Tu1296

Recurrent Acute Pancreatitis in Israel - Genetic and Electrophysiological Aspects

Steven Werlin, Eyal Shteyer, Yasmin Yaakov, Fred M Konikoff, Zamir Halpern, Olga Barkay, Baruch Yerushalmi, Efrat Broide, Erwin Santo, Raanan Shamir, Ron Shaoul, Vered Pinsk, Claude Ferec, Philippe Ruszniewski, Michael Wilschanski

Background: The etiologies of recurrent pancreatitis (RP) include anatomical anomalies, hereditary, metabolic and autoimmune disorders After conventional evaluation a significant number of patients remain with a diagnosis of idiopathic RP The advent of genetic analysis and electrophysiologic testing further assists in the diagnostic process Specific genetic mutations in the cationic trypsinogen gene PRSS1, SPINK1, CTRC and CFTR genes may cause RP. The aim was to present the work-up of patients with RP referred for genetic analysis and electrophysiological testing. Methods: Patients with acute recurrent pancreatitis with no known etiology were referred to the Electrophysiology Laboratory, Division of Pediatric GI at Hadassah University Hospital for genetic testing as well as evaluation of CFTR function by Nasal Potential Difference (NPD) testing Results: 80 patients with recurrent pancreatitis who had no anatomical anomalies and normal fasting lipids and IgG4 were evaluated The mean age was 27±18 years (range 1 5-72 yrs), 89% were Jewish, 11% Arab 12 (15%) patients carried PRSS1 gene mutation (K23R(8), R112H(2) and D21A(2)) 1 patient had K172E/- (CTRC) mutation, 1 had I42M(SPINK1)/V235I(CTRC) together with ΔF508/5T, 1 patient had R67H(SPINK1)/V235I(CTRC), 1 patient had V235I(CTRC)/- and 1 patient was homozygote for R67H (SPINK1) 10 of 80 submitted for CFTR gene testing carried mutations (ΔF508/L997F, ΔF508/5T, W1282/5T(12TG), W1282X/-, D1152H/-, 5T/- and L997F/-) 59 (74%) patients underwent sweat testing 8 had sweat chloride >60mEq/L. 62 (77 5%) patients had NPD testing, 4 (6%) with abnormal results Conclusion. 21% of Israeli patients with recurrent pancreatitis carry mutations for Hereditary Pancreatitis including rare mutations (K23R) and 12 5% have evidence of cftr mutations and 10% had CFTR dysfunction showing the importance of genetic and functional work up of these patients.

Tu1297

Hospital Admission and Readmission Rates of Patients With Chronic Pancreatitis

Carmi S. Punzalan, Tina Park, Justin Yamin, Thu Nguyen, Wahid Wassef

Background: Chronic pancreatitis (CP) is a chronic inflammatory disorder of the pancreas characterized by pain Painful exacerbations may require hospitalization for intravenous analgesics The hospitalization rate for chronic pancreatitis in one Pennsylvania county was 8 1 per 100,000 persons, and 57 9% of the patients were readmitted for acute or chronic pancreatitis within several years after the initial visit (2). There is limited data on the characteristics of the patients who have multiple admissions for chronic pancreatitis and readmission within 30 days of discharge (1-3) This study is a retrospective chart review of hospitalization admission and 30-day readmission rates for patients with the primary diagnosis of chronic pancreatitis Method: Patients over the age of 18 who were admitted to our hospital in 2012 with CP were included in the study Clinical variables, such as age, sex, race, tobacco use, narcotic use, follow-up in the pancreas clinic and missed appointments, and active alcohol use, were obtained These variables were regressed with univariate analysis using the student T test The primary endpoint was admissions and 30-day readmission rates. IRB approval was obtained Results: Forty patients were admitted with CP accounting for 156 visits. The majority were Caucasian, female, and with a mean age of 46. Thirty six percent of 40 patients were admitted more than 5 times and comprised 65% of the total admissions and 88% of the total 30-day readmissions Only the number of missed appointments (P<0.004) was significantly associated with admissions and readmissions Conclusion: A minority of patients accounted for the majority of admissions and 30-day readmissions. Clinical factors were not significantly associated with admissions and 30-day readmissions except for the number of missed appointments in the pancreas clinic Missed appointments leading to inadequate outpatient pain control may increase hospitalizations An alternative explanation is that frequent hospitalizations prevent the patients from attending scheduled appointments. Patients who are frequently admitted for CP should be encouraged to attend their outpatient appointments A larger study may identify other variables that are associated with admission and readmissions for CP Sources. 1 Lowenfels AB, Sullivan T, Fiorianti J, Maisonneuve P. The epidemiology and impact of pancreatic diseases in the United States. Current Gastroenterology Reports 2005;7:90-95. 2. Yadav D, Muddana V, O'Connell M Hospitalizations for chronic pancreatitis in Allegheny County, Pennsylvania, USA Pancreatology 2011; 11 3. Yang AL, Vadhavkar S, Singh G, Omary MB Epidemiology of alcohol-related liver and pancreatic disease in the United States Arch Intern Med 2008;6:649-656 Explanatory variables and estimated p-values from univariate regression

Variable	Number in sample (% of total)	P value
Number of patients	40 (100)	NA
Male	12 (40)	0.220
Mean age in years at first visit	46	0.716
Caucasian	32 (80)	0.094
African American	5 (12.5)	0.051
Hispanic	3 (7.5)	0.910
Current tobacco use	21 (52.5)	0.911
Chronic pain medication	33 (82.5)	0.313
Current alcohol use	8 (20)	0.255
Pancreatic enzyme	33 (82.5)	0.367
*Pancreas clinic	33 (82.5)	0.965
#Number of clinic visits	257 (100)	0.351
^Missed clinic appointments	21 (8.1)	0.004

*Seen at least once in the pancreas clinic in 2012 #Total number of attended visits to the pancreas clinic by cohort ^Total number of missed clinic appointments with percentage of total scheduled visits

Distribution of both admissions and 30-day readmissions across patient groups

Patients with given number of visits	% total patients	Total number of admissions	% of total admissions	Number of 30 day readmissions	% of total 30 day readmissions
All	100	156	100	69	100
≥3	62.5	138	86.8	68	98.6
≥5	36	102	65	58	87.9

Tu1298

High Incidence of Pancreatic Cancer in Patients With Autoimmune Pancreatitis Undergoing Surgery

Peter Macinga, Adela Pulkertova, Jana Maluskova, Martin Oliverius, Julius Spicak, Tomas Hucl

Introduction: Autoimmune pancreatitis (AIP) is a rare, benign, fibroinflammatory disease that may present with signs and symptoms mimicking pancreatic cancer (PC). AIP is characterized by a dramatic response to corticosteroid therapy. Thus, patients diagnosed with AIP can avoid surgery and undergo immunosuppressive treatment Despite the availability of well-defined AIP criteria, still a large portion of AIP patients undergoes unnecessary surgery. Only a few cases of PC in AIP patients have so far been reported worldwide **Aims:** The objective of our study was to assess the proportion of AIP in all pancreatic resections performed in our center for focal pancreatic enlargement and to determine clinical characteristics of this subgroup **Methods:** We performed a retrospective analysis of data of all patients who underwent pancreatic resection in our center for suspected cancer/focal pancreatic enlargement between january 2000 and july 2013 **Results:** Two hundred and ninety-five pancreatic resections were performed in 201 males and 94 females (mean age 60 years, range 36-78 years) Indication for surgery was tumor suspicion based on clinical symptoms, imaging methods and laboratory findings. In 19 patients (6.4%, 13 males, 6 females), autoimmune pancreatitis was diagnosed based on histology of the resected specimen. 10 patients were diagnosed as AIP type 1 (9 males, 1 female), 9 patients had distinct histopathological features of AIP type 2 (4 males, 5 females) In 6 AIP patients (31 6%, all males, 3 AIP type 1), pancreatic adenocarcinoma was also present in the resected tissue No differences were observed in the preoperative characteristics of patients with and without cancer (CT, EUS, ERCP, bile duct involvement, laboratory findings including Ca 19-9). In none of the patients the diagnosis of AIP was made prior to surgery; however the diagnostic algorithm was not fully completed. **Conclusions:** A considerable number of resected patients with AIP had synchronous PC in our study The preoperative diagnosis of AIP in patients with focal pancreatic enlargement may not always rule out the simultaneous presence of cancer

Tu1299

International Prospective Study of Distal Intestinal Obstruction Syndrome (DIOS)

Michael Wilschanski, Carla Colombo, Nataliya Y Kashirskaya, Helmut Ellemunter, Maria Fotoulaki, Roderick Houwen, Eddy Robberecht, Anne Munck

Objectives & Study: DIOS is a unique intestinal complication of CF characterized by complete or incomplete intestinal obstruction by viscid faecal material in the terminal ileum and proximal colon An increase in incidence has been noted and this is the first multinational prospective study on the natural history of DIOS Methods: 28 Centers in 10 countries reported new cases of DIOS in children from 2009-2012 in a study organized by the CF ESPGHAN Working Group DIOS classification was based on the ESPGHAN CF Working Group Criteria Each new case was reported and sent to the coordinating center in Paris (Ethical approval was obtained in each country) Results: 102 cases were reported, 60% were males; age was 14 4 [6 5-23 5] years The patients were divided into 2 groups: complete obstruction (A) and incomplete obstruction (B) There was no difference in age, genotype, CF liver disease, or chronic Pseudomonas infection, 54% had a previous episode of DIOS BMI mean (SD) was 20 1 (2 2), half the patients had mild wt loss, anorexia in 63%, only A had vomiting Outdoor temperature was >20° in 52% Only 2% and 9% patients respectively were on a high fiber or high fat diet. Poor compliance with enzymes was uncommon and over half the patients were on PPI. All A required IV hydration, non-opioid (85%) or opioid

(17%) relief, 87% Gastrografflin enema or polyethylene glycol (PEG) lavage , 4% required a colonoscopy and 9% surgery in 2 centers only; and B mostly received IV hydration (97%) and non opioid pain relief (55%) and 58% Gastrografflin enema or PEG lavage. Overall, 84 % were prescribed maintenance therapy. Conclusion: DIOS in children has a multifactorial cause; it may be related to climate but not to compliance.

DIOS	Complete Obstruction (A)	Incomplete Obstruction (B)
patients %	45	55
Meconium Ileus %	48	33
Pancreatic Insufficient %	96	89
Constipation %	26	51
Hospitalisation duration, days	5 (3-7)	3 (1-4)

Tu1300

The Value of Serial EUS Exams to Establish the Diagnosis of Chronic Pancreatitis

Suzannah J. Luft, Stuart R. Gordon, Timothy B. Gardner

Background & Aims: Endoscopic ultrasound (EUS) is often used as the gold standard to diagnose chronic pancreatitis (CP) despite concerns about its intra-operator reliability and validity. We sought to determine the benefit of repeat EUS in patients suspected of having CP but having an equivocal or negative initial EUS exam for CP. Methods. Patients who underwent at least two EUS exams at our medical center to evaluate for CP from 2001-2012 were identified. Demographic, procedural and etiologic factors were abstracted via chart review. Specifically, EUS minimal standard criteria (MST) for CP (hyperechoic foci, hyperechoic strands, lobularity, cysts, ectatic duct, hyperechoic ductal wall, dilated side branches, ductal stones, ductal dilation) were abstracted for all exams. Diagnosis of CP was based on physician impression following each EUS. Results: Between the first and second EUS exams, the number of patients diagnosed with CP increased from 49% to 76% (p<0.01). Additionally, the number of patients with an indeterminate diagnosis after the first exam decreased significantly after the second exam (41% vs 21%, p<0.01). The presence of hyperechoic foci increased on the second exam (50% vs. 68%, p=0.04), but no other parenchymal or duct features were found to reliably increase. On subgroup analysis, significant increases in hyperechoic foci identified on repeat EUS were found in women (43% vs 67%, p=0.03), patients under the age of 50 (47% vs 74%, p<0.02) and patients in whom recurrent acute pancreatitis is the etiology of their CP (18% vs 73%, p=0.03). Conclusions: Serial EUS exams are valuable in patients with indeterminate prior EUS exams in whom the diagnosis of CP is not secure. In particular, women and those <50 years old appear to benefit the most from serial evaluation.

Tu1301

Predictors of Severe Dysplasia in Surgically Resected Non-Malignant Intraductal Papillary Mucinous Neoplasms (IPMN)

Brett C. Sklaw, Kevin M. Cronley, Veeral Oza, Jean R. Park, Jordan Thomas, Michael Wellner, Feng Li, Mark Bloomston, Peter Muscarella, Samer El-Dika, Jon P. Walker, Kyle Porter, Benjamin Swanson, Darwin Conwell, Somashekar G. Krishna

Background: IPMNs are potentially malignant lesions that arise from stem cells in the pancreatic ducts that generally follow a progression from benign neoplasm to invasive carcinoma. Predicting the risk for more advanced lesions, including those with severe or high-grade dysplasia, remains a challenge. Prior studies have described discrepancies in pre-resection differentiation of IPMN-subtypes when compared to final pathology **Aims:** To determine predictors for severe dysplasia in patients with pathological confirmation of non-malignant IPMNs **Methods:** A retrospective review of the pathology database from January 2000 to July 2013 at a tertiary care center. Demographic information, patient's history, cross-sectional imaging studies of the abdomen, endoscopic ultrasound (EUS), and surgical pathology were reviewed. **Results:** A total of 607 resected cystic and solid pancreatic lesions were reviewed. 48 patients were excluded due to preceding neo-adjuvant chemotherapy. Among the remaining 559 total patients, 247 had cystic lesions. A total of 132 patients had IPMNs, among which 93 (70.5%) patients did not have associated adenocarcinoma. Dysplasia was seen in 77 (95.1%) of 81 patients with complete pathology reports. For all IPMN-types, 61/77 (79%) patients had mild to moderate dysplasia, while 16/77 (21%) patients had severe dysplasia. Review of pathology revealed that the majority of severe dysplasia were seen in main duct (MD)- or mixed-IPMN compared to branch duct (BD)-IPMN [13 of 28 (46.4%) vs. 3 of 49 (6.1%), p < 0.001]. Evaluation with EUS was available only in 53.8% of patients. By univariate analysis (table 1), factors predicting severe dysplasia in non-malignant IPMNs were the presence of diarrhea, main pancreatic duct (MPD) dilation on either EUS or imaging (CT or MRI), and acute pancreatitis (either prior history of or as a presenting disease). Cyst size was available in 75 of 77 IPMN lesions and was not predictive of severe dysplasia. After multivariate analysis, any history of acute pancreatitis [Odds ratio (OR) 6.20, p-value 0.03, 95% confident interval (CI) 1.21-31.78] and dilation of the MPD (OR 10.12, p-value 0.008, 95% CI 1.83-44.94) were found to be predictive of severe dysplasia in non-malignant IPMNs. Subset analysis among branch duct-IPMN did not reveal any significant variables predictive of severe dysplasia. **Conclusion:** Retrospective analysis of patients who had resected non-malignant IPMNs suggests a low prevalence of severe dysplasia among BD-IPM. A history of acute pancreatitis and imaging evidence of MPD dilation appear to predict the presence of severe dysplasia for all IPMN-subtypes.

Categorical Variables	Total	Mild Dysplasia	Severe Dysplasia	P-Value
Gender (male)	76	24	11	0.051
Caucasian race	66	47	14	1.0
Symptoms				
Weight loss	60	5	4	0.20
Diarrhea	56	2	4	0.03
Abdomen pain	65	28	11	0.13
Nausea or vomiting	59	9	3	0.72
Other history				
History of acute pancreatitis	67	8	7	0.01
History of diabetes mellitus	70	15	7	0.21
History of chronic pancreatitis	66	2	0	1
Smoking (never, past, current)	61	22	6	0.73
Alcohol use (any)	58	17	3	0.73
Endoscopic ultrasound (EUS)				
Solid component or intracystic debris	40	4	0	1.0
Fluid opacity	27	3	0	1.0
Fluid: Viscous or thick	31	17	3	1.0
Cytology. Presence of mucin	24	4	3	0.06
Combined imaging (CT/MRI/EUS) results				
Chronic pancreatitis	58	8	4	0.44
Multi-focality	47	27	3	1.0
Pancreatic duct dilation	63	17	11	0.001
CONTINUOUS VARIABLES		Mean ± Std deviation	Mean ± Std deviation	P-value
Age (in years)	77	64.20±11.88	63.15±9.92	0.75
CA 19-9 (U/mL)	43	276.01±1017.28	22.40±15.75	0.42
Total bilirubin (mg/dL)	65	0.77±0.36	0.82±0.66	0.69
Cyst CEA (U/mL)	32	10680 ± 32681	332 ± 45	0.66
Maximum diameter of main pancreatic duct (in mm)	12	0.98±1.31	0.93±0.73	0.94
Size of lesion (in cm)	75	3.10±3.08	3.39±1.33	0.73

Table 1: Univariate analysis of factors predicting dysplasia in non-malignant intraductal papillary mucinous neoplasms (IPMNs)

Tu1302

Outcome of Branch Duct IPMN Follow Up Cases

Daisuke Masuda, Takeshi Ogura, Akira Imoto, Ken Narabayashi, Sadaharu Nouda, Toshihiko Okada, Kumi Ishida, Yosuke Abe, Toshihisa Takeuchi, Takuya Inoue, Michiaki Takii, Eiji Umegaki, Kazuhide Higuchi

Background and Aim: New International Consensus Guidelines for IPMN were published in 2012. We have several unsolved problems on diagnosis of branch duct type IPMN (BD-IPMN) follow-up time. In this study we evaluated how to follow up BD-IPMN. Methods: We studied retrospectively BD-IPMN cases in Osaka Medical College Hospital along the new IPMN guidelines. We classified BD-IPMN in three criteria; "high-risk stigmata" (HRS), "worrisome features" (WF) or "no high-risk or worrisome features" (NHW) on the respect of imaging findings, and studied on imaging findings, imaging progression rate in BD-IPMN follow-up cases. Subjects: Subjects were 336 BD-IPMN follow-up cases (Mean ages; 67.9±0.5 years, gender; male/female 182/154) in Osaka Medical College Hospital from 1995 to 2013. We had 21 HRS, 84 WF, 231 NHW. Mean follow-up time was 1465 days. Results: 1) MPD diameter; HRS: 6.3±1.0mm, WF: 4.2±0.2mm, NHW: 2.8±0.1mm (HRS:WF p=0.0006, HRS:NHW p<0.0001, WF:NHW p<0.0001). Cyst size; HRS: 32.3±4.9mm, WF: 24.6±1.3mm, NHW: 13.9±0.4mm (HRS:WF p=0.0351, HRS:NHW p<0.0001, WF:NHW p<0.0001). Mural nodule diameter; HRS: 11.7±0.6mm, WF: 4.4±0.5mm (HRS:WF p<0.0001). 2) There were total 49 progression cases for 959 days in this subjects. Imaging progression rate was 71.4% (15/21) in HRS, 16.7% (14/84) in WF, and 8.7% (20/231) in NHW, there were significant differences among 3 groupes (p<0.0001 between HRS and WF, HRS and NHW, p=0.0428 between WF and NHW). Time to imaging progression were 673 days in HRS, 831 days in WF, and 1264 days in NHW, there was significant difference (p=0.0186) between HRS and NHW in time to progression. 3) In 15 HRS progression cases, 4 had MPD size enlargement, 5 had cyst size enlargement, 2 was nodule size enlargement. 46.7% (7/15) were dead of invasive ductal carcinoma (IDC) derived from IPMN for 668 days, 6.7% (1/15) underwent resection, 46.7% (7/15) were followed because of other disease treatment or high age. 4) WF had 5 MPD size enlargement, 9 cyst size enlargement, 2 mural nodule appearance, 1 nodule enlargement. 3 appeared invasive ductal cancer derived from IPMN. 7 of 14 progressed to HRS for mean 768 days. 28.5% (2/7) died of IDC, 1/7 underwent resection, other 57.1% (4/7) were followed because of pancreatic cytology negative. 5) NHW: 10 cases had MPD size enlargement, 16 had cyst size enlargement, 3 had nodule size enlargement. 13 cases progressed to WF for mean 1170 days, 2 cases appeared IDC 1573days and 1477days, one died of other disease, and the other is now alive. Conclusions: HRS cases had higher imaging progression than WF or NHW, so HRS should be treated as malignancy along new guideline. But in NHW we had also 2 IDC in follow-up cases, so we thought that careful follow-up is also needed for appearance of IDC.

Tu1303

Risk of Adenocarcinoma in Resected Intraductal Papillary Mucinous Neoplasm (IPMN) With Involvement of the Main Pancreatic Duct (MD)

Veeral Oza, Brett C. Sklaw, Kevin M. Cronley, Feng Li, Jean R. Park, Jordan Thomas, Michael Wellner, Kyle Porter, Mark Bloomston, Peter Muscarella, Samer El-Dika, Jeffery R. Groce, Benjamin Swanson, Darwin Conwell, Somashekar G. Krishna

Background: The 2012 Sendai guidelines recommend resecting all IPMN-MD provided the patient is a good surgical candidate. The risk of progression to cancer in IPMN-MD is estimated to be about 60%. The Sendai guidelines also recommend close monitoring of patients with a duct size of 5 to 9 mm. So far, there have been no consistent predictive factors for malignancy in IPMN-MD. **Aims:** Define risk factors for adenocarcinoma in IPMN-MD and long-term follow up of resected IPMN-MD. **Methods:** A retrospective review of the pathology database 1/2000 to 1/2013 was performed at a tertiary care center. Patient