Acute Coronary Syndromes

IMMUNOLOGICAL MECHANISM AND HISTOLOGIC CHARACTERISTICS OF CLOPIDOGREL HYPERSENSITIVITY

Poster Contributions
Poster Sessions, Expo North
Monday, March 11, 2013, 9:45 a.m.-10:30 a.m.

Session Title: ACS Therapy: Basic and Translational
Abstract Category: 3. Acute Coronary Syndromes: Therapy
Presentation Number: 1301-204

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Background: Hypersensitivity reactions to Clopidogrel (CS) are seen in 2-3% of treated patients and commonly present as a diffuse erythematous rash. Despite significant morbidity associated with CS in susceptible individuals, the immunologic mechanism responsible for CS are poorly understood. In this report, we describe the histological characteristics and delineate the immunologic basis of CS.

Methods: After informed consent, consecutive patients with CS underwent punch biopsy of the affected area for histologic characterization and immunostaining. The hematoxylin and eosin stained sections were used for histologic characterization and antibodies against CD4, CD8, CD1a, CD68 and caspase-3 were used to determine the immunologic response in CS. Qualitative review by an experienced pathologist and quantitative assessment in a blinded manner was performed to assess the severity and type of immunologic response in affected tissue.

Results: A total of 66 patients were diagnosed with CS during the study period and immunologic characterization completed in 19 (29%) patients. The microscopic examination demonstrated perivascular lymphocyte and histiocytic infiltration in superficial and mid layers of the dermis. Spongiosis and focal parakeratosis were observed within epidermal regions. Both qualitative and quantitative assessment were consistent and demonstrated marked infiltration of T lymphocytes (CD4+ and CD8+), dendritic cells (CD1a+) and presence of macrophages (CD68+) in the affected tissue. Caspase-3 staining was characteristically absent.

Conclusions: CS is caused by type IV, delayed type hypersensitivity immune response and suggests the presence of prior sensitization to active or inactive ingredients in clopidogrel. Delayed hypersensitivity response via activation of dendritic cells have been previously described for heparin and iodine contrast media but reported here for the first time with a thienopyridine.