Title: Relationship between clinical diagnoses and pathology findings among patients with cutaneous immune-related adverse events

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Abstract

Background: Cutaneous immune-related adverse events (cirAEs) represent one of the most common and heterogeneous side effects of immune checkpoint inhibitor (ICI) therapy, impacting more than a third of patients. Though cirAEs may morphologically mimic "wild-type" skin diseases (i.e. psoriasis), these reactions can differ from their wild-type counterparts in timeline, severity, and treatment responsiveness. Despite these known differences, cirAEs are rarely biopsied in clinical practice and linkages between presumed clinical diagnoses and pathologic diagnoses remain under-explored.

Methods: Epic billing data and pathology requisition codes were used to identify patients who received ICI therapy and underwent skin biopsy at our institution between May 25, 2011 and November 1, 2019. Clinicopathologic findings for each patient were then reviewed, with exclusion of biopsies occurring prior to ICI start date as well biopsies of non-cirAEs. For each patient with one or more biopsied cirAE, data was collected from the electronic medical record delineating each patient's demographic profile, cancer history, and cirAE episodes. Existing hematoxylin and eosin slides from each biopsied cirAE were also re-reviewed to identify granular histopathologic features. Descriptive statistics were then used to summarize clinicopathologic features and agreement between pre-biopsy clinical diagnoses and histopathology findings.

Results: Of the 3,193 patients who received a checkpoint inhibitor at our institution between 2011 and 2019, 43 (1.4%) had a biopsied cirAE. Three-quarters of these cirAEs (74.4%) had at least one atypical histopathological feature, and in approximately half of cases (48.8%), the histopathology was not consistent with the treating dermatologist's clinical impression at the time of biopsy. Nearly half of patients received systemic immunosuppression (46.5%) for their biopsied cirAE, with a substantial proportion (9.3%) receiving doses exceeding 1 mg/kg daily prednisone for one week or longer.

Conclusions: Despite substantial discordance between presumed clinical diagnoses and histopathological findings, cirAEs were rarely biopsied. To support early cirAE identification and optimize treatment, more frequent biopsy of suspected cirAEs may be merited.