

PANCREAS ALERTS

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Association between autoimmune pancreatitis and systemic autoimmune diseases.

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AIM: To investigate the association between autoimmune pancreatitis (AIP) and systemic autoimmune diseases (SAIDs) by measurement of serum immunoglobulin G4 (IgG4). **METHODS:** The serum level of IgG4 was measured in 61 patients with SAIDs of different types who had not yet participated in glucocorticosteroid treatment. Patients with an elevated IgG4 level were examined by abdominal ultrasonography (US) and, in some cases, by computer tomography (CT). **RESULTS:** Elevated serum IgG4 levels (919 ± 996 mg/L) were detected in 17 (28%) of the 61 SAID patients. Ten patients had Sjögren's syndrome (SS) (IgG4: 590 ± 232 mg/L), 2 of them in association with Hashimoto's thyroiditis, and 7 patients (IgG4: $1,388 \pm 985.5$ mg/L) had systemic lupus erythematosus (SLE). The IgG4 level in the SLE patients and that in patients with SS were not significantly different from that in AIP patients (783 ± 522 mg/L). Abdominal US and CT did not reveal any characteristic features of AIP among the SAID patients with an elevated IgG4 level. **CONCLUSION:** The serum IgG4 level may be elevated in SAIDs without the presence of AIP. The determination of serum IgG4 does not seem to be suitable for the differentiation between IgG4-related diseases and SAIDs.

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Strategy to differentiate autoimmune pancreatitis from pancreas cancer.

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Autoimmune pancreatitis (AIP) is a newly described entity of pancreatitis in which the pathogenesis appears to involve autoimmune mechanisms. Based on histological and immunohistochemical examinations of

various organs of AIP patients, AIP appears to be a pancreatic lesion reflecting a systemic "IgG4-related sclerosing disease". Clinically, AIP patients and patients with pancreatic cancer share many features, such as preponderance of elderly males, frequent initial symptom of painless jaundice, development of new-onset diabetes mellitus, and elevated levels of serum tumor markers. It is of uppermost importance not to misdiagnose AIP as pancreatic cancer. Since there is currently no diagnostic serological marker for AIP, and approach to the pancreas for histological examination is generally difficult, AIP is diagnosed using a combination of clinical, serological, morphological, and histopathological features. Findings suggesting AIP rather than pancreatic cancer include: fluctuating obstructive jaundice; elevated serum IgG4 levels; diffuse enlargement of the pancreas; delayed enhancement of the enlarged pancreas and presence of a capsule-like rim on dynamic computed tomography; low apparent diffusion coefficient values on diffusion-weighted magnetic resonance image; irregular narrowing of the main pancreatic duct on endoscopic retrograde cholangiopancreatography; less upstream dilatation of the main pancreatic duct on magnetic resonance cholangiopancreatography, presence of other organ involvement such as bilateral salivary gland swelling, retroperitoneal fibrosis and hilar or intrahepatic sclerosing cholangitis; negative work-up for malignancy including endoscopic ultrasound-guided fine needle aspiration; and steroid responsiveness. Since AIP responds dramatically to steroid therapy, accurate diagnosis of AIP can avoid unnecessary laparotomy or pancreatic resection.

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Value of serum IgG4 in the diagnosis of IgG4-related disease and in differentiation from rheumatic diseases and other diseases.

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CONTEXT: IgG4-related disease (IgG4-RD) is a novel disease entity that includes Mikulicz's disease, autoimmune pancreatitis (AIP), and many other conditions. It is characterized by elevated serum IgG4 levels and abundant IgG4-bearing plasmacyte infiltration of involved organs. The authors postulated that high levels of serum IgG4 would comprise a useful

diagnostic tool, but little information is available about IgG4 in conditions other than IgG4-RD, including rheumatic diseases. Several reports have described cut-off values for serum IgG4 when diagnosing IgG4-RD, but these studies mostly used 135 mg/dL in AIP to differentiate from pancreatic cancer instead of rheumatic and other common diseases. There is no evidence for a cut-off serum IgG4 level of 135 mg/dL for rheumatic diseases and common diseases that are often complicated with rheumatic diseases. **OBJECTIVE:** The aim of this work was to re-evaluate the usual cut-off serum IgG4 value in AIP (135 mg/dL) that is used to diagnose whole IgG4-RD in the setting of a rheumatic clinic by measuring serum IgG4 levels in IgG4-RD and various disorders. **METHODS** The authors constructed ROC curves of serum IgG4 levels in 418 patients who attended Sapporo Medical University Hospital due to IgG4-RD and various rheumatic and common disorders. The optimal cut-off value of serum IgG4 for a diagnosis of IgG4-RD was 144 mg/dL, and the sensitivity and specificity were 95.10% and 90.76%, respectively. Levels of serum IgG4 were elevated in IgG4-RD, Churg-Strauss syndrome, multicentric Castleman's disease, eosinophilic disorders, and in some patients with rheumatoid arthritis, systemic sclerosis, chronic hepatitis, and liver cirrhosis. **CONCLUSION:** The usual cut-off value of 135 mg/dL in AIP is useful for diagnosing whole IgG4-RD, but high levels of serum IgG4 are sometimes observed in not only IgG4-RD but also other rheumatic and common diseases.

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Systemic lupus erythematosus related acute pancreatitis: A cohort from South China.

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CONTEXT: Acute pancreatitis (AP) is a rare but life-threatening complication of systemic lupus erythematosus (SLE). **OBJECTIVE:** The current study evaluated the clinical characteristics and risk factors for the mortality of patients with SLE-related AP in a cohort of South China. **METHODS:** Inpatient medical records of SLE-related AP were retrospectively reviewed. **RESULTS:** Twenty-seven out of 4,053 SLE patients were diagnosed as SLE-related AP, with an overall prevalence of 0.67%, annual incidence of 0.56% and mortality of 37.04%. SLE patients with AP presented with higher SLEDAI score (21.70 ± 10.32 versus 16.17 ± 7.51 , $P=0.03$), more organ system

involvement (5.70 ± 1.56 versus 3.96 ± 1.15 , $P=0.001$), and higher mortality (37.04% versus 0, $P=0.001$), compared to patients without AP. Severe AP (SAP) patients had a significant higher mortality rate compared to mild AP (MAP) (75% versus 21.05%, $P=0.014$). Sixteen SLE-related AP patients received intensive glucocorticosteroid treatment, 75% of them exhibited favorable prognosis. **CONCLUSION:** SLE-related AP is rare but concomitant with high mortality in South Chinese people, especially in those SAP patients. Activity of SLE, multiple-organ systems involvement may attribute to the severity and mortality of AP. Appropriate glucocorticosteroid treatment leads to better prognosis in majority of SLE patients with AP.

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Pancreatitis in systemic lupus erythematosus: Case series from a tertiary care center in South India.

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CONTEXT: Pancreatitis in systemic lupus erythematosus (SLE) is a rare, but life threatening complication. **OBJECTIVE:** The authors aimed to study the characteristics and treatment outcome of SLE patients with acute pancreatitis in comparison with those with abdominal pain due to causes other than pancreatitis. **METHODS:** Records of SLE patients admitted in the authors' ward with pain abdomen between January 2008 and July 2010 were studied retrospectively. Of 551 SLE in-patients during the study period, 28 (5%) had abdominal pain and 11 (2%) of them were diagnosed to have acute pancreatitis. Five of the 11 patients had severe pancreatitis and 6 had mild pancreatitis. Seizures, arthritis and lack of prior use of steroids were significantly more common in patients with pancreatitis as compared to those with abdominal pain of non pancreatic origin. Seizure occurred more often in severe pancreatitis group as compared to mild pancreatitis. There was no difference in prevalence of lupus anticoagulant and anticardiolipin antibody (40%) between SLE patients with pancreatitis and those with other causes of abdominal pain. **CONCLUSION:** Association of pancreatitis in this cohort of SLE patients include withdrawal of maintenance dose of steroids, seizures and arthritis in univariate analysis.

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Non-operative treatment versus percutaneous drainage of pancreatic pseudocysts in children.

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OBJECTIVE: The purpose of this study was to characterize the clinical course and outcomes of children with pancreatic pseudocysts that were initially treated non-operatively or with percutaneous drainage. **METHODS:** A retrospective review of children with pancreatic pseudocysts over a 12-year period was completed. Categorical variables were compared using Fischer's exact method and the Student's t test was used to compare continuous variables. Analysis was done using logistic and linear regression models. **RESULTS:** Thirty-six children met the criteria for pancreatic pseudocyst and 33 children were treated either non-operatively or with percutaneous drainage. Of the 22 children managed non-operatively, 17 required no additional intervention (77%) and five required surgery. Operative procedures were: Frey procedure (n=3), distal pancreatectomy (n=1), and cystgastrostomy (n=1). Eight of the 11 children treated with initial percutaneous drainage required no additional treatment (72%). The other three children underwent distal pancreatectomy. Success of non-operative management or percutaneous drainage was not dependent on size or complexity of the pseudocyst. Logistic regression did not identify any patient demographic (gender, age, and weight), etiologic (trauma, non-traumatic pancreatitis) or pseudocyst characteristic (size, septations) that predicted failure of non-operative therapy. **CONCLUSIONS:** In children, pancreatic pseudocysts can frequently be managed without surgery regardless of size or complexity of the pseudocyst. When an intervention is needed, percutaneous drainage can be performed successfully, avoiding the need for major surgical intervention in the majority of patients.

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Transmural endoscopic necrosectomy of infected pancreatic necroses and drainage of infected pseudocysts: A tailored approach.

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OBJECTIVE: Transmural endoscopic drainage and necrosectomy have become favored treatment modes for infected pancreatic pseudocysts and necroses. **OBJECTIVE:** In this analysis, we summarize the outcome of 40 patients with complicated course of acute pancreatitis after endoscopic treatment. **MATERIAL AND METHODS:** From January 2006 through May 2011, 40 patients with complicated pancreatitis were included in this retrospective analysis. All patients underwent endosonographic transgastric puncture followed by wire-guided insertion of one or more double pigtail stents. Patients with extensive necroses were treated repeatedly with transgastric necrosectomy. Treatment success was determined by clinical, laboratory, and radiological parameters. **RESULTS:** Nine patients had interstitial pancreatitis (IP) with pancreatic pseudocysts. Thirty-one patients had necrotizing pancreatitis (NP) with acute pancreatic necroses (n=4) or walled-off pancreatic necrosis (n=27). All patients with IP and nine patients with NP had pseudocysts without solid material and underwent transgastric drainage only. In this group major complications occurred in 11.1% and no mortality was observed. Twenty-two NP patients were treated with additional repeated necrosectomy. In patients with localized peripancreatic necroses (n=10) no need of surgery or mortality was observed, major complications occurred in 10%. In patients with extensive necroses reaching the lower abdomen (n=12), three needed subsequent surgery and three died. **CONCLUSIONS:** Transgastric endoscopy is an effective minimally invasive procedure even in patients with advanced pancreatic necroses. Complication rate is low particularly in patients with sole pseudocysts or localized necroses. The extent of the fluid collections and necroses is a new predictive parameter for the outcome of the patients.

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A comparative analysis of K-ras mutation and carcinoembryonic antigen in pancreatic cyst fluid.

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CONTEXT: Analysis of cystic fluid may be useful in distinguishing between benign and malignant cysts which has significant impact on their management. **OBJECTIVE:** The aim of this study was to assess the diagnostic utility of carcinoembryonic antigen (CEA) and K-ras gene mutation in pancreatic cysts fluid. **METHODS:** The study included 56 patients with pancreatic cystic fluid collected for analysis. The cysts were classified as benign (simple cysts, pseudocysts, serous cystadenoma: 39 patients) or premalignant/

malignant (mucinous cystadenoma, IPMN, cystadenocarcinoma: 17 patients). The patients' history, CEA fluid concentrations and presence of *K-ras* mutation were analyzed. RESULTS: CEA were higher in patients with malignant cysts (mean levels 238 ± 12.5 ng/mL; range 32.8-4,985 ng/mL) compared to benign lesions (mean levels 34.5 ± 3.7 ng/mL; range 3.9-693 ng/mL; $P < 0.001$). *K-ras* mutation correctly classified 11 of 17 patients with premalignant/malignant lesions. It was also detected in one patient with final diagnosis of benign cyst (the sensitivity was

64.7% and the specificity was 97.4%; $P < 0.01$). If CEA and molecular analysis were combined in that cysts with either CEA level greater than 45 ng/mL or presence of *K-ras* mutation, than 16 of 17 premalignant/malignant cysts were correctly identified (94.1%). CONCLUSION: Molecular analysis of pancreatic cyst fluid adds diagnostic value to the preoperative diagnosis and should be considered when cyst cytologic examination is negative for malignancy.

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