GLUT-1 staining of squamous cell carcinomas of the uterine cervix identifies a novel element of invasion.

Abstract:

Perturbation of the normal tissue architecture in solid malignant tumors is perceived to be the consequence of actively migrating cancer cells which invade the adjacent normal host tissue. The opposite, invasion of cancer cell clusters by a vascularized stroma, has not been considered. The latter process should, however, be expected to occur since the hypoxic cores of tumor cell aggregates, under the control of HIF-1, are known to secrete cytokines (e.g., bFGF, VEGF) which attract fibroblasts and induce blood vessel formation. In this study, the expression of glucose transporter (GLUT)-1, a major HIF-1 target gene, was examined in 51 squamous cell carcinomas of the uterine cervix by immunohistochemistry to identify the localization of hypoxic tumor cell areas. The relationship of the expression pattern of GLUT-1 with the localization and morphology of the tumor stroma was analyzed. We identified three recurrent histological signs which represent strong evidence in favor of an invasion of solid tumor masses by actively migrating stromal cells. According to our findings, the histological structure of squamous cell carcinomas of the uterine cervix may in part result from the interplay between the inherent tendency of neoplastic epithelial cells to expand in the form of coherent aggregates and the fragmentation of these aggregates by invading, finger- or wedge-like stromal protrusions which carry new blood vessels, driven by gradients of hypoxia-induced pro-angiogenic,
pro-migratory and growth-promoting molecules emanating from the hypoxic core.