Psoriatic nail complex: thick as thieves

This editorial refers to the article ‘Association of the clinical components in the DIP joint synovio-enthesal complex and subsequent response to ixekizumab or adalimumab in PsA’, published by McGonagle et al., Rheumatology, 2024, keae060.

The article by McGonagle et al [1], presents relevant information on the connection between nail psoriasis and distal interphalangeal (DIP) joint disease psoriatic arthritis (PsA), and their value together as a global indicator of treatment response, in a post hoc analysis of data from the SPIRIT-H2H study (NCT03151551), in which the effects of treatment with ixekizumab (IXE) or adalimumab (ADA) were assessed for each finger unit with nail psoriasis and adjacent joint disease, both the DIP of the fingers and the interphalangeal joint of the thumbs, defining "finger unit" as the nail and adjacent joint of an individual digit.

PsA, which is not a co-morbidity of psoriasis (PsO) but a manifestation of psoriatic disease, increases its incidence with time, mainly after the onset of PsO, reaching up to 20% after 30 years, and can manifests clinically in several ways including peripheral synovitis, enthesitis, dactylitis, and axial involvement, being the presence of psoriatic onychopathy a risk factor for the development of PsA [2]. Nail psoriasis has been associated with an increased risk of developing PsA, affecting up to 80% of patients with joint involvement [2-3]. Psoriatic nails are associated with arthritis in the adjacent DIP of the fingers or the interphalangeal joint of the thumbs (see Figure 1), and both locations of PsA are very common and can lead to severe functional impairment [4].

The basis for this association is a close relationship between the extensor tendon fibers and the periosteum of the distal phalanx, nail bed and nail matrix [5-6], suggesting that the enthesal complex is the site of initiation of inflammation in PsA. The spread of inflammation to the enthesal tissues and the DIP joint is considered an early indicator of the presence of PsA and is associated with increased disease severity [7].

In the study by McGonagle et al [1], a total of 1309 finger units (IXE=639, ADA=670) with simultaneous DIP joint involvement (tenderness and/or swelling) and adjacent nail psoriasis (total NAPSI score >0) at baseline are examined in the selected patient population (N=354). The DIP joint was tender in 1217 (IXE=594, ADA=623) of these finger units, and swollen in 928 (IXE=463, ADA=465). The nail had nail matrix involvement in 1033 (IXE=516, ADA=517) finger units, and nail bed psoriasis in 944 (IXE=465, ADA=479). The difference between treatment arms was 38.8% vs. 28.4%, (p<0.0001) and was maintained until week 52 (64.9% vs. 57.5%, p=0.0055). Nail bed psoriasis was less frequent among the finger unit population than among nail matrix psoriasis, but proportionally more finger units had resolved nail bed psoriasis compared to nail matrix psoriasis at earlier time points.

The recent emergence of biologics has revolutionized the treatment of nail psoriasis with numerous clinical trials showing improvement in nail psoriasis in patients with PsO and/or PsA following biologic treatment. However, not all biologics have demonstrated the same level of efficacy or speed in resolving nail psoriasis. Ixekizumab, a biologic targeting IL-17A has proven clinical efficacy and real-world effectiveness [8, 9] at achieving skin and difficult-to-treat areas clearance compared to biologics targeting TNF-α, and several trials in both PsO and PsA have highlighted the efficacy of IXE in clearing nail PsO, which often precedes the development of PsA and may be the earliest visible sign of psoriatic joint involvement [10].
In the clinical trial SPIRIT-H2H, at the finger unit level, IXE showed significant benefit over the TNF inhibitor ADA in achieving complete resolution of DIP joint tenderness, DIP joint swelling, and adjacent nail psoriasis. However, as the authors comment, the limitations of this post hoc analysis were the lack of measures of pain and quality of life specific to nail psoriasis, as well as the lack of comparison between patients with and without nail psoriasis. In addition, it is recognised that tenderness in the DIP region without inflammation in subjects with nail psoriasis could represent nail disease of the matrix or lateral anchorage region, and not of the DIP joint per se. Another drawback would be the difficulty, on many occasions, in differentiating inflammation from DIP in the context of PsA or with erosive osteoarthritis from DIP joints.

Future clinical trials in PsA should incorporate as a secondary or, why not, even primary objective a joint assessment of efficacy at the cutaneous-nail and joint level, using this concept of the “finger unit”, which allows treatment of psoriatic disease to be approached to obtain an improvement as a whole and not just in some of the domains that make up the disease. In psoriatic disease, we find, in short, pieces of a puzzle that we cannot understand separately, but which, on the other hand, form part of an indissoluble whole.

**Data availability**

No new data were generated or analysed in support of this article. Data from the article by McGonagle *et al.* [1] are available within the manuscript and its supplementary material.

**Authors’ contributions**

Dr. J.A. Pinto-Tasende drafted the article and Dr. R. Queiro-Silva revised it critically for important intellectual content. Both authors approved the version to be published.

**Funding**

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

*Disclosure statement:* J.A.P.T and R.Q.S. have received consulting and advisory boards fees and research grants from Bristol Myers Squibb, Celgene, AbbVie, BMS, Janssen, Novartis, Pfizer and UCB.

Jose A. Pinto-Tasende¹,* and Rubén Queiro-Silva²

¹ Division of Rheumatology. INIBIC. Complexo Hospitalario Universitario de A Coruña, Spain

ORCiD 0000-0002-4993-8185

² Faculty of Medicine, Oviedo. Division of Rheumatology. Hospital Universitario Central de Asturias, Oviedo, Spain

*Correspondence to: Jose A. Pinto-Tasende, Complexo Hospitalario Universitario de A Coruña, 84 Xubias de Arriba St, CIP 15009, A Coruña, Spain. E-mail: japt1965@gmail.com

**References**

1.- Dennis McGonagle, Arthur Kavanaugh, Iain B McInnes, Lars Erik Kristensen, Joseph F Merola, Bruce Strober, et al. Association of the clinical components in the distal interphalangeal joint synovio-enthesal complex and subsequent response to ixekizumab or adalimumab in psoriatic arthritis, Rheumatology, 2024;., keae060


Figure 1.

In this image (taken with the patient's permission) the affected DIP joints are those with adjacent damaged nails.