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Pancreatic neuropathy and neuropathic pain--a comprehensive pathomorphological study of 546 cases

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Abstract

Background & aims: Chronic pancreatitis (CP) and pancreatic adenocarcinoma (PCa) are characterized by intrapancreatic neural alterations and pain. Our aims were to: (a) Investigate whether neuropathic changes like pancreatic neuritis, increased neural density, and hypertrophy are phenomena only in CP or whether they are also evident in other pancreatic disorders as well, (b) study possible variations in neural cancer cell invasion among malignant pancreatic tumors, and (c) explore whether these neuropathic changes contribute to pain sensation.

Methods: Neuropathic changes were studied in PCa (n=149), in CP (n=141), in pancreatic tumors (PTm) including serous/mucinous cystadenomas, invasive/noninvasive intraductal papillary mucinous neoplasias, benign/malignant neuroendocrine tumors, ampullary cancers (n=196), and in normal pancreas (n=60). The results were correlated with GAP-43 expression, tissue inflammation, pancreatic neuritis, neural invasion, fibrosis, desmoplasia, pain, and patient survival.

Results: Increased neural density and hypertrophy were only detected in PCa and CP and were strongly associated with GAP-43 over expression and abdominal pain. The severity of pancreatic neuritis was strongest in PCa and was closely linked to changes in neural density and hypertrophy. The aggressiveness of neural cancer cell invasion was most prominent in PCa and was related to neuropathic changes, desmoplasia, and pain. Severe and enduring pain were strongly associated with poor prognosis in PCa patients.

Conclusions: Enhanced neural density and hypertrophy are only typical features of CP and PCa among all investigated pancreatic disorders. Such neuropathic changes, including damage to

nerves by inflammatory and/or cancer cells, seem to enhance and generate pancreatic neuropathic pain.

Similar articles

- Pancreatic neuropathy results in "neural remodeling" and altered pancreatic innervation in chronic pancreatitis and pancreatic cancer. Ceyhan GO, Demir IE, Rauch U, Bergmann F, Müller MW, Büchler MW, Friess H, Schäfer KH. Am J Gastroenterol. 2009 Oct; 104(10):2555-65. doi: 10.1038/ajg.2009.380. Epub 2009 Jun 30. PMID: 19568227

- Neural fractalkine expression is closely linked to pain and pancreatic neuritis in human chronic pancreatitis. Ceyhan GO, Deucker S, Demir IE, Erkan M, Schmelz M, Bergmann F, Müller MW, Giese T, Büchler MW, Giese NA, Friess H. Lab Invest. 2009 Mar;89(3): 347-61. doi: 10.1038/labinvest.2008.170. Epub 2009 Jan 19. PMID: 19153557

- Nerve growth factor and artemin are paracrine mediators of pancreatic neuropathy in pancreatic adenocarcinoma. Ceyhan GO, Schäfer KH, Kerscher AG, Rauch U, Demir IE, Kadihasanoglu M, Böhm C, Müller MW, Büchler MW, Giese NA, Erkan M, Friess H. Ann Surg. 2010 May;251(5):923-31. doi: 10.1097/SLA.0b013e3181d974d4. PMID: 20395845

- Pancreatic pain. Ceyhan GO, Michalski CW, Demir IE, Müller MW, Friess H. Best Pract Res Clin Gastroenterol. 2008;22(1):31-44. doi: 10.1016/j.bpg.2007.10.016. PMID: 18206811 Review.

- Fate of nerves in chronic pancreatitis: Neural remodeling and pancreatic neuropathy. Ceyhan GO, Demir IE, Maak M, Friess H. Best Pract Res Clin Gastroenterol. 2010 Jun; 24(3):311-22. doi: 10.1016/j.bpg.2010.03.001. PMID: 20510831 Review.

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- A Novel Role of Interleukin 13 Receptor alpha2 in Perineural Invasion and its Association with Poor Prognosis of Patients with Pancreatic Ductal Adenocarcinoma. Fujisawa T, Shimamura T, Goto K, Nakagawa R, Muroyama R, Ino Y, Horiuchi H, Endo I, Maeda S, Harihara Y, Nakajima A, Matsuhashi N, Kato N, Isayama H, Puri A, Suzuki A, Bellayr I, Leland P, Joshi BH, Puri RK. Cancers (Basel). 2020 May 20;12(5):1294. doi: 10.3390/cancers12051294. PMID: 32443847 Free PMC article.

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- Pathogenesis and Treatment of Pancreatic Cancer Related Pain. Lohse I, Brothers SP. Anticancer Res. 2020 Apr;40(4):1789-1796. doi: 10.21873/anticanres.14133. PMID: 32234867 Free PMC article. Review.

- Ping-Pong-Tumor and Host in Pancreatic Cancer Progression. Mu W, Wang Z, Zöller M. Front Oncol. 2019 Dec 16;9:1359. doi: 10.3389/fonc.2019.01359. eCollection 2019. PMID: 31921628 Free PMC article. Review.