Pembrolizumab-Induced Neutrophilic Dermatosis of the Dorsal Hands

Rabia Z Mayer1*, George Ansstas2 and Milan J Anadkat1

1Division of Dermatology, Washington University School of Medicine, USA
2Division of Oncology, Washington University School of Medicine, USA

Abstract

The prognosis for advanced and metastatic malignancies has been significantly altered due to the use of checkpoint inhibitors. Due to the activation of CD4+/CD8+ cytotoxic T-cells, these drugs have a unique spectrum of adverse effects, of which cutaneous manifestations are the most common. This case report describes the first instance of pembrolizumab-induced neutrophilic dermatosis of the dorsal hands, a rare and localized variant of Sweet’s syndrome in a patient being treated for metastatic melanoma.

Introduction

The use of immune checkpoint inhibitors has revolutionized the therapeutic approach for advanced malignancies. Pembrolizumab is a monoclonal antibody targeted against programmed cell death protein-1 (PD-1) which was initially approved in 2015 for unresectable or metastatic melanoma [1]. Due to its unique mechanism of action, immune related adverse effects may result, with cutaneous adverse effects being the most prevalent [2]. The morphology of cutaneous eruptions that have been reported vary. Most commonly, eczematous, psoriasiform, or lichenoid dermatoses occur, each with underlying pruritus. In addition, autoimmune reactions such as vitiligo, alopecia areata, dermatomyositis, and bullous pemphigoid have been reported [2]. Here we report a case of Neutrophilic Dermatosis of the Dorsal Hands (NDDH) as a novel cutaneous adverse effect of pembrolizumab.

Case Presentation

A 63 year old male with a history of recurrent and metastatic desmoplastic melanoma receiving treatment with pembrolizumab for six months presented with a two-week history of an exquisitely painful rash on the dorsal hands. The patient reported using topical silver sulfadiazine for the past two days without significant improvement. Physical exam revealed tender, erythematous, ulcerated and bullous plaques over the dorsum of both hands (Figure 1). A punch biopsy was performed, revealing a diffuse infiltrate of neutrophils throughout the upper part of the dermis with subepidermal edema (Figure 2). Staining for microorganisms and fungi was negative, and a diagnosis of neutrophilic dermatosis of the hands was confirmed. A complete blood count revealed neutrophilia and leukocytosis. Of note, the patient did not endorse any fever.

The patient was started on high dose oral steroids (prednisone 60 mg daily) and follow up in a week revealed significant improvement (Figure 3), at which point a rapid taper over the ensuing two weeks was instituted along with initiation of dapsone, with no evidence of relapse on subsequent clinic visits.

Discussion

Neutrophilic dermatosis of the dorsal hands is considered a localized and rare subtype of acute febrile neutrophilic dermatosis (Sweet’s syndrome). It was first described in 1995 as a pustular vasculitis [3] and later renamed based on the dense neutrophilic infiltrate ubiquitously present in the dermis without vasculitis being a constitutive feature [4]. While several cases of Sweet’s syndrome have been documented with the use of ipilimumab (CTLA-4 inhibitor) (Table 1), no documented evidence of localized acral variants occurring with pembrolizumab exist in the literature thus far.

Activated T-cells can be inactivated by the interaction of programmed cell death 1 (PD-1) with its ligand (PD-L1) that is expressed in peripheral tissues and tumors [5]. Immune checkpoint inhibitors like pembrolizumab serve to inhibit PD-1, thereby promoting anti-tumor activity via
literature on neutrophilic dermatosis of the dorsal hands elucidates most common associations with hematologic malignancies, solid organ tumors, inflammatory bowel disease or antecedent infections [8]. This case is the first report of NDDH induced by pembrolizumab.

It is important for dermatologists and oncologists to be aware of this entity as this clinical presentation may commonly be misdiagnosed as an infectious process, which could result in undue cessation of therapy for advanced or metastatic disease. Most cases of neutrophilic dermatoses are highly sensitive to treatment with systemic steroids as was illustrated in our case as well as steroid-sparing agents like dapsone, colchicine and tetracyclines with good prognosis overall.

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References


