

that of patients with chronic pancreatitis (12). In a study by Malka et al. (13) in patients with chronic pancreatitis (predominantly of alcoholic origin) they report pancreatic cancer in 1.1% of, in total, 3437 patients with chronic pancreatitis.

AIP is still a rare disease, so most of the work on it is in the category of case reports. Studies with higher numbers of test subjects show somewhat different results. In a study evaluating a group of 68 patients with AIP at 75-month intervals, no cancer was found (14). A multicentric study from the Mayo Clinic (15), including 23 departments from 10 countries, and a total of 1064 patients with AIP, did not show a significant increased risk of malignancies (57 malignancies and of those only 5 cases of pancreatic cancer, 0.8%). However, Ikeura et al. (16) in a single-centre trial showed a trend towards higher pancreatic cancer development in patients with AIP (4.8%) against patients with other chronic pancreatitis (2.4%). Ikeura et al. (17), also in his review article, summarizes the incidence risk of pancreatic cancer in AIP patients at between 0% and 4.8%. Pancreatic cancer occurs in the vast majority of people with type 1 AIP (8,18).

AIP is a clinical manifestation of a group of diseases called IgG4-RD. In this context, the question arose whether IgG4-RD were associated with the induction of the process of carcinogenesis. Shiokawa et al. in a retrospective study of 108 subjects with AIP, found malignancy present in 13.9% (19), with a standardized incidence rate of 2.7. In the study of Asano et al. of 109 subjects with AIP, cancer was found in 26% of cases (20). However, only 4 cases were of pancreatic cancer. These results indicate that IgG4-RD can be a risk factor for cancer in various organ localities. Also in a study from Hirano et al. (21), which evaluated a set of 113 patients with IgG4-RD, a malignancy was diagnosed at the time of IgG4-RD onset in 15 cases. Most frequently this was lung cancer, with pancreatic cancer detected only in two cases. Interestingly, in patients with AIP, cancer is diagnosed mostly in the years immediately after or soon after the diagnosis of autoimmune disease.

Macinga et al. (22) in a retrospective study assess the occurrence of AIP in pancreatic masses resected for a focal pancreatic enlargement. In 295 pancreatic resections, AIP was diagnosed in 15 patients (5.1%). Six of them had AIP type 1, nine were diagnosed as AIP type 2. In the group of patients with AIP pancreatic adenocarcinoma were diagnosed

in 6 cases (40%). An important fact here is that AIP was not diagnosed before surgery.

It's in no doubt that focal pancreatic enlargement, low density on CT, female gender, and rim enhancement on MRI in patients with AIP type 1 are suggestive of pancreatic cancer in these patients (18).

The incidence of malignancies in patients with AIP is described by Schneider et al (23). It's important that the incidence of malignancy in patients with AIP, versus regular population is higher by 17.9%.

In our study, published by Bojkova et al. (12), we examined the presence of the serum IgG4 in 106 patients with histologically documented pancreatic cancer, without any previous diagnose of AIP. Higher serum IgG4 over the normal level of 135 mg/dL was found in 11 patients. Of these 11 patients, 7 (65.6%) had a level twice higher than the limit of 135 mg/dL. The average IgG4 value in the pancreatic carcinoma group was 263 mg/dL. Pancreatic tissue biopsy material was obtained from all subjects and pancreatic adenocarcinoma was detected simultaneously in 2 subjects with a diagnosis of AIP.

In summary, IgG4 has been considered useful for AIP diagnosis, however, IgG4 levels can be slightly elevated also in patients with pancreatic adenocarcinoma. IgG4 levels of over twice the upper limit are rare among patients with pancreatic adenocarcinoma. However, cases of simultaneous presentation of pancreatic cancer and AIP have been documented and should not be neglected.

The role of NF-kappaB

Despite a number of new findings in recent years, the mechanisms of the relationship of chronic inflammation and the induction of tumor growth are still not entirely clear (24). However, what is unequivocally accepted is the relationship between chronic inflammation, nuclear factor-kappaB (NF-kappaB) activation and tumor growth (25). The role of NF-kappaB in the process of inflammation and inflammation associated with tumor growth is shown in Figure 1 (edited according to (24) - created in collaboration with Service Center for E-Learning at Masaryk University, Faculty of Informatics).

NF-kappaB is a factor that regulates pro-inflammatory processes. Activation of NF-kappaB involves translocation of active dimers into the cell

Tab. 1. Characteristics and essential differences between Type-1 and Type-2 autoimmune pancreatitis (adapted according to Webster [11])

	TYPE-1	TYPE-2
IgG4 – RD	Yes	No
Prevalence	Asia > USA/Europe	USA/Europe > Asia
Gender	Male > Female	Male = Female
AIP in the world in %	> 90	< 10
Predominant age	> 50	30-50
Initial jaundice	> 60	< 30
Acute abdomen pain	< 30	> 60
Increased IgG4 in serum	> 70	< 10
Histopathology	IgG4-LPSP Storiform fibrosis Obliterative phlebitis	IDCP GEL
Other organ disabilities	Yes	No
Presence of IBD in %	< 10	> 40
Response to steroids	> 90	> 90
Relapse after steroid therapy	> 40	< 10

IgG4-RD – IgG4-related disease, LPSP – lymphoplasmatic sclerosing pancreatitis, IDCP – idiopathic duct centric pancreatitis, GEL – granulocytic epithelial lesions, IBD – Inflammatory bowel disease