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Case Report

Pancreatic Cancer-Associated Diabetes: Is a Nihilistic Approach Justifiable?

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Abstract

We present a black African man with pancreatic cancer-associated diabetes managed by a nihilistic approach in a low-resourced setting and discuss the justifiability.

Keywords: Pancreas; Cancer; Diabetes; Management

Case Presentation

A 58-year old black African man, who was a retired store accountant, was admitted as an emergency for management of his decompensating diabetes mellitus. This was associated with body weakness, vertigo, fatigue at rest, anorexia and weight loss of 27kg within 4 months and pruritus. He had been diagnosed type 2 diabetes mellitus 7 years previously for which he was on oral hypoglycemic medication. He had no altered bowel habit but complained of passing pale stools and dark urine. On examination he was in a good general state, and well orientated. His BP was 98/68mmHg, Pulse 97/min and temperature 36.10C. He was clinically jaundiced with a palpable distended gallbladder but no stigmata of chronic liver disease. Chest and cardiovascular examination were unremarkable. Fasting Blood Sugar (FBS) was 265mg/dl (normal: 60-110mg/dl), haemoglobin level of 9.4g/dl and blood film showed a moderate hypochromic, normochromic anaemia. The liver transaminases were raised -aspartate transaminase (ASAT) 100u/l (n<35), Alanine Transaminase (ALAT) 162u/l (n <45) but the biliary enzyme, alkaline phosphatase was not available. Hepatitis B surface antigen and hepatitis C virus antigen tests were negative. Renal function test was normal. He was started on Human mixtard 30/70 and the FBS returned to 106mg/dl by the third day. An abdominal ultrasound showed a normal liver, intra and extrahepatic biliary dilatation and a distended gallbladder suggesting a distal bile duct obstruction. A Computed Tomography (CT) scan of the abdomen confirmed a 38mm tumour of the head of pancreas with intra and extrahepatic biliary dilatation but no local invasion nor extra pancreatic spread. He was hydrated with intravenous fluids and started on cholestyramine (bile salt chelator), prophylactic antibiotics and intramuscular vitamin K 10mg daily. His jaundice progressively deepened and he rapidly emaciated to be unfit (ASA III-IV) for palliative surgical bypass. He continued to be managed symptomatically until his death almost 4 months from admission.

Discussion

Pancreatic ductal adenocarcinoma is the 13th commonest cancer but the fourth most common cause of cancer-related death [1]. The prognosis for patients with this disease is dismal. The overall worldwide incidence has increased over the past few decades such that over 265,000 cases are diagnosed annually and it is projected that it will be the leading cause of cancer-related deaths in the USA by 2050 [2]. The dismal overall median survival of 4.4 months, and a five year survival of 5% is primarily due to the disease-specific symptoms occurring late in the course of the disease. As 50% present with metastatic disease and 35% present with locally advanced disease, only 10-20% with head and less than 3% of body/tail cancers are candidates for resection [3]. Risk factors include family history, smoking, obesity, chronic pancreatitis and Diabetes Mellitus (DM). The aetiology of Pancreatic Carcinoma (PC) is complex and poorly understood. Long-standing diabetes is an aetiologic factor but new-onset diabetes may be a manifestation of PC [4]. Long-standing diabetes increases the risk of PC by 40-100%. Type 2 and type 1 DM increase the risk of PC with a latency period of more than 5 years. New-onset diabetes (within 3 years) is associated with PC in nearly 50% of patients. Type 3 DM is an effect and harbinger of PC in 30% of patients [5]. Experimental studies have suggested that PC cell lines produce soluble factor(s) that can impair glucose metabolism *in vitro* and cause hyperglycemia *in vivo* [6].

This case demonstrated the dilemma of pancreatic carcinoma which is the late and non-specific symptoms, no effective screening process and no specific high risk group [7,8]. It also demonstrated the persistent dilemma in the management of pancreatic cancer (Table 1) because of the preconceived knowledge of its poor prognosis [9,10]. Although surgical resection is the most important factor that determines survival, the arguments for the nihilistic approach are that PC usually has an insidious presentation and physical signs of metastatic spread are commonly present at initial consultation. It is a disease of elderly patients and 50% are >70 years, many are

Table 1: AJCC TNM staging of pancreatic cancer.

Stage 0	Tis	N0	M0	Localized within pancreas
Stage 1A	T1	N0	M0	Localized within pancreas
Stage 1B	T2	N0	M0	Localized within pancreas
Stage IIA	T3	N0	M0	Locally invasive, resectable
Stage IIB	T1-3	N1	M0	Locally invasive, resectable
Stage III	T4 any	N	M0	Locally advanced, unresectable
Stage IV	Any T	Any N	M1	Distant metastases

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Table 2: Favourable prognostic features.

T0	no evidence of primary tumour
Tis	carcinoma in situ
T1	tumour limited to the pancreas, <2cm in greatest diameter
T2	tumour limited to the pancreas, >2cm in greatest diameter
T3	tumour extends beyond pancreas but no involvement of coeliac axis or superior mesenteric artery(SMA)
T4	tumour involves the coeliac axis or SMA (unresectable)
N0	no regional lymph node metastases
N1	regional lymph node metastases
M0	no distant metastasis
M1	distant metastasis

unfit, weak, emaciated and suffer from other concomitant medical conditions [11]. Endoscopic bypass is all that can be offered [9-11]. A realist argument is that bypass procedures are all that can be offered in the vast majority. The palliation of biliary and gastric outlet obstruction is by surgical bypass (hepaticojejunostomy or gastrojejunostomy), if endoscopic/percutaneous methods fail and patient is fit for surgery. In some cases, resectability can only be defined intraoperatively, however. An unsuccessful resection for a carcinoma can result in a high mortality, a very high morbidity and an extremely costly period of treatment for the patient [9,10]. The arguments for the activist are that PC is increasing in incidence and although it is considered a disease of the elderly more than 40% of men and 35% of women present under the age of 70 years as in this case [2]. The use of modern diagnostic imaging techniques or protein markers especially glypican -1(PC1) can pick up tumours at an early stage [8,12]. Even though the chances of cure are <1%, the only hope for cure of early PC is by surgical resection [13]. After a potentially curative R0 (no involved margins) resection in which all margins of the specimen are histologically tumor-free, median survival is 12months, and 5- year survival rate is 15-26% [14]. The resection ameliorates the diabetes in those who had diabetes preoperatively (new-onset) but not patients with long standing diabetes [5,15]. This provides further evidence that PC induces glucose intolerance and recent-onset diabetes may not only define a high risk group for PC but a marker of early, asymptomatic cancer [16]. Moreover, several studies have demonstrated the prevalence of diabetes in early stage PC which would favour the argument for the activist's resection approach [17,18]. As nearly half the patients with early stage, resectable tumours have diabetes, PC-associated diabetes is not a contraindication for the surgical resection approach [19,20]. The prompt diagnosis of type 3 DM (newly diagnosed diabetes mellitus) may allow detection of a tumour at a potentially curable stage. Although widely viewed as a complex procedure associated with considerable perioperative morbidity and mortality, complete surgical removal of the pancreatic tumour is the most important factor that determines survival [9,10,13,14]. The operative mortality has fallen to 5% or less in experience hands [9,21]. The surgical procedure for tumour in head of pancreas is either a Whipple's pancreaticoduodenectomy (PD) or Pylorus-Preserving Pancreaticoduodenectomy (PPPD) or PD with en bloc vascular resection and reconstruction and for tumour in body/tail is either a distal pancreatectomy or a total pancreatectomy [9]. If we excluded all patients from consideration for surgery we may also exclude patients suffering from cancer of the distal common bile duct, the duodenal mucosa and ampulla of Vata with the latter tumour having a 5 year survival rate of 30%. A nihilistic approach is therefore not justified, as in many cases resectability can only be defined intraoperatively (Table 2). The favourable prognostic features are negative resection margin, negative lymph nodes, well/moderately differentiated carcinoma, primary < 2cm diameter and no perineural or lymph vascular invasion [9, 22]. Neoadjuvant and adjuvant chemotherapy or chemo radiotherapy improves the chance of cure for early PC [23,24]. Screening for pancreatic cancer in high risk individuals including recent-onset diabetics especially with the novel protein markers holds promise with regards improving long-term survival (Table 3).

Table 3: Management options.

Resectable diseases (Stages *I-II)*	Locally advanced unresectable disease (Stage *III)*	Metastatic disease (Stage *IV*)
Surgical resection (with or without adjuvant chemotherapy or chemoradiotherapy)	Neoadjuvant chemo radiotherapy then restaging CT with or without resection if down-staged	Poakliative chemotherapy (gemcitabine)
	Palliative chemotherapy: 5-FU, folinic acid, and gemcitabine; Palliative chemo radiotherapy	Best supportive care, Pain control. Consider coeliac plexus block.
	Palliation of biliary and gastric outlet obstruction	Palliation of biliary and gastric outlet obstruction

Authors' Contribution

EPW was the main researcher and carried out literature search, EN assisted with the literature search.

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