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Indium-labelled Autologous Dendritic Cells Migrate to Local Lymph Nodes after Intratumoural Injection in Head and Neck Cancer Patients

Sir - The various functions of dendritic cells in a tumour microenvironment may be compromised by tumour-associated factors and regulatory T cells and thereby limit their ability to generate anti-tumour responses in human cancers [1]. This study established whether monocyte-derived dendritic cells injected into primary tumours were capable of overcoming this environment and migrating to local lymph nodes.

Dendritic cells were generated from CD14þ monocytes from two patients with head and neck cancer using granulocyteemacrophage colony-stimulating factor and interleukin-4 and labelled with indium-111. The two patients in this study were both males with clinically visible and accessible head and neck tumours to allow direct injection of labelled dendritic cells (Fig. 1). Informed consent and ethical approval was obtained for this study.

Dendritic cells were cultured from peripheral blood monocytes and labelled in an aseptic blood handling isolator in a grade A sterile environment. Indium-111 was chosen as the isotope for labelling because the half-life of 65 h allows the analysis of the in vivo distribution of dendritic cells for several days, but also minimises exposure of the patient to radiation. Neither the phenotype nor the potent allostimulatory activities of the dendritic cells were altered by radiolabelling. Images were undertaken using gamma camera imaging for both patients at 30 min, 45 min, 60 min, 2 h, 4 h and 24 h. For patient 1, a positive signal in the local lymph node was detected within 3 h (Fig. 2). Marked activitywas still present in the primary tumour at 24 h. For patient 2 there was some inhibition of dendritic cell migration, as the first evidence of tracking to local lymph nodes was at 24 h, but marked activity within the primary tumour persisted at 24 h. Large numbers of dendritic cells were observed in immunohistochemical sections in the resected lymph node by HLA-DR staining (Fig. 3).

The clinical relevance of dendritic cells at the site of the tumour remains a matter of debate regarding their role in the generation of successful anti-tumour immune responses in human cancers. Our findings suggest that intratumoural dendritic cells may be used as a vehicle to deliver antigenic peptides or therapeutic drugs and expect a proportion to track to regional nodes to prime T-cell responses. In future, Intratumoural delivery of antigen-presenting cells may be a potential method for overcoming immune tolerance by injecting immature unmodified dendritic cells into tumours in the neoadjuvant setting, attempting to generate antitumour primary immune responses in local nodes.

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Reference

[1] Strauss L, Bergmann C, Szczepanski M, et al. A unique subset of CD4þ CD23highFoxp3þ T cells secreting IL10 and TGFbeta1 mediates suppression in the tumour microenvironment. *Clin Cancer Res* 2007;13:4345e4354

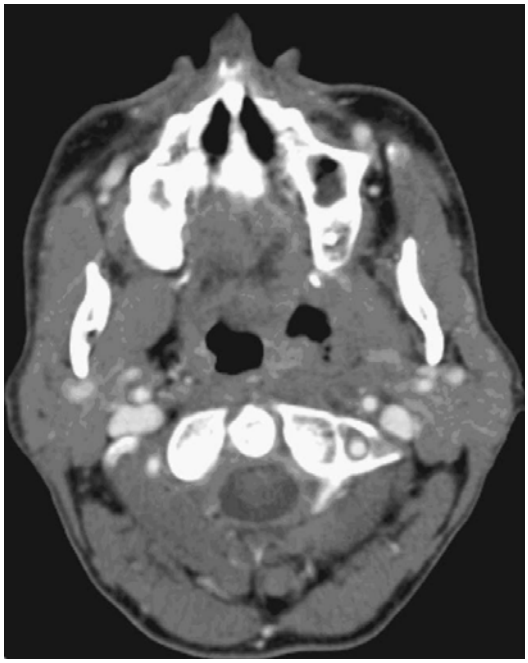

Fig. 1 — Axial computed tomography showing a large necrotic mass in the left tonsillar bed containing gas representing the primary squamous cell carcinoma.

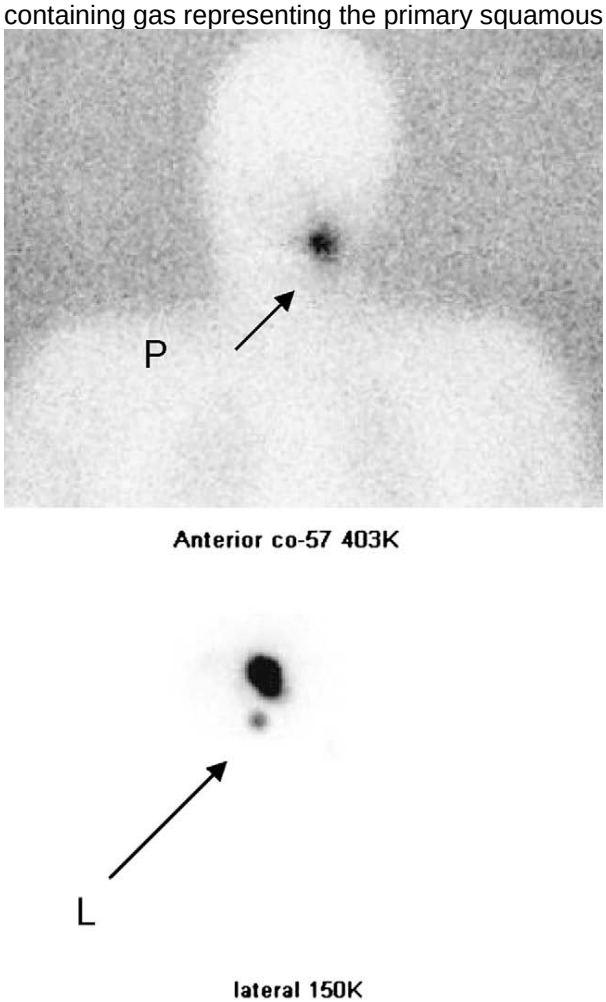

Fig. 2 — Gamma camera scans of treated patient 1. Intratumourally injected dendritic cells are seen to migrate from the primary (P) to the local lymph node (L) in 3 and 24 h, respectively. Note the residually high signal in the primary site indicating that many dendritic cells remain within the primary tumour.

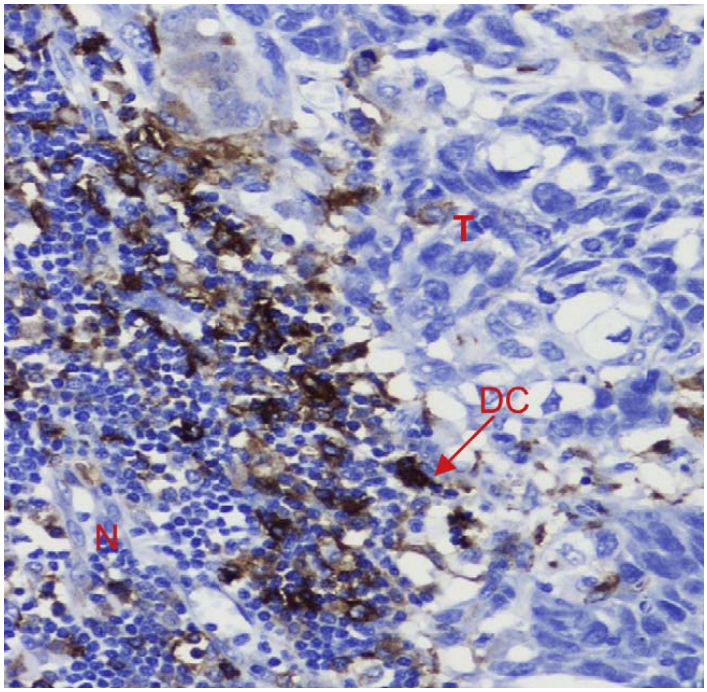

Fig. 3 — HLA-DR-positive dendritic cells (dark brown) between the tumour (T) and the lymph node (N) and within the tumour and adjacent stroma.