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Dermatomyositis associated with capecitabine in the setting of malignancy

To the Editor: Dermatomyositis (DM) is a rare autoimmune condition characterized by cutaneous and muscle inflammation. In addition to malignancy, 24 medications have also been implicated in triggering DM.[1] Herein, we report a new case of DM triggered by oral capecitabine, a prodrug of 5-fluorouracil (5-FU), in the setting of underlying malignancy.

A 76-year-old man with a recent diagnosis of metastatic gastric adenocarcinoma presented with diffuse rash and muscle weakness 2 weeks after receiving a cycle of carboplatin with capecitabine (1 g orally twice daily). He had previously received 1 infusion of carboplatin alone 3 weeks before this cycle without any adverse effects. On examination, the patient was noted to have poikilodermatous plaques with shallow erosions scattered in a V-distribution on his upper chest and upper back (Fig 1). His hands contained erythematous, scaly papules symmetrically distributed over the metacarpophalangeal and interphalangeal joints (Gottron papules) as well as periungual erythema (Fig 1). Muscle strength testing revealed severe proximal weakness of the lower extremities, leading to an inability to ambulate. No electromyography (EMG) was conducted in this case.

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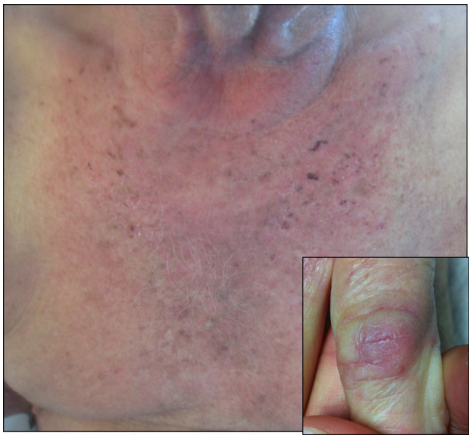

Fig 1. Dermatomyositis, clinical images. Erosive erythematous patches on chest. Inset shows erythematous papules on interphalangeal joints (Gottron sign) and periungual erythema.

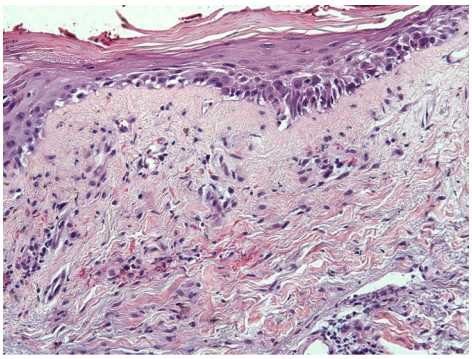

Fig 2. Dermatomyositis, histopathology. Punch biopsy of poikilodermatous erosive plaque on the shoulder shows an interface dermatitis with mild spongiosis, epidermal necrosis, and subepidermal vesicle formation. (Hematoxylin-eosin stain; original magnification ×20.)

Laboratory analysis revealed an elevated creatine kinase (CK) of 2630 U/L, aldolase of 10.9 U/L, erythrocyte sedimentation rate (ESR) of 66 mm/hr, C-reactive protein (CRP) of 1.46 mg/dL, and lactate dehydrogenase (LDH) of 294 IU/L. Results were negative for antinuclear antibody (ANA), anti-Jo, and anti-centromere antibodies. A punch biopsy of the shoulder revealed an interface dermatitis with mild spongiosis, epidermal necrosis, and subepidermal vesicle formation (Fig 2). Thus, clinical, laboratory, and histopathologic findings were consistent with a diagnosis of DM. Capecitabine was discontinued and oral prednisone was initiated, resulting in reduction in CK level to 698 U/L and improved strength and ability to ambulate. The patient was discharged home. Due to the oncologic need to treat the patient's gastric adenocarcinoma, he was restarted

on a cycle of carboplatin and capecitabine 13 days later. After reinitiation of capecitabine 1 g twice daily, the patient was readmitted to the hospital with a CK of 938 U/L. This time, he experienced a flare of his rash on his chest and back, accompanied by severely worsened proximal lower extremity weakness and dysphagia. Upon admission, capecitabine was withheld, and both intravenous methylprednisone (80 mg per day) and intravenous immunoglobulin (2 g/kg over 2 days) were initiated; his condition improved.

We report a novel case in which rechallenge with capecitabine resulted in a DM flare following interval corticosteroid therapy. DM has previously been controversially associated with 5-FU, in that 2 cases have been previously reported, but it remains unclear if this was due to the 5-FU or was incidental to the malignancy.[2,3] Our patient underwent rechallenge of capecitabine, with relapse of cutaneous and muscular symptoms, definitively implicating this 5-FU prodrug as triggering DM in the setting of underlying malignancy. We hypothesize that DM triggered by capecitabine and, likely, 5-FU may require the hypermetabolic state of cancer and the release of tumor antigens. However, it may be challenging to distinguish whether medication or underlying malignancy is the inciting cause of DM, in that both may result in an inflammatory myopathy with similar pathophysiology and cutaneous findings. Researchers have found that statins are associated with the production of autoantibodies against targets related to muscle differentiation and regeneration.[4] It is possible that capecitabine may directly lead to an inflammatory response causing DM in a similar way as statins. Patients with cancer treated with capecitabine who present with skin rash and muscle weakness should be promptly evaluated for potential DM.

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