Rom J Rheumatol 2024, 33(4):156-162 ISSN (print) 1843–0791, ISSN (online) 2069–6086

Revista Română de Reumatologie
Romanian Journal of Rheumatology

CASE REPORT

Breast Cancer and Dermatomyositis - A story of Resilience and Medical Insights: Case Report

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Abstract

Background: Dermatomyositis (DM) is an inflammatory myopathy associated with the presence of certain antibodies, such as transcription intermediary factor 1γ (TIF-1γ), which can be linked to a higher malignant risk.

Case Report: A 52-year-old female developed proximal muscle weakness, heliotrope rash, Gottron's papules, V-sign, and Shawl's sign, and was diagnosed with dermatomyositis with an anti-TIF-1γ phenotype. A complete oncologic screening was performed, including PET-CT, but the results were negative. Seventeen months later, the patient developed breast cancer, which was treated with neoadjuvant chemotherapy and left mastectomy with axillary lymphadenectomy. Clinical and paraclinical remission was maintained since oncologic treatment was initiated.

Conclusions: The appearance of dermatomyositis may have been in the context of a paraneoplastic syndrome due to breast cancer.

Keywords: dermatomyositis, TIF-1γ antibody, breast cancer, paraneoplastic syndrome.

Introduction

Dermatomyositis (DM) is a rare, heterogeneous autoimmune disease with an estimated prevalence of 1 per 100,000 populations [1]. It is part of the immune-mediated inflammatory myopathies (IIM) group, alongside other subtypes such as polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM) and others. These diseases share common clinical manifestations that involve the muscles in various distributions but differ in extramuscular clinical manifestations, laboratory and histological findings, progression, and treatment.

Unlike other subtypes, DM is also characterized by skin lesions. These include periorbital edema, a violaceous rash known as "heliotrope rash," erythematous rash on the elbows and fingers (Gottron's papules and signs), or on the anterior and posterior upper chest ("V-sign" and "Shawl sign") [2].

Studies have shown that DM is frequently associated with a range of myositis-specific antibodies, such as anti-Mi-2, anti- melanoma differentiation-associated protein-5 (MDA-5), anti-nuclear matrix protein-2 (NXP-2), anti–transcriptional intermediary factor 1 γ antibody (TIF-1γ) [3]. Additionally, individuals with anti- TIF-1γ antibodies have a significantly higher risk of malignancy, showing a 9.37-fold increase [4]. These antibodies are identified in up to 40% of patients diagnosed with DM. Thus, regular oncologic screening is crucial for patients with positive anti-TIF-1γ antibodies, as studies have shown that they are strong predictors of neoplastic lesions [5].

In this study, we present the case of a 53-year-old female with positive anti-TIF-1γ antibodies, but no malignancy detected at the time of diagnosis.

Case Report

We present the case of a 53-year-old female who was admitted to our clinic through the Emergency Department in December 2022 with suspicion of DM.

Her symptoms first began in November 2022 when she was admitted into an emergency ward in her hometown with intense muscle weakness in the pelvic and scapular girdle, periorbital edema, anterior and posterior chest erythema, Gottron's signs and papules. Blood tests showed significant inflammatory syndrome, with high C-reactive protein (CRP) 2 mg/dl, erythrocyte sedimentation rate (ESR) 60mm/hour, and elevated muscle enzymes, with serum creatine kinase (CK) levels over 14,000 U/L, alanine transaminase (ALT) levels of 361 U/mL and aspartate transaminase (AST) of 204 U/mL. A suspicion of dermatomyositis was raised, so further investigations were recommended, and treatment with oral corticosteroids at a dose of 0.5 mg/kg of prednisone was initiated.

A muscle biopsy was performed and showed uneven muscle fibers, mild perifascicular atrophy,

interstitial edema, myocytolysis, isolated homogenized fibers, absent transverse striations or signs of regeneration and an interstitial fibrosis associated with moderate inflammation predominantly lymphocytic-plasmacytic with a perivascular arrangement, a pattern suggestive for DM (fig1).

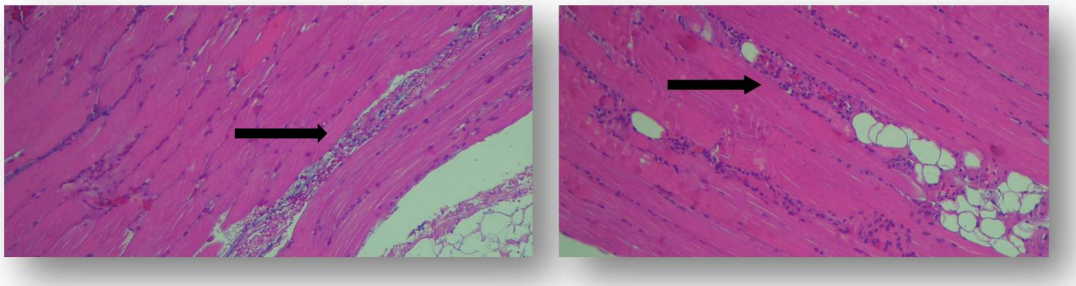

Figure 1. *Muscle biopsy of the patient that shows necrosis of the muscle fiber (left) and lymphocytic-plasmacytic inflammation (right).*

Electromyography (EMG) revealed an inflammatory myopathic pattern with increased spontaneous activity, fibrillation potentials, positive sharp waves, and small polyphasic motor unit potentials (Fig. 2).

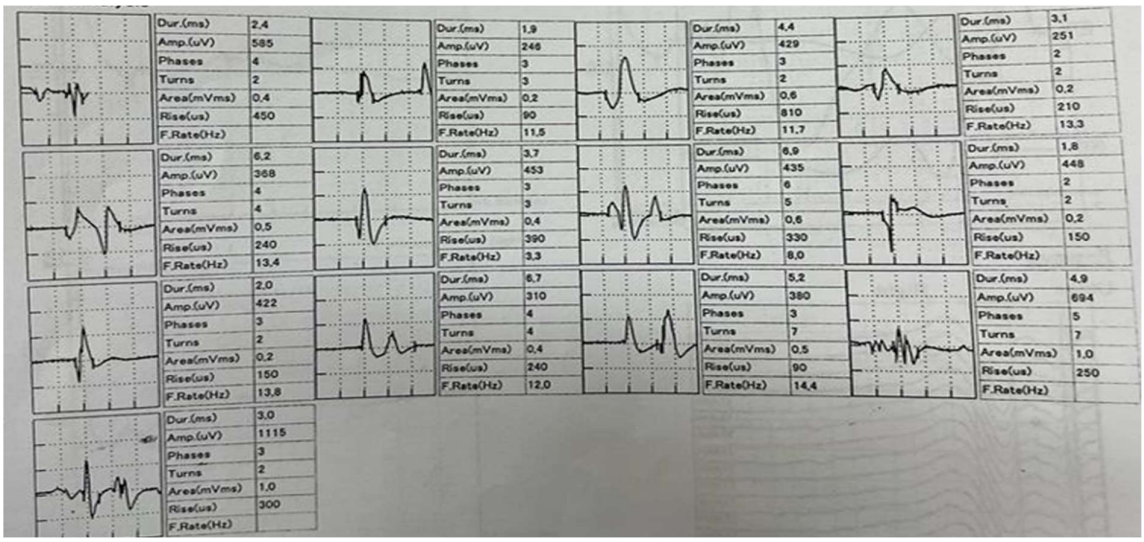

Figure 2. *EMG shows a myopathic pattern with the presence of polyphasic MUAPs, reduced amplitude and duration.*

Despite corticosteroid treatment, muscle involvement rapidly progressed to the cervical paravertebral muscles, and the skin lesions extended to the scalp and new axillary bullous lesions, thus in December she presented to our Emergency Department and was admitted (Fig. 3, 4). No clinical signs of other organ involvement were present at the time of admission.

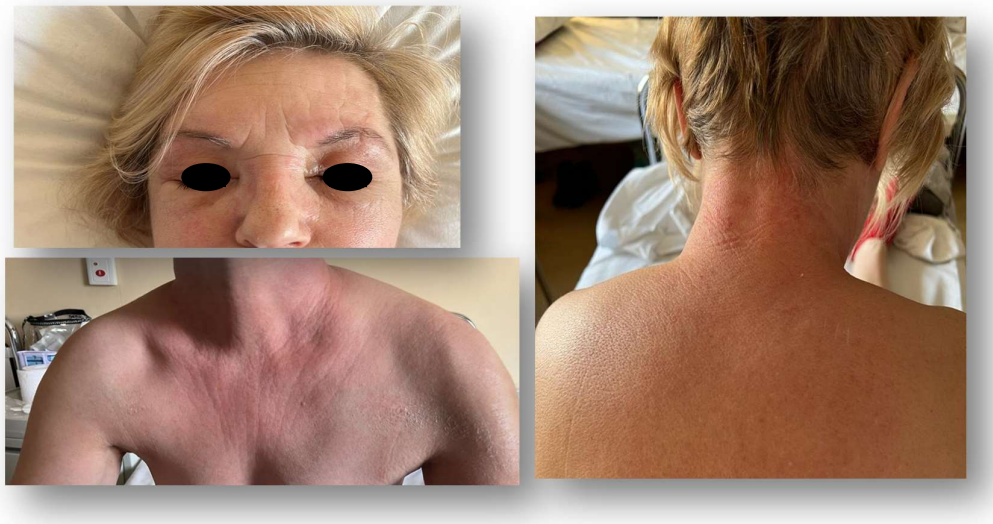

Figure 3. *Heliotrope rash (left up). V-sign (left down). Swal's sign (right).*

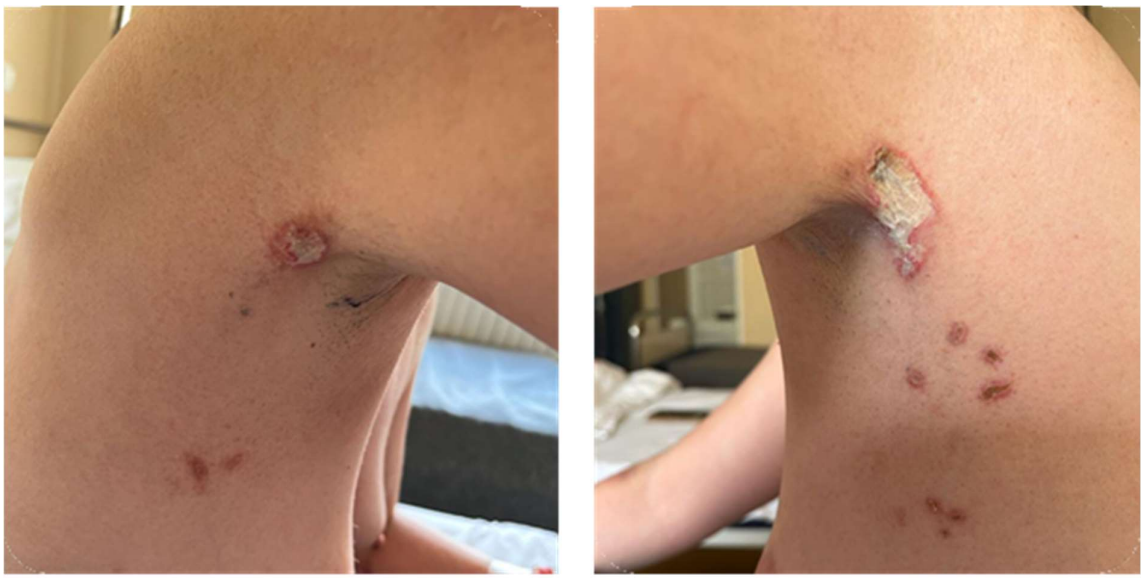

Figure 4. *Bullous lesions in the axillary region.*

Blood tests showed a remission of inflammatory syndrome, with normal serum levels of CRP and ESR and lower but persistent elevated serum levels of muscle enzymes, such as a CK of 2277 U/L, AST 56U/mL, ALT 111 U/mL with . A full myositis antibody panel was performed, which returned equivocal results for anti-TIF1γ and anti-Mi-2 antibodies. We also excluded other causes of myositis and cutaneous infections, such as viral infections (negative for hepatitis, HIV, toxocara, toxoplasma), thyroid markers, and oncologic markers, which were all within normal limits.

After reviewing the data, we applied the Bohan and Peter criteria for DM and established the diagnosis. Intravenous SoluMedrol 500 mg/day for 6 days was administered during hospital stay, followed by oral corticosteroids at 0.75 mg/kg/day and Methotrexate (MTX) at a dose of 15 mg/week. Considering the results of the myositis panel, we performed an extensive neoplastic workup, including thoracic, abdominal, and pelvic CT scans, head and neck CT, mammography, gynecological consult, and upper and lower endoscopies, all of which were within normal limits.

The patient showed good improvement, with resolution of muscle and skin involvement.

However, in April 2023, she began to experience dysphagia for semisolid foods. Barium upper gastrointestinal test showed Moderate stasis in the right piriform sinus (fig. 5).

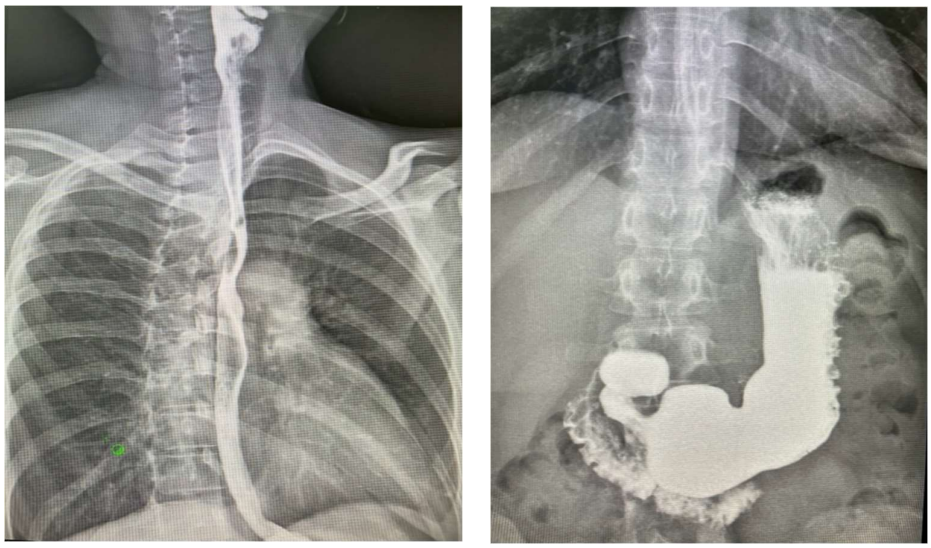

Figure 5. *Barium transit that shows moderate stasis in the piriform sinus.*

MTX dose was increased to 20 mg/week, and the myositis panel was repeated, returning positive results for anti-TIF1γ and anti-Mi-2 antibodies. Considering the rapid progression of the disease, with the esophageal involvement despite the high-dose corticosteroid therapy associated with MTX and the positive anti-TIF1γ antibodies, we decided to extend our oncologic screening and perform a PET-CT scan. The test showed nodular lesions in the superior pulmonary lobes suggestive of pulmonary fibrosis and metabolic activity in the colon and muscles, suggestive of diverticulitis. MTX was switched to mycophenolate mofetil (MMF) 2.5 g/day, with corticosteroid therapy at progressively lower doses, which resulted in a good outcome. Paraclinical remission was achieved and muscle weakness was improved.

In April 2023, the patient presented with intense lower back pain. A magnetic resonance imaging (MRI) of the vertebral column showed collapse of several thoracic vertebrae. Due to the long-term treatment with high-dose corticosteroids, the patient further investigated and diagnosed with osteoporosis through a dual-energy x-ray absorptiometry (DEXA). A vertebroplasty was performed and treatment with zoledronic acid every 6 months was initiated (figure 6).

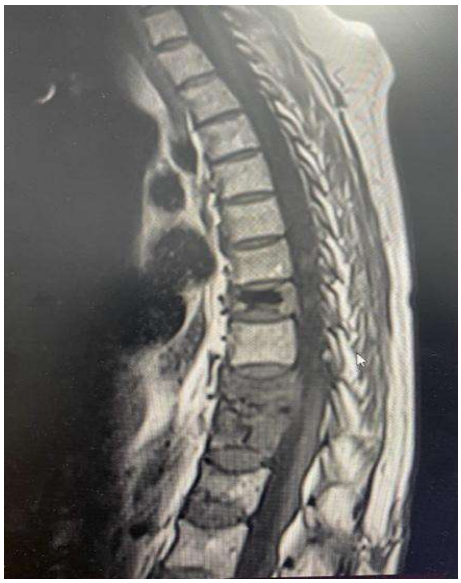

Figure 6. *MRI of the vertebral column shows collapse of thoracic T8,10,11,12 vertebrae.*

In March 2024, the patient presented for a check-up, and a physical exam revealed a nodule in the left breast. Ultrasound showed an irregular hypoechoic nodule measuring 15 x 18 mm (fig. 7).

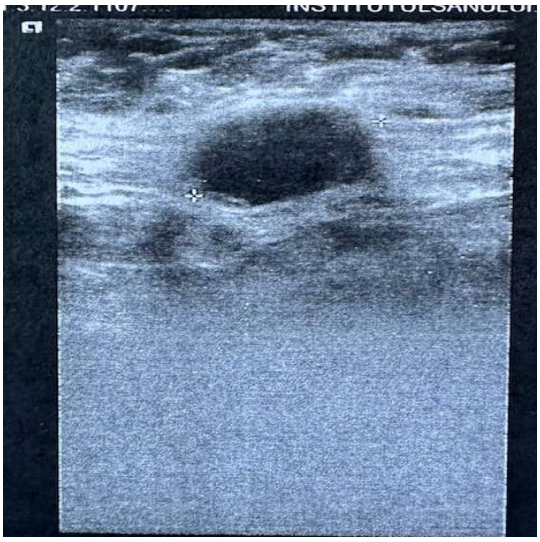

Figure 7. *Ultrasound of the left breast shows an irregular hypoechoic nodule.*

A thoracic CT and mammography raised suspicion of breast malignancy, and a biopsy was requested. The histopathologic exam confirmed the diagnosis of high-grade invasive ductal breast carcinoma (G3) (fig. 8).

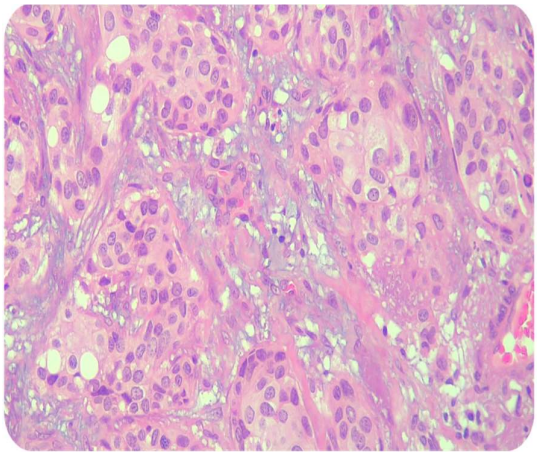

Figure 8. *Hematoxylin-eosin stain with ×200 magnification shows fragments of high-grade invasive ductal breast carcinoma (G3) with marked cellular pleomorphism, abundant mitotic activity, and reduced lymphocytic reactivity.*

Full oncologic screening and consultations such as thoracic, abdomen and pelvic CT, whole-body scintigraphy, head MRI, were performed to exclude the presence of secondary neoplastic lesions and they all came back negative.

The patient followed neoadjuvant chemotherapy with doxorubicin, uromitexan, and cyclophosphamide until September 2024 (16 rounds), when she underwent surgery for left mastectomy and axillary lymphadenectomy, with clear resection margins.

Currently, the patient is in remission with no clinical or paraclinical evidence of disease activity, and no signs of oncologic lesions. Therefore, we have determined that reinitiating immunosuppressive treatment is not necessary at this time.

This type of case is difficult and unpredictable, highlighting the importance of interdisciplinary collaboration among healthcare providers for proper management.

Discussions

DM is an autoimmune myopathy characterized by proximal muscle weakness and skin lesions. It is associated with a four- to six-fold higher risk of neoplasm development compared to the general population, including breast cancer, which may present before, concurrently, or after the diagnosis of dermatomyositis [6] [7]. Among the specific myositis antibodies, anti-TIF1-γ, anti-NXP2, and anti-MDA5 have been shown to predict a higher risk of cancer development [8]. Furthermore, those with anti-TIF-1 gamma antibodies have a significantly higher risk, with a 9.37-fold increase.

Our patient tested positive for anti-Mi-2 antibodies, which are commonly observed in DM (in 20-25% of cases) and are associated with a better response to treatment and a more favorable overall prognosis. She also tested positive for anti-TIF1-γ antibodies, which target two different antigens (140-kDa and 155-kDa proteins). These antibodies were first reported in Japan as specific autoantibodies for dermatomyositis, with a 70% higher risk of cancer [9]. Therefore, close monitoring and vigorous oncologic screening was necessary, especially in the first year of evolution [10].

Several risk factors for oncologic development need to be considered, according to a meta-analysis of clinical trials: advanced age, male sex, cutaneous ulceration, dysphagia, and the presence of anti-TIF1-γ, anti-NXP2 antibodies [11].

Currently, no validated classification criteria for IIM exist. The 2017 EULAR/ACR criteria is the gold standard for identifying the probability of having IIM, including DM, with higher sensitivity and specificity than previous criteria. The clinical features and the use of classification criteria guided the diagnosis and subsequent treatment plan [12].

Although outdated, we used the Bohan and Peter criteria, the oldest classification system. The diagnosis of definite dermatomyositis was established by presenting all five variables: proximal and symmetrical muscle weakness with dysphagia, elevation of serum muscle enzyme levels such as creatine kinase, aspartate aminotransferase, and lactate dehydrogenase, suggestive myopathy findings on EMG, positive biopsy, and skin changes with heliotrope rash and Gottron's signs [13].

Regarding treatment, glucocorticoids are the mainstay for DM, with disease-modifying anti-rheumatic drugs (DMARDs), intravenous immunoglobulins, biologics, and topical antibiotics serving as adjunctive treatments. In our case, intravenous methylprednisolone was initiated at 500 mg/day for 6 days, followed by oral prednisone at 0.75

mg/kg/day. MTX was also started at 15 mg/week and later increased to 20 mg/week due to the onset of dysphagia, which is a clinical sign of severity. Dysphagia appears in 10-73% of cases, is associated with malignancy development and can lead to nutritional deficiencies, aspiration pneumonia, and overall low life quality [14].

Therefore, we have decided to perform a PET-CT to exclude the presence of any oncologic finding. PET-CT is highly sensitive for detecting occult malignancies, which might not be detectable through other imaging modalities. Due to its high sensitivity, it helps detect both primary and metastatic tumors even before they become clinically apparent, allowing for early intervention [15].

After identifying pulmonary fibrosis on PET-CT, MTX was switched to MMF 2.5 g/day. Supportive therapy, including calcium and vitamin D, was concurrently initiated, but the patient developed osteoporosis, and zoledronic acid was started.

In addition to pharmacological treatment, cancer screening remains a critical aspect of managing dermatomyositis. Given the patient's positive anti-TIF-1 gamma status, which is a strong predictor of malignancy, cancer screenings were performed. Initially, the results were negative, but 17 months after disease onset, a breast lump was discovered. This time frame is common in cohorts of patients studying the incidence of malignancy in DM, which often develops within 2 years after diagnosis [6] [16].

Conclusions

The unique aspect of this case is the late appearance of positive antibodies and the rapid progression of the disease until the development of malignancy and the initiation of its treatment. Patients with positive anti-TIF1γ and anti-Mi-2 antibodies present a complex clinical scenario. Early identification of autoantibodies, understanding the interplay between these conditions, and coordinated treatment are essential for optimizing patient outcomes. A multidisciplinary management team must tailor both cancer treatment and autoimmune disease therapy to provide the best care possible for these patients.

Acknowledgments: We would like to thank all the medical staff involved in the diagnosis and management of the patient.

Conflicts of Interest: The authors declare no conflicts of interest related to the research, authorship, or publication of this article.

Patient Consent for Publication: Written informed consent for publication of the clinical details and any accompanying images was obtained from the patient. The identity of the patient has been kept anonymous in accordance with ethical standards.

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Received: 08.12.2024

Accepted: 29.12.2024