FP30

Adhesion molecule expression pattern in primary sclerosing cholangitis and disease controls

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Background. The interaction between cell adhesion molecules [i.e. intercellular adhesion molecule-1 (ICAM-1), the vascular adhesion molecule (VCAM-1), and the mucosal addressin cell adhesion molecule-1 (MAdCAM-1)] and lymphocyte recruitment to the liver is critical in primary sclerosing cholangitis (PSC) pathogenesis. Therefore, we aimed to analyze the expression pattern of ICAM-1, PECAM and MAdCAM-1 in explanted liver samples from patients with PSC and other chronic liver diseases.
Methods. Twelve PSC cases and eleven disease controls were stained for ICAM-1, PECAM-1, and MAdCAM-1 expression using immunohistochemistry. The control cohort comprised four alcoholic steatohepatitis (ASH), three autoimmune hepatitis (AIH), two primary biliary cirrhosis (PBC), and two chronic viral hepatitis C (CHC) cases. Immunohistochemical expression was scored in three categories according to staining intensity.
Results. ICAM-1 was detected on biliary epithelium on proliferating bile ducts in 7/12 and PECAM-1 in 6/12 PSC cases. 3/7 ICAM-1 positive and 2/6 PECAM-1 positive PSC samples, showed immunoreactivity also in medium sized and larger ducts. In control livers, bile ducts were positive for ICAM-1 in 2/4 ASH, 1/3 AIH, 2/2 PBC, and 1/2 CHC cases. All disease controls stained positive for PECAM-1 on proliferating bile ducts. All liver samples, irrespective of disease-background, showed strong immunoreactivity of ICAM-1 on sinusoidal endothelial cells and of PECAM-1 on endothelial cells of small vessels. Staining of MAdCAM-1 was detected on sinusoidal endothelial cells and endothelial cells of portal vessels in 5/12 of PSC patients. Similarly, MAdCAM-1 was also positive on sinusoidal endothelial cells and endothelial cells of portal vessels in control livers: in 1/4 ASH, 3/3 AIH, 1/2 PBC and 1/2 CHC patients.
Conclusions. ICAM-1 and PECAM-1 proved to be markers for reactive cholangiocytes. MAdCAM-1 was identified on sinusoidal endothelial cells and endothelial cells of portal vessels. No difference was observed between PSC and control livers in expression pattern of ICAM-1, PECAM-1 and MAdCAM-1. Further studies are needed to clarify whether ICAM-1 and PECAM-1 expression on biliary epithelium is an early event in the development of disease or a secondary response to inflammation.

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FP31

Decreased CD8+ lymphocytes/tumor-budding ratio is associated with metastasis and venous invasion in pancreatic ductal adenocarcinoma (PDAC)

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Background. T-Lymphocytes can be a major part of tumor microenvironment, especially at the area of tumor-host interaction where tumor progression, reflected by epithelial-mesenchymal transition (EMT) and its hallmark tumor-budding is taking place. Our aim was to determine the role of CD8+ lymphocytes in correlation with tumor-budding in PDAC.
Methods. Double immunostaining for AE1-AE3/CD8 was performed on a multipunch tissue microarray of 120 well-characterized PDACs. Tumor-buds, CD8+ and tumor-budding/CD8+ lymphocytes indices were evaluated and associated with clinico-pathological features, follow-up and adjuvant therapy information.
Results. There was a strong negative correlation between the number of buds and CD8+ counts (p=0.01). Increased numbers of tumor-buds were associated with venous invasion (p=0.0272) and reduced overall survival (p=0.0147). Low CD8+ peritumoral lymphocytes showed only a marginal association with metastasis (p=0.0683). CD8+lymphocytes/tumor-budding ratio was strongly associated with venous invasion (p=0.0078) and metastasis (p=0.0452). Almost no intratumoral CD8+ lymphocytes were detected.
Conclusions. Low counts of CD8+ peritumoral lymphocytes in the micro-environment of PDAC promote EMT as reflected by tumor-budding and facilitate tumor progression, since tumor-buds seem to display metastatic potential only when coupled by decreased counts of CD8+ lymphocytes. However, unlike to other tumor types, no prognostic effect was found, probably reflecting the fact of the absence of intratumoral CD8+ lymphocytes.

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FP32

Loss of Raf-1 kinase inhibitor protein (RKIP) promotes epithelial mesenchymal transition (EMT) in form of tumor budding in pancreatic ductal adenocarcinoma (PDAC)

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Background. Raf-1 kinase inhibitor protein (RKIP) has emerged as a significant metastatic suppressor in a variety of human cancers and is known to inhibit Ras/Raf/MEK/ERK signaling. By suppressing the activation of the NFkB/SNAIL circuit, RKIP can regulate the induction of epithelial-mesenchymal transition (EMT). The aim of