

From diabetes, chronic pancreatitis to pancreatic cancer: miRNA – a new marker of pancreatic cancer?

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Abstract

Introduction: Pancreatic cancer ranks among the cancers with the worst prognosis. High lethality of the disease is caused by late diagnose and a lack of powerful and early markers. The goal of this study was to observe the presence of early unspecific signs of the disease (new-onset diabetes mellitus and weight loss) and to test selected miRNAs as markers of pancreatic cancer, with subanalysis according to specific criteria (diabetes mellitus/prediabetes, its type, weight loss, cancer stage and size of the primary tumor, presence of chronic pancreatitis in cancer patients).

Patients and methods: We have included 77 patients with ductal pancreatic adenocarcinoma, 26 with chronic pancreatitis, 39 patients with type 2 diabetes mellitus without any tumor disease and 25 control subjects. In the cancer group, there were 60 patients who also had diabetes/prediabetes and 18 with chronic pancreatitis in their personal history. Significant weight loss (> 5 % of body weight in 3 months or > 10 % of body weight in 6 months) was observed in 52 patients with the cancer. Relative expressions of miRNAs (miR-21, miR-30, miR-192, miR-196, miR-200, miR-423) were measured in the serum by real-time PCR method. MicroRNA-191 and -454 were used as comparators.

Results: Variable miRNA expressions among all 3 groups (pancreatic cancer – chronic pancreatitis – controls) were distinguished in miR-196: 1,9 (1,6-2,2); 0,4 (0,3-0,4); 1,0 (0,8-1,2) [U]. No significant difference was observed between diabetic and non-diabetic patients within the groups. Elevated expressions of miR-200 were observed in patients with significant weight loss, compared to those without weight loss and to the control subjects. Greater expressions in miR-21, miR-192, miR-196 and miR-200 were shown together with the more advanced stages of the cancer and the bigger size of the primary tumor. A correlation was found between CA 19-9 and miR-21, miR-192 and miR-200.

MicroRNA-423 was expressed less in chronic pancreatitis compared to the other groups. MicroRNA-192 and -200 were more powerful than CA 19-9 in symptomatic patients with the cancer (new-onset diabetes and significant weight loss): AUCmiR-192=0,81, AUCmiR-200=0,88, AUCCA 19-9=0,78.

Conclusion: MicroRNA-192, -200 and -423 may improve the pancreatic cancer diagnosis. The advantage of such an examination consists (similarly to CA 19-9) in non-invasiveness, miR-423 can even clearly distinguish chronic pancreatitis from the cancer, which is not possible by CA 19-9. In the future, miRNA examination in the patients before and after a surgical resection of the cancer is planned, as well as in the early cancer stages and precancerosis.