

Abstract Information

First Name :	Ahmed Olalekan
Last Name :	Bakare
Email :	abakare6@jh.edu
Address :	Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, School of Medicine; Baltimore, MD, 21205, USA
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Title :	An assessment of T-cell involvement in CIPN
Co-Authors :	Eellan Sivanesan, Johns Hopkins University, School of Medicine; USA

Abstract :

Background and Objectives: Conflicting reports on the role of T cells in chemotherapy-induced peripheral neuropathy (CIPN) create uncertainty regarding their influence on neuropathic pain, hindering progress in CIPN treatment and prevention. This study compares T-cell competent (RNU+/-) and T-cell deficient (RNU-/-) rats to explore the role of T cells in painful paclitaxel (PTX)-induced peripheral neuropathy (PIPn).

Methods: Adult male, T-cell competent and T-cell deficient rats were treated with paclitaxel (8 mg/kg i.p. total dose) in a model of non-squamous cell lung carcinoma. Reflexive (mechanical, heat, cold) and spontaneous (burrowing, gait, open field) pain behaviors were evaluated before and after the induction of PIPn. Immunohistochemistry (CD206, CD68, CX3CL1, CX3CR1) and flow cytometry (CD3, CD161a, CD45RA, CD163, CD86) were employed to assess macrophages and lymphocytes in the dorsal root ganglia (DRG), sciatic nerves, and spleen.

Results: Our findings demonstrate that T cells are essential for the development of PTX-induced cold hypersensitivity. T cells delayed the onset of mechanical hypersensitivity and decreased burrowing activity. Flow cytometry revealed an increased CD4+/CD8+ T-cell ratio in paclitaxel-treated T-cell competent rats in the DRG, sciatic nerve, and spleen. Additionally, paclitaxel treatment led to a reduction in B cells and a shift in macrophage polarization towards the M1 phenotype, reducing the M2/M1 ratio, which was independent of T cells. However, an increase in M2 macrophages (M2[?] and M2a) in sciatic nerves was

dependent on the absence of T cells. NK cell levels were reduced in paclitaxel-treated T-cell deficient rats but remained unchanged in T-cell competent rats.

Discussion: T cells are essential for the development of cold hypersensitivity and reduce mechanical hypersensitivity and spontaneous pain at the onset of CIPN. These T-cell dependent effects may be mediated by an increased CD4+/CD8+ T-cell ratio, decreased M2? macrophages in sciatic nerves, and maintenance of NK cells in T-cell competent rats.

Key words: Carcinoma, chemotherapy-induced peripheral neuropathy, macrophage, T cells, pain