

PANCREAS

How to Deal with a Periapillary Mass?

Claudio Bassi MD.
Giovanni Butturini MD.
Roberto Salvia MD.
Hazem Abbas MD.
Massimo Falconi MD.
Paolo Pederzoli Prof.

From the Surgical and
Gastroenterological Department
Pancreatic Unit Hospital
G.B. Rossi University of Verona

Today Pancreaticoduodenectomy has less than 5% mortality rate in experienced centers. As a consequence, surgeons in high volume centre are more willing to embark on resecting periampullary mass without tissue diagnosis and extensive work up to identify its pathological nature: diagnosis seems to be less important than appropriate staging. Whenever jaundice is present the endoscopic placement of biliary stents should be considered both after consultation with the surgeon and radiological staging to avoid “wild management” in potentially resectable cases and difficult readings by CT and/or MRI imaging carried out with “in situ” stents.

The aims of imaging are:

- to identify resectable mass;
- correct staging (avoiding useless surgery);
- to distinguish pancreatic cancer with other periampullary malignant or benign diseases.

US, CN scan and/or “all in one” CWMRI are the essential steps in the work up.

Clear cut resectable cases should move to surgery directly. At the same time clear cut not resectable patients have to undergo FNA for final diagnosis and neo adjuvant treatments, if any.

Despite formidable imaging improvement some patients still undergo laparotomy only to be found to have unresectable disease.

Optional tools such as endoscopic US, PET and pancreatoscopy should be claimed in selected patients. ERCP should be still used for citological aims in particular cases; today angiography seems to be useless.

Laparoscopy (in association with US) could play a role in larger primary tumours and whenever equivocal findings occur, for example in the case of potentially resectable mass with very high Ca 19-9 serum levels.

Last but not least, some cases may still deserve intraoperative palpation and US.

Today’s pancreatic surgeon philosophy facing periampullary mass should be more in the sense of “can I take it out” than “what this mass is?”

Keywords: periampullary tumors, pancreatic cancer, pancreaticoduodenectomy

Introduction

Facing with a periampullary mass, the first step is to reach a diagnosis, if possible, before surgery. The second step in the case of malignancy is the accurate staging and then deciding whether it is resectable or not.

Even if obtaining information about the characteristics of the disease (nature, size, exact location) and establishing the tissue diagnosis preoperatively may simplify the decision to operate and the operation itself (saving both time, human and economic costs), nowadays pancreaticoduodenectomy has less than 5 percent mortality rate in experienced centers. As a consequence, surgeons in high volume centre are more willing to embark on resecting a periampullary mass without a tissue diagnosis and an extensive work-up. Diagnosis then seems to be less important than appropriate staging [1].

In this paper we discuss the limitation of the diagnostic methods in periampullary lesions suggesting the way to follow on the basis of actual acknowledgements.

The Work-up

Frequently benign or malignant periampullary diseases may present with the same symptoms [2]. A variety of non-invasive and invasive diagnostic methods are available to differentiate tumors from pancreatitis, and,

used in combination, they can accomplish these goals with accuracy. Despite technical advances in diagnosis within the last decade, there is more potential for misclassification of cancer of the pancreas, than for any other type of cancer because of the difficulty of an accurate diagnosis. Major differential diagnoses are proximal duct dilation or pancreatic carcinoma that has developed from pre-existing chronic pancreatitis [3, 4]. The definitive diagnosis can be difficult or impossible, even at surgery. Direct biopsies are about 60% sensitive for malignancy. So many carcinoma of the pancreas are not detected until late in its course.

Moreover, there is a subgroup of patients with periampullary mass, in whom the complexity of differential diagnosis is enhanced. The majority of pancreatic tumors are localized to the head and also chronic pancreatitis seems to prefer the head region.

The cancer is frequently associated with secondary inflammatory changes, and since pancreatic carcinoma may develop from chronic pancreatitis the changes are very important due to the increased risk of developing malignancy. Chronic pancreatitis has been suggested as a risk factor for pancreatic carcinoma, and can mimic pancreatic carcinoma as well [5].

Gulik et al. reported a 6% incidence of chronic pancreatitis among 220 pancreaticoduodenectomies performed as a result of suspected pancreatic head carcinoma.

noma [6]. In a larger series of patients who underwent resection for chronic pancreatitis, cancers were found in 4/64 cases [7] and 4/250 cases [8] but the number of patients who underwent pancreatoduodenectomy due to false positive tumor diagnosis is not known.

The management and prognosis in the case of chronic pancreatitis or periampullary cancers is different and the diagnosis still problematic.

Unnecessary laparotomies in the case of pancreatic cancer are avoided since resectability can be correctly predicted with a computed tomography scan and laparoscopy in more than 80% of the cases, but no preoperative diagnostic procedures can completely differentiate between pancreatic head mass caused by chronic pancreatitis or that caused by tumor. Sometimes the diagnosis can be impossible at surgery and "blind" resection must be done to avoid missing a suspected tumor [9].

Biochemical study

A part from the routine efforts to determine, for example, the degree of jaundice it involves the analysis of multiple assays of tumor-associated antigens including oligosaccharides which can help in the diagnosis.

CA 19-9

This is the most important and popular. The specificity may vary from as low as 73% to more than 95%. False negative results are frequent in patients with a Lewis blood group negative phenotype in addition false positive assays can occur in patients with chronic pancreatitis and cirrhosis.

Changes in the quantity of elastase 1 also appear to be of diagnostic value. Multivariate tumor marker analysis could become an important screening method in cases involving an uncertain differential diagnosis between pancreatic cancer and chronic pancreatitis [10].

K-ras gene

More than 80% of pancreatic carcinomas contain mutations of the K-ras gene. Screening duodenal fluid for these mutations may lead to early detection of these cancers. Some pancreas without cancer, however, may also harbour K-ras mutations, and non-mutated K-ras is observed in 15% of cancer potentially limiting the specificity of K-ras based tests. Detection of mutations of the K-ras gene in cells shed in pancreatic secretions may improve the still difficult differential diagnosis of chronic pancreatitis versus malignancies.

Ultrasound (U.S.)

The specificity and sensitivity of U.S. in advanced cases can achieve 90% but it is low in the early stages. It can detect biliary and pancreatic ductal dilation, but it may not be useful in differentiating different periampullary neoplasms from surrounding chronic pancreatitis.

However, it is the most sensitive test for excluding gallstones.

Computed tomography (C.T.)

It can detect the changes of shape and size of the pancreas and the irregularities of the pancreatic ducts, and has a more important role in detecting changes earlier than any other imaging procedure. C.T. sensitivity has been reported to be between 70–90% and specificity has been reported to reach 80–100%, respectively. The sensitivity depends on the stage of the disease, but it is higher than that of ultrasound. The C.T. scan with i.v. contrast is the initial diagnostic imaging procedure of choice for patients with periampullary lesions.

The C.T. staging should be performed before any kind of stenting decompression of the biliary tract: the presence of stents can jeopardize the quality of C.T. imaging leading to not correct conclusions.

Endoscopic retrograde cholangiopancreatography (ERCP)

It has considerable value in patients together with normal and atypical CT and in making a differential diagnosis using cytology. The sensitivity of ERCP for the diagnosis of ductal cancer approaches 95% [12]. A major role for ERCP is palliative therapy of cholestasis by stenting of the malignant bile duct stenosis. ERCP has not lost its importance due to the possibilities of transpapillary biopsy or brush cytology.

Fine-needle aspiration biopsy (FNAB)

Percutaneous core biopsies for fine-needle-needle-spiration cytology is highly specific (90%) and has a high positive predictive value. Reported sensitivity and negative predictive values for pancreatic cancer are generally lower (ranging from 60/70%), and thus a negative aspirate cannot exclude malignancy.

Because of its low sensitivity, negative predictive value and potential complications, we believe that FNAB has little or no role in evaluating patients having resectable mass. There is a definite role for FNAB in non resectable cases, in poor risk patients for whom a major resection is not possible, but who are candidates for palliative chemioradiation therapy.

Upper gastro-intestinal endoscopy

It can play a role in case of Vater papilla tumors, duodenal tumors and for the evolution of duodenal stenosis.

Endoscopic ultrasound

At present, it can be regarded as the most sensitive procedure for detecting those with early chronic pancreatitis and small pancreatic tumors. It is a promising and very reliable method of preoperative T staging [13].

Magnetic resonance imaging: MRI

The overall accuracy of imaging in assessing extra-pancreatic tumor spread, lymph node metastases, liver metastases and vascular involvement was 95.7%, 80.4%, 93.5% and 89.1% respectively [14].

Magnetic resonance colangiopancreatography: MRICW

In contrast to invasive ERCP, MRICW is non invasive and safer, but ERCP is preferable when a therapeutic procedure is necessary. In association MRI and MRICW give complete informations on the presence and extension of the lesion ("all in one") [15].

Positron emission tomography: PET

It is suitable as a tool for differential diagnosis. PET shows an overall sensitivity of 85% and a specificity of 84%. The diagnostic accuracy is very dependent on serum glucose levels [16].

Pancreatoscopy

It has been reported to be associated with high success rates (75–90%). This technique has been proposed to distinguish between chronic pancreatitis and pancreatic cancer. Endoscopic brush-citology of biliary and pancreatic strictures can also confirm cancer [17].

Laparoscopic staging

It is suitable in establishing the operability of pancreatic tumors, and gives the possibility of performing ultrasonographically guided fine-needle aspiration biopsy, which provides a rapid, safe diagnosis [18].

The technique should be always performed if suspicion of peritoneal involvement is present. Small liver metastasis not detectable by US, CT and MRI should be shown by laparoscopy. A recent review [19] suggests that it can avoid unuseful laparotomy in a range of 3–14% of cases.

Conclusion

Facing with a periampullary mass the most important question to answer is whether or not it is malignant.

In experienced centre morbidity for pancreaticoduodenectomy is acceptable and management of complications leads to low mortality rate [20]. As a consequence surgeons are more prone to resect on the bases of precise staging than appropriate nature diagnosis. The need for surgery is often determined by the presence or absence of jaundice or duodenal obstruction. In a patient with obstructive symptoms resection may be the treatment of choice regardless of the diagnosis. Obviously, in these cases, preoperative histological confirmation is not essential before surgical intervention. By contrast adjuvant treatment of advanced cases depends on accurate diagnosis. Thus, the need for

diagnosis is inversely proportional to the degree of resectability of the lesion [21, 22, 23].

Cystic lesions are easily identified by CT or MRI. Fine-needle aspiration biopsy cannot sufficiently differentiate between malignant and benign cystic tumors, with a failure rate of about 30%. Rapid tumor enhancement and specific biochemical features may suggest an endocrine tumor. The vast majority of periampullary tumors are ductal carcinomas, which are almost always solid masses. Even though nonductal tumors are often solid, cystic components demonstrated radiographically in an isolated pancreatic mass suggest a nonductal tumor, which has a far better prognosis [22, 24].

Then, the first step is the staging of the disease and the evaluation of the fitness of the patient. Various imaging techniques may suggest the diagnosis or the potential for resectability, but even with all the cytological techniques in 15–20% of the cases it is impossible to differentiate among several different periampullary lesions. This means that in practice one in five patients with a suspected cancer may have no confirmed diagnosis after having completed a staging protocol.

What can we do with a mass intraoperatively without previous cytologic or histologic verification? When must we strive to establish definite diagnosis at all costs, and how can we achieve it?

Intraoperative FNA cytology is the most common method. The sensitivity is reported to be 70 to 100%, most often it is around 90%. Tissue biopsy of pancreatic lesions can be done as incisional or wedge biopsies or by use of Trucut needles. The sensitivity of pancreatic biopsy for histological evaluation has been reported to be 83–92%. False positive results are extremely rare. The reported rate of complications related to the biopsy varies from 0% to 10% and the mortality rate from 0% to 4% [23].

The reason that the sensitivity of intraoperative tissue biopsies is not better than FNA cytologies is the surgeon's fear of complications. Cautious wedge biopsies, obtaining specimens which are too superficial, can result in false negative reports because pancreatic cancer is often surrounded by a large rim of pancreatitis. Therefore, needle biopsy is recommended for masses located deep in the head of the pancreas, reserving tissue biopsy only for superficial lesions [3].

When should pancreatic biopsies be done? If pathological confirmation alters our decision about resection, all efforts should be made to confirm the diagnosis keeping in mind that resection remains a valuable form of treatment for painful or complicated chronic inflammatory head mass; therefore, if the tumor seems to be resectable, it should be resected when this is feasible with a low mortality rate.

The most questionable cases are those patients who have a mass without any obstructive symptoms. It may also be a chance finding of suspected pancreatic cancer. On the other hand, an asymptomatic focal mass secondary to chronic pancreatitis may require no surgical treatment. In these cases accurate biopsy should be done. If the biopsy is positive, resection may be done.

Evaluating the result we have to take into consideration that a benign finding in itself never excludes the presence of a malignancy [25].

In conclusion, whenever the periampullary solid mass is resectable and your mortality rate for pancreaticoduodenectomy is less than 5%, take it out [26]!

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