Chemokine receptor expression profiles in nasopharyngeal carcinoma and their association with metastasis and radiotherapy

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摘要

Abstract

Nasopharyngeal carcinoma (NPC) is an epithelial cancer that metastasizes predictably to cervical lymph nodes or distant organs. To assess whether the chemokine receptors of NPC cells play important roles in metastasis and are associated with radiotherapy history, the significance of various chemokine receptors (CCR1-10, CXCR1-6, XCR1, and CX3CR1) in NPC cell lines (TW01, TW04, HONE1, BM1, and AS1) and 52 NPC tumour biopsies from 48 patients with NPC was evaluated by mRNA and cytometric analyses, chemotaxis and actin polymerization assays, and immunohistochemical staining. Quantitative real-time reverse transcription-polymerase chain reaction revealed substantial expression of CCR7, CCR9, CXCR4, and CXCR6 mRNA in all the NPC cell lines. Of these, however, only CCR7, CXCR4, and CXCR6 were functional in NPC cells. Negative immunoreactivity for CCR7, CXCR4, and CXCR6 was demonstrated in almost all nasopharyngeal (NP) specimens from patients with primary NPC (n = 12) and in those with regional metastatic NPC (n = 15). However, expression of two or three of these chemokine receptors was demonstrated in NP specimens from patients with liver metastasis. Strong positivity was demonstrated for all three of these chemokine receptors in almost all of the regional and distant metastasis specimens. Significant differences in the expression of CCR7, CXCR4, and CXCR6 were found between primary tumours and metastases ($p < 0.001$, $p < 0.001$, and $p < 0.002$, respectively). This observation was further confirmed by laser capture microdissection of freshly frozen tumours from primary (n = 5) and metastatic (n = 8) NPC sites ($p = 0.04$, 0.03, and 0.03 for CCR7, CXCR4, and CXCR6, respectively). Finally, significant differences in CXCR4 expression were demonstrated between de novo and post-radiotherapy groups (1/22 vs. 5/8; $p < 0.003$). It appears reasonable to conclude, therefore, that CCR7, CXCR4, and CXCR6 are expressed and active in human NPC metastases, while CXCR4 expression is associated with radiotherapy history.