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Unexpected Skin And Nail Manifestations Following Treatment With Ustekinumab In A Patient With Crohn's Disease

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Abstract:
The management of chronic inflammatory bowel diseases requires a therapeutic arsenal. Among the treatments offered, we have biological therapies including ustekinumab, a monoclonal antibody, which acts by inhibiting interleukins 12 and 23, thus reducing the inflammatory activity observed in this type of disease. We report the case of a patient suffering from Crohn's disease who developed unexpected nail and skin involvement such as trachyonychia and erythematous axillary plaques following initiation of treatment with ustekinumab. Despite its rarity, this case highlights the importance of vigilance for adverse reactions and the need for continued monitoring as well as a thorough understanding of the mechanisms of biologic drugs in the management of chronic inflammatory diseases.

Key Word*: Ustekinumab; nail damage; paradoxical psoriasis; anti IL 12/23; Crohn's disease*

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I. Introduction

Managing chronic inflammatory diseases, such as Crohn's disease, poses a complex challenge for clinicians, often requiring a multifaceted therapeutic approach. In this context, the increasing use of biologic therapies has revolutionized the management of these conditions, offering new perspectives in symptom and inflammation control for patients refractory to conventional treatments. Among these biologic therapies is ustekinumab, a monoclonal antibody targeting interleukins 12 and 23, which has proven to be a promising therapeutic option. However, like any medication, ustekinumab is not without side effects, including symptoms such as dizziness, headaches, diarrheal episodes, nausea, or muscle pains. More rarely, paradoxical psoriasis-like manifestations have been reported, raising questions about the pathophysiology and underlying mechanisms. However, a less explored aspect remains that of nail involvement associated with its use.

II. Case Report

We report the case of a 37-year-old patient followed for ileal Crohn's disease initially treated with Adalimumab since April 2015, but stopped in February 2021 due to the occurrence of an infectious complication such as meningo-herpetic encephalitis treated with valaciclovir. Then the patient was treated with Budesonide, a local corticosteroid used in the treatment of Crohn's disease of ileal or ileo-cecal localization, but this treatment proved insufficient since the patient presented clinical symptoms consisting of diarrhea and abdominal pain. also on the endoscopic level, moderate inflammatory damage and ulcerations of the last ileal loop were observed, hence the decision to introduce a new basic treatment was taken. Treatment with ustekinumab was the most suitable therapeutic option for his case. Started in January 2023 at a rate of 90 mg every eight weeks, the digestive effectiveness was excellent with complete remission of the disease clinically and endoscopically. But since October 2023, the patient has presented nail lesions that appeared quickly and exclusively on the hands. Seven fingernails were affected with respect for the first three rays of the left hand and the toenails. An antifungal treatment with varnish has been tried but ineffective. The patient also described lesions on the axillary and inguinal folds, with the latter spontaneously resolving. Clinical examination revealed trachyonychia of the 7 fingernails, with a whitish-grey appearance of the nail plates and respect for the paronychium, without subungual hyperkeratosis or onycholysis (Figs 1, 2). We also noted a relative respect for the first three fingers of the right hand with the presence of thimble punctuations. The skin showed bilateral axillary lesions in the form of relatively well circumscribed, slightly papular, erythematous plaques, with rhagades of erosions on the left. A skin biopsy of the axillary lesion revealed an excoriated chronic eczematiform dermatosis. In the nail lesions, the trachyonychial appearance was not very specific, reflecting a

diffuse matrix infiltration. Given the context and the associated axillary lesions, the diagnosis of paradoxical psoriasis was made. Reverse psoriasis is known to occur with ustekinumab, but induced trachyonychia is not. No specific treatment was prescribed for the nail lesions, as they were mainly cosmetic with no functional impairment, and as her Crohn's disease was well controlled with this drug, the risk-benefit ratio was in favour of continuing his treatment with ustekinumab.

Figs 1, 2: Trachyonychia appearance of the 7 fingernails with a rough whitish appearance of the nail plates

III. Discussion

Ustekinumab is a fully humanized monoclonal antibody, directed against interleukins 12 and 23 by binding with great specificity and affinity to the p40 protein subunit of these two interleukins which are involved in the inflammatory process observed during chronic inflammatory diseases of the intestine. [5] By inhibiting their functioning, ustekinumab reduces the activity of the immune system as well as the manifestations of the disease. Produced by the recombinant DNA technique, a laboratory process consisting of extracting DNA fragments from one or more organisms, then reassembling them with the DNA of the host cells. This genetic modification gives these cells the ability to produce anti IL-12 and anti-IL 23 antibodies. [6] It obtained its first Marketing Authorization in France in 2010 in the treatment of psoriasis, then an ATU for the treatment of Crohn's disease before obtaining a European Marketing Authorization in 2016 from the European Medicines Agency in this indication in specifying that its prescription is indicated in the treatment of moderate to severe active Crohn's disease in adults who have had an insufficient response, loss of response or intolerance to conventional treatment or anti-TNFα treatment or who have a contraindication medical to these treatments. [7] Like most drugs, this molecule has known and described side effects such as dizziness, headache, diarrhea, nausea, vomiting, muscle pain and fatigue which occur in 1 to 10% of cases, others are rather rare. which occur in less than 1% of cases such as pustular psoriasis, acne, hives and dental or vaginal infections. [3][8][9] A review published in 2020 on paradoxical psoriasis found that ustekinumab was linked to 11 cases of developing this condition, usually occurring within 3 months of starting treatment. However, longer delays of up to 15 months have also been observed.[4] The pathophysiology remains poorly understood, the current hypothesis speaks of an increase in the production of interferon alpha (IFN) known for its role in the aggravation of psoriasis due to a decrease in TNF alpha which normally suppresses the 'INF alpha. This decrease in TNF alpha is caused by ustekinumab which blocks the activity of IL23 cells which induces the production of TNF alpha. [10] On the other hand, for nail damage no case of this type was found in the French national pharmacovigilance database, however in the international pharmacovigilance database 89 cases of nail and nail bed disease were reported, including 27 cases of nail disorders, 10 cases of onychomadesis and 13 cases of onychoplasty.[11] In the literature, no case has been published of nail damage with ustekinumab.

IV. Conclusion

The presented case highlights the complex challenges associated with the management of chronic inflammatory diseases such as Crohn's disease. The use of biologic therapies like ustekinumab offers a glimmer of hope in disease control in patients with insufficient response to conventional treatments. However, this case highlights the need for constant vigilance regarding adverse effects and paradoxical reactions associated with these medications. Likewise, the occurrence of this unexpected nail damage raises questions about the underlying mechanisms and underlines the importance of careful monitoring, multidisciplinary collaboration and an in-depth understanding of the mechanisms of action of biological drugs.

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