

Tocilizumab Treatment in COVID-19 Patients: Comparing Cutaneous Disease and Adverse Drug Effects

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ABSTRACT

Actemra (tocilizumab) received emergency use authorization for the treatment of coronavirus disease 2019 (COVID-19) in June 2021. Literature has linked numerous cutaneous adverse effects to tocilizumab. In this current survey, investigators reviewed and compared these adverse effects to the common cutaneous manifestations of COVID-19. While similarities in patient presentation exist, important distinctions are made to aid dermatologists in their clinical diagnosis.

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INTRODUCTION

Over 40 million cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), have been reported in the United States (US).¹ Pulsipher et al.² previously compared the cutaneous manifestations of COVID-19 and adverse effects of remdesivir, an antiviral drug approved by the US Food and Drug Administration (FDA) for SARS-CoV-2. This present survey of Actemra (tocilizumab), a recombinant humanized interleukin 6 (IL-6) receptor antagonist, aims to distinguish COVID-19 disease manifestations from adverse drug reactions.³

Tocilizumab, FDA-approved for rheumatoid arthritis, giant cell arteritis, juvenile idiopathic arthritis, and cytokine release syndrome, received emergency use authorization for hospitalized COVID-19 patients requiring oxygen, mechanical ventilation, or extracorporeal membrane oxygenation.⁴ Tocilizumab may lower risk of mortality, hospital length of stay, and mechanical ventilation requirements.⁵

Cutaneous changes from COVID-19 and tocilizumab are reported in the literature and summarized in Table 1. Tocilizumab adverse reactions include serious skin infections (i.e., cellulitis and necrotizing fasciitis) and cutaneous eruptions.⁶⁻⁸ Maculopapular

TABLE 1.

Summary of Cutaneous Manifestations Observed in COVID-19 Compared to Adverse Drug Reactions from Tocilizumab Treatment Based on Current Peer-Reviewed Literature

Cutaneous Manifestations	
COVID-19 Morphology	Tocilizumab Adverse Reactions
Maculopapular eruptions ⁹	Cellulitis ⁷
Pseudo-chilblain lesions ⁹	Necrotizing fasciitis ^{6,7}
Urticaria ⁹	Urticaria ⁷
Polymorphic diffuse or localized monomorphic vesicles ⁹	Cutaneous sarcoidosis ⁷
Acral vesicular-pustulous lesions ⁷	Maculopapular eruptions ^{7,8}
Livedo ⁹	Pustulous lesions ^{7,8}
Petechiae ¹⁰	Skin ulcer ⁸
Erythema multiforme ⁹	Psoriasiform eruptions ⁸

rash and urticarial lesions characterize the prominent cutaneous manifestations of COVID-19.^{9,10}

A cross-sectional study of tocilizumab treatment for COVID-19 reports associated morbilliform (10% of n=80) and other maculopapular (2.8% of n=36) eruptions.¹¹ Prospective cohort analysis (n=51) similarly found a nonspecific cutaneous

rash necessitating drug discontinuation in one patient.¹² Furthermore, development of a pruritic generalized cutaneous toxic erythematous rash with eosinophilia (similar to DRESS syndrome) was also reported in a SARS-CoV-2 patient receiving tocilizumab treatment.¹³

As cutaneous manifestations of COVID-19 and adverse dermatologic reactions of tocilizumab overlap, distinguishing disease and drug effects is imperative. Sharing and reporting cutaneous findings will be an important role of dermatologists as we deepen our understanding of novel SARS-CoV-2 manifestations. As cases of SARS-CoV-2 continue to rise, increased use of tocilizumab will require greater attention to potential cutaneous toxicity.

DISCLOSURES

Dr Dellavalle is Editor in Chief of Journal of Medical Internet Research Dermatology, a Joint Coordinating Editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a Social Media Editor for the *Journal of the American Academy of Dermatology (JAAD)*, and a Podcast Editor for the *Journal of Investigative Dermatology (JID)*. He is a coordinating editor representative on *Cochrane Council*.

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