REVIEW ARTICLE

Sarcoidosis-Like Reactions Induced by Checkpoint Inhibitors

Ioannis Gkiozos, MD, PhD,[a,*] Alexandra Kopitopoulou, MD,[a] Alexandros Kalkanis, MD, PhD,[b] Ioannis N. Vamvakaris, MD,[c] Marc A. Judson, MD,[d] Konstantinos N. Syrigos, MD, PhD[a]

[a]*Third Department of Medicine, Athens Medical School, National & Kapodistrian University of Athens, Athens, Greece*
[b]*Division of Pulmonary and Critical Care Medicine, 401 Military and VA Hospital, Athens, Greece*
[c]*First Pathology Department, Athens Medical School, National & Kapodistrian University of Athens, Athens, Greece*
[d]*Division of Pulmonary and Critical Care Medicine, Albany Medical College, Albany, New York*

ABSTRACT

Immune checkpoint inhibitors (ICIs) are a newly developed component of cancer care that expands the treatment possibilities for patients. Their use has been associated with several immune-related adverse events, including ICI-induced sarcoidosis-like reactions. This article reviews the data concerning ICI-induced sarcoidosis-like reactions currently available in the medical literature. These reactions have been reported in three classes of ICIs: anti–cytotoxic T-lymphocyte associated protein 4 antibodies, programmed death 1 inhibitors and programmed death ligand 1 inhibitors. These reactions are indistinguishable from sarcoidosis with a similar histology, pattern of organ involvement, and pattern of clinical manifestations. The most common locations to observe granulomatous inflammation from these reactions is in intrathoracic locations (the lung and/or mediastinal lymph nodes) and the skin. The median time between initiation of an ICI and the development of a sarcoidosis-like reaction averaged 14 weeks. Clinicians have opted to use corticosteroids and/or discontinue the ICI, or take no action when these reactions have developed. Regardless of whether the clinician performed an intervention or not, these reactions have uniformly improved or resolved after ICI-treatment, which provides additional temporal evidence supporting the presence of a sarcoidosis-like reaction as opposed to sarcoidosis. There is even evidence that the development of an ICI-induced sarcoidosis-like reaction suggests that the ICI is effective as an anti-tumor agent and should be continued. As is the case for sarcoidosis, sarcoidosis-like reactions do not mandate antisarcoidosis therapy, especially if the condition is asymptomatic. When treatment of sarcoidosis-like reaction is required, it may be prudent to continue ICI therapy and add antisarcoidosis therapy because standard antisarcoidosis regimens seem to be effective. Further research into the mechanisms involved in the development of ICI-induced sarcoidosis-like reactions may give insights into the immunopathogenesis of sarcoidosis.

Keywords: Checkpoint inhibitors; Immune-related adverse events; Sarcoidosis-like reactions

Introduction

Several drugs have been associated with the development of syndromes indistinguishable from sarcoidosis that are described as "sarcoidosis-like reactions." Because the exact immunopathogenesis of sarcoidosis is unknown, it is not clear if these drugs are truly causing sarcoidosis, rendering the immune system more susceptible to the development of sarcoidosis, or are distinct entities from sarcoidosis. Drugs associated with sarcoidosis-like reactions include interferon-α, highly active antiretroviral therapy, and tumor necrosis factor alpha antagonists.[1-10]

Immunotherapy is a newly developed component of cancer care that expands the treatment possibilities for

*Corresponding author.

Disclosure: Dr. Gkiozos has received personal fees from Boehringer Ingelheim, Bristol-Myers Squibb, and Roche. Dr. Kopitopoulou has received personal fees from Bristol-Myers Squibb. Dr. Judson has received grants from Mallinckrodt Pharmaceuticals and Novartis; and he has received personal fees from Biogen.

Dr. Syrigos has received grants from Boeringer Ingelheim, Bristol-Myers Squibb, Merck Sarono, and Roche; and has received personal fees from Roche, Bayer, Astra Zeneca, and MSD. The remaining authors declare no conflict of interest.

Address for correspondence: Ioannis Gkiozos, MD, PhD, 3rd Department of Medicine, Athens Medical School, National & Kapodistrian University Of Athens, Mesogion 152, 11527, Athens, Greece. E-mail: yiannisgk@hotmail.com

ISSN: 1556-0864

https://doi.org/10.1016/j.jtho.2018.04.031