

Tertiary Lymphoid Structures in Ameloblastoma

C. H. Siar* , Z. A. Bin Abdul Rahman, H. Tsujigiwa, H. Nagatsuka, K. H. Ng * University of Malaya, Oral & Maxillofacial Clin. Sciences, Kuala Lumpur, Malaysia .

Objective: The ameloblastoma is a benign but locally-invasive odontogenic epithelial tumour with a high recurrence rate after treatment. Tertiary lymphoid structures (TLS) are ectopic lymphoid formations representing an adaptive immune response to either specific pathogen, inflammatory challenge or neoplastic process. Although these structures are acknowledged measures of disease outcome in many cancer types, their role in ameloblastoma remains unclear. To address this, we investigated for their distribution, morphologic and immunophenotypic characteristics, and evaluated their relevance. Method: Formalin-fixed paraffin-embedded specimens from 63 primary and 14 recurrent ameloblastoma cases were subjected to immunohistochemistry for expression of CD20, CD45RO, CD3, cortactin, NWASP, WIP, RANK, RANKL and osteoprotegerin. Intra- and peri-tumoural lymphocytic infiltrate, lymphoid aggregates and TLS findings were correlated with clinicopathologic parameters. Results: There is a positive association between lymphocytic response with tumour status (primary versus recurrent). Peritumoural lymphocytic infiltrate, lymphoid aggregates and TLS were significantly higher in patients presenting with recurrent ameloblastoma ($P > 0.05$). Actin cytoskeletal regulators NWASP and WIP (except cortactin) overexpression within TLS and lymphoid aggregates suggests enhanced motility of T and B lymphocytes. A low RANK-RANKL and high osteoprotegerin profile within these lymphoid structures indicate an altered tumoural osteoimmunologic microenvironment.

Conclusion: Our results show that neogenesis of lymphoid organs do occur in ameloblastoma albeit in low frequency. Their enhanced presence in recurrent tumours may represent locally generated immune response with potential antitumour activity to control growth and progression. (Grant: FP032-2015A)