RATIONAL IMAGING

Investigation of abdominal pain to detect pancreatic cancer

J Ashley Guthrie, Maria B Sheridan

Department of Clinical Radiology, Lincoln Wing, St James's University Hospital, Leeds LS9 7TF

Correspondence to: J A Guthrie ashley.guthrie@leedsth.nhs.uk

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When a patient presents with abdominal pain, which investigations should clinicians use to establish whether the pain results from pancreatic cancer?

The patient

A 76 year old woman with no important medical history presented after six months of intermittent epigastric discomfort and back pain. These symptoms were associated with 1 stone (6.4 kg) of weight loss despite a good appetite. Immediately before referral, she had developed increased flatulence and loose stools. Physical examination was normal. Test results were normal for full blood count; glucose; urea and electrolytes; liver function; upper gastrointestinal endoscopy; and duodenal biopsy.

What is the next investigation?

The differential diagnosis of upper abdominal pain is wide, and investigation depends on eliciting either features in the history or signs that point to an organ of origin. Pancreatic pain, due to either cancer or chronic pancreatitis, classically radiates to the back and is provoked by eating. Occasionally the onset of diabetes helps to point to a pancreatic cause.

In practice, abdominal pain of pancreatic origin has few specific features, and consequently other diagnoses are likely to be considered. Gallstone disease, peptic ulceration, and gastric or colonic cancer are all more common than pancreatic disease, often leading to these systems being investigated first. Ductal adenocarcinoma, the commonest pancreatic neoplasm, has a propensity to affect the pancreatic head and to obstruct the common bile duct so as to cause jaundice. If jaundice develops, the diagnostic pathway becomes straightforward, with ultrasonography used to differentiate between parenchymal liver and obstructive causes. With the onset of jaundice, pain is often disregarded or leads to gallstones being considered as the cause. In the absence of jaundice, as in this case, the choice of investigation is usually between transabdominal ultrasonography for biliary disease, endoscopy of either the upper or lower gastrointestinal tract, or computed tomography. Distal obstruction of the

pancreatic duct can cause steatorrhoea, and the associated change in bowel habit may prompt colonic investigation.

Transabdominal ultrasonography

Ultrasonography is the primary investigation in patients with pain if cholelithiasis is the leading diagnosis. In addition to the gall bladder and common bile duct, the liver, spleen, pancreas, kidneys, and aorta will also be examined. Ultrasonography may reveal an array of alternative causes of pain arising from these organs, ranging from disseminated malignant disease with liver deposits or bulky lymphadenopathy to benign conditions such as renal stones or an aortic aneurysm. Retroperitoneal structures such as the pancreas may be seen with ultrasonography; however, overlying bowel gas or fat may obscure much of the gland, and it is for this reason that ultrasonography is not the investigation of choice for pancreatic disease. Despite this shortcoming, the sensitivity of ultrasonography for detecting pancreatic cancer was 76% in a meta-analysis¹ and 85% in one population study.² These high rates are primarily due to pancreatic cancer being advanced at presentation.

If after ultrasonography the pain remains unexplained—particularly when associated with features such as weight loss or when the scan elicits unexplained findings such as a dilated pancreatic or common bile duct—investigation with computed tomography is needed.

Computed tomography

Computed tomography is used increasingly in the investigation of the abdomen as it is of value in assessing the solid organs and the aorta and in identifying advanced disease of the bowel. Ultrasonography is more sensitive to gallstones than computed tomography, and endoscopy is more sensitive to inflammatory conditions and earlier stage neoplasms arising in the bowel. A more focused clinical question may lead to modification in computed tomography technique so as to increase the sensitivity for specific diseases—for example, computed tomographic colonography for colon cancer.

Computed tomography should not be used indiscriminately, given its relatively high radiation dose. A

This series provides an update on the best use of different imaging methods for common or important clinical presentations. The series advisers are Fergus Gleeson, consultant radiologist, Churchill Hospital, Oxford, and Kamini Patel, consultant radiologist, Homerton University Hospital, London.

Pancreatic phase computed tomography showing low attenuation mass (between the two left hand arrows) in the medial aspect of the pancreatic head involving the portal vein and superior mesenteric artery (bottom right hand arrow). The splenic vein (top right hand arrow) traverses to the left of the image to form the portal vein. The portal vein has flattened rather than rounded walls owing to tumour involvement

dedicated computed tomography study of the pancreas with intravenous contrast is, however, the imaging method of choice for patients suspected of having pancreatic cancer or chronic pancreatitis. The introduction of helical and multidetector computed tomography allows the pancreas to be scanned in pancreatic and portal venous vascular phases, resulting in improved rates of tumour detection. The sensitivity of such computed tomography for small, potentially resectable tumours is 86-100%³ and 91% in a meta-analysis.¹

Computed tomography also allows assessment of resectability of the tumour. Local invasion of the major peripancreatic blood vessels (superior mesenteric artery and vein, portal vein, and coeliac axis) usually precludes surgical resection. Identification of peritoneal disease, liver metastases (which are often small and therefore difficult to see in an ultrasound scan), and distant lymphadenopathy indicate that the tumour is metastatic and therefore curative surgery will not be possible. The positive predictive value of computed tomography for local vascular invasion is above 90%. The negative predictive value is lower, at about 75%; this is likely to improve with further improvements in computed tomography technology.

Magnetic resonance imaging

Magnetic resonance imaging is not used as a primary means of investigating abdominal pain. Magnetic resonance cholangiopancreatography is commonly used to investigate the cause of a dilated common bile duct shown in an ultrasound scan. If stones are not shown or the pancreatic duct is dilated and a tumour suspected, then imaging without gadolinium enhancement and then with gadolinium enhancement can show

the relation between the tumour and vascular system. A full diagnostic and staging study is technically more difficult to achieve than with computed tomography.

Despite the superior contrast resolution of magnetic resonance imaging, the limited comparative studies with computed tomography have been contradictory in their results for tumour detection and staging. Meta-analysis of the performance of magnetic resonance imaging in detection yielded a sensitivity of 84% and specificity of 82%.¹ Magnetic resonance imaging can be of value in differentiating from and evaluation of inflammatory pancreatic conditions and cystic lesions. It is also superior in evaluating small liver lesions.

Endoscopic retrograde cholangiopancreatography

Endoscopic retrograde cholangiopancreatography can demonstrate the tumour as an area of stenosis in the main pancreatic duct along with a field defect in the side branches. This invasive technique affords limited information about tumour size and no information about local vascular invasion or metastatic disease, and it has therefore been largely superseded as a primary means of diagnosis by more recent imaging techniques.

In those patients who develop jaundice, endoscopic retrograde cholangiopancreatography is the best method for insertion of a biliary endoprosthesis to allow biliary drainage. Brushings can also be taken from either the common bile duct or the pancreatic duct stricture during endoscopic retrograde cholangiopancreatography, which may allow cytological diagnosis of adenocarcinoma. The sensitivity of brushings is 30-75%.⁴

Endoscopic ultrasonography

Endoscopic ultrasonography is the most sensitive method for diagnosing small pancreatic tumours as it has excellent spatial resolution for detecting tumours that do not deform organs. The sensitivity for tumour detection with endoscopic ultrasonography is reported to be as high as 98%.⁵ In some patients these tumours may only be inferred on computed tomography owing to lack of contrast between the tumour and pancreatic parenchyma on multiple vascular phases.⁶ The limited depth of penetration of endoscopic ultrasonography, however, limits the overall staging capability. Tissue can be obtained using both targeted fine needle and cutting biopsy. Endoscopic ultrasonography may also be used to perform coeliac plexus neurolysis to treat poorly controlled pain.⁷

FURTHER READING

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LEARNING POINTS

Abdominal ultrasonography identifies about three quarters of pancreatic cancers

Dedicated pancreatic computed tomography is the imaging method of choice both for diagnosis and staging of pancreatic pathology

Endoscopic retrograde cholangiopancreatography should be reserved for insertion of biliary endoprotheses in those patients who develop jaundice

Brush cytology can be done during endoscopic retrograde cholangiopancreatography, with brushings taken from duct strictures

Skilled endoscopic ultrasonography is the most sensitive method of detecting small pancreatic tumours and allows biopsy

The outcome

After the gastroenterologist had performed a gastro-oesophageal endoscopy that yielded a normal result, he considered a pancreatic cause for the pain as the next leading diagnosis, and dedicated pancreatic computed tomography was performed. Gallstones were not considered to be the cause of the pain and ultrasonography was not performed. Given the location of the tumour, ultrasonography might well have been negative, serving only to lengthen the diagnostic pathway. When to refer directly for computed tomography and omit ultrasonography is a judgment based on the suspected diagnosis and on the likelihood that computed tomography will need to be performed regardless of the ultrasound findings versus the radiation dose.

Computed tomography showed a mass in the neck of the pancreas, deforming the portal vein and infiltrating the retroperitoneum and extending to involve the origin of the superior mesenteric artery (figure). The vascular involvement precluded surgical resection despite the absence of evidence of distant

dissemination. Focal pancreatitis may mimic pancreatic cancer, and therefore it is preferable to obtain a tissue diagnosis in non-surgical cases; this can be done using guidance with ultrasonography, computed tomography, or endoscopic ultrasonography.

In this case endoscopic ultrasonography was performed to obtain a tissue sample and to confirm the computed tomography findings. The diagnosis of adenocarcinoma was established and palliative chemotherapy started. The pain was controlled by oral analgesics. Pancreatic cancer presenting with pain is less frequently amenable to resection.⁸

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The golden tooth

Let us be well assured of the matter of fact, before we trouble ourselves with enquiring into the cause. It is true, that this method is too slow for the greatest part of mankind, who run naturally to the cause, and pass over the truth of the matter of fact; but for my part, I will not be too ridiculous as to find out a cause for what is not. This kind of misfortune happened so pleasantly, at the end of the last age, to some learned Germans, that I cannot forbear speaking of it.

"In the year 1593, there was a report that the teeth of a child of Silesia of seven years old dropped out, and that one of gold came in the place of one of his great teeth. Horatius, a professor of physic in the university of Helmstad, wrote in the year 1595, the history of this tooth, and pretended that it was partly natural, and partly miraculous, and that it was sent from God to this child, to comfort the Christians who were then afflicted by the Turks."

Now fancy to yourself what a consolation this was, and what this tooth could signify, either to the Christians or to the Turks. In the same year (that this tooth of gold might

not want for historians) one Rullandus wrote the history of it: two years after, Ingolsteterus, another learned man, wrote against the opinion of Rullandus concerning this golden tooth; and Rullandus presently makes a fine learned reply. Libavius, another great man, collected all that had been laid of this tooth, to which he added his own opinion.

After all, there wanted nothing to so many famous works, but the truth of its being a tooth of gold. When a Goldsmith had examined it, he found, that it was only a leaf of gold laid on the tooth with a great deal of art. Thus they first compiled books, and they consulted the Goldsmith.

Bernard le Bovier de Fontenelle, (1657-1757). *The History of Oracles*. Translated from the best edition of the original French.

Submitted by Olivier Nardi, consultant, Raymond Poinaré Hospital-Université de Versailles Saint Quentin en Yvelines, Garches, France