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Invited Publications

Thursday, 10 March 2016, 8.30–10.00

Session 1: Cystic Neoplasms of the Pancreas

Chairs: Jean-Charles Nault (France), Arnaud Roth (Switzerland)

PG 1.1 SPEAKER ABSTRACT

Discriminating pancreatic cystic neoplasms: histopathological and molecular features

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Cystic lesions of the pancreas are increasingly identified with a reported prevalence of 3–5%, increasing with age. Pancreatic cysts comprise a broad spectrum of entities, including inflammatory lesions, benign neoplasms and carcinomas. Nevertheless, most resected – and therefore clinically relevant – pancreatic cystic lesions belong to one of the following entities: intraductal papillary mucinous-cystic neoplasms (IPMN), mucinous-cystic neoplasms (MCN), serous-cystic neoplasms (SCN), neuroendocrine cystic tumors (NECT) and solid-pseudopapillary neoplasms (SPN). IPMN and MCN are precursors of ductal adenocarcinoma, whereas NECT and SPN are low-grade, potentially malignant lesions and SCN are usually benign tumors. Due to their distinct biological behavior, a pre-operative stratification of pancreatic cysts according to their malignant potential is mandatory in order to choose the appropriate treatment and possibly avoid unnecessary surgery. On the other side, a careful post-operative assessment is important for further clinical management and follow-up. A combination of high-resolution imaging methods, biochemical cyst fluid analysis as well conventional cyto- and histopathology and immunohistochemistry are helpful in the pre- and postoperative assessment of pancreatic cystic lesions. Moreover, novel molecular markers and methods are being increasingly used to improve diagnostic accuracy. A combination of clinical and imaging features, morphological characterization and molecular subtyping will lead to a better understanding of the natural history and biological behavior of this heterogeneous group of lesions.

Conflict of interests: No conflict of interests

PG 1.2 SPEAKER ABSTRACT

Cystic neoplasms of the pancreas. Differential diagnosis of pancreatic cystic neoplasms

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Pancreatic cystic neoplasms account for 10–15% of all pancreatic cystic lesions and approximately 1% of pancreatic neoplasms.
The reported overall prevalence of pancreatic cystic neoplasms in the general population ranged from 3% (in studies using CT imaging) to 15% (in studies using MR imaging) and increased with age.
Serous cystic neoplasms (SCN), mucinous cystic neoplasms (MCN) and intraductal papillary mucinous neoplasms (IPMN) are the most common types of neoplastic cysts of the pancreas.
Less frequently observed are the solid pseudopapillary neoplasm (SPN) and the cystic pancreatic endocrine neoplasm (CPEN).
Some demographic characteristics (age and gender), location in the pancreas and specific imaging or cystic fluid analysis features may be useful for the differential diagnosis of these cystic lesions.
The distinction between the mucin-producing cystic neoplasms (MCN, IPMN) and those that do not produce a mucin-rich fluid is important, because an increased malignant potential has been attributed to the mucin-producing variants.
High-resolution CT using thin sections with both enhanced and unenhanced technique may provide a presumptive diagnosis if characteristic features are present (i.e. central calcified scar specific of SCN).
MR imaging/MRCP has the potential of determining communication between the cyst and pancreatic duct.
EUS, in addition to the evaluation of the cyst morphology can provide cyst fluid through fine needle aspiration for further biochemical and molecular analysis.
SCN are frequently asymptomatic, their growth rate is slow and features associated to aggressive behavior include tumor location in the head of pancreas and tumor diameter > 6 cm.
Malignant potential of MCN ranged from 15 to 30%. Factors associated with malignancy are the presence of mural nodule (that should be distinguished from mucus) and tumor diameter ≥ 6 cm.
SPN is an uncommon pancreatic cystic neoplasm occurring in young woman, with a low malignant potential and a very god prognosis after resection.
IPMN are characterized by ductal involvement, which distinguishes them from MCN. Ductal dilatation is caused by excessive mucin secretion from the intraductal dysplastic epithelium. IPMN can be divided into main-duct IPMN (MD-IPMN), branch-duct IPMN (BD-IPMN), and mixed-type IPMN (MT-IPMN) depending on the main pancreatic duct (MPD) involvement (defined by dilatation of the MPD to > 5 mm in the absence of obstruction), alone in MD-IPMN, associated with side-branch dilatation in MT-IPMN or absent in BD-IPMN.
Overall, BD-IPMN are more indolent with lower malignant potential than MD-IPMN.
In conclusion, differential diagnosis of pancreatic cystic neoplasms is important as surveillance and management strategy is dependent on the type of lesions, with the aim to prevent the development of invasive cancer in these cysts.

PG 1.3 SPEAKER ABSTRACT

Clinical relevance of pancreatic cystic neoplasms: treatment or watchful waiting?

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Background: Cyst-like lesions in and around the pancreas are a frequent finding. In the absence of a history of pancreatitis a pseudocyst is less likely and the focus is on a cystic neoplasm.
Pancreatic cystic neoplasms (PCNs) are being increasingly detected. Their clinical relevance and the "correct" management are debated. Some guidelines either regarding PCN in general [1] or specifically focusing on intraductal mucinous neoplasms [2] are published. But since there are many relevant questions open and evidence for recommendations is missing this topic truly is a work in progress.
There is a broad differential diagnosis and there are different biological properties of one entity. PCN include mucinous and serous cystic neoplasms as well as the far less common cystic neuroendocrine tumours and pseudopapillary cystic neoplasms. If clinical or imaging data suggest that the lesion may be one of the latter two, resection is warranted in surgically fit patients due to the malignant potential of both these lesions.
In the vast majority of non inflammatory pancreatic cystic lesions we are talking about either serous or mucinous PCN. The distinction between serous and mucinous (producing a mucin rich fluid) neoplasms is important because the former bare almost no malignant potential whereas the latter do so in a various degree.
What is known about the specific lesions?
Serous cystadenomas, either microcystic or macrocystic, occur more commonly in women in the 6th decade. If presenting with a so called honeycomb pattern and a central calcification the diagnosis is made and neither surveillance nor resection are indicated due to the benign character of the lesion. However if the may slowly growing lesion causes symptoms or exhibits worrisome features such as cyst wall thickening or pancreatic duct obstruction further diagnostic tests (e.g. EUS), surveillance or even resection may become adequate.

The term mucinous cystic neoplasms was often used in a broader sense for all mucin producing neoplasms but today should be limited in a narrower sense to one specific entity (MCN) distinct from intraductal papillary mucinous neoplasms (IPMN).
The characteristics of MCN are: Perimenopausal women, no connection to the pancreatic duct, primarily located in the tale of the pancreas, thick wall and calcification in up to 30%. Because they bear a relevant malignant potential laparoscopic or open resection is the first choice and watchful waiting is not recommended especially for neoplasms of > 3 cm. If histology shows an ovarian-type stroma the diagnosis is confirmed and no further surveillance is indicated in case the lesion was benign.
The characteristics of IPMN are: Originating from or communicating with the main duct, side branches, or both. Often multifocal disease, risk for malignancy depending on the subtype (main duct vs branch duct type). For main duct and mixed type disease the risk for invasive cancer is clearly above 30% (up to 63%) and resection is recommended if the diagnosis is established or highly likely. Watchful waiting may be an option in small lesions with diagnostic uncertainty depending on the characteristics of the lesion and the general condition of the patient.
There are some criteria that help to discriminate premalignant from malignant lesions or at least help to better assess the risk of a PCN: main duct dilatation, wall thickening, septation, calcification, solid components within cyst and a cyst size of > 3 cm.

What is unresolved?

There are many open questions. The most important ones are:

– How to proceed with a PCN that cannot be assigned to one of the entities. What is the best work-up?
– The different high-risk stigmata are associated with unequal risks of malignancy. It is unclear how to weigh each risk factor
– Once the diagnosis of a branch duct IPMN is made, what is the best tool for surveillance and in which time intervals this may be needed.
– What is the risk of a pancreatic surgical resection in branch type IPMN with usually soft tissue and an undilated main pancreatic duct
– In which patients prophylactic total pancreatectomy is warranted in order to prevent future pancreatic adenocarcinoma

References

[1] Scheiman JM, Hwang JH, Moayyedi P. American Gastroenterological Association Technical Review on the Diagnosis and Management of Asymptomatic Neoplastic Pancreatic Cysts. Gastroenterology 2015;148: 824–848.
[2] Tanaka M, Fernández-del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, Kimura W, Levy P, Pitman MB, Schmidt CM, Shimizu M, Wolfgang CL, Yamaguchi K, Yamao K; International Association of Pancreatology. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology 2012; 12: 183-197.

Thursday, 10 March 2016, 10.30–12.00

Session 2: Biliary Tract – Extrahepatic Cholangiocarcinoma I

Chairs: Daniela Aust (Germany), Florian Lordick (Germany)

PG 2.1 SPEAKER ABSTRACT

Molecular differences between intra-hepatic and extra-hepatic cholangiocarcinoma

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Cholangiocarcinoma (CCA) is the second primary liver cancer following hepatocellular carcinoma. CCAs are divided on the basis of the anatomical location of the tumor in intrahepatic CCA, extrahepatic CCA (that includes hilar CCA and distal CCA) and gallbladder cancer. The incidence of intrahepatic CCA is rising worldwide whereas the incidence of extrahepatic CCA remains stable or slightly decreases. An old dogma considered that CCA derived from the malignant transformation of cholangiocytes. However, recent in cellulo studies and mouse models have shown that CCA could derive from liver stem cells but also from the de-differenciation of mature hepatocytes. The relevance of these phenomena in human diseases is still unknown. Moreover, next-generation sequencing has helped to drawn the genetic landscape of CCA with strong differences between genetic alterations observed in intrahepatic and extrahepatic CCA. Intrahepatic and extrahepatic CCA shared common genetic alterations such as *KRAS*, *ARID1A*, *SMAD4* and *GNAS* mutations. However, extrahepatic CCAs have mutations in *ARID1B* and *ATP1B-PRKACA/ATP1B-PRKACB* fusion genes. In contrast, intrahepatic CCA harbored *IDH1*/*IDH2* mutations, *BAP1* mutation, *ROS1* kinase fusion genes and *FGFR2* fusion genes. Interestingly, *IDH1*/*IDH2* mutations (14%) and *FGFR2* fusion genes (6% to 40%) could be considered as genetic hallmarks of intrahepatic CCA because there were never identified in extrahepatic CCA. Gallbladder cancer has also specific mutations in *EGFR*, *ERRB3*, *PTEN* and in the genes of the *MLL* family.
Finally, unresecable CCAs have limited therapeutic options and the combination of gemcitabine and cisplatine is the only treatment approved in this setting with a median overall survival of 11.7 months. The identification of the main driver genes in CCA by next-generation sequencing has defined new therapeutic targets. For example, *IDH1* and *IDH2* mutations could be targeted by AG-120 and AG-221 respectively and *FGFR2* fusion genes are potential druggable genetic alterations using FGF inhibitors such as BGJ398 or ponatinib. Recent studies have shown that at least 40% of CCA patients harbor potential actionable alterations that are amenable to therapeutic targeting. The first clinical trials driven by molecular alterations in CCA are currently underway.

PG 2.2 SPEAKER ABSTRACT

Patterns of recurrence after surgery for extrahepatic cholangiocarcinoma

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Goals: Cholangiocarcinoma (CC) is the most common malignancy of the biliary tract and divided in intrahepatic (iCC) and extrahepatic carcinoma (eCC). eCCs are further divided in hilar (hCC) and distal (dCC) tumours, which makes a profound difference in treatment approach. Surgery remains the only potentially curative approach to this rare disease. 5-year survival rates of 20–40% are reported, reflecting the importance of recurrence in this highly malignant disease.
Methods: A literature review via Pubmed has been performed to highlight the evidence on prognostic factors and patterns of recurrence.
Results: High quality evidence is low. eCC is a rare disease with increasing incidence rates over the last decades. This numbers are variing among different studies due to different ICD-O classification that are currently in use. Surgery remains the mainstay of therapy with resection rates of 60% for hCC and up to 90% for dCC. Diagnosis is based on modern cross sectional imaging, endoscopic or percutaneous transhepatic interventions and Magnetic Resonance Cholangiopancreaticography (MRCP). The surgical approach includes liver and bile duct resections for the hilar subtype and duodenopancreatectomies for dCC. Both procedures carry significant risks of postoperative morbidity and even mortality (3–10%). Factors influencing recurrence rates and survival are resection margins (R classification), positive lymph nodes (N stage), microscopic venous invasion, tumour histology and depth of invasion. The most common sites of recurrence are liver, local, distant lymph nodes, lungs and peritoneum.
Conclusion: Mainstay of treatment is surgery with high primary resection rates. Aiming for negative margins is crucial and can be influenced by the surgeon. High volume centers seem to be beneficial for positive outcomes. Patients with high risk recurrence patterns based on histology should be evaluated for adjuvant multimodal treatment strategies. Further research is needed to decode the biology of this increasingly diagnosed, highly malignant disease.

Disclosure of Interest: The author has no conflicts of interest to disclose.

PG 2.3 SPEAKER ABSTRACT

Adjuvant therapy for biliary tract cancer

J. Bridgewater
UCL Cancer Institute, London

Biliary tract cancer is an uncommon cancer in the western world although the incidence is rising the cause of which is uncertain. In the Far East, incidence is related to endemic liver fluke related hepatic inflammation the biology of which differs from that in the western world.
Significant advances have been made in the management of advanced disease with the optimisation of systemic therapy strategies and an increase in academic activity has followed. Significant issues remain with respect to adjuvant therapy the extant data for which will be considered. These issues will be partly addressed in the next 12 months with data from 2 adjuvant studies of systemic treatment. International collaborations have been established to maintain the research narrative.

Thursday, 10 March 2016, 12.00–12.30

Keynote Lecture

Chair: Florian Lordick (Germany)

KN I SPEAKER ABSTRACT

Keynote I: Molecular biology of pancreatic cancer

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Pancreatic cancer remains one of the most deadly cancers with very little progress made over the last few years with regards to treatment and prevention approaches. Recent studies have continued to elucidate the molecular biology of this disease. At the genetic level, studies show that pancreatic cancer (PDAC) develops as the consequence of accumulation of mutations in key oncogenes and tumour suppressor genes. The disease, once established, is characterized by high complexity, heterogeneity and genomic instability. Despite this facts, some patients harbour actionable mutations which targeting has resulted in significant clinical benefit. Indeed, one of the most active