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The WDC Journal is the official, peer-reviewed publication of the Worldwide Dermatology Collaboration (WDC). It aims to foster global cooperation in dermatology by providing a platform for the latest research, innovative practices, and advancements in the field of dermatology. We believe that collaboration among dermatologists worldwide is key to improving patient outcomes and advancing skin health. The journal covers diverse topics, from dermatopathology and skin cancer research to dermoscopy, community dermatology, and more

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Editorial

It is with great pleasure that we introduce the inaugural issue of the *WDC Journal*. This new platform is dedicated to fostering the exchange of clinical knowledge, case-based insights, and original research across disciplines in medicine and healthcare. Our mission is to provide a forum for clinicians, researchers, and academics to share experiences that advance both scientific understanding and clinical practice.

In this first issue, readers will find a stimulating collection of case reports and original research studies that reflect the diversity and depth of contemporary clinical challenges. Among them, a rare case of dermatomyositis coexisting with type 1 diabetes mellitus underscores the importance of recognizing unusual autoimmune associations in clinical practice. The prospective study on the prevalence of metabolic syndrome in Albanian psoriatic patients highlights the systemic nature of psoriasis and its strong links with metabolic and cardiovascular comorbidities.

Equally significant are the contributions that document rare but clinically relevant entities, such as cellular neurothekeoma and lymphangitic sporotrichosis, which remind us of the importance of accurate diagnosis and awareness of uncommon presentations. Moreover, the case report on botulinum toxin type A for refractory trigeminal neuralgia provides valuable insight into innovative therapeutic approaches for patients unresponsive to standard treatment. Finally, the report on the effects of TNF-blockers in psoriatic arthritis emphasizes the dual clinical and biochemical benefits of targeted therapy in autoimmune disease.

As we embark on this journey, we warmly thank our contributors, reviewers, and editorial team for their commitment to high-quality scientific communication. We also invite our readers to actively engage with the journal, submit their work, and share their perspectives. Together, we aim to build a dynamic community of knowledge and collaboration that will enrich medical practice and research.

We look forward to the continued growth of the *WDC Journal* and to many future issues that will reflect both the challenges and the progress of contemporary medicine.

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Editor in Chief WDC Journal

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Case Report

Exploring the Rare Association: A Case Report of Dermatomyositis Coexisting with Type 1 Diabetes Mellitus

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KEYWORDS

Dermatomyositis, Type 1 diabetes mellitus, rare association, contradictory management

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ABSTRACT

Type 1 Diabetes Mellitus (T1DM) is an autoimmune disease characterized by pancreatic β-cell destruction, leading to insulin deficiency and hyperglycemia. Coexisting autoimmune conditions are common, with thyroid diseases being prevalent. Dermatomyositis, a rare systemic autoimmune disorder, primarily affecting muscles and skin, has been infrequently reported in association with Type 1 Diabetes Mellitus, indicating a potential shared genetic susceptibility. This article aims to present a rare case of a 32-year-old patient with the simultaneous occurrence of Type 1 Diabetes Mellitus and dermatomyositis, with focus on the unique challenges and considerations in managing these coexisting autoimmune conditions.

1. Introduction

Type 1 Diabetes Mellitus or insulin-dependent diabetes mellitus (IDDM) is an autoimmune disease characterized by the destruction of pancreatic β-cells, leading to insulin deficiency and hyperglycemia. According to available literature, there is a high prevalence of additional autoimmune diseases in patients with Type 1 Diabetes Mellitus, most commonly those affecting the thyroid gland. Dermatomyositis is a rare, systemic autoimmune disease that is defined by inflammation of the muscles and skin. The coexistence of Type 1 Diabetes Mellitus and Dermatomyositis is extremely rare, with few reports published worldwide. Certain genetic factors may contribute to an increased risk of developing autoimmune diseases and shared genetic susceptibility could explain why some individuals may have both conditions. In this article, we present the case of a patient with such rare association.

2. Case Report

A 32-year-old man was admitted to the Dermatology Department complaining of pruritic skin lesions and muscle weakness. On physical examination, he presented with periorbital, confluent, macular, violaceous (heliotrope) erythema/edema and discolorations on the face (Fig. 1a); erythematous papules over the metacarpophalangeal/interphalangeal joints along with periungual erythema and dystrophic cuticles (Gottron sign) (Fig. 1b); symmetrical confluent, macular erythema over the neck and chest, extending over the deltoid areas and posterior shoulders (the shawl sign) (Fig. 1c, d). The patient reported a history of 6 months with these skin lesions, accompanied by proximal muscle weakness in the upper extremities over the last three months. This weakness led to difficulties in routine activities, such as lifting weights or ironing clothes.

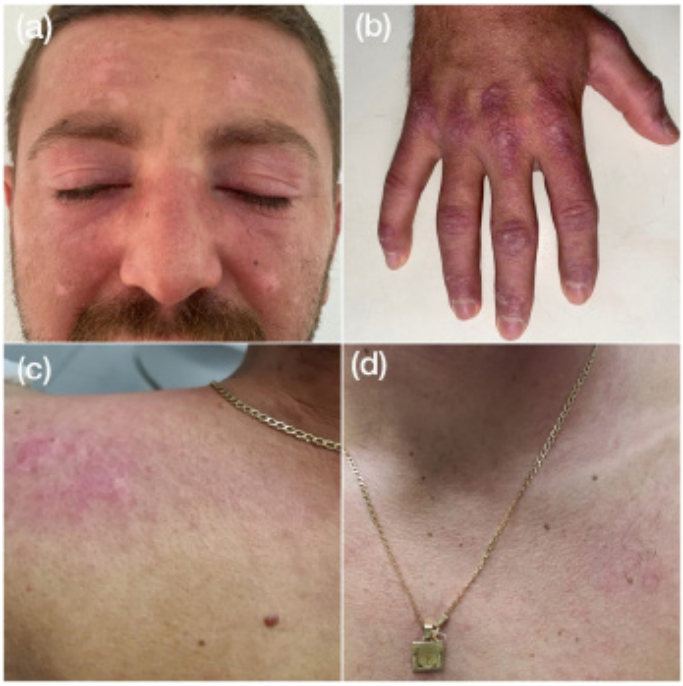

Fig. 1. ***a:*** *Periorbital confluent, macular, violaceous (heliotrope) erythema and discolorations;* ***b:*** *Gottron papules over the distal metacarpophalangeal/interphalangeal joints along with periungual erythema and dystrophic cuticles;* ***c, d:*** *Confluent erythematous papules over the upper back and neck (shawl sign).*

His personal history includes a diagnosis of Type 1 Diabetes Mellitus at the age of 9. He was actually being treated with Insulin Glargine 22 UI/sc and Insulin Aspart 8-12-8 UI/sc. His family history was negative.

Laboratory findings were as follows: glucosuria 1000 mg/dl; fasting plasma glucose level 222 mg/dl, glycosylated haemoglobin (HbA1c) 8.6% (normal <5.7%). Red blood cell count was within normal range. Aspartate aminotransferase (AST) 48 U/L (normal 5-34 U/L), lactate dehydrogenase (LDH) 282 U/L (normal 125-220 U/L), creatine kinase (CK) 433 U/L (normal 30-200), C reactive protein (CRP) 0.21 mg/dL (normal <0.5), Fibrinogen activity 375 mg/dL (normal 200-400 mg/dL). CEA 18.2 ng/ml (normal <5); AFP < 2 ng/ml (normal <8.8 ng/ml), CA 125 negative; CA 19-9 negative. Antinuclear antibodies (ANA) titer 1:320 positive (normal < 1:160); Anti ds DNA 5.8 IU/ml (normal <100); extractable nuclear antigen (ENA) negative.

Dermoscopy of the nailfolds (capillaroscopy) was performed on the patient and it showed the presence of elongated capillaries, dilated capillary loops, cuticular hemorrhage and cuticular overgrowth (Fig. 2).

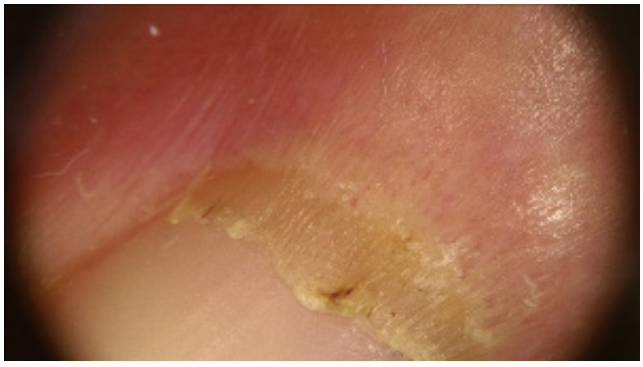

Fig. 2. *Dermoscopy of nailfold (capillaroscopy) shows elongated capillaries, dilated loop capillaries, capillary hemorrhage and cuticular overgrowth.*

Histological examination of a skin specimen revealed hyperkeratosis, inflammatory perivascular plasmo-lymphocytic infiltrates and perivascular/periadnexal myxoid changes; features compatible with dermatomyositis (Fig. 3a, b).

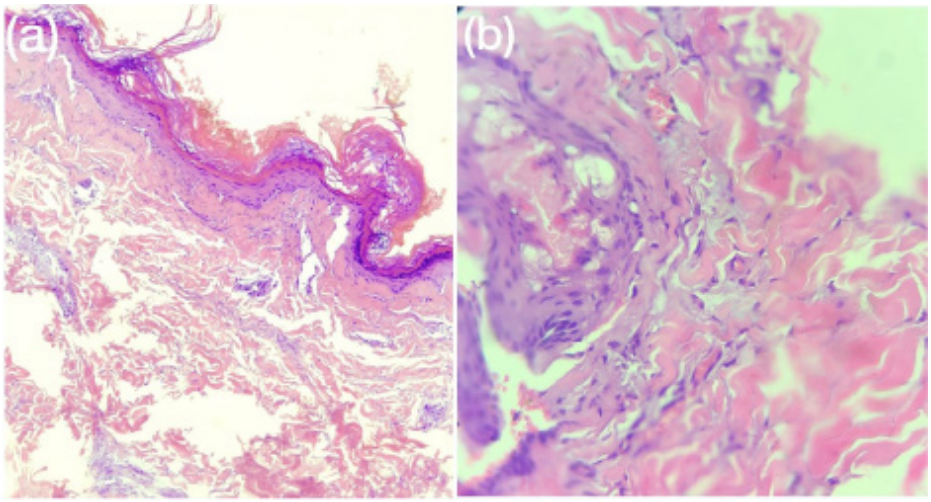

Fig. 3. ***a:*** *Hyperkeratosis, subtle vacuolar interface change, and increased dermal mucin;* ***b:*** *Increased dermal mucin between collagen fibers.*

An electromyogram revealed lesions of degeneration with myopathic pattern of the motor unit action potential along with a myopathic recruitment pattern, compatible with myositis.

Electrocardiogram (ECG) was normal.

The physical examination and laboratories findings, as well as skin and muscle biopsies, confirmed the diagnosis of Dermatomyositis in a patient with a previously diagnosed Type 1 Diabetes Mellitus.

3. Discussion

Dermatomyositis (DM) is a rare, systemic autoimmune disease that is defined by inflammation of the muscles (myositis) and skin (dermatitis). It is presented with a characteristic rash and progressive symmetrical proximal muscle weakness (1). Based on the inflammatory nature of the muscle and skin manifestations, as well as the characteristic humoral autoimmune abnormalities, DM is believed to be caused by a genetically determined, aberrant autoimmune response to environmental factors (2, 3). In the majority of cases, the strongest genetic association is with Human Leucocyte Antigen (HLA) class II alleles. In addition, an array of environmental factors has been linked to DM pathogenesis, including infections (particularly viruses), ultraviolet radiation (DM rates are correlated with proximity to the equator), vitamin D deficiency (common with several autoimmune diseases) and drugs (4).

Dermatomyositis is also associated with a 6-fold increased risk of malignancy compared with the general population (5). Dermatomyositis has been linked to various types of cancer, with breast, ovarian, lung, and hematologic cancers being commonly reported. DM in these cases is considered a paraneoplastic syndrome (5, 6).

Additionally, DM can be associated with non-neoplastic conditions such as vasculitis. Connective tissue disorders like progressive systemic sclerosis, rheumatoid arthritis, mixed connective disease, and systemic lupus erythematosus can also coexist in an overlap group with dermatomyositis. Endocrine diseases like thyroiditis, Cushing syndrome, Crohn disease, and hypophysism have also been linked to DM (6).

Diabetes mellitus is a chronic metabolic disorder, defined by elevated blood sugar over a prolonged period of time. It occurs when the body either doesn't produce enough insulin or cannot effectively utilize it (7). There are two main types of diabetes mellitus: Type 1 Diabetes Mellitus or insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes which is an autoimmune condition where the body's immune system attacks and destroys the insulin producing cells in the pancreas, which results in little to no insulin production; and Type 2 Diabetes Mellitus, non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes, the most common type, which is characterized by insulin resistance, meaning the body's cells do not respond effectively to insulin (7, 8).

Type 1 Diabetes Mellitus affects around 5-10% of diabetes cases. It is an autoimmune disorder characterized by the destruction of pancreatic β-cells, leading to insulin deficiency and hyperglycemia. The disease's progression varies, with some cases showing rapid β-cell destruction in children and adolescents, resulting in diabetic ketoacidosis. In other cases, the disease progresses slowly, with mild increases in fasting blood glucose levels, only becoming severe under physiological stress conditions (9).

Type 1 Diabetes Mellitus (T1DM) is associated with immune markers, particularly autoantibodies, such as glutamic acid decarboxylase autoantibodies (GADAs), islet cell autoantibodies (ICAs), and insulin autoantibodies (IAAs). Multiple genes, including major histocompatibility complex (MHC) class II alleles and human leukocyte antigen (HLA)-DR3 and DR4, have been found in a large percentage of T1DM patients (8, 9).

According to available evidence, individuals with Type 1 Diabetes Mellitus are more likely to have additional autoimmune diseases due to a common genetic background (10). A total of 80 different autoimmune diseases can be observed in Type 1 Diabetes Mellitus, but celiac disease and hypothyroidism are the most frequently observed, followed by vitiligo, hyperthyroidism, autoimmune adrenalitis, gonadal insufficiency, autoimmune hepatitis, dermatomyositis, and myasthenia gravis (10, 11). Due to the similar pathogenesis and immunological processes of various autoimmune diseases, they sometimes occur in the same family or individual (11).

The co-occurrence of Dermatomyositis and Type 1 Diabetes Mellitus has been reported in medical literature, but it is considered very rare. A study conducted by Petrasovicová, V et al. found a relatively high incidence of Type 1 Diabetes Mellitus occurring in 16% of patients with polymyositis. This suggests a potential coexistence of T1DM and dermatomyositis (12). Certain genetic factors may contribute to an increased risk of developing autoimmune diseases like dermatomyositis and Type 1 Diabetes Mellitus. Shared genetic susceptibility could explain why

some individuals may have both conditions (13).

Sattar, M A et al. describes the coexistence of rheumatoid arthritis, ankylosing spondylitis and dermatomyositis in a patient with diabetes mellitus and the associated linked HLA antigens A2, A9, B8, B27, DR3, and DR4 (14). Charalabopoulos, Konstantinos et al. also reports a rare case of DM in association with Type 1 Diabetes Mellitus in a 28-year-old man (15). The limited literature reports indicate the uncommon occurrence of the association between these two diseases.

It is important to note that the presence of one autoimmune condition may increase the risk of developing other autoimmune conditions. The exact underlying mechanisms and factors contributing to the simultaneous occurrence of these two conditions are not fully understood, but it is thought that it might be influenced by autoimmune predisposition, shared genetic factors, environmental factors and chronic inflammation (16).

A potential shared immunopathogenic mechanism involves molecular mimicry, wherein viral or environmental triggers induce an aberrant immune response leading to autoimmunity. Viral infections, such as enteroviruses, have been implicated in both T1DM and DM, possibly initiating immune-mediated tissue destruction. Chronic inflammation and cytokine dysregulation, particularly involving interferon pathways (e.g., Type I and Type II interferons), have also been implicated in both diseases. This suggests that an innate immune response driven by viral or other environmental exposures could contribute to the simultaneous development of these autoimmune disorders (17).

In the presented case the diagnosis of T1DM is confirmed by the presence of glucosuria 1000 mg/dl; fasting plasma glucose level 222 mg/dl, glycosylated hemoglobin (HbA1c) 8.6%; while the diagnosis of DM is based on the histopathologic examination of skin and muscle specimen and electromyography (EMG), both with features compatible with dermatomyositis.

There is a contradiction in the management of the diseases, since the therapy for DM includes Prednisone, a corticosteroid which is contraindicated in diabetic patients due to the risk of disrupting glucose control and causing acute decompensation.

In such cases, alternative immunosuppressive strategies should be considered. Steroid-sparing agents such as mycophenolate mofetil, azathioprine, methotrexate, and calcineurin inhibitors have demonstrated efficacy in managing dermatomyositis while minimizing the metabolic complications associated with long-term corticosteroid use. Additionally, biologic therapies like rituximab, which targets B cells, have shown promising results in refractory dermatomyositis and may provide a viable treatment option in patients with diabetes (18).

When corticosteroid therapy is necessary despite its risks, careful insulin therapy adjustments are crucial to prevent hyperglycemia and acute decompensation. Patients may require an increase in both basal and prandial insulin doses, with close glucose monitoring to assess and modify the regimen accordingly. Continuous glucose monitoring can aid in identifying fluctuations and optimizing insulin delivery (19).

A multidisciplinary approach involving rheumatologists, endocrinologists, and dermatologists would be necessary to provide comprehensive care and management of both diseases.

4. Conclusions

In summary, in addition to the well-established associations between autoimmune diseases, it is important for clinicians to be aware that a coexistence of Type 1 Diabetes Mellitus with dermatomyositis (DM) may also occur. Regular monitoring and coordination between specialists are crucial to ensure the best possible outcomes for the patient and prevent any potential complications.

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All authors report no conflict of interest.

DISCLOSURE

All authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ETHICS STATEMENT

The patients in this manuscript have given written informed consent to publication of their case details.

References

1. Hilton-Jones D. Inflammatory myopathies. Curr Opin Neurol 2001; 14(5): 591–6.

2. Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K. eds. Fitzpatrick's Dermatology in General Medicine, 8e. The McGraw-Hill Companies; 2012. Accessed February 20, 2025.

3. Pokhrel S, Pardhe BD, Giri N, Pokhrel R, Paudel D. Classical Dermatomyositis: A Case Report. Clin Cosmet Investig Dermatol. 2020; 13:123-126. doi: 10.2147/CCID.S234452. PMID: 32104038; PMCID: PMC7008393.

4. Thompson C, Piguet V, Choy E. The pathogenesis of dermatomyositis. Br J Dermatol. 2018 Dec;179(6):1256-1262. doi: 10.1111/bjd.15607. Epub 2017 May 24. PMID: 28542733.

5. Buchbinder R, Forbes A, Hall S, Dennett X, Giles G. Incidence of malignant disease in biopsy-proven inflammatory myopathy: a population-based cohort study. Ann Intern Med. 2001; 134(12):1087–95.

6. Dalakas MC. Polymyositis, dermatomyositis, and inclusion body myositis. N Engl J Med 1991; 325: 1487–98.

7. Radha V, Vimaleswaran KS, Deepa R, et al. The genetics of diabetes mellitus. Indian J Med Res. 2003; 117: 225–38.

8. Grimaldi A, Hartemann-Heurtier A. Insulin-dependent diabetes. Etiology, physiopathology, diagnosis, complications, treatment. La Revue Praticien. 2000; 50: 1473–84.

9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010 Jan;33 Suppl 1(Suppl 1):S62-9. doi: 10.2337/dc10-S062. Erratum in: Diabetes Care. 2010 Apr;33(4):e57. PMID: 20042775; PMCID: PMC2797383.

10. Nederstigt C, Uitbeijerse BS, Janssen LGM, Corssmit EPM, de Koning EJP, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. Eur J Endocrinol. 2019; 180:135–144.

11. Menconi F, Osman R, Monti MC, Greenberg DA, Concepcion ES, Tomer Y. Shared molecular amino acid signature in the HLA-DR peptide binding pocket predisposes to both autoimmune diabetes and thyroiditis. Proc Natl Acad Sci U S A. 2010; 107:16899–16903.

12. Petrasovicova V, Alusik S, Zamrazil V. Systemic rheumatic diseases and diabetes mellitus. Casopis Lekaru Ceskych. 1989; 128: 51–5.

13. Hui-Qi Qu and others, Genetic analysis for type 1 diabetes genes in juvenile dermatomyositis unveils genetic disease overlap, Rheumatology, Volume 61, Issue 8, August 2022, Pages 3497–3501, https://doi.org/10.1093/rheumatology/keac100

14. Sattar MA, Al-Sughyer AA, Siboo R. Coexistence of rheumatoid arthritis, ankylosing spondylitis and dermatomyositis in a patient with diabetes mellitus and the associated linked HLA antigens. Br J Rheumatol. 1988; 27(2):146-9.

15. Charalabopoulos K, Charalabopoulos A, Papaioannides D. Diabetes mellitus type I associated with dermatomyositis: an extraordinary rare case with a brief literature review. BMJ Case Rep. 2009;2009:bcr10.2008.1158. doi: 10.1136/bcr.10.2008.1158. Epub 2009 Apr 14. PMID: 21686441; PMCID: PMC3029914.

16. Ekhzaimy A, Masood A, Alzahrani S, Al-Ghamdi W, Alotaibi D, Mujammami M. Rare occurrence of central diabetes insipidus with dermatomyositis in

a young male. Endocrinol Diabetes Metab Case Rep. 2020; 2020:19-0070. doi: 10.1530/EDM-19-0070. Epub ahead of print. PMID: 32031964; PMCID: PMC7040529.

17. Fernandez-Ruiz R, Niewold TB. Type I Interferons in Autoimmunity. J Invest Dermatol. 2022; 142(3 Pt B):793-803. doi: 10.1016/j.jid.2021.11.031. Epub 2022 Jan 10. PMID: 35016780; PMCID: PMC8860872.

18. Oddis CV, Reed AM, Aggarwal R, et al. RIM Study Group. Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: a randomized, placebo-phase trial. Arthritis Rheum. 2013; 65(2):314-24. doi: 10.1002/art.37754. PMID: 23124935; PMCID: PMC3558563.

19. Jannot-Lamotte MF, Raccah D. Management of diabetes during corticosteroid therapy. Presse Medical 2000; 29: 263–6.

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A Prospective Sudy

The prevalence of metabolic syndrome in psoriatic patients in Albania

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KEYWORDS

psoriasis, metabolic syndrome, comorbidities, obesity, cohort study, prevalence, Albania

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ABSTRACT

Psoriasis is a chronic, immune-mediated skin, now recognized as a systemic inflammatory disease linked to comorbidities such as metabolic syndrome (MetS), cardiovascular disease, and psychiatric disorders. This study explores the prevalence of MetS among psoriasis patients in Albania. This is a prospective case-control study conducted in the University Hospital Center "Mother Theresa", Tirana, Albania. It included 148 psoriasis patients and 150 age- and sex-matched controls. Data collected from patients included age, sex, psoriasis severity (PASI score), and metabolic parameters such as fasting blood glucose, lipid levels, and blood pressure. MetS was diagnosed based on NCEP-ATP III criteria. Statistical analyses were performed using SPSS software. The mean age was 52.3±12.6 years in psoriatic patients and 54.46±15.18 years in controls. Psoriatic patients were 38,5% women and 61,5 % men. The prevalence of MetS was significantly higher in psoriasis patients (62.8%) compared to controls (37.2%) ($p<0.002$). PASI score was greater in patients with MetS than those without MetS ($p=0.004$). Psoriasis severity correlated with an increased likelihood of MetS (OR: 2.6, $p<0.0001$). There was a significant relationship between PASI>10 and obesity ($p=0.0152$). Significant positive correlations were observed between age, disease duration, and MetS ($p<0.0001$). Stress was also significantly associated with MetS ($p=0.006$). No significant associations were found between smoking or sex and MetS in this cohort. The study confirms a high prevalence of MetS in psoriasis patients in Albania. Disease severity, age, and duration are significantly associated with MetS, underscoring the importance of early identification and comprehensive management. Addressing both physical and psychological factors is critical for improving patient outcomes.

1. Introduction

Psoriasis is a chronic, immune-mediated skin condition characterized by erythematous plaques with silvery scales, affecting approximately 2-3% of the global population. The prevalence varies significantly by region and affects individuals of all ages, but it often manifests in early adulthood or between the ages of 50 and 60 years (1). The public health implications of psoriasis extend beyond its cutaneous manifestations. Psoriasis is associated with a significant psychosocial burden, negatively impacting patients' quality of life. Furthermore, psoriasis is increasingly recognized as a systemic inflammatory disease linked to various comorbidities, including metabolic syndrome, cardiovascular disease, and psychiatric disorders (2, 3). This dual burden underscores the importance of prioritizing psoriasis in public health policies to reduce its physical, psychological, and systemic impacts.

Metabolic syndrome (MetS), a cluster of interrelated conditions including central obesity, hypertension, dyslipidemia, and insulin resistance, is strongly linked to psoriasis (4). Numerous global studies have confirmed that patients with psoriasis are more likely to develop metabolic syndrome than the general population. This association persists across diverse populations, suggesting a universal underlying mechanism involving chronic systemic inflammation. However, study methodologies and population demographic variations warrant cautious interpretation (5).

Psoriasis and metabolic syndrome share several pathophysiological mechanisms. One key link is the role of pro-inflammatory cytokines, particularly IL-17 and TNF-α, which contribute to both psoriasis pathogenesis and metabolic dysfunction. IL-17 has been implicated in insulin resistance, type 2 diabetes, vascular inflammation, and hypertension. Targeting IL-17 with biologics like secukinumab has shown not only improvements in psoriasis but also reductions in body weight, fasting glucose levels, and metabolic parameters. Similarly, TNF-α inhibitors, widely used in psoriasis treatment, have demonstrated beneficial effects on lipid metabolism, blood pressure, and insulin sensitivity, though some studies indicate conflicting results regarding their overall metabolic impact (6, 7). Adipocytokines, particularly leptin, and adiponectin, also play a crucial role in linking psoriasis and MetS. While leptin is pro-inflammatory and associated with obesity and psoriasis severity, adiponectin has anti-inflammatory and insulin-sensitizing properties, and its levels are reduced in psoriasis patients. The imbalance between these adipokines may contribute to the development of metabolic complications in psoriasis (8). Elevated oxidative stress markers correlate with psoriasis severity and metabolic dysfunction, suggesting that targeting oxidative pathways could have therapeutic potential for both conditions (9). Changes in gut microbial composition can influence systemic inflammation, intestinal permeability, and metabolic homeostasis. Reduced levels of beneficial bacteria have been observed in both psoriasis and MetS, and gut barrier dysfunction may exacerbate systemic inflammation and metabolic complications (10, 11). Overall, these shared pathways suggest that psoriasis and MetS are closely interconnected through inflammatory, metabolic, and microbial factors. Targeting these common mechanisms may provide a more comprehensive approach to managing both conditions (6, 12).

Severe psoriasis is strongly linked to cardiovascular diseases, though the exact mechanisms remain unclear. Furthermore, both conditions share common genetic pathways, including genetic factors such as IL-23R and IL-23 polymorphisms, as well as genes related to lipid metabolism, the renin–angiotensin system, and endothelial function. Further research is needed to clarify these mechanisms, which could lead to personalized treatment strategies based on an individual's molecular and clinical, biological, and immunological profile (10).

This study marks the first exploration of the psoriasis-metabolic syndrome relationship in Albania, addressing a significant knowledge gap. Albania's healthcare system, like those in many developing countries, faces challenges related to non-communicable diseases, which are a leading cause of morbidity and mortality. In Albania, non-communicable diseases account for about 85% of the overall disease burden and 94% of mortality related to risk factors such as hypertension and smoking (13). This research can inform public health strategies tailored to Albania's context by elucidating the prevalence and characteristics of metabolic syndrome in psoriasis

patients. Policymakers can leverage these findings to implement multidisciplinary care models, enhance patient education (focused on promoting healthy lifestyles, implement gender-sensitive antismoking initiatives, and encourage physical activity), and integrate psoriasis and metabolic syndrome screening into primary care.

2. Materials and methods

Study subjects

This prospective case-control study includes 148 patients with psoriasis and 150 age and sex-matched controls admitted to the Service of Dermatology at "Mother Theresa" University Hospital Center, the only tertiary center in Tirana. The controls were subjects referred during the study period for various dermatological complaints other than psoriasis. Individuals who were less than 18 years old, pregnant, or who had received and/or were receiving systemic and topical treatment for psoriasis were excluded from the study.

Data collection

Data collected from enrolled subjects include age, sex, medical history, personal history of psoriasis and psoriatic arthritis, dermatologic condition for controls, age onset of psoriasis, smoking habit, and stress presence (defined as yes or no). Weight and height were measured barefoot. Waist circumference was measured by pacing a measuring tape at the level of the iliac crest. Psoriasis severity was assessed by the psoriasis area severity index (PASI) (14). Psoriasis was considered mild to moderate if the PASI score was <10 and severe if the PASI score was >10. Venous blood samples were collected from fasting subjects and tested for glucose, HDL cholesterol, and triglycerides.

MetS was diagnosed in the presence of three or more criteria of the National Cholesterol Education Program Adult Panel III:

1. Fasting blood sugar ≥100mg/dl or treatment for hyperglycemia,
2. Serum HDL level <40mg/dl in men or <50mg/dl in women or treatment for low HDL,
3. Serum triglyceride level ≥150mg/dl or treatment for elevated triglycerides,
4. Obesity defined by waist circumference ≥102 cm in men or ≥88 in women,
5. Blood pressure ≥130/85mm Hg or treatment for hypertension.

Statistical analyses

Statistical analyses were made using the SPSS version 20.0 software package. Continuous variables are presented as means ±SD unless stated otherwise. Data were considered statistically significant if $p< 0,05$. The Chi-squared test and binary logistic regression assessed the relationship between two categorical variables. The independent t-test was used to compare mean values of continuous variables such as age between patients and controls, the mean of age, disease duration, and PASI score between patients with psoriasis with MetS and those without MetS. Multivariate binary logistic regression models were built to assess the relationship between MetS and psoriasis.

The authors have followed and reported the necessary elements that comply with STROBE guidelines for observational studies.

3. Results

Baseline characteristics

The study included 148 psoriatic patients and 150 control individuals. The mean age of psoriatic patients was 52.3 ±12.6 years, while the mean age in the control group was 54.46 ±15.18 years, with no significant difference observed between the two groups. In psoriatic patients, the mean disease duration was 10 years±7.78 years. Among the psoriatic patients, 57 (38.5%) were women, and 91 (61.5%) were men. Conversely, the control group comprised 74 women (49.3%) and 76 men (50.7%).

Psoriasis and MetS

Patients with psoriasis exhibited a significantly higher prevalence of MetS (93 patients, 62.8%) compared to controls (56 patients, 37.2%) ($p<0.002$). The confidence intervals for the prevalence of MetS in psoriatic patients (95% CI: 0.001-0.003) and controls (95% CI: 0.800-0.816) confirmed the statistical significance. However, individual components of MetS, including hypertension ($p=0.491$), triglycerides ($p=0.473$), HDL cholesterol ($p=0.572$), and obesity ($p=0.747$), did not show significant differences between the groups**.**

Psoriasis Area and Severity Index (PASI) and MetS

Among the psoriatic cohort, 107 patients (72.3%) had a PASI score >10, while 41 patients (27.7%) had a PASI score ≤10. Psoriatic patients with a PASI score >10 were more likely to have MetS than those with PASI ≤10 ($p<0.0001$). Furthermore, individuals with severe psoriasis (PASI >10) had an odds ratio (OR) of 2.6 for developing MetS compared to those with milder disease. A significant relationship was identified between PASI >10 and type II diabetes mellitus ($p<0.0001$).

Correlation analysis

Table I. The results of study There was a significant positive correlation between age, disease duration, and MetS in psoriatic patients. The Pearson correlation coefficients were as follows: age and MetS ($r=0.771$, $p<0.0001$), disease duration and MetS ($r=0.416$, $p<0.0001$), and age and disease duration ($r=0.604$, $p<0.0001$).

Stress, smoking, and MetS

Stress was significantly associated with MetS in psoriatic patients ($p=0.006$). However, no significant relationship was observed between smoking and MBS ($p=0.167$). Sex did not significantly affect MetS in this cohort ($p=0.404$).

The results are summarized in Table I.

Table I. *The results of study*

Variable	Psoriatic Patients (n=148)	Control Group (n=150)	Comments
Age (mean ± SD, years)	52.3 ± 12.6	54.46 ± 15.18	
Disease duration (mean ± SD, years)	10 ± 7.78	N/A	
Sex [female, n (%)]	57 (38.5%)	74 (49.3%)	
Sex [male, n (%)]	91 (61.5%)	76 (50.7%)	
MetS prevalence [n (%)]	93 (62.8%)	56 (37.2%)	p <0.002
95% CI for MetS	0.001–0.003	0.800–0.816	
PASI score >10 [n (%)]	107 (72.3%)	N/A	
PASI score ≤10 [n (%)]	41 (27.7%)	N/A	
PASI >10 and MetS (OR)	2.6	N/A	p <0.0001
Correlation: age & MetS (r, p)	0.771, <0.0001	N/A	Positive correlation
Correlation: disease duration & MetS (r, p)	0.416, <0.0001	N/A	Positive correlation
Correlation: age & disease duration (r, p)	0.604, <0.0001	N/A	Positive correlation

(N/A= not applicable)

4. Discussion

The understanding of psoriasis has evolved from a purely dermatologic disorder to a systemic inflammatory disease with significant metabolic and cardiovascular implications. In 1988, Gerald Reaven introduced the term Syndrome X, describing the cluster of insulin resistance, hyperglycemia, dyslipidemia, and hypertension (15). In 1999, the World Health Organization (WHO) formalized the definition of metabolic syndrome, linking it to cardiovascular disease and diabetes risk (16). The Third Report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) introduced metabolic syndrome as a critical target for intervention, highlighting its role in increasing CHD risk. The findings and definitions provided by NCEP-ATP III were adopted as criteria for the inclusion and registration of our patients in the current study (17).

Understanding the link between psoriasis and metabolic syndrome is crucial for several reasons. Firstly, metabolic syndrome is a significant contributor to morbidity and mortality, primarily due to its role in escalating cardiovascular disease risk. Secondly, the systemic inflammation underlying psoriasis exacerbates metabolic syndrome's pathogenesis, creating a vicious cycle that amplifies disease severity and complications (18, 19). By studying this association, healthcare providers can develop targeted screening and intervention strategies to prevent complications in psoriasis patients. Early identification of metabolic syndrome components in psoriasis patients allows timely intervention, reducing long-term cardiovascular risks. Moreover, such studies have provided a scientific foundation for public health initiatives, fostering integrated care approaches and raising awareness about the systemic nature of psoriasis (20). Inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-17 (IL-17), play central roles in both psoriasis and metabolic syndrome, creating a pro-inflammatory milieu that promotes insulin resistance, endothelial dysfunction, and lipid abnormalities. The interplay between these conditions emphasizes the need for holistic management strategies addressing the dermatological and systemic

components of psoriasis (12).

Our findings show a significantly higher prevalence of MetS among psoriatic patients than controls (62.8% vs. 37.2%, p<0.002), aligning with previous research suggesting systemic inflammation in psoriasis contributes to metabolic dysregulation (21, 22). Male predominance in the psoriasis group might have independently affected the high prevalence of MetS in our study. Meta-analyses provide robust evidence on the psoriasis-metabolic syndrome relationship. For instance, Singh et al. analyzed 15 studies involving over 46.714 psoriasis patients and reported a pooled odds ratio of 2.14 for metabolic syndrome (23). Similarly, a systemic review found a global MetS prevalence of 32% in patients with psoriasis, with higher rates in adults (32%) compared to children and adolescents (9%); regionally, Latin America had the highest prevalence (47%), while North America had the lowest (26%) (24).

While the link between psoriasis and metabolic syndrome is well-documented, several controversies persist. One key debate concerns causality: whether psoriasis directly contributes to metabolic syndrome or if shared risk factors, such as obesity and sedentary lifestyles, drive the association. Additionally, some studies suggest that lifestyle modifications alone can reduce metabolic syndrome in psoriasis patients, challenging the emphasis on systemic inflammation as the primary mechanism. Another area of contention involves the role of biological therapies. While TNF-α inhibitors and IL-17 blockers improve psoriasis symptoms and some metabolic parameters, their long-term effects on cardiovascular outcomes remain unclear (25, 26).

Interestingly, in our study, while the prevalence of MetS was markedly higher in psoriatic patients, individual MetS components such as hypertension, triglycerides, HDL cholesterol, and obesity did not show significant differences between the psoriatic and control groups. Geographic and climatic factors regard sunlight and vitamin D protection potential, and the Mediterranean diet influences cardiovascular heart disease risk in Albania, as mentioned by Grimes et al. (27).

Additionally, this study presents the relationship between disease severity, as measured by PASI and MetS. Psoriatic patients with a PASI score >10 had a significantly higher likelihood of developing MetS than those with milder disease (OR: 2.6, p<0.0001). Severe psoriasis is associated with an increased risk of developing metabolic syndrome through complex mechanisms. The heightened systemic inflammation characteristic of severe disease, driven by elevated levels of TNF-α and interleukins, extends beyond the skin and impacts multiple organ systems. This pro-inflammatory state promotes adipose tissue dysfunction, favoring the secretion of pro-inflammatory adipokines while reducing protective factors such as adiponectin, thereby exacerbating insulin resistance. Concurrently, oxidative stress and endothelial dysfunction accelerate vascular injury and hypertension, while dyslipidemia, characterized by elevated triglycerides and small dense LDL particles, further enhances cardiovascular risk. Together, these pathological alterations—chronic inflammation, metabolic imbalance, vascular damage, and impaired glucose homeostasis—converge to substantially increase the prevalence of metabolic syndrome among patients with more severe forms of psoriasis (28). Numerous studies affirm the correlation between psoriasis severity and metabolic syndrome, although exceptions have been reported (29, 30). This association extends to specific metabolic components such as type II diabetes mellitus, which was significantly correlated with higher PASI scores (p<0.0001). These findings suggest that severe psoriasis acts as a systemic pro-inflammatory state, heightening the risk of metabolic disturbances. Psoriasis is strongly associated with diabetes, with studies reporting an increased risk of type 2 diabetes in psoriasis patients. Chronic inflammation plays a vital role in this relationship, as elevated levels of TNF-α and IL-6 impair insulin signaling pathways, promoting insulin resistance. Moreover, psoriasis-related inflammation exacerbates pancreatic beta-cell dysfunction, further contributing to hyperglycemia (31, 32).

Age and disease duration were strongly correlated with MetS in the psoriatic cohort, as evidenced by Pearson correlation coefficients for age and MetS (r=0.771, p<0.0001) and disease duration and MetS (r=0.416, p<0.0001). These results reinforce the concept of psoriasis as a chronic condition whose cumulative inflammatory and metabolic impact increases with time (33). The significant correlation between age and disease duration (r=0.604, p<0.0001) further underscores the potential compounded risk in older individuals with longstanding

disease.

Psychosocial factors also play a role in the metabolic complications associated with psoriasis. Stress, significantly associated with MetS in this study (p=0.006), may exacerbate systemic inflammation through neuroendocrine pathways. This finding highlights the importance of addressing psychological well-being in a comprehensive management plan for psoriatic patients (33). Smoking is a significant modifiable risk factor for MetS. It contributes to the pathogenesis of MetS through multiple mechanisms, including increased adiposity, insulin resistance, leptin resistance, low-grade systemic inflammation, endothelial dysfunction, and autonomic dysfunction. It promotes central obesity by increasing waist circumference and waist-to-hip ratio in a dose-dependent manner while also disrupting lipid metabolism by elevating triglycerides and reducing HDL cholesterol. Additionally, smoking induces a proinflammatory and prothrombotic state by increasing C-reactive protein, fibrinogen, and endothelial dysfunction, further exacerbating MetS development (35, 36). A meta-analysis based on 13 prospective cohort studies (56,691 participants) confirms a strong association between smoking and an increased risk of metabolic syndrome (MetS), with active smokers having a 26% higher risk than nonsmokers. Furthermore, smoking cessation showed potential benefits in reducing MetS risk, particularly in males (37).

In our study, smoking and sex did not exhibit significant associations with MetS, suggesting that these factors may play a less direct role in metabolic dysregulation in this context in our population. However, potential bias due to self-reported smoking habits and cultural and racial disparities in study data must be considered key confounders in every report (37). Research has indicated that smoking independently contributes to an increased risk of developing both psoriasis and metabolic syndrome because it induces inflammation (38).

Different reports observe variances between sex and metabolic syndrome in psoriatic patients, some indicating distinct male or female risk, and some others report no association (39-41). In a population-based study in the UK, the strongest association was observed among women in younger age groups, with nearly fourfold increased odds of MetS, while the odds decreased with age. In contrast, men with psoriasis had a consistent 35% increase in odds of MetS across all age groups compared to men without psoriasis (42).

While this study provides valuable insights, some limitations should be considered. The single-center setting may limit the broader applicability of the results. Stress was evaluated based on personal perceptions rather than standardized scales, and lifestyle factors such as diet and physical activity, which significantly impact metabolic syndrome risk, were not included in the assessment.

5. Conclusion

The interplay between psoriasis and metabolic syndrome is a critical area of research with significant implications for public health and clinical practice. This study, the first of its kind in Albania, aims to illuminate this relationship, providing valuable insights for healthcare providers and policymakers. The significant association between PASI scores, age, disease duration, and MetS highlights the need for early identification and holistic management of metabolic risk factors in psoriatic patients. Addressing both physical and psychological dimensions of care could improve outcomes and reduce the long-term burden of comorbidities in this vulnerable population.

References

1. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015;386:983-94.

2. Kovitwanichkanont T, Chong AH, Foley P. Beyond skin deep: addressing comorbidities in psoriasis. Med J Aust. 2020;212:528-534.

3. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol. 1999:401-7.

4. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112:2735-2752.

5. Chan WMM, Yew YW, Theng TSC, et al. Prevalence of metabolic syndrome in patients with psoriasis: a cross-sectional study in Singapore. Singapore Med J. 2020;61:194-199.

6. Piaserico S, Orlando G, Messina F. Psoriasis and Cardiometabolic Diseases: Shared Genetic and Molecular Pathways. Int J Mol Sci. 2022;23:9063.

7. Timis TL, Beni L, Florian IA, et al. Prevalence of metabolic syndrome and chronic inflammation in psoriasis before and after biologic therapy: a prospective study. Med Pharm Rep. 2023;96:368-383.

8. Goolam Mahyoodeen N, Crowther NJ, Pillay L, et al. Relationship of Visceral Fat and Adipokines with Cardiometabolic Diseases in Psoriasis. Acta Derm Venereol. 2019;99:1218-1223.

9. Holmannova D, Borsky P, Andrys C, et al. Chromosomal Aberrations and Oxidative Stress in Psoriatic Patients with and without Metabolic Syndrome. Metabolites. 2022;12:688.

10. Mustata ML, Neagoe CD, Ionescu M, et al. Clinical Implications of Metabolic Syndrome in Psoriasis Management. Diagnostics. 2024;14:1774.

11. Secchiero P, Rimondi E, Marcuzzi A, et al. Metabolic Syndrome and Psoriasis: Pivotal Roles of Chronic Inflammation and Gut Microbiota. Int J Mol Sci. 2024;25:8098.

12. Hao Y, Zhu YJ, Zou S, et al. Metabolic Syndrome and Psoriasis: Mechanisms and Future Directions. Front Immunol. 2021;12:711060.

13. Burazeri G. Burden of non-communicable diseases and behavioral risk factors in Albania. Eur J Public Health. 2020;30(Suppl 5).

14. New Zealand Dermatological Society page on PASI with scoring pictures. https://dermnetnz.org/topics/pasi-score

15. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37:1595–1607.

16. WHO. Definition, diagnosis and classification of diabetes mellitus and its complications. 1999.

17. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285:2486-2497.

18. Davidovici BB, Sattar N, Prinz J, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol. 2010;130:1785-1796.

19. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol. 2010;56:1113-1132.

20. Wu JJ, Suryavanshi M, Davidson D, et al. Economic Burden of Comorbidities in Patients with Psoriasis in the USA. Dermatol Ther (Heidelb). 2023;13:207-219.

21. Patwekar S, Chaudhari N, Poulkar CB, et al. A Case-Control Study to Find Out the Prevalence of Metabolic Syndrome in Patients With Psoriasis As

Compared to Age and Sex Matched Controls. Int J Res Dermatol. 2021;8:15-20.

22. Tas B, Kabeloglu V. Prevalence of Metabolic Syndrome and Its Parameters and Their Correlations With Psoriasis Duration, Severity, and Sleep Quality In Psoriasis Patients: A Cross-Sectional Study. Dermatol Pract Concept. 2021:2021049.

23. Singh S, Young P, Armstrong AW. An update on psoriasis and metabolic syndrome: A meta-analysis of observational studies. PLoS One. 2017;12:e0181039.

24. Liu L, Cai XC, Sun XY, et al. Global prevalence of metabolic syndrome in patients with psoriasis in the past two decades: current evidence. J Eur Acad Dermatol Venereol. 2022;36:1969-1979.

25. Patrick MT, Li Q, Wasikowski R, et al. Shared genetic risk factors and causal association between psoriasis and coronary artery disease. Nat Commun. 2022;13:6565.

26. Wu JJ, Kavanaugh A, Lebwohl MG, et al. Psoriasis and metabolic syndrome: implications for the management and treatment of psoriasis. J Eur Acad Dermatol Venereol. 2022;36:797-806.

27. Grimes DS, Hindle E, Dyer T. Albanian paradox, another example of protective effect of Mediterranean lifestyle? Lancet. 1998;351(9105):835-836.

28. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and metabolic syndrome: a systematic review and meta-analysis of observational studies. J Am Acad Dermatol. 2013;68:654–662.

29. Sommer DM, Jenisch S, Suchan M, et al. Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. Arch Dermatol Res. 2006;298:321-328.

30. Gisondi P, Tessari G, Conti A, et al. Prevalence of metabolic syndrome in patients with psoriasis: a hospital-based case-control study. Br J Dermatol. 2007;157:68-73.

31. Takeshita J, Grewal S, Langan SM, et al. Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol. 2017;76:377-390.

32. Abramczyk R, Queller JN, Rachfal AW, Schwartz SS. Diabetes and Psoriasis: Different Sides of the Same Prism. Diabetes Metab Syndr Obes. 2020;13:3571-3577.

33. Praveenkumar U, Ganguly S, Ray L, et al. Prevalence of Metabolic Syndrome in Psoriasis Patients and its Relation to Disease Duration: A Hospital Based Case-Control Study. J Clin Diagn Res. 2016;10:WC01-WC5.

34. Blackstone B, Patel R, Bewley A. Assessing and Improving Psychological Well-Being in Psoriasis: Considerations for the Clinician. Psoriasis (Auckl). 2022;12:25-33.

35. Behl TA, Stamford BA, Moffatt RJ. The Effects of Smoking on the Diagnostic Characteristics of Metabolic Syndrome: A Review. Am J Lifestyle Med. 2022;17:397-412.

36. Balhara YP. Tobacco and metabolic syndrome. Indian J Endocrinol Metab. 2012;16:81-87.

37. Sun K, Liu J, Ning G. Active smoking and risk of metabolic syndrome: a meta-analysis of prospective studies. PLoS One. 2012;7:e47791.

38. Wei L, Chen S, Qiang Y, et al. Tobacco smoking was positively associated with metabolic syndrome among patients with psoriasis in Shanghai: A cross-sectional study. Tob Induc Dis. 2022;20:05.

39. Zindancı I, Albayrak O, Kavala M, et al. Prevalence of metabolic syndrome in patients with psoriasis. Scientific World Journal. 2012;2012:312463.

40. Lee HJ, Han KD, Park HE, et al. Changes in metabolic syndrome and risk of psoriasis: a nationwide population-based study. Sci Rep. 2021;11:24043.

41. Kim GW, Park HJ, Kim HS, et al. Analysis of cardiovascular risk factors and metabolic syndrome in Korean patients with psoriasis. Ann Dermatol. 2012;24:11–5.

42. Danielsen K, Wilsgaard T, Olsen AO, et al. Elevated odds of metabolic syndrome in psoriasis: a population-based study of age and sex differences. Br J Dermatol. 2015;172:419-427.

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Case Report

Cellular Neurothekeoma – Rare but exists

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KEYWORDS

Cellular Neurothekeoma, benign skin tumor, dermoscopy, histopathological diagnosis

ABSTRACT

Cellular neurothekeoma is a rare, benign cutaneous neoplasm with uncertain histogenesis, that most commonly develops on the head or neck. It predominantly affects females in their third or fourth decade. Usually, they do not have any symptoms, but there may be pressure-related pain. Since cellular neurothekeomas are typically rare and do not have well defined clinical symptoms, it is often difficult to distinguish them from other types of skin tumors. We present the case of a 40-year-old female with a slowly growing violaceous nodule on her scalp, noted since childhood but recently exhibiting growth. We describe the diagnostic and therapeutic approach. This case highlights the diagnostic challenges posed by cellular neurothekeoma due to its histological and clinical variability. Accurate diagnosis through histopathology and immunohistochemistry is crucial to avoid misdiagnosis and ensure appropriate management.

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1. Introduction

Cellular neurothekeoma is a rare, benign cutaneous neoplasm of uncertain histogenesis. Unlike dermal nerve sheath myxomas (formerly known as classic or myxoid neurothekeomas), cellular neurothekeomas are not related to tumors of nerve sheath origin. They typically appear as a slow-growing, painless nodule on the head and neck. Most common in women during their third or fourth decade of life, it can be challenging to diagnose due to its histological variability. Accurate diagnosis is essential to distinguish it from other similar skin tumors, ensuring proper treatment. We present a case of a 40-years old female with cellular neurothekeoma and describe the diagnostic and therapeutic approach.

2. Case Report

A 40-years old female presented with an asymptomatic, slowly growing nodule on scalp. The patient reported that she had noticed it since childhood, but it had recently exhibited growth.

On physical examination, the lesion appeared as a well-circumscribed, violaceous-colored nodule of soft consistency (Fig.1a). No other lesions were found, and examination of her neck and supraclavicular lymph nodes revealed no abnormalities. The patient had no other medical conditions and her family history was negative.

Dermatoscopy examination revealed a non-specific pattern with a central purple structure, white structureless areas at the center, and linear irregular vessels (Fig.1b).

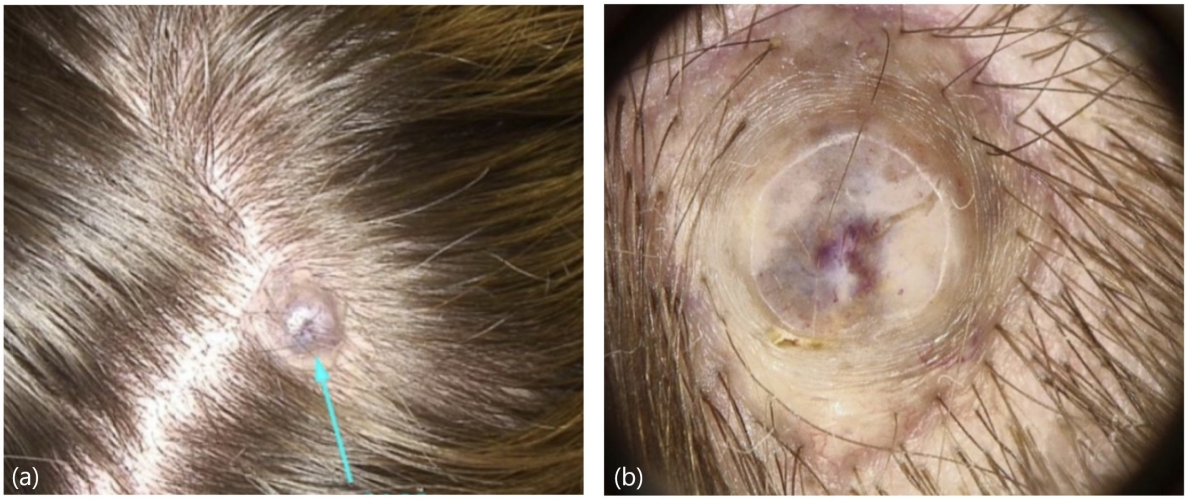

Fig. 1. *(a) Violaceous-coloured well-circumscribed nodule of soft consistency with a diameter of 7mm; (b) Dermatoscopic image showing linear vessels, whitish streak area, purple central structure, structureless white area.*

It was decided for an excisional biopsy with 1-mm margins around the lesion in the form of an ellipse with measures of 4x1.5, and the nodular lesion of 7mm (Fig. 2). The lesion was entirely excised and sent for histopathological examination.

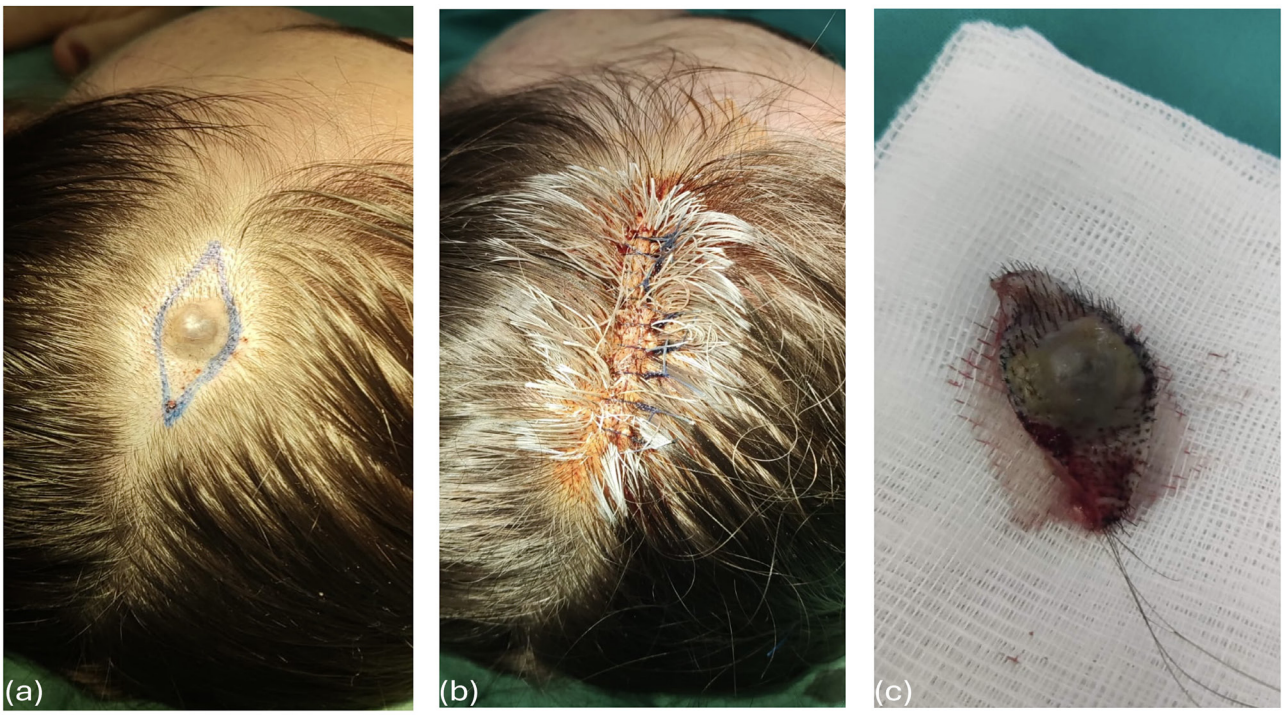

Fig. 2. *(a) Preoperative image of the lesion measuring 4 x 1.5 cm; (b) Postoperative image after complete excision; (c) The specimen.*

Histopathological analysis revealed a lobular growth pattern with infiltration of the subcutaneous tissue and chronic inflammation around histio-epithelioid lobules. The tumor consisted of fused cell neoplasia with a monomorphic appearance arranged in short bundles. No cytologic atypia or significant mitotic activity was observed. There were noticed focal deposits of melanin. Immunohistochemical reactions for protein S100 and CD34 were negative, ruling out nerve sheath tumors. The picture appears compatible with cellular neurothekeoma (Fig. 3).

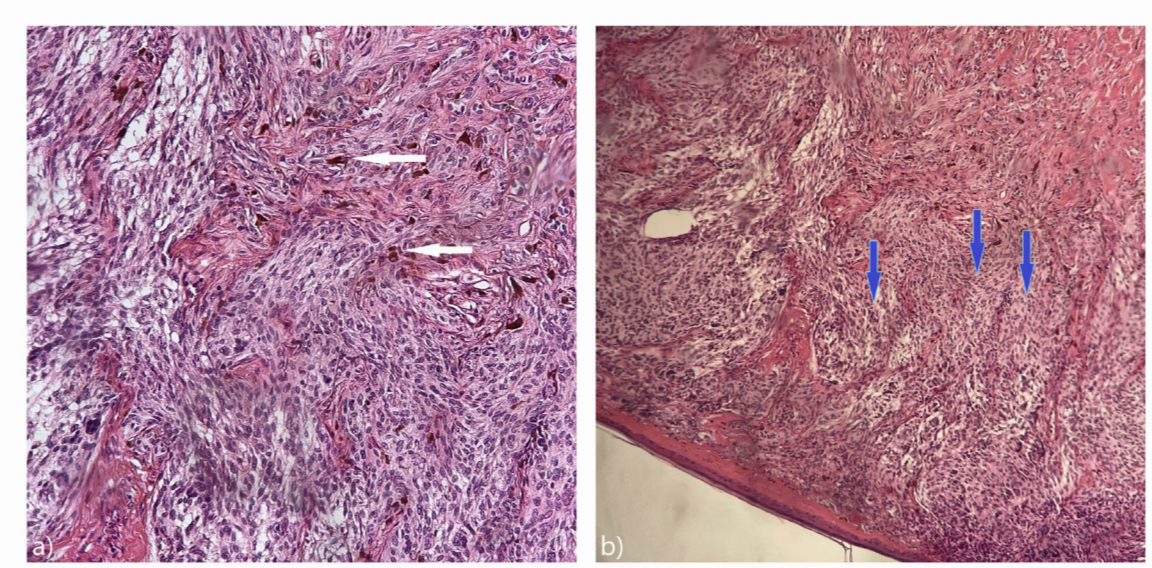

Fig. 3. *(a, b) Histopathology image of the lesion, H&E. Fascicular patterns of spindled and epithelioid mononuclear cells with abundant cytoplasm, indistinct cell borders (blue arrows). Focal deposits of melanin (white arrows).*

3. Discussion

Cellular neurothekeoma is a benign superficial skin tumor of uncertain origin, distinct from dermal nerve sheath myxomas. Previously classified as a subtype of nerve sheath myxomas, cellular neurothekeomas are now recognized as separate entities, with differences in immunohistochemical profiles and histogenesis. Cellular neurothekeomas do not express S100 protein, unlike dermal nerve sheath myxomas, suggesting a fibrohistiocytic origin. It usually occurs during the third and fourth decade of life, often affecting females more than males, with a predilection for the head and neck (1, 2). Neurothekeomas clinically appear as painless, slowly growing, red-colored cutaneous nodule with good mobility. They have a variety of histologic patterns, including myxoid, cellular, or mixed types depending on the amount of myxoid matrix (2, 3).

For many years, neurothekeomas were diagnosed and reported as one of the subtypes of dermal nerve sheath myxomas, because it was initially thought that they originated from Schwann cells (4).

Harkin and Reed described the first neurothekeoma in 1969 as a myxoma originating from the nerve sheath (5). It was only after 1980 that Gallager and Helwig gave this type of tumor its current definition of neurothekeoma (3). There were later two large case studies published in 2007 by Fetsch et al. and Hornick and Fletcher, establishing the immunoprofile of neurothekeomas and further distinguishing it from nerve sheath myxomas (2, 6). In contrast to dermal nerve sheath myxomas, neurothekeomas do not express the S-100 protein, according to recent studies (2, 7). Rather than emerging from peripheral nerve sheath, neurothekeomas have been proposed to originate from fibrohistiocytic cells (2, 3).

Most of these lesions are small and show no cytologic atypia and minimal invasion into other tissues. However, there have been studies that report atypical features of neurothekeomas, which include cytologic atypia, size greater than 1 cm, invasion into surrounding tissues and high mitotic index. The rate of recurrence remains low, in spite of their atypical features (8, 9).

The lack of clearly defined clinical symptoms and physical examination, makes them difficult to distinguish from other skin tumors. The differential diagnosis includes sebaceous cysts, fibrous histiocytoma, pilomatricoma, neurofibroma, basal cell carcinoma or other melanocytic lesions (2, 3). These diseases are clinically similar, but have different pathological features.

In this case, dermoscopy revealed a non-specific pattern that did not provide a definitive diagnosis but guided clinical suspicion for further investigation. Although dermoscopic features are not pathognomonic, these findings overlap with benign fibrohistiocytic tumors. Unlike melanocytic lesions, neurothekeomas typically lack a pigment network. In comparison, basal cell carcinoma may exhibit arborizing vessels, while pilomatricoma often shows a “rolled border” and central calcifications. Dermoscopy can occasionally aid in differentiating benign lesions from malignancies, but its utility in cellular neurothekeoma remains limited. Further studies may elucidate dermoscopic features specific to this tumor (10).

Thus, the confirmation of the diagnosis must be done by histopathological and immunohistochemical examination (7, 9).

Excisional biopsy remains the treatment of choice for cellular neurothekeomas. Most lesions show no cytologic atypia or significant invasion, and recurrence rates are low when margins are clear. However, atypical cases, characterized by cytologic atypia, deep tissue invasion, or increased mitotic activity, may have a higher recurrence risk. Literature suggests that follow-up for at least 12–24 months is beneficial in detecting recurrences, especially in cases with positive margins. While our case showed clear margins, periodic follow-up is recommended (11).

4. Conclusions

It is essential to diagnose neurothekeomas accurately since these lesions can be mistaken for malignancies, resulting in unnecessary treatment. The inclusion of dermoscopic features in diagnostic algorithms may aid in earlier recognition. While the prognosis is excellent, long-term follow-up is recommended for atypical cases to monitor recurrence risk. Dermatologists and pathologist should be aware of the clinical presentation of this rare tumor and the similar clinical and histologic features it shares with other benign and malignant tumors, in order to provide an accurate diagnosis, management and follow-up care.

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DISCLOSURE

All authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ETHICS STATEMENT

The patients in this manuscript have given written informed consent to publication of their case details.

References

1. Barnhill RL, Mihm MC. Cellular neurothekeoma: A distinctive variant of neurothekeoma mimicking nevomelanocytic tumors. Am J Surg Pathol. 1990; 14(2):113-120.

2. Hornick JL, Fletcher CD. Cellular neurothekeoma: Detailed characterization in a series of 133 cases. Am J Surg Pathol. 2007; 31(3):329-340.

3. Fetsch JF, Laskin WB, Hallman JR, Lupton GP, Miettinen M. Neurothekeoma: An analysis of 178 tumors with detailed immunohistochemical data and long-term patient follow-up information. Am J Surg Pathol. 2007; 31(7):1103-1114.

4. Vetrano IG, Levi V, Pollo B, Chiapparini L, Messina G, Nazzi V. Sleeve-shaped neurothekeoma of the ulnar nerve: A unique case of a still unclear pathological entity. Hand (N Y). 2020;15:NP7-NP10.

5. Harkin JC, Reed RJ. Tumors of the Peripheral Nervous System. Washington, DC: Armed Forces Institutes of Pathology; 1969:60-64.

6. Abuawad YG, Saraiva MI, Westin AT, Valente NY. S-100 negative myxoid neurothekeoma: A new type of neurothekeoma? An Bras Dermatol. 2017; 92:153-155.

7. Tran P, Mclemore M. Atypical cellular neurothekeoma: A potential diagnostic pitfall for benign and malignant spindle cell lesions in skin. J Cutan Pathol. 2018; 45(8):619-622.

8. Busam KJ, Mentzel T, Colpaert C, Barnhill RL, Fletcher CD. Atypical or worrisome features in cellular neurothekeoma: A study of 10 cases. Am J Surg Pathol. 1998; 22(9):1067-1072.

9. De la Guardia V, Castro-Pérez E, Porcell AI, et al. Atypical cellular neurothekeoma: a case report with a novel NF1 mutation. Diagn Pathol. 2024; 19:151. doi:10.1186/s13000-024-01578-y.

10. Choi S, Cho SI, Lee C, Kwak Y, Mun JH. Dermoscopy of multiple cellular neurothekeoma: An analysis of 11 neurothekeomas in a middle-aged woman. Australas J Dermatol. 2020; 61(1):e73-e76. doi:10.1111/ajd.13185

11. Boukovalas S, Rogers H, Boroumand N, Cole EL. Cellular neurothekeoma: A rare tumor with a common clinical presentation. Plast Reconstr Surg Glob Open. 2016; 4(8):e1006.

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Case Report

Lymphangitic sporotrichosis caused by cat scratch in an area of eastern Mexico

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KEYWORDS

sporotrichosis, Sporothrix schenckii sensu stricto, feline sporotrichosis, sporotrichosis in Mexico

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ABSTRACT

Sporotrichosis is an endemic mycosis caused by the dimorphic fungus *Sporothrix schenckii* sensu lato. This phenomenon has gained prominence in recent years due to its global prevalence, the recognition of multiple cryptic species within the originally described species, and its distinctive ecology, distribution, and epidemiology worldwide. Sporotrichosis, a human and animal disease caused by the *Sporothrix* species, is the most prevalent implantation mycosis worldwide. The classification of *Sporothrix* has undergone significant refinement in recent years, resulting in substantial progress in the fields of diagnosis, epidemiology, and treatment. Material and methods: we present the clinical case of a 15-year-old male, who was scratched by his cat on the back of the right hand, after 5 days developed erythematous-violaceous lesions. *Sporothrix schenckii sensu stricto* was diagnosed as the causal agent of both infections by using microbiological and proteomic tools (mycological culture and MALDI-TOF). Itraconazole 200mg twice daily for three months was prescribed with excellent clinical improvement.

1. Introduction

Sporotrichosis is an endemic mycosis caused by the dimorphic fungus *Sporothrix schenckii* sensu lato, is prevalent worldwide in tropical and subtropical areas. Patients with this infection usually present with "implantation mycoses" that is caused by transcutaneous trauma through which the fungal conidia enter the host. Such infections may progress into chronic cutaneous, subcutaneous, and/or even deeper infections involving the lymphatics, fascia, muscles, cartilage, and bones. Although sporotrichosis causes considerable morbidity, it is only rarely associated with mortality.

Among endemic mycoses, sporotrichosis is distinct in the supposed high prevalence of animal-to-human transmission of the disease. However, it is not clear how the yeast phase transmits the infection through this route since it is generally accepted that conidia of the mycelial phase are the infectious propagules for humans. However, the evidence from several studies of feline transmission provides compelling support for this means of transmission.

In a study by the Evandro Chagas Clinical Research Institute, Rio de Janeiro, Brazil, 83% of patients and 85% of dogs were reported to have contact with cats, 56% of humans reported being bitten or scratched by a cat with sporotrichosis preceding the occurrence of the disease among owners, and *S. schenckii* sensu lato was isolated from the skin and nasal and oral cavities of the animals (1).

Cutaneous sporotrichosis is contracted in two ways: through traumatic inoculation of the fungi through the skin. The classical clinical presentation is transmitted by plant debris, and the second (zoonotic form) is by animal transmission. Cat scratches are a well-documented source of the latter, but inoculation through a wound or open skin can also occur. Transmission through contact with the exudate (oozing fluid) of infected cats has also been reported. This zoonotic disease has prompted significant public health concern due to its persistence and subsequent dissemination throughout South America (2). The following factors have been identified as contributing to the potential for zoonotic transmission: engagement in activities such as playing in rural environments, residence in dwellings with unsealed flooring, and the presence of domestic felines within the household. In addition, the majority of documented cases have been observed in patients with a low socioeconomic status, females, and children. This is due to the fact that these demographic groups are more likely to engage in play activities with these animals.

Typically, patients deny the occurrence of the bite or scratch.

However, a preponderance of evidence indicates that the subjects in question cohabitate with felines (3).

2. Case report

We present the clinical case of a 15-year-old male, native and resident of Xalapa, Veracruz, Mexico, student, without significant personal pathological history who attended the infectious disease department of the General Hospital north of Xalapa with an erythematous-violaceous lesion with necrotic center and multiple nodules with lymphatic tract in the right upper extremity of five days of evolution (Fig. 1A), when questioning the parents of the minor, they stated that he was scratched by his cat on the back of his hand (Fig. 1B), and after five days he developed the aforementioned lesion with drainage of sero-purulent material, clinically it was diagnosed as lymphangitic sporotrichosis; however, samples were sent for mycological cultures to the center for diagnosis and research in microbiology and infectious diseases based in guadalajara, jalisco, mexico with the objective of evidencing the causal agent.

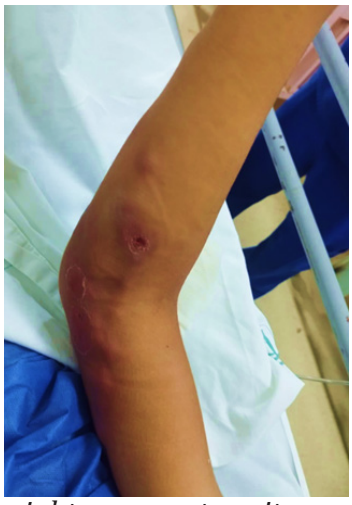

Fig. 1A. *Lymphangitic sporotrichosis on right upper extremity.*

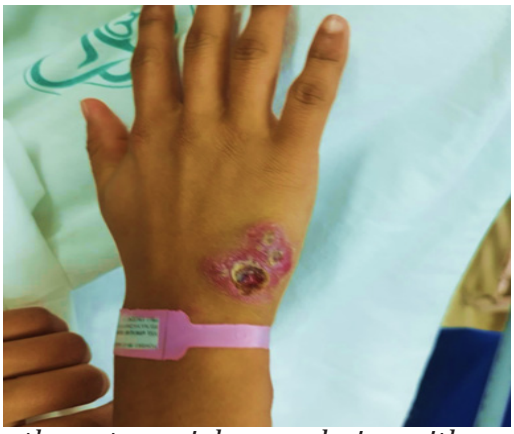

Fig. 1B. *Sporotrichoid chancre, erythematous-violaceous lesion with necrotic center at the level of the back of right hand.*

After 7 days of incubation on Sabouraud's agar with and without antibiotic, the mycology laboratory reported the growth of a membranous, radiate, dark brown pigmented fungus (Fig. 2A), which microscopically revealed sympoduloconidia and thin filaments compatible with *Sporothrix spp*. (Fig. 2B).

Fig. 2A. *White, membranous, radiate and folded colony with melanocytic pigment compatible with Sporothrix spp.*

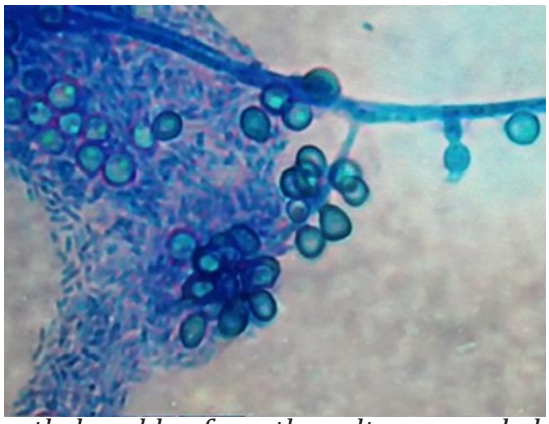

Fig. 2B. *Direct examination with methylene blue from the culture revealed a substantial quantity of sympoduloconidia organized into a "daisy-like configuration", accompanied by thin, branched filaments.*

Subsequently a fragment of the strain was transferred to the laboratory of microbiology and pathology of the University of Guadalajara to perform proteomic tests with MALDI-TOF having as causal agent *Sporothrix schenckii sensu stricto* with a score of 1.88 considering acceptable the identification at species level.

A post-mortem sample of the cat was sent to the microbiology laboratory to confirm that it was infected by *Sporothrix*. The same studies were performed as in the patient, and after seven days a colony with similar characteristics to those isolated in the patient was found, confirming *Sporothrix spp*. as the cause of both infections and the cat as the cause of the zoonosis (Fig. 3A, 3B).

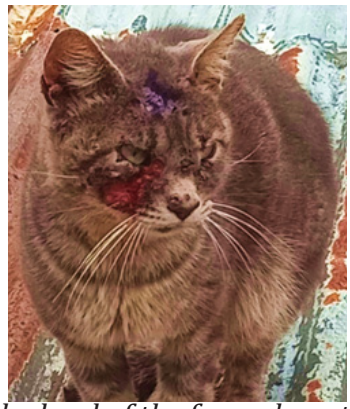

Fig. 3A. *Feline with ulcerated lesions at the level of the face where the post-mortem sample was obtained.*

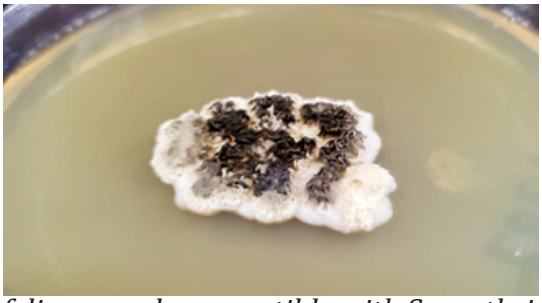

Fig. 3B. *Culture obtained from the feline sample compatible with Sporothrix spp.*

The cat strains were also sent to the microbiology and pathology laboratory of the University of Guadalajara to confirm the causative agent by MALDI-TOF, and the result was *Sporothrix schenckii sensu stricto* with a score of 1.9, corroborating the same species identified in the patient.

The patient was treated with itraconazole 200 mg twice daily for three months. 85% remission of the lesions was achieved, although some keloid scarring remained (Fig. 4A,4B).

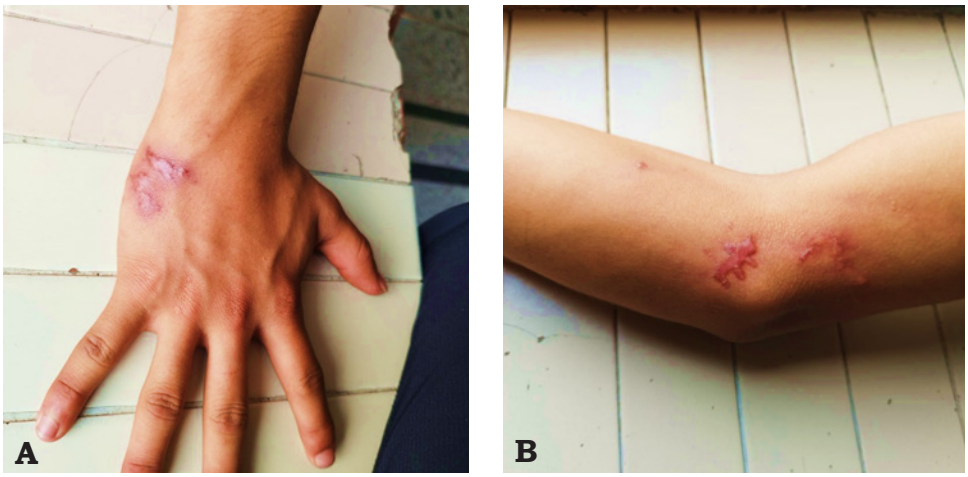

Fig. 4A, 4B. *Right dorsum and forearm of the patient after treatment with itraconazole 200mg twice daily. We observed an almost complete cure, with keloid scars remaining.*

3. Discussion

Sporotrichosis, a subcutaneous mycosis, is caused by the dimorphic fungus *Sporothrix schenckii* and related species. This fungus is found worldwide in vegetation, decaying organic matter, sphagnum moss, and soil. Sporotrichosis, a fungal pathology, is transmitted through traumatic inoculation of *Sporothrix* propagules into skin tissue. The classical route of transmission refers to sapronosis (i.e., from the environment to the warm-blooded vertebrate host). Consequently, it is classified as an occupational mycosis, frequently associated with trauma sustained during outdoor work in professionals such as gardeners, farmers, extractivists, and florists, among others. The alternative route of infection is linked to horizontal animal transmission, which predominantly affects domestic cats and armadillos. In the context of sporotrichosis, a disease transmitted by cats, these animals act as vectors for the spread of the disease by transmitting secretions through scratches and bites, or by direct contact with other cats. This process can lead to the emergence of epizootics or, directly, the transmission of the pathogen to humans (zoonosis) (4).

Cats are the most susceptible hosts to *Sporothrix* contamination and commonly develop the most severe forms of the disease, which can progress to death (5). Multiple ulcerative lesions are usually seen in the cephalic region, mainly in the nose and paw region, due to feline behavior involving scratching and biting during fights (5, 6, 7).

4. Conclusions

This study presents the third documented case of cat scratch sporotrichosis in Mexico. However, this number is estimated to be negligible when considered in the context of the population of the country in question and the prevalence of cats as domestic pets. Consequently, it is imperative to provide more training through awareness campaigns where the care of pets is promoted, to make this fungal pathology known to health personnel who are not familiar with it, in addition to promoting talks in health centers and congresses or symposiums where more and more health professionals, including dermatologists, microbiologists and veterinarians, join every day, thus improving the diagnosis of these zoonoses and optimizing patient care.

References

1. Chakrabarti A, Bonifaz A, Gutierrez-Galhardo MC, et al. Global epidemiology of sporotrichosis. Med Mycol. 2015 Jan;53(1):3-14. doi: 10.1093/mmy/myu062. Epub 2014 Dec 19. PMID: 25526781.
2. World Health Organization, Esporotricosis. [internet], November 15, 2023, due: May 12, 2025. URL: https://www.who.int/es/news-room/fact-sheets/detail/sporotrichosis.
3. Alcocer-Salas M, Torres-Calderón MF, Rodríguez-Mena AC, et al. Esporotricosis cutánea fija trasmitida por un gato, segundo caso reportado en México. Dermatol Rev Mex 2025; 69 (1): 99-104.
4. Rodrigues AM, Gonçalves SS, de Carvalho JA, et al. Current Progress on Epidemiology, Diagnosis, and Treatment of Sporotrichosis and Their Future Trends. J Fungi (Basilea). 2022 Jul 26;8(8):776. doi: 10.3390/jof8080776. PMID: 35893145; PMCID: PMC9331723.
5. Gremião ID, Menezes RC, Schubach TM, et al. Feline sporotrichosis: epidemiological and clinical aspects. Medicine. Micol. 2015;53:15-21. doi: 10.1093/mmy/myu061.
6. Pereira SA, Gremião IDF, Menezes RC Sporotrichosis in Animals: Zoonotic Transmission. In: Zeppone Carlos I., editor. Sporotrichosis: New Developments and Future Perspectives. Springer International Publishing; Cham, Switzerland: 2015. pp. 83-102.
7. Pereira SA, Gremião ID, Kitada AA, et al. The epidemiological scenario of feline sporotrichosis in Rio de janeiro, Rio de janeiro State, Brazil. Rev. da Soc. De Med. tropo. 2014;47:392-393. doi: 10.1590/0037-8682-0092-2013.

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Case Report

Botulinum toxin type A treatment for Trigeminal Neuralgia: Case Report of a patient unresponsive to pharmacotherapy

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KEYWORDS

Trigeminal Neuralgia, Botulinum toxin type A, pain relief

ABSTRACT

Trigeminal Neuralgia (TN) is a chronic neuropathic disorder characterized by episodic, sharp facial pain, often unresponsive to standard pharmacologic treatments. This case report presents a 51-year-old female with classical TN affecting the right maxillary branch (V2), who experienced inadequate relief from conventional anticonvulsants and declined surgical intervention. Botulinum toxin type A (BTX-A) was administered intradermally at the sites of pain, following a protocol based on prior literature. Two weeks post-treatment, the patient reported a significant reduction in pain intensity—from a Visual Analog Scale (VAS) score of 9/10 to 3/10—and decreased frequency of attacks. Symptom relief persisted for approximately 4.5 months with no observed adverse effects. This report highlights BTX-A as a promising alternative therapy for refractory TN, especially in patients unsuitable for invasive procedures. Further studies are warranted to evaluate long-term efficacy and safety.

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1. Introduction

Trigeminal neuralgia manifests as chronic pain characterized by sharp, shock-like sensations in one or more divisions of the trigeminal nerve. In cases where pharmacotherapy proves ineffective, there is an increasing amount of research indicating that, injections of Botulinum toxin type A (BTX-A) into the trigeminal ganglion offer pain relief lasting from several weeks to several months. We present a case of a patient suffering from Trigeminal Neuralgia, unresponsive to pharmacotherapy, who subsequently underwent treatment with local injections of Botulinum toxin type A (BTX-A).

2. Case Report

A 51-year-old female presented with trigeminal neuralgia pain in the region of her right maxillary nerve. She reported a 2-year history of sudden, intense shock-like facial pain, with episodes occurring 5–6 times per day, especially during cold weather or chewing. Recently these symptoms had gotten worse, with attacks of pain that occurred regularly for days to weeks, sometimes several times a day. The diagnosis of Trigeminal Neuralgia (TN) was confirmed by her neurologist, based on the clinical signs and symptoms as well as findings on Magnetic Resonance Imaging (MRI) of the cranium, which showed neurovascular contact of the right trigeminal nerve root entry zone. It is important to note that the MRI was performed 6 months after the onset of symptom exacerbation, helping to correlate imaging with clinical deterioration. The patient declined microvascular decompression due to the associated surgical risks.

She had been treated with anticonvulsants such as carbamazepine (up to 800 mg/day) and gabapentin (up to 1800 mg/day) over several months, but these provided only partial relief, and increasing dosages led to drowsiness, dizziness, and impaired concentration. This was the reason the patient came to our clinic, requesting Botulinum toxin type A (BTX-A) injections for her trigeminal neuralgia pain.

The patient was informed that BTX-A injections for TN was not an FDA-approved procedure, but current literature supports its off-label use. After obtaining informed consent, a treatment plan was initiated. We evaluated the pain intensity with the Visual Analog Scale (VAS) on a score of 9/10. The painful area was mapped according to the patient's symptom description and facial anatomical landmarks (Fig. 1). A total of 100 Units of BTX-A was diluted in 2.5 ml saline. BTX-A was injected intradermally at the sites of pain, guided by pain mapping and anatomical landmarks of the maxillary (V2) distribution (Fig. 1). Each site received 3 Units, chosen based on protocols from prior studies indicating this dose as both safe and effective.

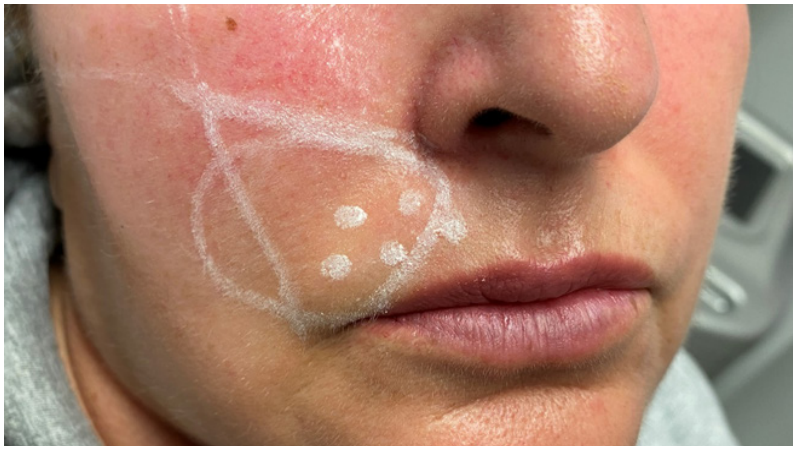

Fig. 1. *Distribution of pain in right maxillary (V2) region and corresponding intradermal BTX-A injection sites (marked by patient pain mapping).*

Two weeks after treatment with BTX-A injections, the patient experienced significant pain relief. The Visual Analog Scale (VAS) decreased from 9/10 to 3/10, and pain episode frequency dropped from 5–6 daily attacks to only 1–2 mild episodes per week. This reduction indicates a substantial improvement in the patient's pain management and quality of life. The patient reported fewer episodes of sharp, shock-like pain and was able to resume daily activities with minimal discomfort.

No adverse effects such as muscle weakness, asymmetry, or allergic reactions were observed during follow-up, and the patient expressed interest in repeating the treatment if symptoms returned. She was monitored monthly for 6 months and remained improved for approximately 4.5 months before mild recurrence of symptoms.

3. Discussion

Trigeminal Neuralgia (TN) is "a disorder characterized by recurrent unilateral brief electric shock-like pain, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve and triggered by innocuous stimuli", as defined by the International Headache Society (1). Symptoms of pain include sharp, lancinating, shock-like or electric-like attacks that can be sudden, severe, and superficial, as well as tic-like cramps (involuntary contraction of facial muscles) (2). Each pain attack lasts up to two minutes, and most patients remain asymptomatic between attacks. This is considered to be Classical TN, which is purely paroxysmal. A persistent background pain of moderate to severe intensity can also follow pain attacks and this is called Classical TN with concomitant persistent facial pain (1).

TN affects mostly the maxillary (V2) and mandibular (V3) trigeminal branches and less commonly the ophthalmic (V1) branch. According to various studies, it has been demonstrated that the right side of the face is affected more often than the left side of the face by TN. Additionally, it has been found a slight female predominance in TN incidence (3).

Regarding the quality of life, it is negatively affected by TN, with studies showing increased psychological distress, depression and anxiety that sometimes may even result in suicide attempts (4). Pain reduction/relief may improve mood disorders and lead to improved quality of life. Thus, multidisciplinary teams are essential for the effective management of TN.

Pharmacotherapy is the first line of treatment, usually with anticonvulsants and antispasmodics. However, these are frequently associated with side effects and are not effective in all cases. Among the other interventions available are microvascular decompression, gamma knife radiosurgery, or rhizotomies, which each has significant risks and side effects (2, 5).

The injection of Botulinum toxin type A (BTX-A) into the trigeminal ganglion has been shown to be effective for patients with trigeminal neuralgia. BTX-A works primarily by inhibiting acetylcholine release by binding to the presynaptic nerve terminals, thus affecting muscle contraction. Its antinociceptive impact on trigeminal neuralgia is brought about by various mechanisms. The identification of a direct analgesic action implies that BTX might operate through an alternative mode of action (6, 7).

Most theories propose that BTX-A not only inhibits the release of acetylcholine (Ach) but also other neurotransmitters. Blocking the release of these neurotransmitters from nociceptive nerve endings is thought to bring about pain relief. Another potential site for the analgesic effect of BTX-A could be postganglionic sympathetic nerve endings that utilize norepinephrine (NE) and adenosine triphosphate (ATP) as neurotransmitters. With NE elevated in chronic pain and ATP linked to the stimulation of muscle nociceptors, it is theorized that BTX-A might inhibit the release of these neurotransmitters, producing an analgesic effect in cases of sympathetically maintained pain associated with complex regional pain syndrome (8, 9).

However, the relief from pain is temporary, usually persisting for a duration ranging from 6 weeks to 6 months, necessitating patients to undergo recurrent injections for sustained benefits (8).

Wu et al. conducted a randomized, double-blind, placebo-controlled study involving 42 patients with trigeminal neuralgia: 22 received BTX-A treatment, while 20 received a placebo. In this class I study, the intervention group received 75 units of BTX-A injected either intradermally or submucosally into the painful regions of each patient. Among those

who received BTX-A injections, 68.18% reported a reduction of more than 50% in pain intensity on the VAS, in contrast to 15% in the placebo group (10).

Turk et al. undertook a class IV, open-ended study to explore the efficacy of administering BTX-A to individuals with trigeminal neuralgia. Eight patients received 100 units of BTX-A around the zygomatic arch, and all experienced positive effects (11). In another class IV, open-label study, 13 patients with idiopathic trigeminal neuralgia underwent transcutaneous BTX-A injections at the trigeminal nerve branches. Four patients achieved pain relief, and nine reported a reduction of over 50% in pain intensity, measured by the VAS score, which persisted for 60 days (12).

Although the relief from pain typically lasts 6–12 weeks, repeated injections have been reported as safe and effective in various small-scale studies and clinical experiences. In a retrospective analysis of patients receiving BTX-A for hemifacial spasm and blepharospasm—neurological conditions that, like TN, require repeated injections over years—no cumulative systemic toxicity or permanent local tissue damage was observed, even after more than 10 years of regular use. Applied to TN, available reports indicate that repeated BTX-A injections do not significantly increase the risk of muscle atrophy, facial asymmetry, or resistance development, provided that the dosage remains within therapeutic range and injections are correctly localized. Additionally, studies have not demonstrated increased risk of neuromuscular junction disorders or systemic side effects over time (13-15).

Another point of consideration is the limited data on BTX-A use in patients with comorbid neuromuscular disorders, such as myasthenia gravis or Lambert-Eaton syndrome, where even small doses can provoke unwanted effects.

Numerous case reports have shown consistent success with BTX-A injections in treating trigeminal neuralgia. However, long-term data on repeated BTX-A use in TN patients are still limited. Future longitudinal, multicenter studies with larger cohorts and extended follow-up durations are necessary to fully characterize the long-term safety and efficacy profile of BTX-A in the treatment of TN.

4. Conclusions

Administering local injections of BTX-A might prove effective and safe for treating trigeminal neuralgia over an extended period, offering a novel strategy for certain patients. This approach could be particularly beneficial for middle-aged and elderly individuals who may struggle with drug side effects and harbor concerns about potential serious complications following microvascular decompression (MVD).

Abbreviation and acronym list

1. Trigeminal Neuralgia (TN)
2. Magnetic Resonance Imaging (MRI)
3. Botulinum toxin type A (BTX-A)
4. Visual Analog Scale (VAS)
5. Norepinephrine (NE)
6. Adenosine Triphosphate (ATP)
7. Microvascular Decompression (MVD).

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All authors report no conflict of interest.

DISCLOSURE

All authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ETHICS STATEMENT

The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors.

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd Edition. Cephalalgia. 2018;38(1):1–211. doi:10.1177/0333102417738202.

2. Araya EI, Guíñez-Molinos S, Carmona-Castro O, Fuentealba-Arévalo E, Chandía-Poblete D. Trigeminal Neuralgia: Basic and Clinical Aspects. Curr Neuropharmacol. 2020;18(2):109-119. doi:10.2174/1570159X17666191010094350.

3. Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945–1984. Ann Neurol. 1990;27(1):89–95. doi:10.1002/ana.410270114.

4. Wu TH, Hu LY, Lu T, et al. Risk of psychiatric disorders following trigeminal neuralgia: A nationwide population-based retrospective cohort study. J Headache Pain. 2015;16(1):64. doi:10.1186/s10194-015-0548-y.

5. Tatli M, Satici O, Kanpolat Y, Sindou M. Various surgical modalities for trigeminal neuralgia: Literature study of respective long-term outcomes. Acta Neurochir (Wien). 2008;150(3):243–255. doi:10.1007/s00701-007-1474-y.

6. Klein AW. The therapeutic potential of botulinum toxin. Dermatol Surg. 2004;30(3):452–455. doi:10.1111/j.1524-4725.2004.30096.x.

7. Kroumpouzos G, Kassir M, Gupta M, Patil A, Goldust M. Complications of botulinum toxin A: An update review. J Cosmet Dermatol. 2021;20(6):1585–1590. doi:10.1111/jocd.14160.

8. Mense S. Neurobiological basis for the use of botulinum toxin in pain therapy. J Neurol. 2004;251(Suppl 1):I/1–I/7. doi:10.1007/s00415-004-1101-9.

9. Verma G. Role of Botulinum Toxin Type-A (BTX-A) in the Management of Trigeminal Neuralgia. Pain Res Treat. 2013;2013:831094. doi:10.1155/2013/831094.

10. Wu CJ, Lian YJ, Zheng YK, et al. Botulinum toxin type A for the treatment of trigeminal neuralgias: Results from a randomized, double-blind, placebo-controlled trial. Cephalalgia. 2012;32(6):443–450. doi:10.1177/0333102412441724.

11. Turk U, Ilhan S, Alp R, Sur H. Botulinum toxin and intractable trigeminal neuralgia. Clin Neuropharmacol. 2005;28(4):161–162. doi:10.1097/01.wnf.0000161994.63016.fc.

12. Bach-Rojecky L, Dominis M, Lackovic Z. Lack of anti-inflammatory effects of botulinum toxin A in experimental models of inflammation. Fundam Clin Pharmacol. 2008;22(5):503–509. doi:10.1111/j.1472-8206.2008.00616.x.

13. Dressler D. Clinical applications of botulinum toxin. Curr Opin Microbiol. 2012;15(3):325-336. doi:10.1016/j.mib.2012.05.012.

14. Thouaye M, Yalcin I. Neuropathic pain: From

actual pharmacological treatments to new therapeutic horizons. Pharmacol Ther. 2023;251:108546.

15. Matak I, Lacković Z. Botulinum toxin A, brain and pain. Prog Neurobiol. 2014;119-120:39-59. doi:10.1016/j.pneurobio.2014.06.001.

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Case Report

Case report: Effects of TNF-blockers in lowering Crp, Esr and D-dimer in Psoriatic arthritis

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KEYWORDS

psoriatic arthritis, TNF-blocker, Etanercept, D-dimer, CRP, ESR, biologic therapy, systemic inflammation

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ABSTRACT

Psoriatic arthritis (PsA) is a chronic inflammatory disease affecting both the joints and skin, often associated with elevated systemic inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and D-dimer. TNF-α inhibitors have become pivotal in the management of moderate to severe PsA. We report the case of a 32-year-old male with a 9-year history of psoriasis who developed PsA following a COVID-19 infection. The patient presented with severe bilateral knee pain, inflammatory arthritis, and markedly elevated inflammatory markers: CRP 139 ng/L, ESR 86 mm/hr, and D-dimer 3303 ng/ml. Treatment with Etanercept over a 24-month period led to significant clinical improvement and normalization of inflammatory markers (CRP 5 ng/L, ESR 16 mm/hr, D-dimer 110 ng/ml). Pain scores decreased from 10/10 to 1/10, and the patient's psoriatic skin lesions resolved. This case highlights the efficacy of Etanercept in achieving both clinical and biochemical remission in PsA and suggests a potential role for D-dimer as a marker of systemic inflammation and thrombotic risk in PsA patients.

1. Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory condition that not only affects the joints but is also often accompanied by systemic features, leading to significant impairment in a patient's quality of life (1). The disease is characterized by both musculoskeletal inflammation and elevated levels of inflammatory biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and, in certain cases, D-dimer—reflecting underlying inflammation and thrombotic risk (2). Managing these inflammatory markers effectively is crucial for controlling disease activity and preventing long-term complications (3).

Tumor necrosis factor (TNF) blockers have emerged as a cornerstone in the treatment of moderate to severe PsA. These biologic agents target key inflammatory pathways and are designed to reduce inflammation, alleviate symptoms, and halt disease progression (3, 4). Beyond their effects on joint and skin manifestations, TNF-blockers have demonstrated the potential to reduce systemic inflammation, as evidenced by declines in laboratory markers such as CRP, ESR, and D-dimer (5).

This case report illustrates the impact of TNF-blocker therapy in a patient with PsA, focusing on its effectiveness in lowering CRP, ESR, and D-dimer levels, while also contributing to a marked improvement in the patient's quality of life. It highlights the broader systemic benefits of targeted biologic therapy and provides insight into the role of TNF-blockers in achieving both clinical and biochemical remission.

2. Case report

The case studied is a 32-year-old patient, with the initials E.D., who presented to our Clinic with bilateral knee pain, inflammatory joint pain, generalized psoriatic squamous plaque-like cutaneous elements, accompanied by pruritus, and a temperature of 38.5 degrees Celsius for two days. He reports that these complaints have started more than 1 year ago (2 months after the patient was diagnosed with Covid-19).

The pain level was assessed 10/10 (The pain level was assessed by the Rheumatologist on a scale of 0-1, where 0 is no pain at all and 10 is very severe pain that affects the quality of life).

The patient has been diagnosed with Psoriasis for 9 years.

The patient had previously been treated with methylprednisolone 40 mg, but no significant improvement in the general condition was observed. On clinical examination, signs of synovitis were evident in the radiocarpal (RC), metacarpophalangeal (MCP), and talocrural (TC) joints, all of which were infiltrated and tender to digital pressure. The bilateral knee joints (genua) were also tender and edematous, with evidence of hypertrophic synovium on palpation. The coxofemoral (CF) joints demonstrated restricted range of motion during maneuvering. Additionally, spinal tenderness was noted during flexion movements.

The patient was admitted to the Rheumatology Clinic for further evaluation and initiation of biologic therapy. Etanercept, a tumor necrosis factor-alpha (TNF-α) inhibitor, was selected as the biological agent for treatment.

Etanercept treatment on dosagee Etanercept 50mg/ml lasted a total of 4 sessions/month (one session/ week) over a period of 24 months (accorded to EULAR, 2019, EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies).

The patient was taken for assessment in periods every 6 months.

After treatment with Etanercept 50mg/ml, an improvement in pain was observed, synovial inflammation was reduced, and psoriatic squamous plaques were reduced. The joints appeared without inflammation, were not edematous, and were not tender to finger pressure and to range of motion.

The pain level after treatment was rated 1/10. (Pain was assessed by the rheumatologist using a scale from 0 to 10, where 0 indicates no pain and 10 indicates severe pain that significantly affects quality of life.)

The examinations performed and included in this case report are summarized in Table I:

Table I. *Laboratory values before and after treatment.*

Laboratory test	Values before treatment	Values after treatment	Normal values
CRP	139	5	0-5ng/l
ERS	86	16	0-20mm/hr
D-Dimer	3303	110ng/ml	0-500ng/ml
ALP	376	267	0-270U/L

3. Discussion

This case highlights the effectiveness of TNF-α inhibitor therapy in the management of severe psoriatic arthritis (PsA), with significant clinical improvement and normalization of inflammatory markers. Of particular interest was the marked reduction of D-dimer levels, which dropped from 3303 ng/mL to 110 ng/mL following treatment.

While C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are routinely used as indicators of disease activity in PsA, the elevation of D-dimer is notable. D-dimer, commonly used in the diagnosis of venous thromboembolism (VTE), has also emerged as a non-specific biomarker of systemic inflammation (6). In this case, thromboembolic disease was clinically excluded, and the elevation was attributed to systemic inflammation associated with active PsA.

There is growing evidence linking chronic inflammatory states such as PsA to a prothrombotic profile, suggesting that D-dimer may serve as a surrogate marker for cardiovascular and thrombotic risk in these patients (7, 8). Elevated D-dimer levels have been documented in patients with PsA, correlating with disease activity and systemic inflammatory load (9). The normalization of D-dimer after anti-TNF therapy in this patient reinforces the hypothesis that biologic treatment may reduce thromboinflammatory risk.

The temporal association with COVID-19 infection—which occurred two months prior to the onset of PsA symptoms—raises the possibility of a viral trigger in the pathogenesis of autoimmune disease. Several mechanisms, including molecular mimicry, bystander activation, and immune dysregulation, have been proposed as ways through which SARS-CoV-2 may precipitate autoimmunity in genetically predisposed individuals (10, 11). Emerging case reports have also described new-onset PsA and psoriasis exacerbations following COVID-19 infection (12, 13), supporting the need for vigilance in post-viral autoimmune manifestations.

This case illustrates the importance of comprehensive disease monitoring in PsA, not only evaluating joint and skin symptoms but also systemic markers like D-dimer, which may provide insights into inflammatory activity and cardiovascular risk.

4. Conclusions

This case underscores the effectiveness of etanercept, a TNF-α inhibitor, in inducing clinical remission in a patient with severe PsA. Treatment resulted in:

- Complete resolution of joint inflammation and skin lesions
- Substantial reduction in pain
- Normalization of inflammatory biomarkers including CRP, ESR, and D-dimer

The sharp decline in D-dimer levels may reflect attenuation of systemic inflammation and thrombotic risk, reinforcing the thromboinflammatory connection in PsA. Moreover, the temporal relationship with COVID-19 infection raises considerations about viral triggers in autoimmune pathogenesis.

This case advocates for the early initiation of biologic therapy in PsA and suggests potential value in monitoring D-dimer as a supplementary biomarker for both disease activity and systemic risk. Further research is needed to validate the prothrombotic role of D-dimer in PsA and the post-viral autoimmu-

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DISCLOSURE

All authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ETHICS STATEMENT

The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understan-ding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors.

References

1. Ogdie, A., & Weiss, P. The epidemiology of psoriatic arthritis. Rheumatic Disease Clinics of North America, 2015; 41(4): 545–568. https://doi.org/10.1016/j.rdc.2015.07.001.
2. Gladman, D. D., Chandran, V., & Mease, P. J. Psoriatic arthritis. Rheumatic Disease Clinics of North America, 2020; 46(2): 195–209. https://doi.org/10.1016/j.rdc.2020.01.003.
3. Mease, P. J., Gladman, D. D., Ritchlin, C. T., Ruderman, E. M., Steinfeld, S. D., Choy, E. H., & Helliwell, P. S. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: Results of a double-blind, randomized, placebo-controlled trial. Arthritis & Rheumatism, 2013; 52(10): 3279–3289. https://doi.org/10.1002/art.21655.
4. Gossec, L., Baraliakos, X., Kerschbaumer, A., de Wit, M., McInnes, I., & Smolen, J. S. (2020). EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Annals of the Rheumatic Diseases. 2019; 79(6): 700–712. https://doi.org/10.1136/annrheumdis-2020-217159.
5. Kavanaugh, A., Mease, P. J., Reimold, A. M., Pablo, A., & Zhang, L. Long-term follow-up of infliximab efficacy and safety in psoriatic arthritis: Results from the IMPACT 2 trial. Annals of the Rheumatic Diseases. 2014; 73(2): 349–356. https://doi.org/10.1136/annrheumdis-2012-202727.
6. Haj Hussen, W., Abou Assi, H., & Farhat, R. D-dimer as a marker of inflammation in autoimmune diseases. Autoimmunity Reviews. 2019; 18(3): 294–299. https://doi.org/10.1016/j.autrev.2018.10.012.
7. Tam, L. S., Li, E. K., & Leung, Y. Y. Inflammation and thrombosis in rheumatic diseases: A review. Nature Reviews Rheumatology. 2014; 10(11): 701–710. https://doi.org/10.1038/nrrheum.2014.143.
8. Li, X., Tian, F., Wang, F., & Zhou, Q. Cardiovascular risk in psoriatic arthritis: A systematic review and meta-analysis. Current Rheumatology Reports. 2020; 22(11): 70. https://doi.org/10.1007/s11926-020-00942-7.
9. Sfikakis, P. P., Iliopoulos, A., & Kitas, G. D. Elevated D-dimer levels in patients with psoriatic arthritis: Correlation with disease activity. Clinical Rheumatology. 2017; 36(6): 1383–1389. https://doi.org/10.1007/s10067-017-3601-2.
10. Muskardin, T. L. W., & Niewold, T. B. SARS-CoV-2 as a trigger for autoimmune disease: Lessons from pandemic infections. Autoimmunity Reviews. 2021; 20(4): 102792. https://doi.org/10.1016/j.autrev.2021.102792.
11. Sattui, S. E., Liew, J. W., & Graef, E. R. COVID-19 and autoimmune disease: The pathophy-

siology of a complex interaction. Nature Reviews Rheumatology. 2021; 17(11): 733–745. https://doi.org/10.1038/s41584-021-00612-1.
12. Ashrafzadeh, F., Rezaei, M., & Omidian, M. New-onset psoriatic arthritis following SARS-CoV-2 infection: A case report. Journal of Clinical Rheumatology. 2022; 28(1): e315–e317. https://doi.org/10.xxxx/jcr.2022.xxxxxx.
13. Gambichler, T., Schroter, U., & Bechara, F. G. Flares of psoriasis and psoriatic arthritis after COVID-19. Dermatologic Therapy. 2021; 34(1): e14778. https://doi.org/10.1111/dth.14778.