe, whereas reinfection is usually mild.

Type of pain: Prodromes (pruritus, burning, tingling pain) prior to the appearance of the signs, then pain presents as acute, constant, shooting, moderate/severe.

C. Fungal Infections: Mould Onychomycosis

Non-dermatophyte mould onychomycosis accounts for approximately 10% of onychomycosis worldwide [16] and is the only type of onychomycosis that is painful. The responsible organisms are *Scopulariopsis brevicaulis* sp., *Aspergillus* sp., *Acremonium* sp., *Fusarium* sp., *Scytalidium* sp., *Onychocola canadensis*, and *Alternaria* sp. [17]. They are difficult to diagnose as moulds are common contaminants of the nails and the laboratories. The toenails are most commonly affected. A distal, lateral subungual onychomycosis with concurrent painful paronychia inflammation (perionyxis) is highly suggestive. Painful perionyxis and purulent discharge may also occur with the proximal subungual onychomycosis subtype.

Mechanism of pain: The pain is due to the presence of cytokines in the pus that causes stretching and activation of the Ruffini corpuscles (Fig. 2d) due to pressure on the

nail folds, as well as the mechanical pressure from the shoe.

Type of pain: Chronic, intermittent, dull, moderate.

Foreign Body

Nail injury following foreign body insertions can happen both in adults and in children and are mainly seen in Emergency Departments. It most commonly affects the nail bed of the dominant hand. It can be splinters of wood [18], sea urchin needles [19], fish bones [20], thorns [20], hair [21], and pieces of glass or metal. Visualizing white radiotransparent foreign bodies (fishbones, white hair) subungually can be difficult and, therefore, using a dermatoscope proves invaluable [20, 22], as well as ultrasound. Sea urchins characteristically cause granulomas with possible splitting of the nail plate [20], whereas fishbones and thorns cause a focal abscess pocket acutely. Occasionally, eventual expulsion of the foreign material can occur or formation of granuloma with caseation and edema or worse, persistently disabling secondary infections in the cases of fragmented residues.

Mechanism of pain: Secondary to acute inflammation and activation of the Pacinian corpuscles (Fig. 2b) that respond to acute pressure changes secondary to granuloma formation, edema, or abscess.

Type of pain: Acute, intermittent, sharp, severe, and more intense on palpation.

Fig. 3. Schematic presentation of pain induction in (a) enchondroma, (b) keratoacanthoma, (c) onychoclavus, and (d) exostosis.

Trauma/Hematoma/Inclusion Cysts

Nail bed injuries can arise from a sudden forceful crush or laceration. The commonest injury is the catching of a finger in a door or the fall of a heavy, sharp object on the toes. An injury in the matrix can result in a permanent nail deformity; hence, quick and efficient assessment is of paramount importance [23]. The size and level of the defect, presence of exposed bone, as well as examination for motor function, sensation, and evaluation of circulation are imperative. Sometimes an incomplete avulsion is present, a sign that might indicate laceration of the nail matrix or even fracture of the distal phalanx. Following injury of the highly vascular nail bed gives rise to sudden blood collection and formation of a subungual hematoma, with a resulting very severe throbbing pain.

Trauma or local surgery may induce inclusion of keratinocytes into the bone that will slowly develop into inclusion cyst over years. The trauma is often not remembered by the patient. Tumefaction of the distal extremity may be observed. Radiography demonstrates a sharp osteolysis [24].

Mechanism of pain: Acute hematoma develops in the unexpandable subungual (Fig. 2c) space exerting sudden and severe pressure and therefore activating the Pacinian corpuscles that transmit pain.

In inclusion cysts (Fig. 1c), the pain comes very late from osteolysis, the bone resorption creating an acidic environment with upregulation of neurotransmitters and ectopic sprouting of the sensory and sympathetic nerve fibers.

Type of pain: Acute, constant, throbbing, very severe.

Enchondroma

This benign cartilaginous bone tumor arises in the medullary cavity (ectopic formation of hyaline cartilage) and grows into the cortex, forming a prominent endogenous mass in the bone. Solitary enchondroma accounts for 90% of all bone tumors of the hand but is rare in the distal phalanx [25].

It is usually asymptomatic, found incidentally on an X-ray. Pathological fracture from the thinning of the bone cortex is the painful common presenting symptom.

Enchondromas may be solitary or multiple [26]. They may enlarge and present as a painful swelling or a white tumor lifting the nail plate or as bluish discoloration of the nail bed with ridging or as paronychia [27]. The risk of malignant transformation (chondrosarcoma) is estimated to 4% [26].

Mechanism of pain: Slow dilation of the medullary cavity will induce no pain. Pain comes from bone fracture due to thinning of the cortex of the bone (Fig. 3a). Sensory nerve fibers innervate the bone and are activated and sensitized within seconds due to mechanical distortion from the fracture. There is ectopic sprouting and bone hyperinnervation, which is not pruned back until the fracture has healed (Fig. 1c). Finally, central sensitization in the brain takes place that further amplifies pain [5].

Type of pain: Depending on the size of the tumor and the fracture: acute, constant, sharp, severe.

Drugs

Nail pain from drugs may come from retinoids and tetracyclines but is essentially a side effect of some anticancer drugs. Whatever the drug, fingernails are much more often affected than toenails.

A. *Retinoids* may very rarely induce a painful onycholysis [28] and ingrown nails with pyogenic granuloma. These signs may appear anytime between 2 weeks and 18 months after initiation of treatment with retinoids and are more frequent in patients with nail psoriasis [28]. Retinoids decrease the attachments between keratinocytes and cause nail brittleness with penetration of fragments between the nail plate and the surrounding tissues; they also have angiogenic properties and inhibit collagenases and gelatinases in vitro [29].

Mechanism of pain: Secondary to the desquamative effect of retinoids on the nails with brittleness, resultant spicules and pyogenic granuloma formation, as well as inflammation from the ingrowing.

B. *Tetracyclines* may induce, very exceptionally, a photo-onycholysis usually sparing the thumbnails, as they are covered by the other fingers. Pain may start several weeks before the onycholysis manifests [30] and may be followed by subungual erythema, subungual hemorrhage, and onycholysis.

Mechanism of pain: It has been postulated that capillaries, terminal vessels, and glomus bodies may be involved in the production of pain [12].

C. *Chemotherapy agents:* Among the anticancer drugs, *taxanes* are very well known for their nail toxicity with a variable incidence that may reach up to 44% of patients [31] or even 80% with docetaxel. The most debilitating symptoms are hemorrhagic onycholysis, subungual abscess, and paronychias with severe morbidity and impact on the patient's quality of life [30]. These severe nail side effects are mostly observed with higher infusion frequency (weekly scheme is mostly responsible) and prolonged exposure to chemotherapy (usually after 3 cycles) [32] in susceptible patients. However, with paclitaxel, a new formulation, the nanoparticle albumin-bound paclitaxel (nab-paclitaxel) can be used instead, which is a solvent-free, colloidal suspension of paclitaxel with fewer side effects [33, 34]. It is suggested that direct nail bed toxicity, inhibition of nail bed angiogenesis, and the release of neuropeptides and prostaglandins from the sympathetic fibers secondary to the taxanes may be the mechanisms leading to onycholysis [35, 36]. The subungual hematoma and hemorrhagic onycholysis could be explained by the taxane-induced thrombocytopenia and vascular abnormalities. The integrity of peripheral nerve fibers is neces-

sary for the development of nail abnormalities as suggested by the absence of nail changes in a denervated hand [37].

Mechanism of pain: (1) Hemorrhagic onycholysis: pressure from the hemorrhage activating the Pacinian corpuscles. (2) Subungual abscess: secondary to acute inflammation, especially the edema exerting pressure and therefore activating the Pacinian corpuscles. (3) Paronychia: secondary to inflamed nail folds. Moreover, the release of neuropeptides and prostaglandins add to the pain.

D. *Epidermal growth factor receptor inhibitors* (inhibitors of kinase proteins or monoclonal antibodies) are widely used. Among other cutaneous side effects, there is a tropism for the nail unit, especially for the thumbs and great toes: fingertip xerosis with subsequent fissuring and pain [38], acute paronychia, pyogenic granuloma, ingrown nails, and periungual abscesses. These signs usually appear 4–8 weeks after initiation of treatment with the epidermal growth factor receptor inhibitors; they may vary in severity during the course of treatment and subside after cessation. On the contrary to the acneiform rash, a correlation between nail toxicity and clinically beneficial response to therapy could not be determined. The pathogenesis is not well understood. The epidermal thinning and the nail brittleness induced by these drugs would favor the initial piercing of or trauma to the periungual skin by the nail plate.

Mechanism of pain: (1) Very dry skin causes the fissuring with subsequent hemorrhage especially in winter. (2) Acute paronychia, pyogenic granuloma, ingrown nails, and periungual abscesses: mechanisms as already mentioned above.

Type of pain: Depending on the cause: the most severe pain is experienced with hemorrhagic onycholysis from taxanes, subungual abscess, and paronychias: *acute/chronic, constant, throbbing or sharp, severe.*

Keratoacanthoma

Subungual keratoacanthoma (SUKA) is a rare, epithelial, benign very painful and rapidly growing tumor (1–2 cm mass within weeks to months). It is commoner in men, between the ages of 35 and 60 with a predilection for the first 3 hand digits, especially the thumb [39]. It presents distally as a small, painful keratotic nodule under the nail and its etiology is still not well understood. The pain starts as mild but as the keratoacanthoma presses onto the bone, the pain becomes severe and constant. It grows vertically and erodes the bone without bone sclerosis and periosteal reaction [40]. SUKA may be solitary or multi-

ple [41]. Multiple lesions have been associated with incontinentia pigmenti [39], but a solitary SUKA has been recently reported in association with it [42]. The rapid growth, the presence of severe pain, and the occurrence in young to middle-aged patients differentiate it from the invasive squamous cell carcinoma, which is painless and occurs in older patients [43]. Spontaneous regression is rare [39, 43] as opposed to the cutaneous form. There are no reports of metastasized SUKA.

Mechanism of pain: The pain starts as mild but as the keratoacanthoma presses onto the bone, the pain becomes severe and constant. There is vertical growth and bone erosion (Fig. 3b) with subsequent activation of the osteoclasts cause bone resorption by the secretion of the matrix metalloproteinases and cathepsin K (organic bone) and the secretion of protons (H^+ and ATP; inorganic bone) with the subsequent formation of an acidic microenvironment that causes pain [5]. The acidic environment upregulates neurotransmitters that will stimulate ectopic sprouting of the sensory and sympathetic nerve fibers (Fig. 1c; see details in Introduction).

Type of pain: Gradual, constant, sharp, severe to very severe. Patients may ask for amputation for relief.

Ice/Frostbites

Frostbite is an injury caused by freezing of the skin and the underlying tissues for a sustained period [44]. The severity of injury depends on the following external factors: the absolute temperature, the presence of wind, the immersion in water, the exposure duration, and the protective ability of clothing. They can be aggravated by the patient's physical status: peripheral vascular disease, Raynaud's phenomenon, perniosis, cryoglobulinemia, acrocyanosis, cold panniculitis, malnutrition, dementia, alcoholism, smoking, β -blockers, substance abuse, and psychiatric illness.

Digits/nails are the most affected areas (90%) [45] with other acral sites (ears, nose, cheeks) and buttocks, perineum, and penis (joggers/Nordic skiers) less affected.

The symptoms are tingling, stinging, numbness, and severe throbbing pain. The digits appear pale, violaceous in color followed by a sensation of tightness, the digits may macerate and finally become gangrenous and necrosed [44]. The prognosis is worsened by a delayed presentation or extended exposure to cold.

Mechanism of pain: The freezing causes vasoconstriction and formation of extracellular ice crystals which then cause cellular dehydration, microvascular occlusion, and endothelial cell membrane injury with the release of the inflammatory mediators such as matrix metalloprotein-

ases, thromboxane TXA_2 , and prostaglandin PGF_{2a} . The release of the mediators together with the thawing of tissues causes edema, platelet aggregation with thrombosis, and progressive dermal ischemia resulting in tissue necrosis and severe pain [46].

Type of pain: Acute, gradual, constant, throbbing, severe.

Droppings (Gout)/Gouty Tophi

This metabolic disease is characterized by monosodium urate crystal deposition in the synovial fluid, crystal formation in soft tissues (tophi), elevated serum urate levels, recurrent attacks of arthritis, renal stone formation, and renal failure [47]. Tophi are collections of solid crystals (monosodium urate crystals), which present in the joints, cartilage, tendons, and skin and less commonly in parenchymal organs. They are surrounded by granulomatous inflammation that denotes a chronic nature, whereas an acute response is unusual [48]. The neutrophil extracellular trap (Fig. 2e) is a web-like structure present in the tophus that shuts down an acute attack by increasing the number of proteases and therefore degrading cytokines (IL-1 β , IL-6, TNF- α) [49]. Hence, the tophi are visible and palpable and typically nontender. They can precede the diagnosis of gout and therefore be the first sign [50]. Periungual gouty tophi can distort the nail apparatus and cause pain from pressure.

Mechanism of pain: The tophi are nontender; however, they may become quite large and break through the skin causing pain due to destruction of the surrounding tissue. Additionally, the chronic inflammatory state and the mechanical deformation within the joint are registered from the Ruffini spindled-shaped mechanoreceptors that transmit the pain (Fig. 2e).

Type of pain: Chronic, intermittent, sharp, mild to severe.

The Causes of Pain in the Toenails (Table 2)

Frostbites

See above.

Onychoclavus (Heloma)

Onychoclavus is a very painful hyperkeratotic papule originating from the median distal nail bed of the great toenail, mainly the right one [51], which often appears dark from hemorrhage. It occurs in patients with hallux erectus [52] secondary to friction on the tip of the shoe with resulting compression between the nail and the

bone. The plate is lifted up by the subungual horn giving rise to a perilesional onycholysis. It has also been described in the little toenail [53] and secondary to subungual exostosis [54].

Mechanism of pain: The heloma is stuck in between the bone and the plate, a virtually unexpansive space (Fig. 3c), exerting sudden and severe pressure and therefore activating the Pacinian corpuscles that transmit pain. The pain is further aggravated by the shoe.

Type of pain: Chronic, constant, sharp, mild to severe.

Mechanical Causes/Trauma: See Above

Incorrectly fitted footwear is common in older people and is strongly associated with forefoot pathology and foot pain. The nail unit may exhibit subungual hyperkeratosis, onycholysis, and nail plate dystrophy. Chronic trauma to the nail unit may also result from superimposed faulty biomechanics [55]. Most orthopedic abnormalities are acquired and precipitated by long-standing use of ill-fitting footwear (especially high heels) and/or underlying osteoarthritis, which accounts for their occurrence in the elderly. The acronym AGNUS (asymmetric gait, nail unit signs) has recently been coined to define nail abnormalities secondary to chronic trauma to the nail unit from footwear and from skeletal abnormalities resulting from an asymmetric walking gait [56].

Mechanism of pain: Long-standing use of ill-fitted shoes, hallux valgus, and the appearance of osteoarthritis, as well as the attempt for a steady gait in the elderly cause the nails to be affected from the rotation of the foot and the constant friction in the shoe. The consequent appearance of subungual hyperkeratosis, onycholysis, and nail plate dystrophy are perceived as painful due to the activation of the Ruffini corpuscles from the proprioception of the toe, as well as the mechanical deformation within the joint from the arthritis.

Type of pain: Chronic, constant, dull ache, mild to severe.

Ingrown Nails/Pincer Nails/Retronychia

A. *Ingrown nails:* They result from a painful conflict between the plate and the nail folds. Sharp spicules of the lateral nail margin are gradually driven into the dermis of the nail groove. These spicules act as a foreign body. An inflammatory response occurs in the area of penetration leading to erythema, edema, and development of granulation tissue (acute stage) with sometimes added infection presenting with discharging pus. Chronic evolution leads to chronic induration of the nail fold [57].

Mechanism of pain: The acute inflammation/edema, the activation of the Pacinian corpuscles, and the presence of cytokines together with the pressure from the shoe pressing on the nail fold cause the sensation of pain. The pain severity depends on the severity of the inflammation formed.

Type of pain: Chronic, intermittent (worse upon pressure), sharp, moderate/severe.

B. *Pincer nails* are hereditary or acquired transverse overcurvature of the nail plate resulting from widening of the base of the distal phalanx [58]. The nail matrix is very tightly attached to the base of the phalanx with the enlarging bone causing the proximal nail to widen and the distal nail to overcurve and narrow. The resulting distal pinching will pull the nail bed up and the collagen fibers attaching the bed to the bone may get ossified. This is visualized on X-rays as a traction osteophyte. If pressure on the distal bed induces a sharp pain, this might be indicative of hyperostosis. The condition is quite common on toes but rare on fingers.

Mechanism of pain: The lateral plate margins roll and dig into the lateral grooves. Amazingly, there is no inflammation or hypertrophic nail folds as in ingrowing nails. There is no real satisfying explanation for the pain in this condition, as some minor forms of pincer nail are extremely painful, even the weight of the sheet may induce pain and some very severe overcurvature of the nail may remain completely painless. Two scenarios may be proposed: either the pressure from the lateral edges of the nail plate onto the lateral folds and pulp rich in Pacinian corpuscles or pain from traction osteophytes upon pressure.

Type of pain: Inconsistency between signs and symptoms. When present, it is chronic, intermittent, very sharp, moderate/severe.

C. *Retronychia* is the proximal embedding of the nail plate [59]. It mainly occurs on the great toenail. Repeated minor trauma is the commonest cause. The disrupted alignment causes multiple ingrown nails with the subsequent elevation of the proximal nail compared to the distal nail, inflammation of the proximal nail fold, thickened adherent yellow nail and distal firm attachment to the nail bed. Granulation tissue may be present proximally where the ingrowing takes place. It has been described in both children and adults [60].

Mechanism of pain: There is inflammation of the nail pocket from digging of the accumulated nail plates and distension of the proximal nail fold with subsequent stretching of the skin in a subacute/chronic fashion, therefore activating the slow-adapting Ruffini mechanoreceptors (Fig. 2f).

Type of pain: Gradual, intermittent, sharp, severe.

Tophi (Gout)

See above.

Exostosis

It is a relatively common, solitary, benign true tumor manifesting as an outward formation of normal bone. It was for a long time considered as a reactive dermal metaplasia resulting from microtrauma [61]. It is now considered a true neoplasm harboring a pathognomonic translocation t (X;6) (q22;q13–14) [62] instead of being a reactive process in response to trauma. It occurs mainly in teenagers, equally common in both genders. It is usually located on the dorsomedial aspect of the distal great toe [63]. It might be found much less commonly in lesser toes and fingers [64]. Microtrauma plays either a contributory or a causative role with the additional pressure from the shoe [65]. It has been found in the toes of ballet dancers [66]. Clinically, the tumor presents as a hard, white, well-circumscribed nodule, surrounded by a collarette. Often a fine layer of telangiectasia runs over, but it may be covered by some hyperkeratosis. The exostosis may elevate the nail plate without causing any destruction or it may emerge from the hyponychium or the lateral sulcus or it may appear as a subungual erythematous patch visible through the nail plate with a possible surrounding onycholysis. In some rare instances, it may present as an ingrowing nail-like picture with pyogenic granuloma.

Exostosis may, very rarely, be part of the multiple exostosis syndrome (autosomal dominant), which has the potential for malignant transformation to chondrosarcomas (1–2%) [67] as opposed to solitary exostosis.

Mechanism of pain: Pain is caused by pressure from a direct mechanical mass effect of the exostosis on the overlying nail bed and on the mechanoreceptor-rich pulp with the activation of the Ruffini corpuscles and the transmission of pain (Fig. 3d).

Type of pain: Chronic, intermittent, mild and provoked by pressure.

Conclusion

Pain in nails is the result of the unique anatomic structure of the terminal phalanx: the high presence of terminal axons, the lack of subcutaneous tissue between the nail plate and the bone and the adherence of collagen fibers between those 2 levels make the possibility of painless dilation almost impossible.

Although the list of disorders that cause onychalgia is nonexhaustive, the authors of this article offered an easy acronym to remember the main causes of pain at the nail unit and tried to shed light to the underlying mechanisms.

Developing a deeper understanding of the mechanisms of pain provides insight and targeted analgesic therapies for a variety of nail disorders, with symptom relief and patient satisfaction.

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