Atypical features and systemic associations in extensive cases of Grover disease: A systematic review

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Background: Grover disease is an acantholytic disorder that typically occurs on the trunk of older individuals, primarily white men, in association with heat and xerosis. Cases with extensive and/or atypical distributions have been reported.

Objective: To review the literature characterizing the population, morphology, associations, and disease course of extensive or atypical eruptions of Grover disease.

Methods: A systematic literature review identified 50 articles with 69 cases.

Results: Patient age ranged from 14 to 83 years (mean age, 56 ± 15), with 71% of patients being male and 29% female. Areas of involvement included the trunk (90%), upper and lower extremities (63% and 61%, respectively), face/scalp (28%), neck (21%), groin (11%), buttocks (8%), and axillae (6%). The most common associations included a history of malignancy (61%), recent chemotherapy (38%), and recent transplant (20%).

Limitations: Extensive cases with typical clinical morphology may not have been examined by biopsy or reported; thus, this review may have publication bias toward more severe or atypical presentations.

Conclusions: Greater variability exists among patients affected by extensive or atypical Grover disease than among those with typical disease. Malignancy is a common association, and there may be a role for immunosuppression in the pathogenesis of extensive or atypical Grover disease. (J Am Acad Dermatol 2017;77:952-7.)

Key words: atypical; extensive; Grover disease; malignancy; toxic erythema of chemotherapy; transient acantholytic dermatosis.

Grover disease, first described by Ralph W. Grover in 1970,[1] is a relatively common skin condition characterized by pruritic, acuminate papules ranging from the color of normal-appearing skin to pink and papulovesicles on the trunk. The key histopathologic finding of Grover disease is acantholysis of keratinocytes.[2] It generally affects white men older than 40 years. Despite the term *transient,* the eruption in transient acantholytic dermatosis may or may not actually be transient.[3]

Abbreviations used:

TEC: toxic erythema of chemotherapy
UV: ultraviolet

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The etiology and pathogenesis are not clearly elucidated; however, the course is generally benign.

Cases of extensive or atypically distributed (trunk plus ≥1 additional area of the body or nontruncal location) Grover disease have been previously reported. One small case series reported extensive Grover disease in association with chemotherapy induction for hematopoietic stem cell transplant,[4] hypothesizing that this condition may be a manifestation of toxic erythema of chemotherapy (TEC).[5] Features of extensive or atypically distributed Grover disease and its systemic associations are not known. In this systematic review we describe the epidemiology, morphology, associations, and course of extensive or atypically distributed Grover disease on the basis of 50 articles reporting 69 cases as well as 3 unpublished cases.

CAPSULE SUMMARY

- Classic Grover disease is a benign truncal eruption associated with heat and xerosis.
- Extensive cases of Grover disease have clinical features distinct from those of classic disease and may be associated with malignancy, chemotherapy, and immune suppression.
- Atypical Grover disease should be recognized as a benign condition that may occur among immunosuppressed and systemically ill patients.

METHODS

Search strategies

To better characterize extensive Grover disease presentations, a comprehensive search of English-language literature was performed in PubMed, EMBASE and Ovid MEDLINE. The following search terms were included: ((("Grover disease" [Supplementary Concept]) OR (Grover disease)) OR "Transient acantholytic dermatosis") AND ((extensive or widespread or disseminated or acral or arm? or leg? or hand? or foot or feet or palm? or sole? or groin or ((upper or lower) adj extremit*) or neck or face or head or scalp)). Bibliographies of select publications were reviewed for eligible studies.

Data sources

Data sources included case reports or series published between 1970 (the year in which Grover disease was first described[1]) and 2016. Inclusion criteria required biopsy-confirmed Grover disease and an extensive or atypical distribution. Extensive distribution was defined as including at least 1 area of the body in addition to the trunk. Atypical distribution was defined as involving at least 1 nontruncal area of the body. Studies that did not satisfy the diagnostic and clinical criteria were excluded (Supplemental Fig 1; available at http://jaad.org). A total of 69 cases were identified for inclusion from 50 articles that met the criteria. Three unpublished cases seen at the University of California, San Francisco were also included, for a total of 72 cases.

Data extraction

Data collected included age, sex, ethnicity, medical issues, medications, timing of rash onset relative to other factors, fever, excessive perspiration, hospitalization, morphology, distribution, biopsy number and site, histopathology, treatments and clinical course. Available reported information was used to calculate mean age and percentages.

RESULTS

Patient population

Patients with extensive Grover disease were older (mean age 56 ± 15) relative to those with typical disease and predominantly male (71%). In the reports describing ethnicity (n = 35), the majority of patients were white (74%), followed by Asian[6-9] (14%), African American[10,11] (6%), Middle Eastern[12] (3%), and Hispanic (3%).

Clinical presentation

The majority of patients presented with an eruption affecting more than 1 area of the body (94%) (Table I). Truncal involvement was reported in 90% of cases (Fig 1). The most common nontruncal areas of involvement were the upper and lower extremities (63% and 61%, respectively) (Fig 2), followed by the face/scalp (24%), neck (21%),[7,8,13-24] groin (11%),[4,8,11,23-25] buttocks (8%),[11,23,24,26,27] and axillae (6%).[15,23,24,28] Rarely involved areas included the palms,[12,13] soles,[12] ear,[13] and oral mucosa.[20] Additional reported patterns of distribution included dermatomal,[28,29] along Blaschko lines,[6,30] and around the port of radiation therapy.[31]

Morphology was reported for 65 patients, many of whom presented with polymorphic lesions. The most common morphologies were papular (94%) and papulovesicular (35%). Bullous variants were infrequently reported (8%).[12,23,24] Five cases were described as an eruption superimposed on solar lentigines.[16,32,33] Papulopustular[34] and plaque-like[9] variants were also reported.

Rash symptoms were described for 55 patients. The predominant symptom was pruritus (76%). The remaining 24% of patients were asymptomatic.

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