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MedPeer Publisher
Abbreviated Key Title: MedPeer
ISSN : 3066-2737
homepage: https://www.medpeerpublishers.com

When Catabolism Triggers Hair Growth: Non-Paraneoplastic Acquired Hypertrichosis in Dermatomyositis with Tuberculosis

DOI: 10.70780/medpeer.000QGTL

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ABSTRACT

Acquired hypertrichosis lanuginosa is a rare cutaneous disorder most commonly recognized as a paraneoplastic phenomenon. Non-malignant associations have been documented, with a severe catabolic state proposed as the common pathophysiologic denominator. We report the first case of diffuse acquired hypertrichosis occurring in the context of dermatomyositis complicated by pulmonary tuberculosis, in the absence of malignancy. A 44-year-old woman with newly diagnosed anti-NXP2-positive dermatomyositis developed diffuse hypertrichosis during a severe catabolic state, with a 22% loss of initial body weight and declining serum protein levels, driven by the convergence of active myositis and pulmonary tuberculosis unmasked by immunosuppressive therapy. The diagnosis of tuberculosis proved particularly challenging, as initial chest CT, three consecutive sputum cultures, sputum PCR, and PCR on cold abscess aspirates were all negative for Mycobacterium tuberculosis. Diagnosis was ultimately established through bronchoscopy with bronchoalveolar lavage PCR. A comprehensive paraneoplastic workup including whole-body ^{18}F-FDG PET/CT excluded an underlying malignancy. The hypertrichosis resolved spontaneously upon initiation of anti-tuberculous therapy and nutritional recovery. This observation expands the spectrum of non-malignant conditions associated with acquired hypertrichosis lanuginosa and highlights the diagnostic challenges of tuberculosis reactivation in immunosuppressed patients with inflammatory myopathies.

KEYWORDS :

acquired hypertrichosis lanuginosa, anti-nxp2, catabolic state, dermatomyositis, paraneoplastic workup, tuberculosis, dermatology

MAIN ARTICLE

INTRODUCTION

Acquired hypertrichosis lanuginosa (AHL) is a rare cutaneous disorder characterized by the diffuse growth of fine, lanugo-type hair. It is most commonly recognized as a paraneoplastic phenomenon associated with gastrointestinal, pulmonary, and breast malignancies [1][2]. In a review of 56 paraneoplastic cases, the malignancy was usually metastatic, and the hypertrichosis preceded or accompanied the cancer diagnosis [2]. Non-malignant associations, including anorexia nervosa, AIDS, porphyria cutanea tarda, and drug-related causes, have also been documented, with a severe catabolic or metabolic stress state proposed as the common pathophysiologic denominator [2]. Its occurrence in the context of autoimmune myopathies complicated by infectious disease, in the absence of malignancy, has not been previously reported.

Dermatomyositis (DM) is an inflammatory myopathy associated with an increased risk of both malignancy and opportunistic infections, including tuberculosis (TB), particularly in patients receiving immunosuppressive therapy [10][11]. We report, to our knowledge, the first case of diffuse acquired hypertrichosis occurring in the context of DM complicated by pulmonary TB, in the absence of malignancy.

CASE PRESENTATION

A 44-year-old woman with no significant past medical history was admitted for suspected DM. She presented with a 4-month history of progressive proximal muscle weakness (strength 1/5 in all four limbs), facial and periorbital edema, heliotrope-like erythema, V-sign, shawl sign, poikiloderma, multiple cutaneous ulcerations, panniculitis, and dysphagia with normal hair distribution noted at admission (Figure 1). Her body mass index (BMI) at admission was 27.6 kg/m² (weight 68 kg, height 1.57 m). Myositis-specific antibody testing revealed a positive anti-NXP2 (anti-MJ) antibody, with all other myositis-specific and myositis-associated antibodies negative. An initial chest CT scan, performed as part of the baseline workup in the endemic setting, showed no pulmonary abnormalities and no evidence of active or latent tuberculosis.

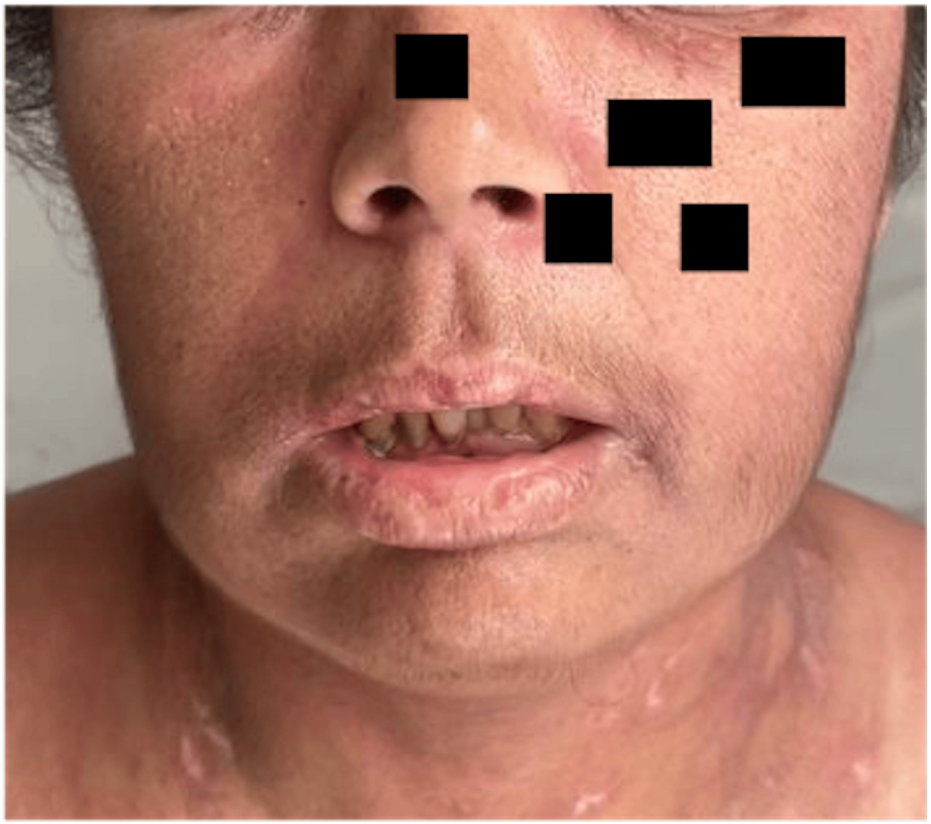

FIGURE 1: Normal hair distribution at admission.

Given the well-established association between DM and malignancy (20-25% in large cohorts), and the increased cancer risk specifically associated with anti-NXP2 positivity (3.68-fold increased risk compared to the general population), a comprehensive malignancy screening was performed as part of the standard workup for newly diagnosed DM [5][6][9]. This included whole-body ^{18}F-FDG PET/CT, which has demonstrated a sensitivity of 67-94% and specificity of 80-98% for detecting occult malignancy in DM, as well as tumor markers, mammography, cervical cancer screening, and upper and lower gastrointestinal endoscopy [5][9]. No evidence of an underlying malignancy was identified.

Treatment was initiated with intravenous methylprednisolone pulse therapy followed by oral prednisone (1.5 mg/kg/day) and methotrexate. Muscle strength improved; however, the course was complicated by gummatous skin lesions and significant weight loss (8 kg over three weeks), raising concern for reactivation of latent TB under immunosuppression.

The diagnostic workup for tuberculosis proved particularly challenging. The initial chest CT scan at admission revealed only a sequellar-appearing calcified lesion located in the basal segments, a distribution atypical for tuberculosis, which classically involves the upper lobes and apical segments of the lower lobes. A second chest CT scan performed following clinical deterioration showed no interval change, further diminishing clinical suspicion for active TB. Sputum cultures for Mycobacterium tuberculosis on three consecutive days were negative, as was sputum PCR for M. tuberculosis. PCR performed on cold abscess aspirates from the cutaneous lesions was also negative for M. tuberculosis but positive for pyogenic organisms (Staphylococcus aureus and Klebsiella species). Targeted antibiotic therapy was initiated against the identified pyogenic organisms; however, the patient failed to improve clinically,

with persistently elevated C-reactive protein (CRP) levels and ongoing clinical deterioration despite adequate antimicrobial coverage. This discordance between targeted treatment and clinical response heightened suspicion for an unidentified underlying infectious process. It was ultimately through bronchoscopy with bronchoalveolar lavage that pulmonary TB was confirmed, with PCR returning strongly positive for M. tuberculosis. A third chest CT scan, performed at three months, demonstrated interval progression with a right lower lobe parenchymal consolidation with posterior-basal predominance and associated air bronchograms, alongside the previously noted calcified right pulmonary nodule consistent with a residual granulomatous lesion, findings now suggestive of active infectious pneumonia (Figure 2).

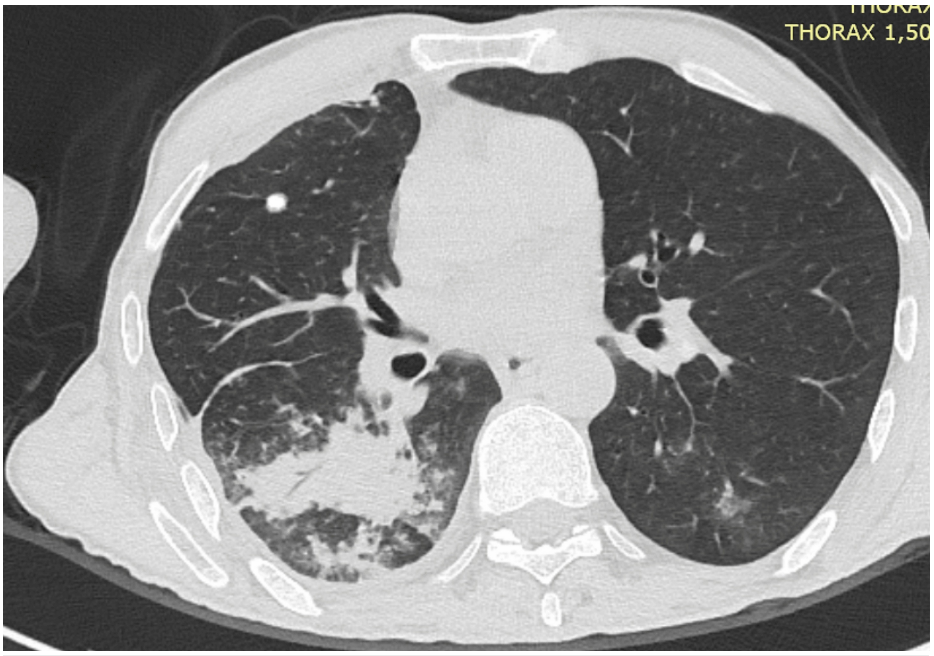

FIGURE 2: Axial chest CT scan at three months. Right lower lobe parenchymal consolidation with posterior-basal predominance and associated air bronchograms. A calcified right pulmonary nodule, consistent with a residual granulomatous lesion, is also visible.

The severity of the catabolic state was objectively documented: the patient's BMI decreased from 27.6 kg/m² at admission to 21.5 kg/m² over three months of hospitalization, representing a total weight loss of 15 kg (22% of initial body weight). Serum total protein levels declined from 61 to 55 g/L (reference range: 64-83 g/L), further reflecting the degree of metabolic derangement. Notably, diffuse acquired hypertrichosis developed concurrently with this progressive catabolic state (Figure 3), driven by the convergence of active DM and undiagnosed pulmonary TB. After initiation of anti-tuberculous therapy and nutritional recovery with weight regain, the hypertrichosis improved spontaneously (Figure 4).

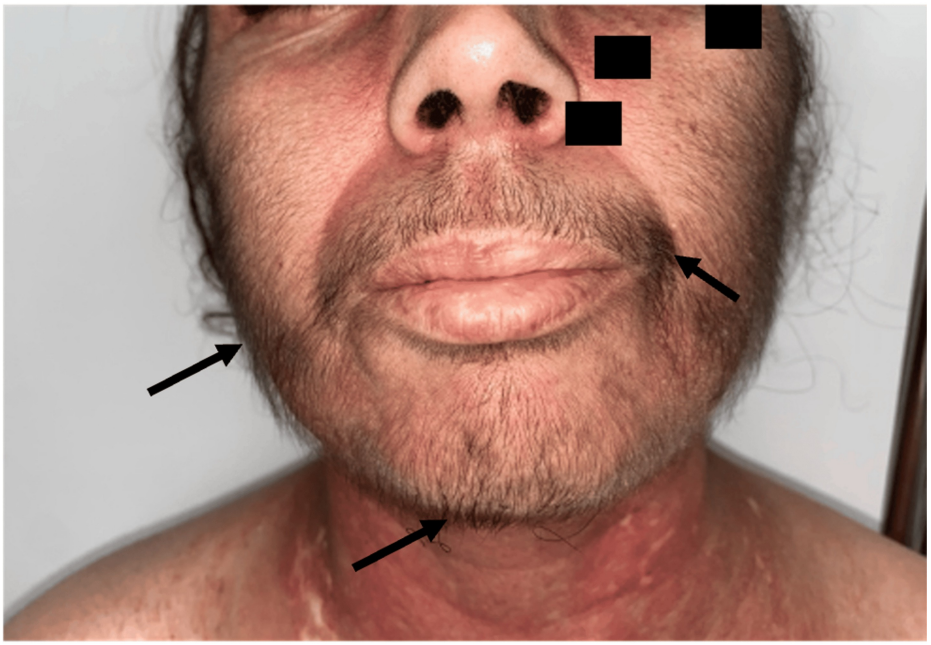

FIGURE 3: Clinical photograph demonstrating localized hypertrichosis (arrows), highlighting the abnormal excessive hair growth in the involved region.

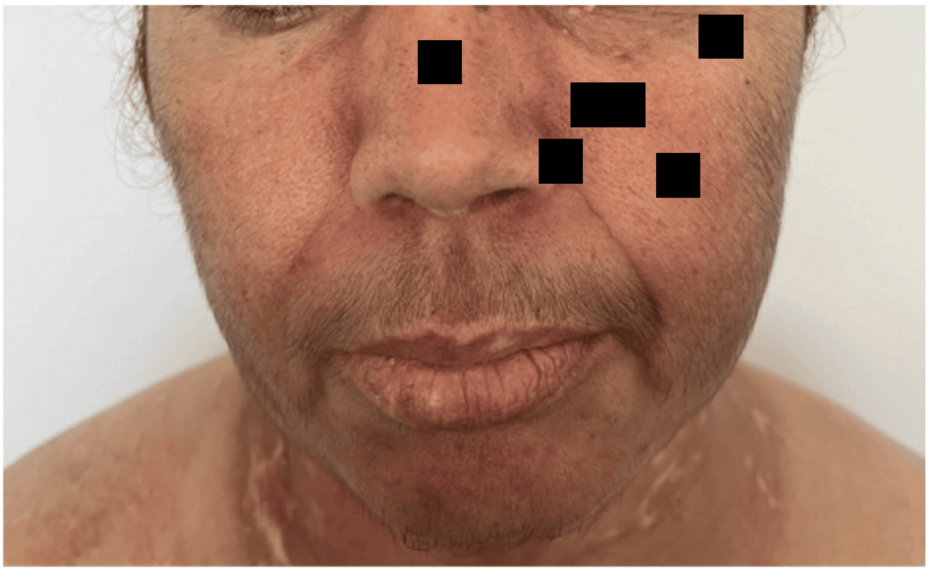

FIGURE 4: Spontaneous improvement of hypertrichosis following anti-tuberculous therapy and nutritional recovery.

DISCUSSION

Several aspects of this case merit discussion.

First, the comprehensive malignancy screening performed as part of the standard DM workup, including PET/CT with a high negative predictive value (93.8-95.7%), had already excluded occult malignancy before the onset of hypertrichosis [9]. This was particularly important given the patient's anti-NXP2 positivity, which places her in a high-risk category for cancer-associated myositis [5][6]. The negative screening allowed diagnostic reasoning to be redirected toward the catabolic state itself as the driver of hypertrichosis, rather than a paraneoplastic mechanism. The severity of the catabolic state was objectively documented by a 22% loss of initial body weight and declining serum protein levels, paralleling the onset of hypertrichosis.

The reversibility upon nutritional recovery, as observed in anorexia nervosa and after successful cancer

treatment, supports the hypothesis that metabolic derangement, rather than DM or TB as such, was the primary trigger, likely through prolongation of the anagen phase of the hair cycle [5][6].

The pathophysiology of this catabolism-driven hypertrichosis can be understood through several converging mechanisms. The most compelling is the recently described macrophage–adipocyte–hair follicle axis: macrophages infiltrating dermal white adipose tissue (dWAT) promote free fatty acid (FFA) release from adipocytes via serum amyloid A3 (SAA3)-dependent lipolysis; the released monounsaturated fatty acids (MUFAs) are then absorbed by epithelial hair follicle stem cells (eHFSCs) via the fatty acid translocase CD36, activating the transcriptional coactivator PGC1-α, which drives fatty acid oxidation, mitochondrial biogenesis, and exit from quiescence into anagen [7]. In our patient, the massive systemic lipolysis, 8 kg lost in three weeks, would have generated a sustained flood of FFAs into the dermal microenvironment, potentially activating this pathway on a diffuse scale. Critically, the panniculitis of dermatomyositis involves macrophage infiltration of dWAT, precisely replicating the initiating event of this axis and potentially serving as a local amplifier of lipolysis-driven hair follicle activation [7][14]. Beyond the FFA–CD36 pathway, dWAT is known to secrete hepatocyte growth factor (HGF), which stimulates hair matrix keratinocyte proliferation through the Wnt/β-catenin pathway; the breakdown of adipocytes during lipolysis releases not only FFAs but also such growth factors, potentially amplifying trichogenic signaling [3][8]. Additionally, the chronic inflammatory milieu of both DM and TB generates moderate levels of TNF-α, which have been shown to activate Lgr5+ hair follicle stem cells via AKT/β-catenin signaling, promoting telogen-to-anagen transition, a biphasic effect where moderate concentrations are stimulatory while high doses are inhibitory [4]. A complementary thermoregulatory mechanism, classically invoked in anorexia nervosa, posits that lanugo hair growth compensates for the loss of subcutaneous insulating fat, an hypothesis supported by the concurrent nutritional depletion in our patient [2]. The spontaneous resolution of hypertrichosis upon nutritional recovery and weight regain, mirroring observations in anorexia nervosa and paraneoplastic AHL after successful cancer treatment, provides the strongest clinical evidence for the metabolic nature of this phenomenon: cessation of systemic lipolysis terminates FFA-mediated eHFSC activation, while restoration of dWAT mass re-establishes physiological hair follicle cycling [2][1][7].

Second, this case highlights the considerable diagnostic difficulty of identifying TB reactivation in immunosuppressed DM patients. The initial chest CT was unremarkable, repeat imaging showed only a basal sequellar lesion in a distribution not suggestive of tuberculosis, and conventional microbiological investigations, including three consecutive sputum cultures, sputum PCR, and PCR on cold abscess aspirates, were all negative for M. tuberculosis. The cold abscesses, which could have been attributed to tuberculous etiology, instead yielded pyogenic organisms, further confounding the clinical picture [13].

Crucially, the failure to respond to targeted antibiotic therapy against the identified pyogenic organisms, with persistently elevated inflammatory markers, served as the key clinical clue that prompted bronchoscopy. Only bronchoalveolar lavage PCR ultimately established the diagnosis. DM patients carry a significantly increased risk of active TB (adjusted HR 2.64; 95% CI 1.97-3.54), with corticosteroid use being a major risk factor, and this case illustrates that standard non-invasive investigations may be insufficient to exclude TB reactivation in this population [14]. Moreover, atypical radiographic presentations of TB, including lower lobe involvement, are well recognized in immunosuppressed patients and should not dissuade clinicians from pursuing the diagnosis.

Third, the diagnostic challenge was compounded by the overlapping clinical features of DM and TB, including weight loss, muscle weakness, and skin lesions with gummatous evolution [10][11]. Cutaneous ulcerations in DM may reflect vasculopathy, specific autoantibody profiles such as anti-MDA5, or a paraneoplastic etiology; in this patient, the negative malignancy screening and infectious complications under immunosuppression pointed toward a multifactorial, non-paraneoplastic mechanism [11][12]. Notably, anti-NXP2-positive DM is associated with subcutaneous edema, calcinosis, dysphagia, and severe muscle involvement, features that were present in our patient and further complicated the clinical picture by overlapping with both the infectious and catabolic manifestations [10][11].

CONCLUSIONS

This observation expands the spectrum of non-malignant conditions associated with AHL and underscores three clinical imperatives: (1) maintaining a high index of suspicion for TB in DM patients from endemic regions who deteriorate under immunosuppression, even when conventional investigations are negative and radiographic findings are atypical; (2) considering early bronchoscopy when clinical suspicion for TB persists despite negative sputum studies and failure to respond to targeted antimicrobial therapy; and (3) recognizing diffuse acquired hypertrichosis as a potential clinical marker of severe catabolism that should prompt investigation for occult systemic disease, ncluding, but not limited to, malignancy.

ACKNOWLEDGEMENTS

The authors have no acknowledgements to declare and report no conflicts of interest.

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