Diagnostic and Therapeutic Challenge of Metatarsalgia in a Patient With Rheumatoid Arthritis

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Abstract

A 63-year-old female patient, with a past history of rheumatoid arthritis, presented with insidious pain on the left foot second and third metatarsophalangeal joints, associated with swelling and morning stiffness (mean time: four hours). Physical examination evidenced a tender and soft nodularity in the third intermetatarsal space, along with sharp pain, consistent with Morton’s neuroma. Foot ultrasound suggested Morton’s neuroma, but not excluding the possibility of rheumatoid arthritis involvement. Foot magnetic resonance imaging suggested the possibility of extensive synovitis of the third metatarsophalangeal joint, but not excluding the coexistence of Morton’s neuroma because of the mass effect. Finally, the patient underwent an ultrasound-guided needle biopsy of the nodule, which confirmed metatarsophalangeal joint synovitis. The foot is a common location of rheumatoid arthritis manifestation, and metatarsophalangeal joint synovitis can mimic Morton’s neuroma. After a definite diagnosis, the patient recovered lower limb functional impairment after introducing adalimumab and a rehabilitation program. This case highlights the importance of an accurate differential diagnosis, pharmacological rheumatoid arthritis control, and physical medicine and rehabilitation programs to optimal clinical and functional improvement.

Introduction

Metatarsalgia refers to pain generally located under one or more metatarsal heads [1]. Forefoot pain includes pain located in the toes and metatarsophalangeal joints [2]. Those locations are among the most common foot pain locations [1,2]. Manifestations of forefoot pain may be similar and a thorough assessment of pain location and associated clinical manifestations is key to differential diagnosis [2]. The causes include plantar callosities, plantar warts, subluxation, dislocation or synovitis of the metatarsophalangeal joints, hallux valgus, hallux rigidus, Freiberg disease, interdigital (Morton’s) neuroma, systemic disorders (such as rheumatoid arthritis, psoriatic arthritis, or gout), structural malalignment of the foot, sesamoiditis, stress fractures and trauma [1,2]. The foot is the second most common location of rheumatoid arthritis manifestation [3]. Foot pain, especially forefoot pain, and rheumatoid forefoot deformity are debilitating and a common reason why these patients seek medical care [3]. Synovitis leads to capsular distension and initiates bone and soft tissue destruction [3-5]. Loss of articular integrity and associated muscle imbalances result in dorsal subluxation of the proximal phalanx, hallux valgus, claw toe deformity, and plantar callosities, and associated with other conditions such as Morton’s neuroma [3-5]. The treatment mainstay is pharmacological rheumatoid arthritis control; notwithstanding it may be necessary other nonoperative measures such as the use of orthoses, or even surgical management [3,4]. The authors report a case of a rheumatoid arthritis patient who presented with metatarsalgia that revealed a challenging differential diagnosis between metatarsophalangeal joint synovitis and Morton’s neuroma, and its implications to therapeutic decision-making.

Case Presentation

A 63-year-old Portuguese female patient, with a past history of rheumatoid arthritis diagnosed in 2005, osteoporosis, and hypercholesterolemia, medicated with methylxate, folate, alendronic acid, cholecalciferol, and atorvastatin. The patient presented with insidious pain evolving through 3 months on the second and third metatarsophalangeal joints of her left foot, associated with swelling and about 4-hour morning stiffness. Physical examination evidenced painless second and third metatarsophalangeal joint deformity and a tender and soft nodularity in the third intermetatarsal space, with sharp pain consistent with Morton’s neuroma. There was no history of trauma or another joint deformity, instability, or diminished range of movement. There were no inflammatory signs or plantar callosities within the skin, nor vascular insufficiency or neurologic deficits within the lower limbs. Disease activity according to disease activity score 28 (DAS28) was low.

There was no seric inflammatory markers elevation. Initially, the patient underwent a foot ultrasound that showed a hypoechogenic and heterogeneous nodule with 23x16x9 mm with vascularity, suggesting...
Morton’s neuroma, not excluding the possibility of rheumatoid arthritis involvement. At this phase, it had been initiated pharmacologic therapy with sulfasalazine, to counter rheumatoid arthritis involvement, with poor response and progressively worse lower limb functional impairment. Subsequently, the patient underwent left foot magnetic resonance imaging that showed marked bone edema of the distal third metatarsal bone and the third proximal phalanx, and a 18x10x17 mm widening of the third intermetatarsal space with T1-weighted iso-signal and T2-weighted heterogeneous signal, seemingly connected to the dorsal aspect of the third metatarsophalangeal joint, suggesting the possibility of extensive synovitis of this joint, but not excluding the coexistence of Morton’s neuroma because of mass effect (Figures 1-2). The doubt remained, so the patient underwent an ultrasound-guided needle biopsy of the nodule, which revealed fibrous connective tissue with mild inflammatory infiltrate and fibrin, compatible with synovitis.

**FIGURE 1**: T1-weighted long-axis left-foot magnetic resonance imaging showing marked bone edema of the third metatarsal bone and the third proximal phalanx, and iso-signal widening of the third intermetatarsal space.
FIGURE 2: T2-weighted long-axis left-foot magnetic resonance imaging showing marked bone edema of the third metatarsal bone and the third proximal phalanx, and heterogeneous signal widening of the third intermetatarsal space.

Treatment was initiated with sulfasalazine 500 mg bid. However, three months later the pain did not subside and was associated with functional lower limb impairment. So, sulfasalazine dose was increased and the patient initiated an outpatient rehabilitation program with cryotherapy, third metatarsophalangeal joint and space-pulsed ultrasound therapy, slow passive range of motion exercises, and deep transverse friction massage to counter joint stiffness and maintain its range of motion, intrinsic foot muscles isometric strengthening exercises and gait training with a foot orthosis with retrocapital support. Two months later she presented with significant but not complete pain relief. At that time, with a definite diagnosis of metatarsophalangeal synovitis with ultrasound-guided needle biopsy, it was decided to initiate biweekly adalimumab while she maintained the same rehabilitation program.

The patient was evaluated about one month after beginning biological therapy. She reported sustained pain relief and no side effects. There were no signs of metatarsophalangeal joint arthritis with physical examination and it was initiated gradual discontinuation of sulfasalazine. Three months later, she presented...
adalimumab was introduced after that. Other conservative measures include the use of foot orthoses, which
hydroxychloroquine
of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis, there is a conditional recommendation
control. This patient was previously medicated with methotrexate. According to the 2021 American College
As mentioned before, rheumatoid forefoot treatment’s mainstay is pharmacological rheumatoid arthritis
imaging can be useful if Morton’s neuroma diagnosis is doubtful
deformities or fractures, ruling out other causes of pain
metatarsophalangeal joint synovitis. Differential injection with anesthetic into the intermetatarsal space, proximal to the metatarsal head, and into
reproduces the patient’s pain suggests metatarsophalangeal synovitis
clinical history suggests the diagnosis
Metatarsophalangeal joint synovitis and Morton’s neuroma can overlap and it can be confusing to separate
metatarsophalangeal joint is inflamed, the soft tissues around can be affected,
including the interdigital nerves. Furthermore, the neuroma can irritate adjacent structures. The clinical history suggests the diagnosis
Pain location, pain quality, chronology, and aggravating and alleviating factors may be the key to the diagnosis. Morton’s neuroma is suggested by pain not located to the metatarsal head, aggravated with tight shoes or high heels, whereas metatarsophalangeal joint synovitis is suggested by pain on weight-bearing, associated with joint swelling, that alleviates with antinflammatory medication. Physical examination should focus on feet inspection, looking for deformities, the foot arches, callosities and swelling, and foot palpation, particularly the intermetatarsal spaces. Other specific tests may be helpful, such as Mulder’s test and the drawer test. Palpable clicking with Mulder’s test is extremely sensitive to Morton’s neuroma diagnosis. A drawer test that reproduces the patient’s pain suggests metatarsophalangeal synovitis. Miller also suggested a differential injection with anesthetic into the intermetatarsal space, proximal to the metatarsal head, and into the metatarsophalangeal joint, alternately, and evaluate and compare the clinical response to distinguish between Morton’s neuroma and metatarsophalangeal joint synovitis.
Diagnosis of Morton’s neuroma is made clinically. If doubt remains after a thorough clinical history and physical examination, imaging may be extremely helpful. Plain radiographs can be useful to assess deformities or fractures, ruling out other causes of pain. Ultrasound scan and magnetic resonance imaging can be useful if Morton’s neuroma diagnosis is doubtful.
As mentioned before, rheumatoid forefoot treatment’s mainstay is pharmacological rheumatoid arthritis control. This patient was previously medicated with methotrexate. According to the 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis, there is a conditional recommendation to add a biologic or targeted synthetic disease-modifying antirheumatic drug over adding sulfasalazine and hydroxychloroquine. In this patient, it was initiated sulfasalazine when the diagnosis was not clear, and adalimumab was introduced after that. Other conservative measures include the use of foot orthoses, which
can help with forefoot pain control, but the available evidence shows conflicting results [3]. Surgical management of rheumatoid forefoot may be necessary to restore ambulation [3]. There are numerous possible procedures, with variable rates of success [3]. One classical procedure is a resection arthroplasty of the metatarsophalangeal joints [3]. Other procedures include first metatarsophalangeal fusion, in isolation or combined with the aforementioned arthroplasty [3]. Other techniques include joint-preserving surgery, consisting of metatarsal osteotomy and soft tissue reconstruction, with metatarsophalangeal joint function preservation [3,13]. Debridement of plantar callus may offer some pain relief [3]. Synovectomy may have a role but is not usually performed because most patients present already with the consequent forefoot deformity [3].

On the other hand, Morton’s neuroma conservative treatment consists of shoe modification and a plantar orthosis with metatarsal unloading [2,6]. In about 30% of cases, conservative treatment and steroid injection provide long-term pain relief [6]. The remaining patients should be considered for surgical excision of Morton’s neuroma [6].

Conclusions

The foot is a common location of rheumatoid arthritis manifestation and should not be overlooked. Metatarsophalangeal joint synovitis can mimic Morton’s neuroma, and Morton’s neuroma can coexist with metatarsophalangeal joint synovitis. Given the different approaches to the different clinical entities, an accurate diagnosis is mandatory to guide treatment. Clinical history and physical examination are important to the differential diagnosis of metatarsalgia and forefoot pain and, in doubtful cases, the diagnostic investigation must be exhaustive, as it was in this case, until a clear diagnosis is reached. After an accurate diagnosis, pharmacological rheumatoid arthritis control and physical medicine and rehabilitation programs are crucial to optimal clinical and functional improvement.

Additional Information

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References

1. Mann RA: Metatarsalgia. Common causes and conservative treatment. Postgrad Med. 1984, 75:150-3, 156-8, 163-7. 10.1080/00325481.1984.11697998
2. Pelly T, Holme T, Tahir MA, Kunasingam K: Forefoot pain. BMJ. 2020, 371:m3704. 10.1136/bmj.m3704
3. Brooks F, Harhiran K: The rheumatoid forefoot. Curr Rev Musculoskelet Med. 2013, 6:320-7. 10.1007/s12178-013-9178-7
4. Louwerens JW, Schrier JC: Rheumatoid forefoot deformity: pathophysiology, evaluation and operative treatment options. Int Orthop. 2013, 37:1719-29. 10.1007/s00264-013-1404-2
5. Doorn PF, Keijzers NL, van Limbeek J, et al.: A clinical classification system for rheumatoid forefoot deformity. Foot Ankle Surg. 2011, 17:158-65. 10.1016/j.fas.2010.05.001
6. Di Caprio F, Meringolo R, Shehab Eddine M, Ponziani L: Morton's interdigital neuroma of the foot: a literature review. Foot Ankle Surg. 2018, 24:92-8. 10.1016/j.fas.2017.01.007
7. England BR, Tiong BK, Bergman MJ, et al.: 2019 update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. Arthritis Care Res (Hoboken). 2019, 71:1540-55. 10.1002acr.24042
8. Dakkak YJ, Boer AC, Boeters DM, Niemantsverdriet E, Reijnierse M, van der Helm-van Mil AH: The relation between physical joint examination and MRI-depicted inflammation of metatarsophalangeal joints in early arthritis. Arthritis Res Ther. 2020, 22:67. 10.1186/s12977-020-0216-7
9. Chagartti S, Joshy S, Harhiran K, Rashid M: Rheumatoid nodule presenting as Morton's neuroma. J Orthop Traumatol. 2013, 14:219-22. 10.1007/s10195-012-0215-x
10. Zielaskowski LA, Klucja SJ, DiStazio JJ, Bastacky S: Multiple neuromas coexisting with rheumatoid synovitis and a rheumatoid nodule. J Am Podiatr Med Assoc. 2000, 90:252-5. 10.1177/75770315-90-5-252
11. Miller SD: Technique tip: forefoot pain: diagnosing metatarsophalangeal joint synovitis from interdigital neuroma. Foot Ankle Int. 2001, 22:914-5. 10.1177/107110070102201112
12. Fraenkel L, Bathon JM, England BR, et al.: 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2021, 73:1108-23. 10.1002/art.41752
13. Yano K, Ikari K, Tobimatsu H, Tominaga A, Okazaki K: Joint-preserving surgery for forefoot deformities in patients with rheumatoid arthritis: a literature review. Int J Environ Res Public Health. 2021, 18:10.3390/ijerph18084093