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NEW-ONSET DIABETES AS PRESENTING FEATURE OF PANCREATIC CARCINOMA: A CASE REPORT

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Summary

Diabetes is often related to pancreatic cancer and sometimes the only symptom of an underlying pancreatic malignancy. We report a case of new-onset diabetes in a 83-year-old male patient that exposed an unknown pancreatic carcinoma. Patient was treated with chemoradiotherapy and diabetes was regulated by glicazide introduction. Taking into account its late recognition and poor prognosis, in a case of sudden new-onset diabetes, pancreatic cancer should be considered.

KEYWORDS: *pancreatic cancer, secondary diabetes, primary chemoradiotherapy*

NOVODIJAGNOSTICIRANI DIJABETES KAO ZNAK KARCINOMA GUŠTERAČE – PRIKAZ SLUČAJA

Sažetak

Dijabetes se često dovodi u vezu s karcinomom gušterače, štoviše, katkad je prvi simptom maligne bolesti gušterače. U ovom radu prikazujemo slučaj novonastalog dijabetesa u 83-godišnjeg bolesnika koji je ukazao na skriveni karcinom gušterače. Bolesnik je liječen primarnom kemoradioterapijom, a dijabetes je reguliran uvođenjem glikazida. Uzimajući u obzir njegovo kasno otkrivanje i lošu prognozu, u slučaju naglog razvoja dijabetesa trebalo bi posumnjati na karcinom gušterače.

KLJUČNE RIJEČI: *karcinom gušterače, sekundarni dijabetes, primarna kemoradioterapija*

INTRODUCTION

Pancreatic cancer represents great frustration for clinicians due to several reasons: there is no adequate screening method, it is asymptomatic until it had advanced locally or metastasized, radical surgical treatment is very mutilating and current available chemotherapy agents are inefficient. All mention the above results in high mortality of this not so frequent malignancy (1). Sudden onset of secondary diabetes with brief history, absence of obesity and lack of family history could be an early manifestation of pancreatic cancer (2). Recognition of this atypical diabetes could lead to earlier diagnosis of pancreatic cancer at a curable stage (2).

CASE REPORT

An 83-year-old male patient was admitted to the emergency unit due to high blood glucose level of 30 mmol/L. He had neither prior history of diabetes nor any kind of hyperglycemic condition. When admitted, patient complained of inapetence,

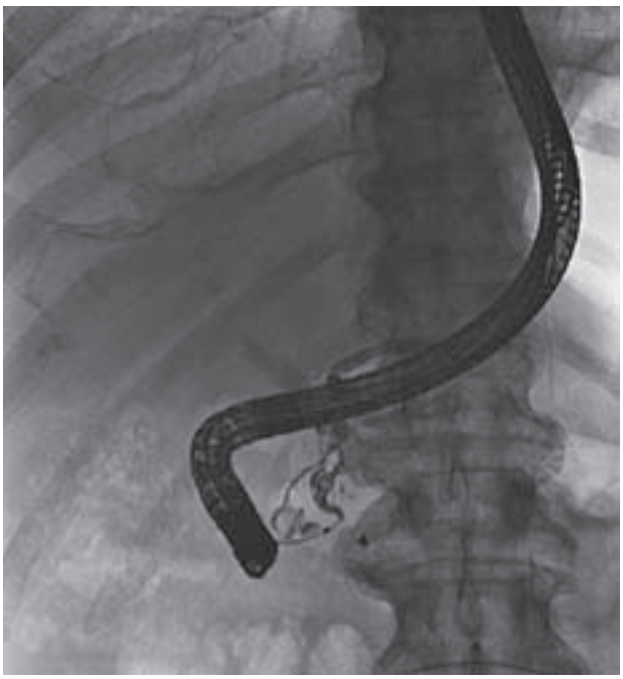

Figure 1. Biductal segmental subtotal stenosis of the common bile duct and main pancreatic duct. Significant poststenotic dilatation of both ducts: common bile duct 14 mm, pancreatic duct 7 mm (diameter). Irregularity of pancreatic duct stenosis implicates malignancy.

dry mouth, body weight loss, polyuria and polydipsia lasting for 3-4 months. Biochemical blood analysis showed severe hyperglycemia, elevated bilirubin level of 40,1 μmol/L, elevated levels of serum and urinary amylase, CRP, ALP and liver enzymes. Serum level of tumor marker CA 19-9 was 307 U/mL (normal range is up to 33 U/mL). Ultrasonography of the abdomen showed a tumor mass in the pancreas head. Endoscopic retrograde cholangiopancreatography, performed in order to locate and treat bile retention, showed subtotal stenosis of the main pancreatic duct and common bile duct with post-stenotic dilatation (Figure 1). Prosthesis placed in the biliar tree normalized bilirubin level (Figure 2). Computerized tomography revealed enlarged, irregularly contoured and weakly oppacificated pancreatic head (Figure 3) with a prominent tumor measuring 6 cm. Few solid nodes were found bilaterally in the basal part of the lungs. Ultrasound-guided cytological puncture of the prominent mass in the pancreatic head found adenocarcinoma cells. Considering the clinical stage of the disease, primary chemoradiotherapy was applied. It consisted of external-

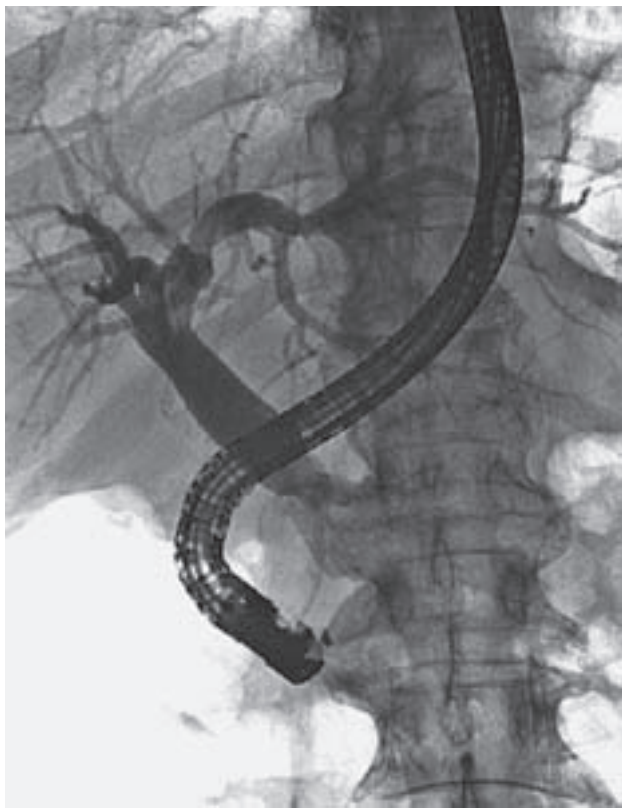

Figure 2. Biliary stent placed in the common bile duct.

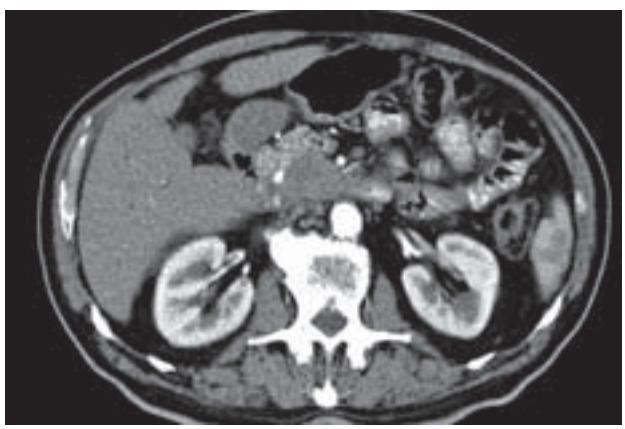

Figure 3. Computer tomography (CT) of the abdomen: enlarged, irregularly contoured and weakly oppacificated pancreatic head with a prominent tumor.

beam radiotherapy on pancreatic head bed and regional lymph drainage concomitant with 5-fluorouracil intravenously for the first three days of radiotherapy. The delivered dose was 45 Gy into 25 fractions. Chemotherapy plan was not fully conducted due to thrombocytopenia. Diabetes

was well regulated by glicazide introduction and HbA1c value was maintained around 7.1 %. In a few months' time, the patient passed away due to disease progression.

DISCUSSION

Pancreatic cancer represents a challenge for physicians and the health system in general. Its relative frequency has been increasing during the last several decades: approximately 30 000 new cases in 2002 and about 32 000 in 2004 were diagnosed in the United States (3). With expected 5-year survival rate less than 4% it is the fourth leading cause of cancer-related deaths in the United States (3, 4) and the eight major form of cancer related death worldwide (5). Pancreatic cancer is difficult to diagnose at an resectable stage. At the time of diagnosis, only 10 to 25% of patients will be eligible for potentially curative resection (6). Namely, most patients present late in the course of the disease with locally advanced cancer or with metastatic spread (7, 8). But, even after timely surgical resection, survival rate does not surpass 20% (9-11).

The standard surgical treatment for pancreatic cancer remains pancreatoduodenectomy. Surgical resection, as part of a multimodality treatment approach, represents the only potentially curative strategy (10). The multimodal approach includes radiotherapy and chemotherapy. Multiple-field, fractionated, external-beam techniques with high-energy photons are used to deliver 45 to 50 Gy in 1.8-Gy fractions to tumor bed, unresected or residual tumor and lymph-node-bearing areas at risk (12). Single chemotherapeutic agents like 5-streptozocin, mitomycin C and 5-flourouracil have response rates of about 20% (13). When drugs are combined, like in FAP or FAM protocol, response rates are up to 40%, with only 5% being complete responses (12). New chemotherapeutic agents include gemcitabine (14), docetaxel (15, 16) and capecitabine (17), used individually or in combination.

Pancreatic cancer is rarely discovered at an early stage because most symptoms are non-specific. Most common ones are jaundice, pain and weight loss - the classic triad, and significant anorexia (12). Other symptoms include changes in bowel habits, constipation, diarrhea, dyspepsia, dysphagia and gas (3, 4). The relationship between diabetes and cancer of the pancreas is still dubious. Nevertheless, in France it is generally agreed that new-onset diabetes in a patient over 50 years old is a classic indication of pancreatic cancer (18). It usually presents within 2 years before the diagnosis of pancreatic cancer and has atypical characteristics: there is no positive family history or obesity and the progression to insulin dependence is rapid (2). Diabetes itself is not a risk factor for pancreatic cancer (19). In the described studies "new-onset diabetes" manifested 2, 3 or 4 years prior to pancreatic cancer diagnosis. In the case of our patient, diabetic symptoms manifested 3-4 months before the diagnosis. During that time he had extremely high blood glucose levels of up to 30 mmol/L. A new and sudden onset of diabetes is not recorded only in pancreatic cancer. A case of uncontrollable diabetes was described in renal cell carcinoma (20). A mild degree of hyperglycemia can be associated with multifunctional neuroendocrine tumors (21). Insulin allergy and insulin resistance were seen in a man with lung cancer (22). Diabetes associated with pancreatic cancer may be a result of β-cell dysfunction in insulin production (3, 4) in which case its progression is proportional with cancer-related islet destruction. Or, like in renal cell carcinoma (23) or lung carcinoma (22), it can be a manifestation of paraneoplastic syndrome.

CONCLUSION

Pancreatic cancer is characterized by late recognition and poor prognosis. New-onset diabetes likely represents a marker for pancreatic cancer in a subset of newly diagnosed individuals with severely controllable disease, presence of gastrointestinal symptoms or young age. In such cases increased rate of subsequent pancreatic cancer diagnosis persists for several years after the diabetes diagnosis. Surveillance of all individuals with new-onset diabetes is not recommended because of the uncertainty of pancreatic cancer incidence and the lack of data showing improvement in survival or quality of life from this surveillance. But, using the knowledge about additional risk factors and individuals at risk, we may be able to identify pancreatic cancer in the early, amenable stage. Any kind of harbinger would be useful in the fight against this silent and vile malignancy.

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