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Perspectives on Pancreatic Cysts: How to Determine Malignancy

Dr. Buch:

Pancreatic cysts may be detected at 40 to 50% of patients undergoing intraabdominal MR imaging for unrelated reasons. Some cysts have the potential for malignancy or malignant transformation. This is your host for ReachMD *GI Insights* Dr. Peter Buch. Here to help us better understand pancreatic cysts is Dr. Rajeev Attam. Dr. Attam is a gastroenterologist at Kaiser Permanente down in California, whose special interest is evaluating pancreatic cysts. Welcome to the program, Dr. Attam.

Dr. Attam:

Thank you, Peter, thank you so much for having me here.

Dr. Buch:

It's a delight. Let's get right into it. Dr. Attam, what are some concerning features when we encounter a pancreatic cyst?

Dr. Attam:

Peter, as you've rightly said, with the wider use of CT and MRI, more and more patients have been diagnosed with pancreatic cyst, and the number that you said, what, 40 to 50% of patients who undergo MRI have a pancreatic cyst is indeed correct. But remember, the overall risk of malignancy in this incidentally-detected pancreatic cyst is low. It is estimated the risk of malignancy in a pancreatic cyst at the time of diagnosis is about 0.01%; it may be higher in cysts that are more than 2 cm in size and number they would be around 0.21%, but again, that's a pretty low number.

The risk of malignancy is higher with older age, in males, and in patients with present symptoms such as jaundice, weight loss, and recurrent pancreatitis. There are also some radiological features that are associated with increased risk of malignancies. These include cyst size of more than 3 cm, finding a solid component within the cyst, presence of a dilated main pancreatic duct, presence of enlarged upper abdominal lymph nodes on the CT scan or MRI, and increase in the cyst over a year by more than 3 mm in size. So these are all concerning features, that should raise your concern for malignancy in a cyst.

Dr. Buch:

Thank you. Let's hone down on a couple of types. Could you please discuss main ductular papillary, mucous neoplasms?

Dr. Attam:

Sure. So as per WHO classification, pancreatic cysts are broadly classified into four broad categories: serous cystadenomas, mucinous adenomas, intraductal mucinous cysto- neoplasms or IPMNs, and the solid pseudopapillary cysts.

IPMNs are intraductal papillary mucinous neoplasm, a potentially malignant intraductal epithelial tumors of pancreas, and these are composed of mucin-producing columnar cells. They are very similar to what we see as in polyps in colon, so that's a good analogy to follow. So IPMNs have been classified as either main duct or branch duct based on the anatomic involvement of the pancreatic duct. Main duct IPMN involves the main pancreatic duct while the branch duct involves the side branches. There's also a mixed duct type of IPMN where both the main and side branches are involved, but these patients tend to behave more like main duct IPMN.

So main duct IPMN, these patients present as diffuse or segmental dilatation of the pancreatic duct without obvious downstream stricture. This expansion of mucin-producing ductal cells, which can be seen as papillary projections into the duct, and many times these patients present with mucin at the pancreatic orifice when ERCP or endoscopy is performed. The pancreatic orifice in such patients are usually patulous and you can see mucin glob sitting right there. The majority of these main duct IPMNs arise in the head of the pancreas and progress distally towards the body and tail, and they can involve the side branches, as in mixed duct IPMNs.

The risk of cancer in these patients is pretty high. It's estimated to be about 70% in patients with main duct IPMN. As I said you could use the analogy of colon polyps while describing pancreatic IPMN cysts, even in the IPMN, the progression of benign neoplasm to invasive pancreatic cancer follows the adenocarcinoma sequence, as you see in the colon polyps.

The branch duct IPMNs on the other side have a lower overall incidence of pancreatic cancer, which is estimated at about 3% at 5 years and then at about 15% at 15 years after diagnosis.

Dr. Buch:

So, let's move on to mucinous cystic neoplasms and could you describe those please.

Dr. Attam:

Sure, so, IPMNs and mucinous cystic neoplasms are two mucin-producing cystic neoplastic lesions of the pancreas. The MCN of mucinous cystic neoplasms occur almost exclusively in men and are usually seen after the age of 40 years. They are more common in the body and tail of the pancreas. Unlike the branch duct IPMN, mucinous cystic neoplasms do not communicate with the main pancreatic duct. These mucin-producing cysts are lined by columnar epithelium which is surrounded by ovarian stroma. Presence of ovarian stroma is pathognomonic for MCNs. On cross-sectional imaging, mucinous cystic neoplasms classically appear as separated cystic lesions, although they can also be unilocular, meaning having one cyst. Sometimes, calcifications can be seen on these cysts, in about 15% of patients.

So mucinous cystic neoplasms have a significant risk of developing cancer. And there are some features that are associated with higher risk of malignant transformation in these cysts, and these features include larger size; usually the cysts that are about 5 cm or larger have a higher risk of forming cancer. Cancer is very rare in cysts less than 3 cm in size, presence of a thickened or irregular cyst wall is associated with higher risk of cancer; presence of internal solid component within the cyst and presence of calcifications of the cyst wall, these are all features associated with malignant transformation in these cysts.

Due to the high risk of malignancy, a resection is usually recommended in appropriate candidates. But again, remember the risk of cancer is higher in larger cysts, the smaller cysts rarely have cancer, especially if they do not have solid component or mural nodules within the cysts.

Dr. Buch:

For those of you just joining us, this is your host Dr. Peter Buch discussing pancreatic cysts with Dr. Rajeev Attam. So Dr. Attam, which patients should be entered into a cyst surveillance program?

Dr. Attam:

That's a great question, Dr. Buch. Cyst surveillance should be offered to patients with asymptomatic mucinous cystic neoplasms and IPMNs who are surgically fit and will likely pursue surgical resection as the need arises. Patients with benign inflammatory cysts like a pseudo-cysts and non-neoplastic cysts such as serous adenomas do not need surveillance. Patients who are surgically fit and have worrisome features, such as solid components within the cyst or have a dilated main pancreatic duct, should be referred for surgical evaluation rather than cyst surveillance.

Before initiating cyst surveillance, it is imperative to evaluate the patient's risk of developing pancreatic cancer, the estimated life expectancy, and other health conditions. It is also important to take consideration of the location of the pancreatic cyst. As you know, cysts in the body and tail of the pancreas are easier to resect with distal pancreatectomy as compared to cysts in the head and the uncinate process, which may require an extensive surgery like Whipple for removal of the cyst.

Dr. Buch:

How should we approach a pancreatic cyst that has concerning features but yet the endoscopic ultrasound fine-needle aspiration is negative for malignancy?

Dr. Attam:

Though highly specific, cytology from pancreatic cyst fluid obtained with EUS-FNA is only about 50 to 55%, so to have a negative cyst fluid cytology does not exclude dysplastic or malignant pancreatic cyst.

Patients with concerning features of malignancy should be referred to a multi-disciplinary group for consideration of surgical resection. There are also newer techniques that are available to improve this sensitivity and diagnostic yield of EUS-FNA to help guide surgical management. These new techniques include testing the cyst fluid for molecular analysis and sampling with novel devices such as micro-biopsy forceps and cytology brush, which can improve diagnostic yield. The micro-biopsy forceps in a recent study showed a sensitivity of 82%, which is much higher than 55% of regular cyst fluid cytology. Also, confocal laser endomicroscopy has been used to help determine malignant cysts from benign cysts.

Again, if the patient has concerning features and they are in good health and are a candidate for surgery, then a referral to a multi-disciplinary team for evaluation for resection should be made, even if the cytology on the EUS-FNA is negative.

Dr. Buch:

Perfect. And that's a wonderful segue to our last question. How do we avoid unnecessary surgery?

Dr. Attam:

That's again a great question, Peter. I've seen many patients being referred to surgery when they do not need surgery for pancreatic cysts, and that's per recent review about 14% of resections that are performed for asymptomatic, benign cysts which appear preoperatively suspected to be potentially pre-malignancies. So it is important to carefully select the patients and send only the patients who have high-risk features for surgery. Again, patients with IPMN or MCN should be evaluated with EUS-FNA to establish a diagnosis and look for malignancy. We went over the features of malignancy which include larger cyst size, presence of solid component within the cyst, presence of main duct dilatation; these features, again, point towards high risk, and these patients should be evaluated with EUS-FNA and be sent to multi-disciplinary team for evaluation.

At the same time, the cysts that do not lead to cancer should not be sent for resection, and these patients should be easy to diagnose. Pseudocysts are benign and can be diagnosed by taking history and looking for features on cross-sectional images, and if there is still doubt EUS-FNA can be used to diagnose these patients and prevent unnecessary surgery.

Serous cysts also do not need surgical resection because the risk of malignancy is exceedingly low in these patients. These patients need surgery only if they develop symptoms due to the space-occupying size of the serous cyst.

Asymptomatic mucinous cysts, such as mucinous cystic neoplasms and IPMNs, without high-grade features, can be followed with cross-sectional imaging and if they remain stable in size, they do not need surgical resection.

Referral for EUS-FNA and surgery should be made only when concerning features arise or if they develop symptoms such as new-onset diabetes, jaundice, recurrent pancreatitis, or the CT scan or MRI start showing change in cyst size over a period of time, or labs show a higher CA 19-9, etc. Otherwise, many of these patients can be followed with surveillance alone.

Lastly and most importantly, patients' health and overall health scales needs to be considered when making these management decisions.

Dr. Buch:

Thank you, so much. I want to reemphasize, multi-disciplinary team. That's all the time we have for today. Dr. Attam, I wanted to thank you so very much for educating us about pancreatic cysts.

Dr. Attam:

Thank you, Dr. Buch, it was a pleasure. I hope this will help our fellow clinicians in deciding which patients to be sent for surveillance and which patients should be sent for multi-disciplinary evaluation for resection.

Dr. Buch:

Absolutely, I think so too. For ReachMD, this is Dr. Peter Buch. To access this episode as well as others from this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for joining us today. See you next time.