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Case Report

Melanonychia is an Adverse Effect of TNF Inhibitors (Adalimumab) in Psoriatic Arthritis Patient: A Case Report

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ABSTRACT

Introduction: Melanonychia, derived from the Greek terms "melas" (black) and "onyx" (nail), is characterized by brown-black discoloration of the nail plate, primarily due to melanin production. This condition can arise from two mechanisms: Melanocytic activation and melanocyte proliferation.

Case presentation: A fully human monoclonal antibody targeting Tumor Necrosis Factor (TNF), adalimumab is used to treat several immune-mediated inflammatory diseases, including rheumatoid arthritis, psoriatic arthritis, and Crohn's disease. Skin-related adverse effects account for approximately 25% of all reported side effects of anti-TNF therapies, which may only become apparent in clinical practice despite thorough preclinical studies.

Results: This case report suggests that adjusting the frequency of adalimumab therapy can effectively manage adverse effects like melanonychia while retaining the drug's therapeutic benefits. Modifying the dosing schedule led to significant improvements in nail pigmentation.

Discussion: The findings are consistent with existing literature, which documents skin-related adverse effects from TNF inhibitors, including melanonychia. This aligns with studies that highlight the potential for TNF antagonists to induce immune-mediated reactions affecting melanocyte activity.

Conclusion: The case of adalimumab-induced melanonychia underscores the need for clinicians to remain vigilant for a broad range of potential side effects. Further research is necessary to better understand the safety profile of biologic therapies and to recognize uncommon adverse effects like melanonychia

Keywords: Melanonychia; Tumour necrosis factor; Adalimumab; Crohn's disease; Psoriasis; Antagonists

INTRODUCTION

Approximately two-thirds of Nail Apparatus Melanoma (NAM) cases exhibit brown to black nail pigmentation derived from melanin, a condition known as melanonychia [1]. It can affect either single or multiple nails, in both fingers and toes [2].

Melanin in the nail plate is typically produced by melanocytes in the nail matrix. These active melanocytes transfer melanin-rich melanosomes to the developing nail cells through dendritic processes. This process usually results in a longitudinal band of melanonychia, though total or transverse melanonychia can occur, albeit rarely. Melanonychia typically originates in the distal nail matrix [3].

Etiology

Melanonychia primarily arises through two mechanisms:

Melanocytic activation: This involves an increase in melanin production from a normal number of activated melanocytes located in the nail matrix.

Melanocyte proliferation: This refers to an elevated melanin pigment level due to an increased number of melanocytes in the nail matrix. The proliferation or hyperplasia of melanocytes can be either benign or malignant [4].

Adalimumab

Adalimumab is a fully human monoclonal antibody that targets Tumor Necrosis Factor (TNF) and is approved for treating six immune-mediated inflammatory diseases: Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Psoriasis (Ps), and Crohn's Disease (CD) [5]. Initially, the FDA approved adalimumab for RA, making it the third TNF-alpha inhibitor to receive FDA approval, following infliximab and etanercept [6].

This recombinant human high-affinity Immunoglobulin G1

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(IgG1) monoclonal antibody works by inhibiting TNF alpha. Injection site reactions are the most common side effects, occurring in nearly 20% of patients, usually within 1-2 days after administration and resolving within 3-5 days. These reactions are less frequent compared to etanercept. Although rare, anaphylactic and anaphylactoid reactions can occur.

As anti-TNF therapy suppresses the immune system, serious infections are the most commonly reported significant adverse events associated with this class of drugs. There has been concern regarding the risk of malignancy due to TNF's role in tumor growth, though studies involving RA have not consistently indicated a safety risk. Additionally, chronic inflammation from the diseases treated with anti-TNF therapy is also linked to a heightened risk of malignancy [7].

Adverse event rates among patients receiving anti-TNF agents can differ based on the therapeutic indication. Variations in populations-such as inherent disease risks, prevalence of comorbidities, and the use of concomitant immunosuppressive medications like corticosteroids-may explain these differences [8].

Skin adverse reaction with biological agents

Skin-related adverse effects from anti-TNF alpha therapies account for nearly 25% of all reported side effects. While preclinical studies aimed to identify potential issues, many adverse effects only became apparent after these biologics were used in clinical settings. The first report linking anti-TNF alpha treatment to induced psoriasis was published in 2004, leading to the recognition of a category of immune-mediated adverse effects, including a variety of paradoxical reactions. Additionally, new cases of hypersensitivity reactions have emerged, often with unclear underlying mechanisms [9].

The skin complications associated with anti-TNF alpha treatment can be categorized into four main groups: skin infections, reactions related to drug administration, immune-mediated reactions, and malignancies [10].

CASE PRESENTATION

50 years old medical staff female patient presented with red painful eye consult an ophthalmologist and diagnosed her as uveitis, which start steroid eye drop and send for rheumatological consultation for chronic backache which she complain. During thorough examination the rheumatologist find bilateral sacroilietis by MRI examination and patient had history of recurrent oral ulcers, and family history of Psoriasis, so by clinical examination and investigation, she diagnosed as psoriatic arthritis and arrange her to start biological treatment.

Patient complete her investigation to start biology and prescribed adalimumab every second week. Patient condition start to resolve after second dose of adalimumab, uveitis resolve and backache also disappear and patient health is good.

After the third dose of adalimumab (6 weeks) from beginning of biology, patient noticed bilateral symmetrical dark brown to black pigmentation of nails as shown in Figure 1, which is longitudinal pigmentation and consult a dermatologist which diagnosed it as melanonychia and suggest either to stop treatment or increasing spaces between doses, so 8 weeks after increasing space between injections to three weeks instead of two weeks, one of discoloration of nail also disappeared completely and other nail discoloration decrease in size.

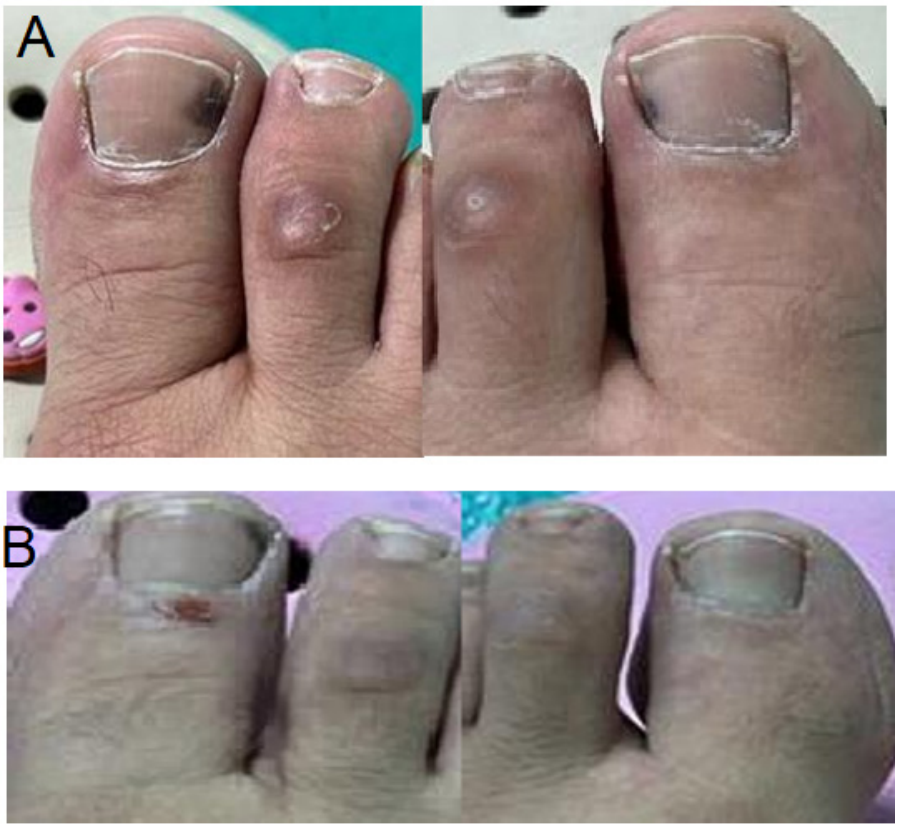

Figure 1: Bilateral symmetrical dark brown to black pigmentation of nails. **Note:** A) Before; B) After.

RESULTS

The resolution of melanonychia after modifying the dosing schedule of adalimumab, in the case report, after extending the interval between injections from two to three weeks, the patient experienced a significant improvement in nail pigmentation, with one nail's discoloration disappearing completely and the others showing a reduction in pigmentation.

This suggests that adjusting the frequency of biologic therapy could be an effective strategy to manage adverse effects like melanonychia while maintaining the therapeutic benefits of the drug. This result underscores the potential for dose modification as a practical approach in managing side effects of TNF inhibitors.

DISCUSSION

This case report about adalimumab induced melanonychia is in agreement with study of Flendrie et al., this study reported that skin-related adverse effects are common in patients treated with TNF inhibitors, including adalimumab [11]. And also in agreement with Lee et al., the study documented a range of skin complications, including pigmentation changes, resulting from TNF inhibitor therapy [12]. These findings support the hypothesis that adalimumab can cause melanonychia due to its impact on skin and nail melanocytes.

Also in agreement with Tracey et al., this comprehensive review indicated that TNF antagonists, including adalimumab, are associated with immune-mediated reactions [13]. The suppression of TNF can alter melanocyte activity, potentially leading to conditions like melanonychia.

CONCLUSION

The case of adalimumab-induced melanonychia presented in the case report aligns with several studies that have documented skin-related adverse effects associated with TNF inhibitors. The evidence supporting the potential for adalimumab to cause melanonychia includes reports of various dermatological reactions and immune-mediated effects on melanocytes. However, larger studies focusing on the safety profile of TNF inhibitors have not prominently reported melanonychia, suggesting it may be an uncommon or under recognized adverse effect. This discrepancy highlights the need for clinicians to be vigilant for a broad range of potential side effects and to report unusual reactions to enhance our understanding of the safety profile of biologic therapies.

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