

# Paraneoplastic dermatomyositis and prostate cancer: Myopathy regression under cancer-directed therapy

Mafalda Miranda Baleiras,  
Luís Maduro, Carolina Vasques,  
Filipa Ferreira, Marta Mesquita Pinto,  
Ana Martins

Hospital São Francisco Xavier, Centro  
Hospitalar Lisboa Ocidental, Portugal

## Abstract

Prostate cancer is the second most frequent malignancy in men worldwide and the fifth leading cause of death. Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy characterized by musculoskeletal manifestations. However, DM can also present as a paraneoplastic syndrome of an underlying neoplasm. We report a case of a 65-year-old man diagnosed with prostate adenocarcinoma in the setting of severe dysphagia, muscle weakness and a facial erythematous rash. At first, the DM-related symptoms resolved with the initial treatment for the underlying malignancy. Yet, they flared up as the tumor progressed. To sum up, DM is a rare systemic disorder with unknown etiology. There is a well-established association between DM and malignancy. Malignancy-headed therapy can improve DM manifestations and the recurrence of DM symptoms may act as an early warning of malignancy relapse.

## Introduction

Paraneoplastic syndrome (PS) is a rare entity, occurring in up to 8% of cancer patients.<sup>1</sup> Dermatomyositis (DM) is an uncommon idiopathic inflammatory myopathy (IIM) characterized by muscle inflammation and weakness, well-defined cutaneous lesions and systemic complications. The extension of muscle and cutaneous manifestations varies. The reported annual incidence of adult DM ranges from 0.5 to 0.89 per 100,000, affecting mostly middle-aged women. The female to male ratio is 2:1.<sup>2</sup> The majority of cases is idiopathic, but in 15-30% of adult-onset DM cases an underlying malignancy precipitates the PS manifested as DM.<sup>3</sup> Patients with simultaneous DM and cancer have a poor prognosis.<sup>4</sup> Hence, early recognition of this disease is important.

Herein, our rare case of concurrent DM

and prostate cancer underlines two remarkable relationships: DM symptoms improve after cancer-specific therapy and work as an early warning of neoplasm progression. The case makes also clear how the diagnosis of DM in an adult should raise suspicion of an underlying malignancy; this may help to secure timely and safe patient care. This result is particularly impactful as the case concerns the second largest worldwide male malignancy, prostate cancer.<sup>5</sup>

## Case Report

A 65-year-old Cape Verdean, with a past medical history of type 2 diabetes and hypertension, presented with a five-month history of progressive asthenia, dysphagia and tetraparesis. He reported no other systemic symptoms and denied a family history of malignancy.

On examination, the subject showed a fixed painless 2 cm-long left supraclavicular lymph node and a mild periorbital violaceous erythema. Neurological examination revealed reduced symmetrical proximal strength in both upper and lower limbs (3/5). He was unable to rise independently from a seated position and displayed a *waddling* gait. General examination was unremarkable.

A clinical diagnosis of DM was made, supported on raised creatine kinase (CK) of 1450 U/L (reference range <190) and lactate dehydrogenase (LDH) of 580 U/L (reference range 135-225). Myositis-specific antibody panel was positive for the anti-nuclear matrix protein 2 (NXP2), thus corroborating this diagnosis. On further investigation, a computed tomography (CT) scan of the chest, abdomen and pelvis revealed a nodular prostate and enlarged left iliac, para-aortic and supraclavicular lymph nodes (Figure 1). A transperineal prostate biopsy showed a Gleason grade group 5 acinar adenocarcinoma. Therefore, the patient was diagnosed with very high-risk metastatic hormone-sensitive prostate cancer with paraneoplastic dermatomyositis.

Following DM diagnosis, physical rehabilitation, and a five-day course of 2 g/kg bodyweight Intravenous Immunoglobulin (IVIG) was prescribed as the initial therapy. Albeit with some improvement of the skin lesions and pre-admission muscle-associated enzyme levels, the muscle weakness persisted, and he developed the inability to dress himself and perform daily hygiene.

Later, the neoplasm was approached with a combination of abiraterone (1 g/day) with prednisolone (10 mg/day) and andro-

Correspondence: Mafalda Miranda Baleiras, Hospital São Francisco Xavier, Centro Hospitalar Lisboa Ocidental, Estr. Forte do Alto Duque, 1449-005 Lisboa.  
Tel.: +351 913147616  
E-mail: ambaleiras@gmail.com

Key words: Prostate Cancer, Paraneoplastic Syndrome, Dermatomyositis, Myositis-Specific Antibody, Recurrence.

Acknowledgments: We acknowledge the important contribution of the patient willingness to collaborate through the conduction of his case.

Contributions: MMB: literature review and writing of the original manuscript. LM: editing. CV: supervision and resources. FF: writing-review and editing, supervision, and resources. MMP: supervision and resources. AM: supervision and resources. All authors have read and agreed to the published version of the manuscript.

Conflict of interest: The authors declare no potential conflict of interests.

Funding: None.

Ethical approval and informed consent: Informed consent was obtained from the patient.

Availability of data and material: Data and materials are available from the authors upon request.

Please cite this article as: Baleiras MM, Maduro L, Vasques C, et al. Paraneoplastic dermatomyositis and prostate cancer: Myopathy regression under cancer-directed therapy. *Dermatol Rep* 2021;13:9262.

Received for publication: 11 May 2021.

Accepted for publication: 29 July 2021.

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*Dermatology Reports* 2021; 13:9262  
doi:10.4081/dr.2021.9262

gen deprivation therapy made up of leuprorelin (22.5 mg every 12 weeks) and bicalutamide (50 mg/day). His weakness and rash resolved and CK levels normalized as the prostate-specific antigen (PSA) started to decrease progressively from 77.6 ng/ml to 14.8 ng/mL. He finally managed to eat solid consistent food and became fully independent in his daily life activities.

Eight months after the prostate cancer-

directed therapy had begun, blood tests showed elevation of PSA levels (to 40 ng/mL). At the same time, the patient complained again of muscle weakness in the limbs – yet, the neurologic exam revealed no deficit of muscle strength. One month later, a recurrence of the DM clearly emerged including proximal weakness, dysphagia, diffused myalgia and raised CK (439 U/L). A CT scan was conducted and revealed ganglionic progression (Figure 2). The patient was then administered with docetaxel-based (75 mg/m<sup>2</sup> every 21 days) systemic chemotherapy. After the first cycle of chemotherapy, his muscle claims decreased remarkably. The authors keep monitoring this case closely.

## Discussion

DM typically presents with characteristic skin lesions and progressive symmetrical proximal muscle weakness. Myopathy is present in approximately 80% of patients with DM and is usually painless. Dysphagia, dysphonia and aspiration pneumonia may also occur and are associated with a poor prognosis. In addition to pathognomonic cutaneous findings, such as Gottron's papules and heliotrope rash, DM often presents with periungual telangiectasias, poikiloderma and cuticular overgrowth.<sup>6</sup> Lesions can precede or follow myositis and may be pruritic, which normally disturbs life quality.<sup>7</sup>

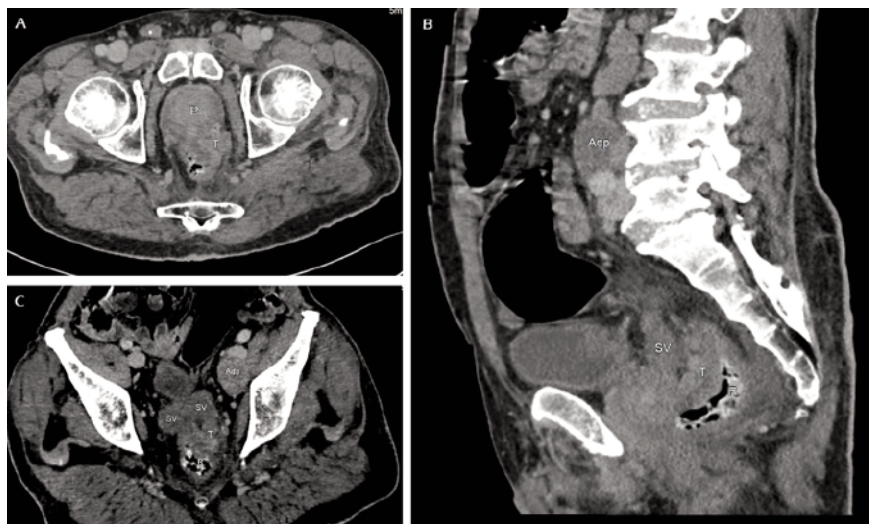
The European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR) criteria for IIM, published in 2017, are a highly sensitive and specific probability-based classification system. A classification tree is then used to assign IIM subtypes.<sup>8</sup> Although its pathogenesis remains unclear, several genetic, immunologic and environmental factors are thought to play a role in DM development.<sup>9</sup> Approximately 70% of DM patients have myositis-specific autoantibodies (MSA) in circulation. Their presence matters for prognosis and clinical management inasmuch as they are associated with distinct clinical phenotypes.<sup>10</sup>

Paraneoplastic dermatomyositis was first described in 1916 and accounts for approximately 30% of dermatomyositis cases.<sup>11</sup> The risk of malignancy is highest within a year of DM diagnosis and remains high for up to five years. A neoplasm can precede, coincide with or follow the diagnosis of DM.<sup>12</sup> Although the precise link between malignancy and DM is poorly understood, cellular and humoral immunologic abnormalities have been suggested. The most frequent associated malignancies

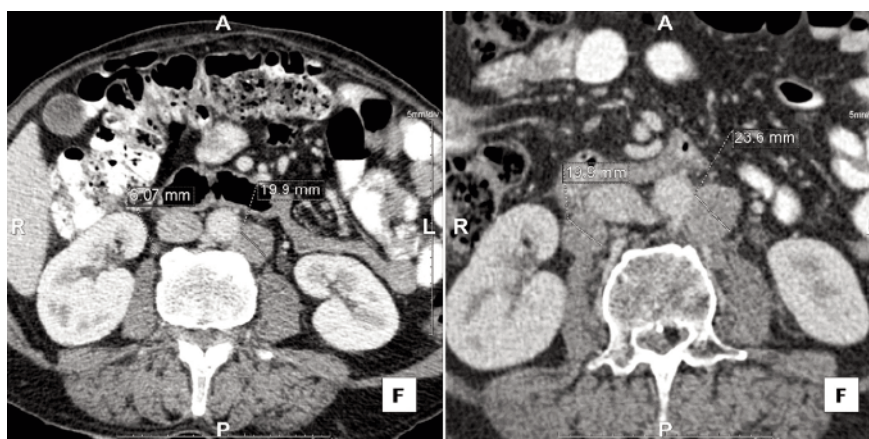
are breast, ovarian, lung, colorectal and Hodgkin's lymphoma. Malignancy-associated DM risk factors are: age over 60, male gender, dysphagia, skin necrosis, cutaneous vasculitis, rapid onset (< weeks), elevated CK and C-reactive protein and an increase in the erythrocyte sedimentation rate (ESR). The association between DM and malignancy is particularly strong in those patients with antibodies to transcription intermediary factor 1γ (TIF1γ) or nuclear matrix protein 2 (NXP2), some of the MSA recently

discovered.<sup>13</sup>

DM treatment goals are the improvement of daily living activities through increased muscle strength and the alleviation of extramuscular manifestations. Systemic corticosteroids are the mainstay of therapy. Second-line therapeutic regimens include methotrexate and azathioprine. If resistance to therapy is developed, rituximab or intravenous immunoglobulin can be used<sup>14</sup>. Supplemental nutrition and rehabilitation are also essential to improve mus-



**Figure 1.** Image A: Oblique axial CT plane shows an enlarged and asymmetric prostate (P) with prominent nodular densities extending posteriorly into the periprostatic space. Transrectal prostate biopsy revealed cancer in this area. Image B: Sagittal CT plane. Image C: different oblique axial CT plane. These latter planes demonstrate the tumor (T) also spreading superiorly, with infiltration of fat between the left seminal vesicle (SV) and the rectum wall (R) and loss of the fat planes between these structures. CT is not accurate to characterize locally the prostatic cancer. MRI is the imaging method for regional staging, but the presence of disseminated disease, shown by non-regional/distant metastatic adenopathies (Adp), made MRI unnecessary.



**Figure 2.** CT images. The right image (Axial CT scan) shows progressive disease with an increase of retroperitoneal lymph nodes, comparing to the CT performed nine months before (left image).

cle strength and endurance. Some studies report improvement of DM symptoms with cancer treatment and the relation of myopathy recurrence with neoplasm relapse, thus supporting a paraneoplastic nature.<sup>15</sup> There are also reports highlighting DM symptom resolution after treatment for the underlying malignancy, thereby avoiding the use of corticotherapy and its side effects.<sup>16,17</sup>

In the current case, the clinical suspicion for DM arose from typical features such as scapular and pelvic girdles muscle weakness, erythematous skin rash and elevated CK. The anti-NXP2 positivity also supported the diagnosis, since this DM-specific autoantibody is present in up to 30% of adult-onset DM. Anti-NXP2 antibodies are associated with heliotrope rash and more extensive myopathy including dysphagia, as observed in our patient. Fiorentino *et al.* reported that 24% of anti-NXP2 positive DM patients had malignancy. This association with cancer is also supported in a Japanese cohort study showing that three out of eight anti-NXP2 positive patients had advanced stage malignancy.<sup>18</sup> The patient hereby considered also met other risk factors for cancer such as male gender, ageing, dysphagia and diabetes. There were two developments in his condition in line with the paraneoplastic origin of DM: i) the significant clinical enhancement with the cancer-directed therapy; and ii) the DM recurrence coincided with the tumor progression.

## Conclusions

To sum up, DM is a rare systemic disorder with unknown etiology. There is a well-established association between DM and malignancy. Thus, the chance of an underlying neoplasm should be ruled out in newly diagnosed DM especially in high-risk patients. A coordinated multidisciplinary approach is essential for early diagnosis and timely treatment to improve the malignan-

cy-associated DM prognosis.

The treatment of the underlying malignancy will usually result in symptom resolution in cases of paraneoplastic DM. It is important to keep in mind that myositis manifestations may relapse in the setting of recurrent or aggravated malignancy. These patients should therefore be monitored closely.

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