

Diabetes as a presenting feature of pancreatic cancer: A case report

Caroline Sharratt, Varadarajan Baskar

The phenomenon of diabetes as a result of exocrine pancreatic cancer is well documented, although not well understood. Currently, people with this condition are managed as having type 2 diabetes, and no differentiation is made. The authors report a person with a recent diagnosis of diabetes who was later found to have a probable pancreatic cancer, and review the literature on the link between these two conditions and the optimal management of diabetes in this context.

As much as 80% of people with pancreatic cancer have diabetes or glucose intolerance at diagnosis (DeMeo, 2001). Yet, whether diabetes is causally associated with pancreatic cancer or simply a consequence of it remains unclear.

The likely cause of diabetes in the context of exocrine pancreatic cancer is believed to be multifactorial, including reduced release of insulin in response to stimuli (more from islet dysfunction than islet destruction by the tumour), and peripheral resistance, which improves following resection of the tumour (Wang et al, 2003). Potentially, there may also be diabetogenic peptides found in people with pancreatic cancer (Wang et al, 2003).

Diabetes and pancreatic cancer

In a retrospective cohort study, Gupta et al (2006) observed that 149 of 36 631 individuals

newly diagnosed with diabetes received a diagnosis of pancreatic cancer over the subsequent 6-year period. The risk was 2.2-fold higher in those newly diagnosed with diabetes than those without diabetes (95% confidence interval 1.84–2.56) and was highest during the first 2 years after diabetes diagnosis. The authors estimated one additional pancreatic cancer diagnosis for every 332 new diagnoses of diabetes over 6 years.

Questions have been raised regarding the possibility of distinguishing this sub-group at increased risk of pancreatic cancer from other people with type 2 diabetes (Chari et al, 2008). If this were possible, people newly diagnosed with diabetes could be screened to detect pancreatic cancer at a stage where it may be operable (Chari et al, 2008). However, there are insufficient and conflicting data supporting improved outcomes following such

Article points

1. A clinical diagnosis of exocrine pancreatic cancer was made in a 79-year-old female presenting with type 2 diabetes, and the tumour was felt to be inoperable.
2. There is no clear guidance on how best to manage diabetes in the context of pancreatic cancer.
3. With most cases of diabetes now being diagnosed and managed in primary care, practitioners should be aware that there may be secondary causes for diabetes.

Key words

- Case report
- Computed tomography
- Pancreatic cancer

Caroline Sharratt is a Foundation Year 2 trainee; Varadarajan Baskar is a Consultant Physician at Wolverhampton Diabetes Centre, New Cross Hospital, Wolverhampton.

Page points

1. Gupta et al (2006) estimated one additional pancreatic cancer diagnosis for every 332 new diagnoses of diabetes over 6 years.
2. Questions have been raised regarding the possibility of distinguishing this subgroup at increased risk of pancreatic cancer from other patients with type 2 diabetes.
3. If this were possible, newly diagnosed patients could be screened to detect pancreatic cancer at a stage where it may be operable.

early detection of pancreatic cancer at the time of diabetes diagnosis (Damiano et al, 2004; Chari et al, 2005; Pelaez-Luna et al, 2007).

Routine imaging (a mixture of ultrasound, computed tomography and magnetic resonance imaging) of all people with new onset acute diabetes ($n=115$) over the age of 50 years, identified pancreatic cancer in 5.2% of patients in a study by Damiano et al (2004). Whether targeted screening based on the presence of other risk factors for pancreatic cancer – including presence of gastrointestinal symptoms, weight loss, or early need for insulin – would have increased the rate of cancer identified, has not been tested.

Guidance

Guidance published in *Gut* (Pancreatic section of the British Society of Gastroenterology et al, 2005) has grade B recommendations that the “diagnosis of pancreatic cancer should be considered in patients with adult onset diabetes who have no predisposing features or family history of diabetes”. They go on to recommend that unexplained diabetes in people over 50

years of age, with no family history, obesity or steroid usage should be referred to a local cancer unit. However, this recommendation is not currently included in NICE (2005) referral guidance for suspected cancer. Where there is suspicion, clinicians, in addition to examining the abdomen, should have a low threshold to seek specialist help and to consider an ultrasound examination.

Management

There is no clear guidance on how best to manage diabetes in the context of pancreatic cancer. The primary concern should be resolution of hyperglycaemic symptoms, safe blood glucose levels and the avoidance of hypoglycaemia. Long-term complications are unlikely to be a major concern in this group. Fluctuations in glucose levels with the potential need for chemotherapy, decreasing appetite and change in weight and dietary input may warrant follow-up.

With recent evidence suggesting a mixed pattern of both islet dysfunction and peripheral resistance (Wang et al, 2003), there may be

Box 1. Case study of a woman with pancreatic cancer.

Narrative

A 79-year-old woman was admitted to hospital after feeling generally unwell and unsteady for 3 weeks. She had been diagnosed with diabetes 3 weeks earlier by her GP. Despite lifestyle changes, she had been commenced on metformin after just 2 weeks due to poor glycaemic control. A right upper quadrant mass and a palpable liver edge were found on examination. Her blood glucose level on admission was 23.5 mmol/L and her HbA_{1c} at 10.7% (93 mmol/mol) confirmed poor control preceding admission. There was no ketonuria or acidosis.

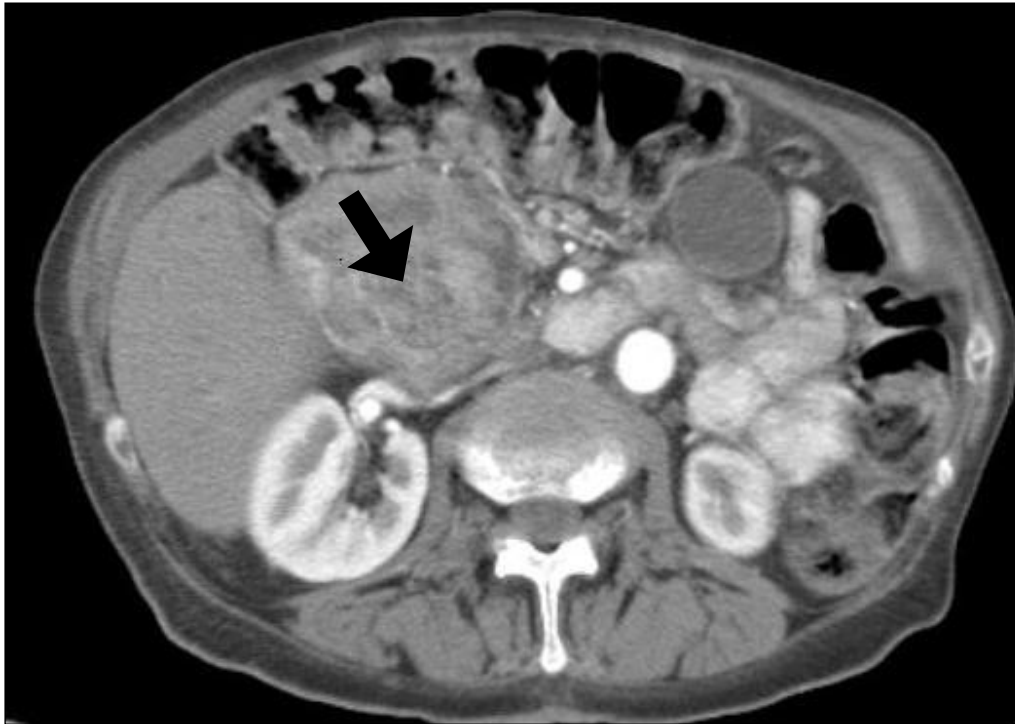
The woman was noted to have deranged liver function tests: alkaline phosphatase 283 IU/L (healthy range: 38–126 IU/L), alanine transaminase 65 IU/L (healthy range: 5–40 IU/L) but with normal total bilirubin at 9 µmol/L.

An abdominal computed tomography (CT) scan suggested a malignant mass in the head of the pancreas (see *Figure 1*) and her cancer antigen 19-9 was elevated at 244 KU/L (healthy range: 0–34 KU/L).

Diagnosis

A clinical diagnosis of exocrine pancreatic cancer was made and the tumour was felt to be inoperable. In accordance with the woman’s wishes, further investigations were not performed. She remained hyperglycaemic and symptomatic, despite maximisation of oral antihyperglycaemic therapy with metformin and a sulphonylurea. Insulin was therefore commenced with good improvement in her wellbeing.

Figure 1. Computed tomography of the abdomen showing a cystic and solid mass (arrow) in the head of the pancreas, highly suggestive of an exocrine carcinoma of the pancreas.



“There is no clear guidance on how best to manage diabetes in the context of pancreatic cancer. The primary concern should be resolution of hyperglycaemic symptoms, safe blood glucose levels and the avoidance of hypoglycaemia.”

benefit in using oral agents before initiating insulin. However, with the nature of this illness, many people are likely to require insulin, and progression may be faster than in type 2 diabetes (Noy and Bilezikian, 1994).

Conclusion

The case study in *Box 1* highlights the fact that, although diabetes is very common, occasionally it may be secondary to another cause, such as pancreatic malignancy.

Despite the fact that there is no evidence to support early diagnosis of cancer improving outcome, with most cases of diabetes now being diagnosed and managed in primary care, practitioners should be aware that there may be secondary causes for diabetes. It also highlights the need for further research in how best to manage this subgroup, and the potential differences compared with other people with type 2 diabetes. ■

Chari S, Leibson C, Rabe K et al (2005) Probability of pancreatic cancer following diabetes: a population based study. *Gastroenterology* **129**: 504–11

Chari S, Leibson C, Rabe K et al (2008) Pancreatic cancer-associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. *Gastroenterology* **134**: 95–101

Damiano J, Bordier L, Le Berre JP et al (2004) Should pancreas imaging be recommended in patients over 50 years when diabetes is discovered because of acute symptoms? *Diabetes Metab* **30**: 203–7

DeMeo M (2001) Pancreatic cancer and sugar diabetes. *Nutr Rev* **59**: 112–15

Gupta S, Vittinghoff E, Bertenthal D et al (2006) New-onset diabetes and pancreatic cancer. *Clin Gastroenterol Hepatol* **4**: 1366–72

NICE (2005) *Clinical Guideline 27. Referral Guidelines for Suspected Cancer*. NICE, London. Available at: <http://tiny.cc/4Z95H> (accessed 9.12.08)

Noy A, Bilezikian JP (1994) Clinical review 63: Diabetes and pancreatic cancer: clues to early diagnosis of pancreatic malignancy. *J Clin Endocrinol Metab* **79**: 1223–31

Pancreatic Section of the British society of Gastroenterology, Pancreatic society of Great Britain and Ireland, Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, Royal College of Pathologists, Special Interest Group for Gastro-I (2005) Guidelines for the management of patients with pancreatic cancer perampullary and ampullary carcinomas. *Gut* **54**: v1–v16

Pelaez-Luna M, Takahashi N, Fletcher JG et al (2007) Resectability of presymptomatic pancreatic cancer and its relationship to the onset of diabetes: a retrospective review of CT scans and fasting glucose values prior to diagnosis. *Am J Gastroenterol* **102**: 2157–63

Wang F, Herrington M, Larsson J et al (2003) The relationship between diabetes and pancreatic cancer. *Mol Cancer* **2**: 4