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" Multidisciplinary Perspectives on Pancreatobiliary Medicine "

Role of neutrophil gelatinase-associated lipocalin in pancreatobiliary cancer

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Authors disclosure

- Nothing

Aim of the study

Objectives:

Aim of the study was to investigate the value of serum and bile neutrophil gelatinase-associated lipocalin (NGAL) for distinguishing malignant strictures caused by cholangiocarcinoma (CCA) or pancreatic cancer from benign biliary strictures

And to assess its diagnostic accuracy.

Introduction

Accurate differentiation between benign and malignant causes of biliary obstruction remains challenging and reliable biomarkers are urgently needed. Bile is a potential source of such biomarkers.

The bile seems to be an attractive medium for diagnostic purposes as it is potentially rich in husking epithelium and tumor-derived products. Considering that obstructive jaundice is usually an indication for endoscopic intervention, the bile is easily accessible.

Neutrophil gelatinase-associated lipocalin (NGAL) is a low molecular weight protein released from activated neutrophils. This protein can bind and transport different hydrophobic substances into the cell cytoplasm, where it forms a complex with the gelatinase, matrix metalloproteinase-9. High NGAL expression was observed in many tumors , including tissues of esophageal cancer, gastric cancer , pancreatic cancer and cell lines of colon cancer and CCA.

Materials and Methods

➢Bile, urine, and serum were collected prospectively from 40 patients undergoing endoscopic or radiologic biliary decompression; with dilated biliary ducts, including 16 cases of CCA, 6 cases of pancreatic cancer, and 18 cases of benign biliary stricture were enrolled. Initially, label-free proteomics and immunoblotting were performed in samples from a subset of these patients.

➢Enzyme-linked immunosorbent assay was then performed for NGAL as a potential biomarker on all samples in this cohort. Routine biochemistry including measurement of serum levels of carbohydrate antigens (CA) 19-9 and carcinoembryonic antigen (CEA) was also performed.

Bile and serum levels of NGAL were measured using a commercially available ELISA kit (R&D Systems) according to each manufacturer's protocol.

NGAL levels were calculated from the standard calibration curve.

Statistical analysis was performed using Statistical 10 software . The Mann-Whitney U test or Student's t-test were used for analysis of quantitative variables asappropriate. Data are presented as mean ±S.D.

Results & Discussion

NGAL levels were significantly raised in bile from the malignant disease group, compared with bile from the benign disease group. The serum CA19-9, serum CEA, and bile NGAL levels were significantly increased in patients with malignant strictures as compared with patients with benign biliary diseases. Serum NGAL had no significant value for discriminating between malignant and benign biliary strictures. Bile NGAL levels had a receiver characteristic area under the curve of 0.74, sensitivity 77.3, and specificity 72.2% for discriminating between pancreatobiliary cancer and benign biliary diseases. Bile NGAL and serum CA19-9 were independent parameters and their combined use improved diagnostic accuracy (sensitivity 91%, negative predictive value 85.7%).

Serum CA19-9 - serum CEA and serum and bile NGAL concentrations in patients with pancreatobiliary malignant and benign bile duct strictures.

	Benign	Malignant	P value benign *vs.* malignant	CCA	P value benign *vs.* CCA	Pancreatic cancer	P value benign *vs.* pancreatic cancer
CA 19-9 (0–37 U/ml)	38.3 (75.4)	5690 (13000)	<0.0001	7267 (15008)	0.0001	1484 (2235)	0.02
CEA (0–5 ng/ml)	1.7 (1.0)	27.7 (65.4)	<0.0001	19.7 (41.2)	0.0001	48.9 (110)	0.01
Serum NGAL ng/ml	95.1 (51.9)	91.9 (57.4)	0.79	97.5 (59.4)	0.94	77.1 (53.8)	0.42
Bile NGAL ng/ml	674 (966)	1244 (1186)	0.01	1379 (1361)	0.02	884 (372)	0.08

CA 19-9 - carbohydrate antigens 19-9; CCA - cholangiocarcinoma; CEA - carcinoembryonic antigen; NGAL - neutrophil gelatinase associated lipocalin. Mean values ±S.D.

Conclusion

- We conclude that measurement of biliary, but not serum NGAL, may differentiate malignant pancreatobiliary from benign biliary strictures, serving as a complementary. NGAL in bile is a novel potential biomarker to help distinguish benign from malignant biliary obstruction.
- Further studies are needed to clarify the role of NGAL in tumorigenesis, its relationship with the biliary cancer stage, and the effect on clinical outcome.

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Questions?

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