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Hyperactivated signaling pathways of chemokine RANTES/CCL5 in osteopathies of jawbone in breast cancer patients

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Hollow spaces in jawbone have been defined as fatty degenerative osteonecrosis of jawbone (FDOJ) and have been linked with a deregulated immune system. Little is known about the underlying relationship. Chemokine RANTES/CCL5 has been associated with the induction or promotion of breast cancer (BC). In our research a case of BC showed extremely high RANTES/CCL5 expression in an area of FDOJ. Parallel, this jawbone area contained metastasizing BC cells. Samples of FDOJ were analyzed to assess expression of cytokines, which can play a role in the pathogenesis of BC. FDOJ extracted from 23 patients with BC and 19 healthy control jawbone samples were analyzed for seven immune messengers by multiplex bead-based immunoassay. We measured RANTES/chemokine ligand (CCL)5, FGF-2, IL-1 receptor antagonist (IL-1ra), IL-6, IL-8, monocyte chemotactic protein-1(MCP-1) and TNF-alpha. Only RANTES/CCL5 was found to be highly overexpressed in disease samples. This research provides a compelling confirmation that FDOJ produces high levels of RANTES/CCL5, a cytokine implicated in BC and metastasis. Levels detected in FDOJ are five-fold higher than that previously reported for BC tissue suggesting its role as a cytokine source in BC. We thus hypothesize that FDOJ may serve as an expeditor of BC progression, through RANTES/CCL5 production. The results provide a rationale for deregulated RANTES/CCL5 expression within FDOJ to have a causal role in a variety of immunological and systemic diseases besides BC. The challenge posed by these discoveries is the need to raise awareness of FDOJ throughout the medical and dental community under the integrative aspect of "silent inflammation".

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