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Anti-TIF-1γ-positive dermatomyositis associated with colorectal adenocarcinoma: a case report

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Abstract

Dermatomyositis (DM) is a rare autoimmune disease characterized by inflammatory involvement of skin and muscles, often associated with malignancy, particularly in the presence of anti-transcription intermediary factor 1 gamma (TIF-1γ) antibodies. This case report describes a 57-year-old Senegalese man with anti-TIF-1γ-positive DM and colorectal adenocarcinoma with liver metastases, presenting with severe dermatological symptoms such as ulcerations, the "red on white" sign, and scalp pustulosis, as well as systemic features including dysphagia and muscle weakness. Diagnosis was confirmed through clinical evaluation, serological testing, and histopathology. Treatment with corticosteroids, intravenous immunoglobulin (IVIG), and surgical tumor resection led to significant improvement. This case underscores the importance of recognizing DM's dermatological signs, conducting thorough malignancy screening, and implementing a multidisciplinary approach for effective management and improved outcomes, given the rarity of the association with colorectal cancer.

Introduction

Dermatomyositis (DM) is a rare autoimmune disease characterized by inflammatory involvement of the skin and muscles. It is marked by the presence of specific autoantibodies that often define clinical subtypes and guide both diagnostic and therapeutic strategies. Among these, anti-transcription intermediary factor 1 gamma (TIF-1γ) antibodies are particularly significant, as they are strongly associated with cancer-associated dermatomyositis (CAD). For this reason, comprehensive malignancy screening is imperative in all patients with anti-TIF-1γ-positive DM, given the high prevalence of underlying neoplasms in this population. The complexity of the case presented lies in the interplay between severe dermatologic manifestations, systemic involvement, and an associated malignancy, highlighting the necessity of a multidisciplinary approach to ensure timely diagnosis, appropriate treatment, and long-term follow-up.

Case Report

A 57-year-old Senegalese man with a past medical history of type II diabetes, hypertension, moderate-to-severe renal insufficiency, and prior lymph node tuberculosis presented with spontaneous ulcerations on the trunk, predominantly in the sternal, axillary, and left thigh regions. These lesions had been evolving over the course of one month and were associated with pustules, pruritus, and pain. Subcutaneous nodules were noted on the left forearm, along with the presence of the "red on white" sign, which was bilaterally evident on the neck, back, shoulders, and arms. Additional findings included pustular eruptions of the scalp and mild edema of the lips and eyelids.

The patient also reported proximal muscle weakness affecting the upper and lower limbs, as well as the hands (Figure 1).

To differentiate between idiopathic DM and CAD, a series of laboratory investigations was performed. Blood tests revealed elevated levels of lactate dehydrogenase (LDH, 730 U/L) and creatine phosphokinase (CPK, 7948 U/L). Autoantibody testing showed positive antinuclear antibodies (ANA, 1:320, speckled/homogeneous pattern), positive anti-TIF-1γ antibodies, and weakly positive anti-melanoma differentiation-associated gene 5 (MDA-5) antibodies. Tests for anti-dsDNA and extractable nuclear antigens (ENA) were negative. Electromyography of the upper limbs demonstrated findings consistent with inflammatory myopathy. Due to the persistence of periorbital and lip edema, dysphagia, and tongue swelling, the patient was hospitalized and initiated on high-dose oral prednisone (up to 75 mg/day). This led to a gradual improvement of symptoms and subsequent discharge.

Based on the clinical presentation, electromyographic findings, and serological profile – particularly the presence of anti-TIF-1γ antibodies – a diagnosis of dermatomyositis was established. A multidisciplinary approach was adopted involving both rheumatology and dermatology specialists. Treatment with oral corticosteroids and intravenous immunoglobulin (IVIG) led to significant improvement in both cutaneous and muscular symptoms.

Given the established association between DM and malignancy, further investigations were conducted. As part of the malignancy screening, fecal occult blood testing was performed and returned positive on three consecutive samples. Further investigations included esophagogastroduodenoscopy, which revealed active chronic atrophic gastritis with intestinal metaplasia and *Helicobacter pylori* infection. Colonoscopy identified an ulcerative-vegetative lesion located 12 cm from the anal verge. Histopathological analysis confirmed a diagnosis of colorectal adenocarcinoma.

Staging with PET-CT imaging showed no significant abnormalities. In December 2022, the patient underwent anterior resection of the rectum with the creation of a protective ileostomy. Histological examination confirmed a moderately differentiated (G2) adenocarcinoma infiltrating the subserosal layer, with lymph node metastases and lymphovascular invasion (pT3N1, WHO classification).

In May 2023, follow-up CT imaging revealed hepatic metastases involving segments VII and VI. In August 2023, a wedge resection of segment VII was performed. Histopathological findings confirmed metastatic colorectal adenocarcinoma. In October 2023, adjuvant chemotherapy with capecitabine was proposed but declined by the patient.

Despite this, regular oncologic surveillance has continued. As of March 2024, the patient is in good general condition (ECOG Performance Status 0), with no radiological evidence of disease recurrence.

DM symptoms remain well-controlled with ongoing treatment consisting of IVIG (400 mg/kg/day for five consecutive days every six weeks) in combination with corticosteroids.

Discussion

DM is a systemic autoimmune disease characterized by inflammation involving multiple organ systems, most prominently the skin and muscles, with the presence of specific autoantibodies. These autoantibodies are not only diagnostic markers but also correlate with distinct clinical phenotypes. DM is also recognized as a paraneoplastic syndrome, with underlying malignancies identified in approximately 20% of adult patients.

Recent advances have led to the identification of novel DM-specific autoantibodies, enhancing our understanding of the disease pathogenesis and clinical subtypes. These include anti-Jo-1 and anti-Mi-2 antibodies, anti-MDA-5 antibody, anti-TIF-1γ antibody, anti-nuclear matrix protein 2 antibody, and anti-small ubiquitin-like modifier 1 activating enzyme (SUMO-1) antibody.[1,2] These advancements have enhanced our understanding of DM and its diverse manifestations, offering opportunities to optimize diagnostic and therapeutic approaches.

Systematic reviews and meta-analyses have shown that adult DM patients positive for anti-TIF-1γ antibodies have a markedly increased risk of malignancy, with an odds ratio of approximately 27.[3] These autoantibodies target proteins, also known as TRIM33 or p155/140, which are involved in critical cellular processes including proliferation, development, apoptosis, and innate immunity. The TIF-1 protein family plays a crucial role in cancer development, particularly through its involvement in regulating the tumor suppressor protein p53. Elevated levels of TIF-1 proteins have been detected in tumor tissues. This suggests that the autoimmune response against TIF-1 proteins may reflect an aberrant or failed antitumor immune surveillance mechanism.[4]

In the majority of cases, malignancy is diagnosed within three years before or after the onset of DM, as illustrated by the case presented. The most frequently associated malignancies include ovarian, breast, lung, gastric, and colorectal cancers, as well as lymphomas.[5]

According to current evidence, patients with anti-TIF-1γ antibodies have a relatively lower risk of developing systemic features of DM, such as interstitial lung disease, Raynaud's phenomenon, and arthritis or arthralgia. However, muscle weakness has been reported in up to 50% of this patient subgroup, with myalgia and facial edema occurring in approximately 14% of cases.[6]

The hallmark and potentially pathognomonic features of DM are the heliotrope rash and Gottron's papules. The heliotrope rash is characterized by violaceous to erythematous discoloration of the palpebral area, often accompanied by facial edema. In individuals with darker skin phototypes, the rash may be less visually prominent, though periorbital swelling may still be appreciable. Gottron's

papules, slightly violaceous raised plaques, are typically located over bony prominences, such as the metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints, as well as on the elbows, knees, and feet.

Other cutaneous features associated with DM, while not pathognomonic, include poikiloderma in photosensitive areas, characterized by a combination of atrophy, dyspigmentation, and telangiectasia. Scalp involvement is also a common feature, presenting as an erythematous psoriasiform dermatitis.[7]

In patients with anti-TIF-1γ antibodies, skin involvement is seen in nearly 100% of cases and tends to be more severe, widespread, and preferentially localized to photo-exposed regions in up to 54% of cases, including the face, scalp, upper chest (V-neck sign), and back. Common skin manifestations include ulcerations with dark red discoloration, erythema, and, in 15% of cases, psoriasis-like lesions.[1]

Additionally, a distinctive skin finding in anti-TIF-1γ-positive patients is the presence of hypopigmented patches intermixed with punctate telangiectatic or erythematous macules, described as a "red on white" appearance. This feature is observed in 12% of anti-TIF-1γ-positive patients compared to only 1% of DM patients without these antibodies. The case we report also exhibits these small hypopigmented macules on an erythematous background, primarily affecting the neck, shoulders, and arms bilaterally.[1,8]

As observed in the case presented, involvement of the oropharyngeal musculature is a frequent feature in individuals with anti-TIF-1γ antibodies. Studies estimate that up to 84.6% of patients with dysphagia associated with DM and polymyositis (PM) test positive for TIFγ-specific autoantibodies.[9] Dysphagia is a significant complication of DM, as it can lead to difficulties with oral feeding and subsequent malnutrition; moreover, it tends to be associated with poorer outcomes.[6]

Additionally, respiratory impairment caused by weakness of the respiratory muscles is a well-documented neurological complication in these cases.[10]

Management of patients with DM who are positive for anti-TIF-1γ antibodies involves comprehensive, age-appropriate cancer screenings, given the strong association between anti-TIF-1γ antibody-positive DM and malignancies. Early cancer detection is critically important, as it significantly influences the therapeutic strategy and prognosis. Although the optimal treatment algorithm for cancer-associated DM remains under discussion, current evidence supports prioritizing surgical resection of the tumor when the patient's clinical status permits, as it is associated with improved outcomes.[6]

Systemic therapies – including glucocorticoids, immunosuppressive agents, and IVIG – form the cornerstone of DM treatment. Among these, IVIG has emerged as an effective and well-tolerated

option, demonstrating improvements in muscle strength, reductions in creatine kinase levels, and enhanced swallowing function in affected patients.[11]

This case represents a complex intersection of dermatologic, rheumatologic, and oncologic domains. The patient's presentation – with spontaneous ulcerative lesions, periorbital and lip edema, dysphagia, and muscle weakness – alongside a distinctive "red on white" sign and anti-TIF-1γ positivity, pointed early toward a paraneoplastic form of DM. These features highlight how skin manifestations can serve as sentinel signs not only of autoimmune disease but also of underlying cancer.

The detection of colorectal adenocarcinoma in this setting emphasizes the pivotal role of cutaneous and serologic findings in triggering timely oncologic evaluation. While DM has been more frequently associated with ovarian, breast, and lung malignancies,[3] cases linked to colorectal cancer remain uncommon, making this report particularly relevant. Moreover, the successful identification and resection of the tumor underscores the potential for disease treatment when diagnosis is prompt.

Despite advances in understanding DM pathogenesis and its immunologic markers, there is still no consensus on the optimal therapeutic strategy in cancer-associated DM. Further research is needed to define evidence-based therapeutic algorithms that address both autoimmune control and oncologic outcomes in these patients.

Conclusions

This case illustrates the importance of recognizing cutaneous signs of DM and investigating the associated autoantibody profile – especially anti-TIF-1γ positivity – as potential indicators of underlying malignancy. It represents a complex dermato-rheumato-oncologic case and, to date, one of the few reported instances of DM associated with colorectal adenocarcinoma. Given the rarity of this association, further research is needed to better understand and define the optimal therapeutic approach for affected patients.

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Figure 1. Clinical presentation at time of diagnosis: spontaneous ulcerations on the trunk and limbs with subcutaneous nodules. Mild edema of the lips and eyelids.