Grover disease associated with docetaxel chemotherapy

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INTRODUCTION

Grover disease (GD) is an acantholytic disorder that primarily affects middle-aged Caucasian men and causes erythematous skin eruptions in the form of papules or vesicle-papules on the upper portion of the trunk and proximal parts of extremities.[1] The pathogenesis and etiology of GD, also commonly called transient acantholytic dermatosis, are poorly understood. In some cases, malignancy has been speculated to be a cause; however, most of these cases are rather associated with chemotherapy.[2,3] Specifically, chemotherapeutic agents such as daunorubicin, cytarabine, idarubicin, and etoposide have been previously reported to be associated with GD.[4,5] Here, we present a case of GD induced by the chemotherapeutic agent docetaxel.

Abbreviations used:

GD: Grover disease
TCS: topical corticosteroid

CASE REPORT

A 73-year-old man on leuprolide for metastatic prostate cancer presented to the dermatology clinic with a rash on his chest for approximately 2 weeks. The rash was mildly pruritic. The patient denied being bedridden or starting any new personal care products but did report starting chemotherapy with intravenous docetaxel 75 mg/m^2 2 weeks prior to the onset of the rash. He denied taking any other new medications or a previous history of similar rashes. Physical examination revealed erythematous papules and eroded macules on the upper and medial portions of his chest (Fig 1) without any pustules or involvement of his back. The clinical differential diagnosis included GD, miliaria rubra, folliculitis, demodicosis, and *Pityrosporum* folliculitis. A punch biopsy of a representative lesion on his chest showed hyperkeratosis, parakeratosis, focal epidermal suprabasilar acantholysis, and dyskeratosis without significant spongiosis (Fig 2). The clinical and histopathologic findings were consistent with a diagnosis of GD. The patient was started on treatment with fluocinonide 0.05% cream and experienced a nearly complete resolution of the rash within 2 weeks. The patient was able to undergo 2 additional cycles of treatment with docetaxel without a recurrence of the rash. A month later, he was switched to chemotherapy with carboplatin and cabazitaxel because of progression of the metastatic prostate cancer. However, the patient was subsequently lost to follow-up.

DISCUSSION

The incidence of GD is 0.8% in hospitalized patients, predominantly affecting White men, with a gender ratio of 2.4:1 and a mean age of 61 years.[6] The rash generally occurs on the trunk and proximal parts of extremities as papules and papulovesicles with pruritus.[4] GD is a more accurate, all-encompassing description than transient acantholytic dermatosis because many cases are not transient but persistent and recurrent.[3] Quirk and Heenan[7] describe 3 different variants of the disease: (1) transient eruptive—sudden and severe pruritus that negatively impacts the quality of life and lasts only a

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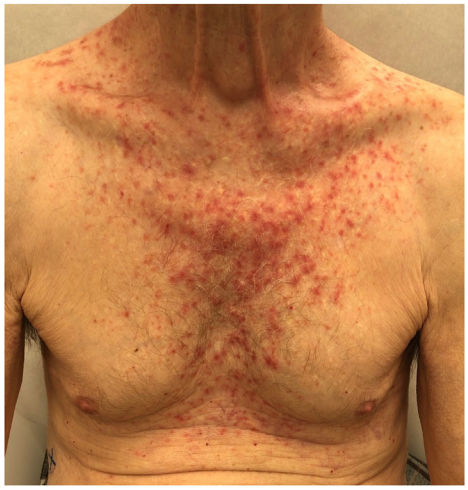

Fig 1. Initial presentation of the patient with erythematous papules and eroded macules on the upper and medial portions of the chest.

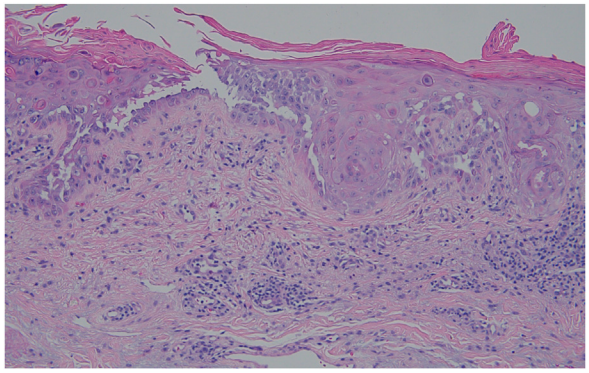

Fig 2. Histopathology showing focal epidermal suprabasilar acantholysis and dyskeratosis as well as variable spongiosis. (Hematoxylin-eosin stain; original magnification: ×20.)

few weeks; (2) persistent pruritic—pruritus of moderate severity that persists for months to years; and (3) chronic asymptomatic—persistent papules without pruritus that may go untreated. Our patient's presentation was most consistent with the transient eruptive form, although he reported his pruritus to be milder than what this variant often presents as. Other chemotherapeutic agents associated with GD include daunorubicin, cytarabine, idarubicin, and etoposide. Similar to our case, the onset of the rash in these cases was approximately 2 weeks after the induction of chemotherapy.[4,5] Drugs of different classes associated with GD include anastrozole, penicillamine, ipilimumab, 2-chlorodeoxyadenosine, ribavirin, vemurafenib, dabrafenib, sulfadoxine-pyrimethamine, and recombinant interleukin 4.[8,9] Although malignancy is the most commonly associated condition for GD, most often GD develops in patients with malignancy shortly after they receive chemotherapy.[3] Although the mechanism for chemotherapy-associated GD is not known, one proposed mechanism of this is the chemotherapeutic agent's accumulation in the eccrine sweat glands, where it leaks into and alters the epidermis to manifest as acantholysis and dyskeratosis.[2] Other associated causes include end-stage renal disease, hemodialysis, bone marrow transplantation, sweating, heat exposure, bedbound hospitalization, and ultraviolet and ionizing radiation.[1]

Histologically, GD is characterized by variable degrees of hyperkeratosis, parakeratosis, acantholysis, dyskeratosis, and spongiosis in predominantly 4 classical patterns: (1) Hailey-Hailey–like, (2) Darier-like, (3) pemphigus-vulgaris–like, and (4) spongiotic-dermatitis–like diseases.[9] Typically, there is a superficial perivascular lymphomononuclear infiltrate with variable numbers of eosinophils within the dermis.[2,10] Patients may present with 1 variant throughout their dermatoses or exhibit multiple histologic patterns in a single biopsy. Recently, additional histologic variants have been recognized and described as lichenoid, lentiginous, porokeratotic, vesicular, pseudoherpetic, bullous, and dysmaturative.[9]

With regard to the treatment options, topical corticosteroids (TCSs) are the most common treatment agent, and both TCSs and oral retinoids are highly effective at symptom regression.[1,10] For cases of persistent and refractory GD, providers may consider combining TCSs and oral retinoids. Typically, the clinical course can range from days to years, and the factors that may cause an early regression or long persistence of symptoms remain unclear. In their review, Bellinato et al[1] found that 42% of the 211 cases that they reviewed showed resolution without treatment within a time range of 1 week to 8 months. In a review by Davis et al,[10] at the Mayo Clinic, a follow-up of 28 patients with GD revealed that 43% of the patients' symptoms completely resolved, whereas 11% persisted and 46% recurred. Some cases of chemotherapy-related GD that have been described have resolved spontaneously or with the use of TCSs and, similar to our case, have remained clear despite continued treatment with the same chemotherapeutic agent.[2,8]

To our knowledge, this association between GD and docetaxel is previously unrecognized. This case serves to inform clinicians of the association between GD and chemotherapy and further demonstrates the need for GD to be considered in the differential diagnosis for patients presenting with a rash while undergoing care for a malignancy.

Conflicts of interest

None disclosed.

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