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Tuberculosis infection in patients with dermatomyositis

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Summary

Patients with dermatomyositis (DM) are particularly susceptible to the development of opportunistic infections due to immunosuppression induced by the disease itself and its treatment. We describe three patients who met the diagnostic criteria for DM and developed tuberculous myositis. The first case, a 54-year-old woman, had a positive polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* detected in a *post-mortem* muscle biopsy. A second patient was diagnosed with a positive Ziehl-Neelsen stain in bronchoalveolar lavage, and a third patient, with multiple collections in the thorax and lower limbs, had positive Ziehl-Neelsen stain and PCR for *Mycobacterium tuberculosis*. In inflammatory myopathies, muscle and soft tissue infection by tuberculosis may produce symptoms similar to the underlying disease. The differential diagnosis of tuberculosis superinfection can be difficult.

Introduction

Dermatomyositis (DM) is considered a rare disease: in Argentina, an incidence of 0.32 per 100,000 person-years has been reported (1). The 5-year survival rate of patients with DM ranges from 60% to 80%, with infections representing one of the main causes of mortality (2). The immunosuppression induced by the disease itself and its treatment make DM patients particularly susceptible to opportunistic infections, including tuberculosis (TB). Extrapulmonary TB involving the musculoskeletal system, in patients with DM, is a real medical challenge.

Here, we present three clinical cases of patients who met the diagnostic criteria of DM and who developed extrapulmonary TB with varying clinical outcomes. None of the three cases had a known history of exposure to TB

Case Report 1

A 54-year-old woman with a history of smoking and nonalcoholic steatohepatitis consulted for erythematous macules in sun-exposed areas, arthralgias, myalgias, muscle weakness in the pelvic girdle, and erythematous papules over the interphalangeal and metacarpophalangeal joints of both hands. The was biopsy compatible with Gottron's papules.

Laboratory findings revealed an erythrocyte sedimentation rate (ESR) of 85 mm/h, C-reactive protein (CRP) of 123 mg/L, and normal total creatine phosphokinase (CPK), negative antinuclear antibodies (ANAs) and positive anti-RO antibody. A computed tomography (CT) scan of the chest was performed and showed isolated pseudo-nodular opacities in both lungs, but bronchoalveolar lavage could not be performed. A magnetic resonance imaging (MRI) scan of the pelvis showed focal muscle edema in the maximus gluteus and right adductor brevis. A muscle biopsy was performed in the gluteal region, which showed no signs of inflammatory myopathy. A diagnosis of amyopathic DM was made and initial treatment with methylprednisone 40 mg/day was indicated.

One month later, the patient reported several episodes of fever and pain in the right buttock, associated with difficulty in hip flexion and extension. Blood cultures were negative, and new laboratory values revealed an ESR of 111 mm/h and a CRP of 203 mg/L. A surgical biopsy of the right sartorius muscle was performed and found no evidence of infection or active inflammatory process. Methotrexate 15 mg and folic acid 5 mg weekly were added, and the dose of methylprednisone was increased to 60 mg/day.

Subsequently, the patient developed asymmetric edema of the lower limbs, predominantly on the right side, episodes of fever, and hemodynamic instability, and was admitted to the intensive care unit. Empiric broad-spectrum antibiotic therapy was initiated. Due to the presence of severe myalgia in the lower limbs, a new MRI was performed, showing interfasciomuscular edema of the posterior and lateral adductors of the right hip and less intense on the left side. Another muscle biopsy was performed, which showed atrophic fibers without specific findings. Fluorodeoxyglucose positron emission tomography was performed, which showed diffusely increased metabolism and muscle edema in the neck, shoulder girdle, upper limbs, right gluteus, and both thighs.

The patient suffered multiple organ failure and died. An enlarged *post-mortem* muscle specimen was obtained from the right quadriceps. Histopathology demonstrated blood vessels with fibrinoid thrombosis associated with necrotizing fasciitis and positive Ziehl-Neelsen staining. Subsequently, polymerase chain reaction (PCR) confirmed the presence of *Mycobacterium tuberculosis*.

Case Report 2

A 49-year-old female with no relevant past medical history consulted for purple macular lesions on the dorsal region of both hands. A skin biopsy was performed, which was compatible with a DM diagnosis. She began treatment with methotrexate 15 mg weekly and hydroxychloroquine 400 mg per day. Eight months later, she presented dry cough and progressive dyspnea to functional class III /IV. A chest CT revealed vitreous infiltrates consistent with the pattern of nonspecific interstitial pneumonia secondary to DM. A panel of antibodies specific for myositis was performed, and anti-MDA5 was positive. She developed later arthralgias in small joints of both hands and muscle

weakness in the shoulder and pelvic girdle. On physical examination, she had Gottron's sign, ulcers on the fingertips of both hands and diffuse erythema on both thighs. Prednisone 20 mg/day was added.

One week later, she developed debilitating right thigh pain associated with infra- and suprapatellar edema. A pelvic muscle MRI was performed, which showed asymmetric muscle edema primarily in the gluteal region and right thigh. A muscle biopsy was performed, which showed perifascicular atrophy suggestive of DM, with negative cultures for common germs, fungi, and *Mycobacterium tuberculosis*.

Due to the persistence of symptoms, a positron emission tomography (PET)-CT was performed, which revealed a pseudonodular consolidation area with an air bronchogram in the posterior segment of the upper lobe of the right lung, soft tissue edema at the level of the right chest wall, bilateral abdominal wall, right pelvic girdle, and bilateral buttocks. Intravenous γ globulin was administered for 3 days without clinical response. Subsequently, hemodynamic instability and respiratory failure occurred. Bronchoalveolar lavage was performed, and a positive Ziehl-Neelsen stain for *Mycobacterium tuberculosis* was obtained; therefore, therapy with rifampicin, isoniazid, pyrazinamide, and ethambutol was started. The patient worsened her general clinical condition, developed multiple organ failure, and died one week later.

Case Report 3

A 33-year-old male patient consulted for myalgias, muscle weakness in lower limbs, and maculopapular lesions on the dorsum of the hands and chest. Laboratory findings showed elevated CPK (7000 IU/L) and transaminases: positive ANA at high titers of 1/1280, with a fine speckled pattern. Muscle MRI showed bilateral muscle edema of both quadriceps, especially the rectus femoris anterior and vastus lateralis. Muscle biopsy was compatible with DM diagnosis. Specific myositis antibodies (S.A.E, Mi2, P.M-SCL, PL12, PL7, JO -I, OJ, E.J, SRP, MDA 5, TIF-1- γ) and neoplasia screening images were all negatives. DM was diagnosed, and methotrexate 15 mg weekly and methylprednisone 20 mg oral per day were started, with a good initial clinical response.

Seven months later, he presented generalized myalgias, skin lesions compatible with Gottron's sign and elevated CPK levels. A new MRI was performed, which showed increased muscle involvement of the adductor and gluteal muscles (Figure 1). The treatment was changed to mycophenolate mofetil 2 gr per day. By the third month, there was an improvement in the skin lesions but greater limitation due to pain and weakness in thigh flexion, associated with low-grade fever and unquantified weight loss. ESR and CRP, which were in normal ranges when DM was diagnosed, were now elevated. A new muscle biopsy was performed, which showed changes of inflammatory myopathy and negative cultures for common germs, mycology, and PCR for TB. The patient persisted with muscle pain, especially in the lower limbs, with elevated CPK levels.

A PET-CT showed the presence of axillary, mesenteric, and retroperitoneal lymph nodes, SUV Max 6.9 (Figure 2), in a non-adenomegaly range, with uptake in the right breast region. This finding was interpreted as refractory DM, and three intravenous pulses of 500 mg of methylprednisolone for 3 consecutive days were indicated.

One month later, he developed multiple collections of purulent fluid in the thorax and lower limbs (Figure 3). An ultrasound-guided puncture of the right thoracic collection was performed, which yielded a positive Ziehl-Neelsen result and PCR for *Mycobacterium tuberculosis*. Treatment with four drugs for TB was initiated. Surgical drainage and rifampicin lavage were performed at the collection sites. He had nephrotoxicity and hypercalcemia not mediated by parathyroid hormone (increased calcitriol due to the presence of granulomas). He required hospitalization for 3 months and multiple surgical drains of collections in the right chest, posterior neck, lower lumbar area, both thighs and left arm.

The patient had a good clinical evolution and received tuberculostatic treatment and mycophenolate on an outpatient basis.

Discussion

In Argentina, TB continues to be a serious public health problem; in 2020, the TB reporting rate was 24 per 100,000 population. Extrapulmonary involvement was found in 11.9% of cases (3).

The prevalence of opportunistic infections, including TB, in DM, ranges from 6.3% to 21.3%, with *Mycobacterium* among the most isolated pathogens (4). A recent meta-analysis showed that countries with a TB incidence rate higher than 40 per 100,000 population have an estimated prevalence of mycobacterial infections in inflammatory myopathies of approximately 6.62% (5).

In a study conducted in Taiwan, patients with DM were found to have a higher risk of global TB [internal rate of return (IRR): 2.95 95% confidence interval (CI): 2.24-3.88; p=0.001] and extrapulmonary TB (IRR: 2.72 95% CI: 1.40- 5.27; p=0.001) compared to the general population. Some variables, such as male gender, diabetes mellitus, corticosteroid use, and azathioprine use, were identified as independent risk factors for the development of TB (6). Compared to other autoimmune diseases, for example, systemic lupus erythematosus, the risk of TB (pulmonary and extrapulmonary) remains higher in DM (odds ratio: 2.24; 95% CI: 1.5-5.4; p=0.007) (7).

TB can affect various structures such as bones, fascia, muscles, joints, tendon sheaths, and others, with or without purulent collections (8-11). The infection may originate from a contiguous pulmonary focus, hematogenous dissemination, or local trauma with implantation of the bacilli. The inflammatory involvement of the skin in DM makes it particularly susceptible to the development of TB (12).

In inflammatory myopathies, infestation of muscles or soft tissues by TB may produce symptoms similar to those of the underlying disease, making differential diagnosis very difficult. In addition, difficulties associated with isolation and culture of *Mycobacterium tuberculosis* are present.

In our series, key signs/symptoms of suspected infection were severe muscle pain with mild weakness, asymmetric lower limb edema, the presence of fever, and persistently elevated acute phase reactants despite immunosuppressive treatment (Table 1).

The development of collections, as in our third patient, may occur late and sometimes allows identification of the TB bacillus. In general, TB abscesses occur more frequently in the abdominal and thoracic walls, paravertebral region, lymph nodes, joints, muscles, and subcutaneous tissues of the extremities (12).

The identification of the TB bacillus can be performed by direct (Ziehl-Neelsen and PCR) and indirect (histopathology) methods. Culture remains the gold standard, with the disadvantage that long periods of time are required to identify the bacilli (13). Extrapulmonary lesions, especially those involving the musculoskeletal system, are usually paucibacillary, and muscle biopsies are often insufficient to identify the germ. In these cases, where patients have an unusual course, PET-CT may be useful to find collections at unusual sites, guide biopsy collection, and distinguish muscle involvement expected in DM.

If clinical suspicion is strong, it is important to consider an enlarged (surgical) muscle biopsy with specimen collection for culture and also to quickly start empiric antibiotic treatment.

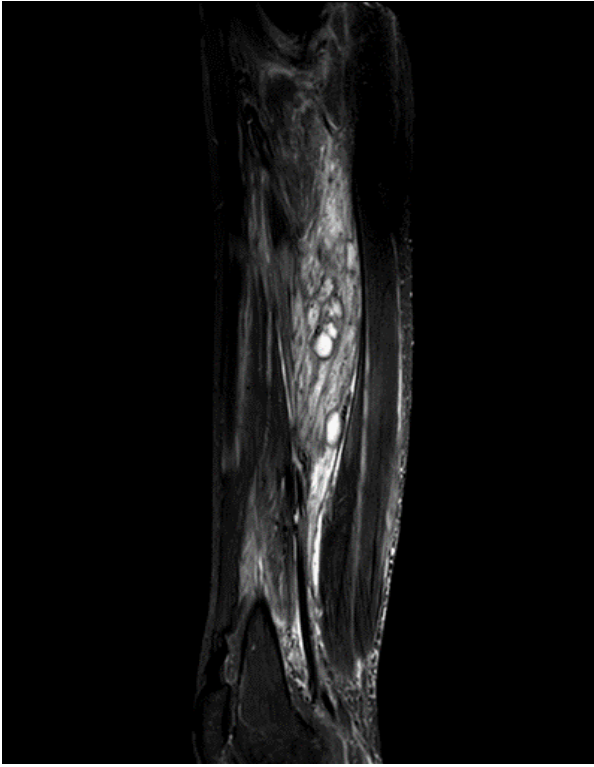
Finally, the purified protein derivative tuberculin test (PPD), used to screen for latent TB, is of limited value in immunocompromised patients, especially those receiving high-dose corticosteroids and immunomodulators (14). In this case series, all patients had a negative PPD at the onset of symptoms of inflammatory myopathy before the start of immunosuppression. In Argentina, we do not have a gamma interferon release assay that would allow more appropriate screening for earlier contact with TB.

Conclusions

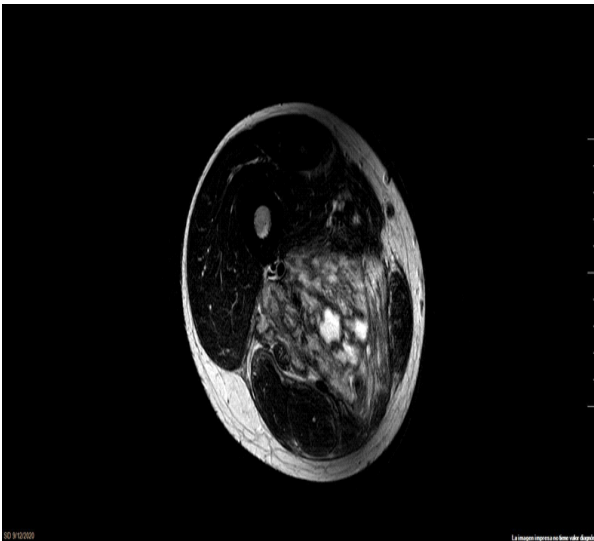
Superinfection with TB in DM patients should be suspected in those with severe muscle pain despite immunosuppressive treatment, especially in countries where TB is endemic.

References

1. Rosa J, Garrot LF, Navarta DA, Saucedo C, Scolnik M, Bedran Z, et al. Incidence and prevalence of polymyositis and dermatomyositis in a health management organization in Buenos Aires. *J Clin Rheumatol* 2013; 19: 303-7.
2. Schioppa E, Phillips K, MacDonald PM, Crofford LJ, Somers EC. Predictors of survival in a cohort of patients with polymyositis and dermatomyositis: effect of corticosteroids, methotrexate and azathioprine. *Arthritis Res Ther* 2012; 14: R22.
3. Argentine Ministry of Health. Bulletin No. 5. Tuberculosis and leprosy in Argentina. 2022.
4. Chen IJ, Tsai WP, Jan Wu YJ, Luo SF, Ho HH, Liou LB, et al. Infections in polymyositis and dermatomyositis: analysis of 192 cases. *Rheumatology* 2010; 49: 2429-37.
5. Haldule S, Chatterjee M, Goswami RP, Vadsaria I, Gaur P, Kavadiachanda C, et al. A systematic review and meta-analysis of mycobacterial infections in patients with idiopathic inflammatory myopathies. *Rheumatology* 2022; 61: 3521-33.
6. Wu PH, Lin YT, Yang YH, Lin YC, Lin YC. The increased risk of active tuberculosis disease in patients with dermatomyositis - a nationwide retrospective cohort study. *Sci Rep* 2015; 5: 16303.
7. Gupta L, Aggarwal R, Naveen R, Lawrence A, Zanwar A, Misra DP, et al. High prevalence of active tuberculosis in adults and children with idiopathic inflammatory myositis as compared with systemic lupus erythematosus in a tuberculosis endemic country: retrospective data review from a tertiary care centre in India. *Mediterr J Rheumatol* 2020; 32: 132-42.
8. Abreu AS, Fernandes GH, Borba EF, Guedes LKN, Ramos JF, Shinjo SK. Musculoskeletal tuberculosis in dermatomyositis: association or coincidence? *Open J Rheumatol Autoimmune Dis* 2014; 04: 58-61.
9. Liu CH, Liu WC, Chen LW, Chen JS. Tuberculous myofasciitis in dermatomyositis. *Clin Rheumatol* 2008; 27: S7-9.
10. Simopoulou T, Varna A, Dailiana Z, Katsiari C, Alexiou I, Basdekis G, et al. Tuberculous pyomyositis: a re-emerging entity of many faces. *Clin Rheumatol* 2016; 35: 1105-10.
11. Rajalingham S, Mohd Said MS, Shaharir SS, Abaziz A, Periyasamy P, Anshar FM. Dermatomyositis masquerading musculoskeletal tuberculosis. *BMJ Case Rep* 2011; 2011: bcr0820114675.
12. Gao W, Zeng Y, Chen W. Multiple subcutaneous tuberculous abscesses in a dermatomyositis patient without pulmonary tuberculosis: a case report and literature review. *BMC Infect Dis* 2020; 20: 409.
13. Purohit M, Mustafa T. Laboratory diagnosis of extra-pulmonary tuberculosis (EPTB) in Resource-constrained Setting: State of the Art, Challenges and the Need. *J Clin Diagn Res* 2015; 9: EE01-6.
14. Anton C, Machado FD, Ahumada Ramirez JM, Manzoni Bernardi R, Palominos PE, Viegas Brenol C, et al. Latent infection in patients with rheumatic diseases. *J Bras Pneumol* 2019; 45: e20190023.



a.



b.

Figure 1. Magnetic resonance imaging T2 sequence of the thigh on sagittal (a) and axial (b) planes. Evidence of hyperintensity at the level of the adductor muscles, more intense in their proximal third, gracilis, and to a lesser extent hamstring muscles. Laminar fluid surrounding the semitendinosus muscle.

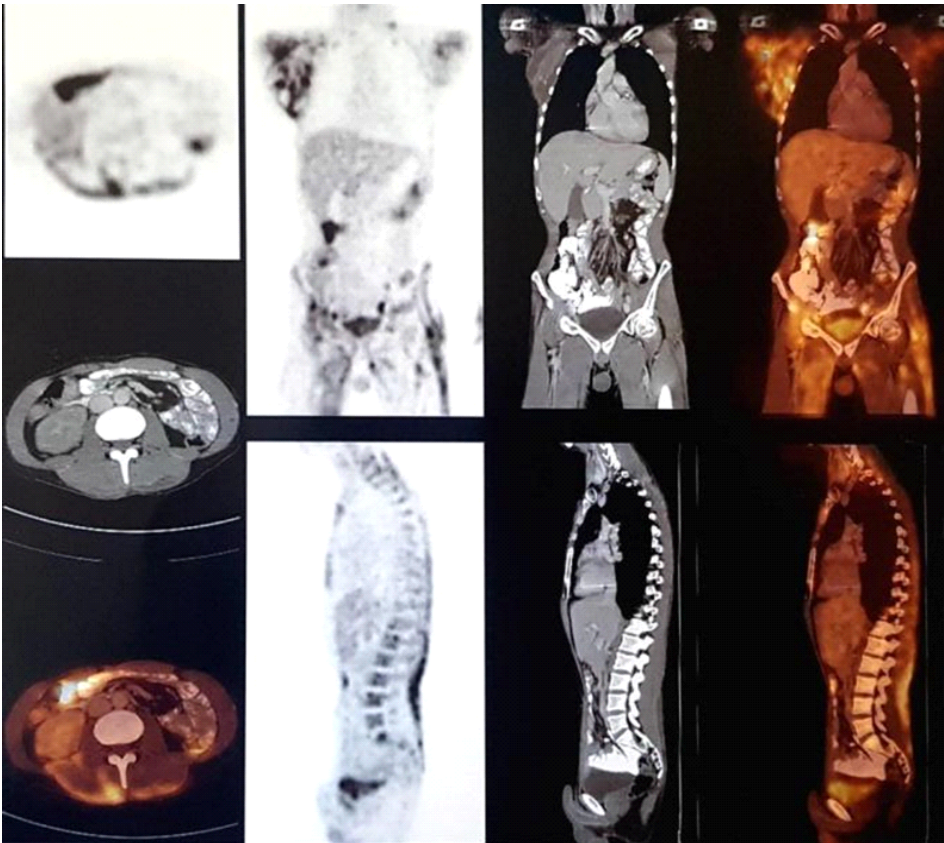


Figure 2. Positron emission tomography-computed tomography. Increased uptake in the right pectoral muscle region and diffusely in most muscle groups, predominantly in the lower extremities. Mesenteric hypermetabolic lymph nodes, the largest on the left flank (32.6 mm; SUV: 4.7).



Figure 3. Subcutaneous collection in the left thoracolumbar region.

Table 1. Characteristics of the cases.

	Case 1	Case 2	Case 3
Age (years)	54	49	33
TB diagnosis delay*	3 months	6 months	15 months
TB diagnostic method	Muscle biopsy (PCR)	Bronchoalveolar lavage (Ziehl Neelsen)	Culture of skin abscess
Muscle biopsies, n (result)	2 (Perifascicular atrophy)	2 (Perifascicular atrophy)	2 (Perifascicular atrophy)
Reason for consultation	Gluteal and RLD edema	Edema RLD	Myalgies
Pain	+++	+++	+++
Weakness	+	+	+
Constitutional symptoms	+	+	+
ESR at DM diagnosis	102	126	12
ESR at TB diagnosis	111	61	64
CRP at DM diagnosis	123	327	7
CRP at TB diagnosis	203	126	167
CPK at DM diagnosis	24	136	5382
CPK at TB diagnosis	62	316	<10
Antibodies	Anti-Ro (+)	Anti-MDA5 (+)	ANA (+) 1/1280 (AC-4)
Chest CT	Pseudonodular opacity (7mm)	Scars sequelae in upper lobe	Calcified granuloma
MRI	Interfibrillar, interfasciomuscular and SCT edema	Interfibrillar, interfasciomuscular and SCT edema	Edema and fluid collections
Positron emission tomography-CT	positive	positive	positive

TB, tuberculosis; ESR, erythrocyte sedimentation rate; DM, dermatomyositis; CRP, C-reactive protein; CPK, creatine phosphokinase; CT, computed tomography; RLD; right lower limb, ANA; antinuclear antibodies, SCT; subcutaneous cellular tissue. *Time from DM diagnosis to TB diagnosis.