

## Rare Case of Pancreatic Cancer Presenting with Leg Cramps

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### Abstract

Leg cramps is a very common complaint in primary care office. More than 50% of the patients are found to have diabetes who presented with leg cramps and up to 80% [1] of pancreatic cancer patients present with either new-onset type 2 diabetes or impaired glucose tolerance at the time of diagnosis. Leg cramps should be worked up to look for new onset diabetes that could essentially lead to and unmask underlying pancreatic cancer. The data linking high glucose levels with an elevated risk of pancreatic cancer have led some to suggest that the new onset of diabetes in a thin older adult should prompt consideration of screening for early diagnosis of a potentially resectable pancreatic cancer. But so far no clear-cut guidelines over there that suggest which parameters should be taken to consideration for CT screening for pancreatic cancer in a newly diagnosed diabetic patient.

**Keywords:** Leg cramps; Diabetes mellitus; Pancreatic cancer.

### Introduction

Muscle cramping is a very common presentation for diabetes. It could be due to low potassium or peripheral vascular disease-causing peripheral neuropathy. The cramps tend to be more common in the lower extremities and may be seen more commonly at night. Sometimes patient is a diagnosed with restless syndrome. But unfortunately, patient could have underlying pancreatic cancer that could be the cause of diabetes as up to 80% of pancreatic cancer patients present with either new-onset type 2 diabetes or impaired glucose tolerance at the time of diagnosis [1].

### Background

This case demonstrates patient is presenting with severe leg cramps looks like restless leg syndrome could have underlying diabetes from pancreatic cancer.

61 years old male with past medical history of hypertension and anxiety on amlodipine and Diovan and clonazepam presented to the office with severe Leg cramps. Not able to sleep at night leg cramps are more worse at night. Denies any polyuria polydipsia or any dry mouth. Legs were hurting at nighttime when he is trying to come downstairs goes up stairs and subsequently gets severe leg cramps at night when he is sleeping. Denies any weight loss any nausea and vomiting no other complaints. Initially was given muscle relaxants for couple of days and also told to get the blood test done to rule out diabetes. His A1c came surprisingly 9.1 he was immediately put on metformin considering normal renal functions but patient after couple of days reported nausea symptoms earlier it was thought nausea could be due to side effect of metformin and he was suggested to take some alternative medication

### Article Information

**Article Type:** Case Report

**Article Number:** SJASR210

**Received Date:** 11 January, 2019

**Accepted Date:** 24 January, 2019

**Published Date:** 31 January, 2019

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**Citation:** Singla M, Singla M (2019) Rare Case of Pancreatic Cancer Presenting with Leg Cramps. Sch J Appl Sci Res Vol: 2, Issu: 1 (25-28).

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sitagliptin but diabetes. Patient called next day his eyes also yellow and he is vomiting he was sent to the emergency room and found to have severe obstructive jaundice, CT scan abdomen and pelvis showed pancreatic mass with metastasis. Patient not a candidate for any surgery palliative therapy started with poor prognosis.

### Investigations

Labs:

	Ref. Range	6/9/2018	10/17/2018
ALT	7 - 52 IU/L	31	206 (H)

	Ref. Range	6/9/2018	10/17/2018
AST	13 - 39 IU/L	19	101 (H)

	Ref. Range	6/9/2018	10/17/2018
Bilirubin Total	0.3 - 1.0 mg/dL	0.9	16.2 (H)

	Ref. Range	6/9/2018	10/17/2018
Alk Phos	34 - 104 IU/L	64	386 (H)

	Ref. Range	1/13/2018	9/22/2018
HA1C - Glycohemoglobin	4.9 - 6.0 %	5.7	9.1 (H)

A CT abdomen/pelvis scan with contrast was performed, which is demonstrated in Figures 1 and 2.

### Discussion

Leg cramps are common and frequently unreported to clinicians. In the general population, they are present in 40 percent of those over the age of 50, have an increased frequency with age, show no gender preference, and are associated with sleep disturbance and overall poor health. But could be related to diabetes and that diabetes could be from underlying pancreatic cancer. The early symptoms of pancreatic cancer, such as abdominal pain, weight loss, fatigue, jaundice, and nausea, are nonspecific and may occur late in the course of the disease [1,2]. As a result, pancreatic cancer is usually diagnosed at an advanced stage, frequently after the tumor has already metastasized. Pancreatic cancer is insensitive to pharmacological and radiological intervention and often recurs after apparently curative surgery. All these factors contribute to the dismal prognosis of the disease.

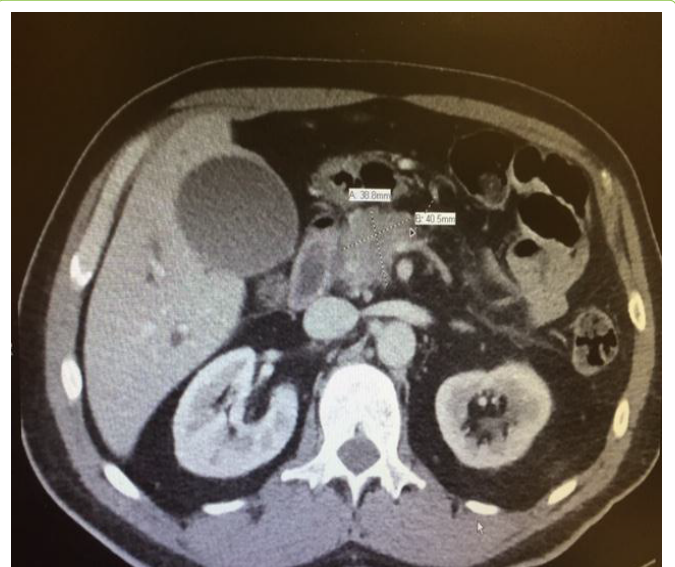
A recent onset of atypical diabetes mellitus [3-5] may be noted. Several studies have addressed whether earlier detection of nonspecific signs of an evolving pancreatic neoplasm (particularly in adults with new-onset diabetes mellitus) might improve respectability and overall outcomes, but the results are inconclusive.

Numerous epidemiologic studies describe an association between diabetes mellitus and pancreatic cancer [6-13]. In a meta-analysis of 88 studies (50 cohort and 30 case-control, predominantly of patients with type 2 diabetes) the pooled relative risk (RR) for pancreatic cancer in diabetics compared with patients without diabetes was 2.08 (95% CI 1.87-2.32) [13].

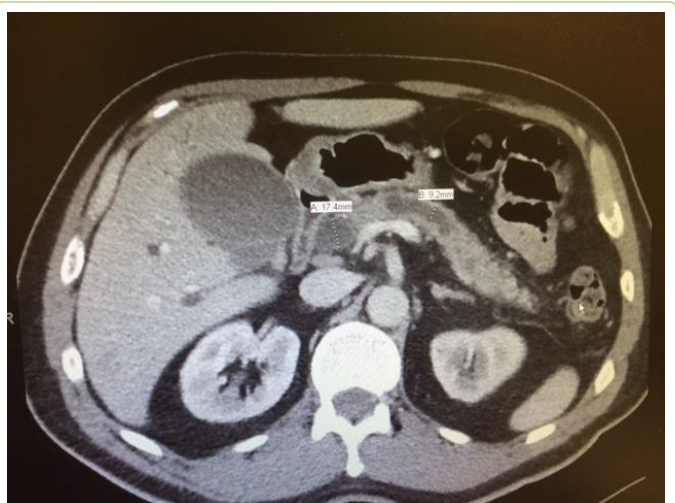
It has been suggested that diabetes may be a consequence rather than a cause of pancreatic cancer [14-16]. As an example, one study compared 512 patients with newly

diagnosed pancreatic cancer to 933 controls of similar age [16]. Compared with controls, diabetes was more prevalent in pancreatic cancer cases (47 versus 7 percent) and more likely to have been diagnosed in the preceding two years (74 versus 53 percent). After pancreaticoduodenectomy, diabetes resolved in 17 of 30 patients (57 percent) with new-onset diabetes, while its prevalence was unchanged in the 11 patients who had longstanding diabetes. One intriguing possibility derived from in vitro work is that pancreatic cancers might induce paraneoplastic beta cell dysfunction and inhibition of insulin secretion by shedding exosomes containing adrenomedullin (a vasodilator peptide hormone that regulates insulin balance and may participate in the development of diabetes [17]) into the systemic circulation [18].

On the other hand, other data support the view that abnormal glucose metabolism and insulin resistance are etiologic factors rather than the result of a subclinical cancer [19-23].



**Figure 1:** Common bile duct measures 17 mm as it courses through the pancreatic head. There is dilatation of the pancreatic duct throughout the length of the pancreas.



**Figure 2:** Pancreas Mass: Location: Pancreatic head and neck; Size: 41 x 31 mm; Enhancement: Heterogeneous; Pancreatic Duct: Dilated to 9 mm.

An association between pre-diagnosis serum levels of glucose, insulin, insulin resistance, and pancreatic cancer risk was suggested in a case-cohort study within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study, a primary prevention trial enrolling 29,133 male Finnish smokers aged 50 to 69 [20]. Fasting serum concentrations of glucose and insulin, and levels of insulin resistance were assessed. The interval between serum collection and follow-up was up to 16.7 years. The study included 169 incident cases of pancreatic cancer that were diagnosed after the fifth year of follow-up and 400 randomly selected controls.

After adjustment for age, years of smoking, and BMI, higher pre-diagnosis serum concentrations of glucose and insulin, as well as insulin resistance were significantly correlated with the risk of pancreatic cancer. The positive associations were stronger among the cases that occurred more than 10 years after baseline (highest versus lowest quartile for glucose, HR 2.16, 95% CI 1.05-4.42; for insulin, HR 2.90, 95% CI 1.22-6.92; for insulin resistance, HR 2.71, 95% CI 1.19-6.18). The prospective study design, with a minimum five-year follow-up prior to the detection of incident pancreatic cancer, minimizes the possibility that the identified insulin and glucose abnormalities resulted from "subclinical" pancreatic cancer.

The mechanism underlying this association is unclear. However, at least some data suggest that the increased risk of pancreatic cancer in patients with metabolic diseases such as diabetes mellitus and other states of insulin resistance as well as obesity may be mediated by reduced levels of plasma adiponectin, a fat-derived hormone that has insulin-sensitizing and anti-inflammatory properties [24].

The data linking high glucose levels with an elevated risk of pancreatic cancer have led some to suggest that the new onset of diabetes in a thin older adult should prompt consideration of screening for early diagnosis of a potentially resectable pancreatic cancer. At least three studies have addressed the utility of CT screening for early detection of pancreatic cancer in adults with new-onset diabetes. Two uncovered mainly unresectable tumors, but they selected patients for screening based upon the presence of cancer-related symptoms. A third series from the Mayo Clinic suggested that CT scans done at the time of newly diagnosed diabetes in otherwise asymptomatic patients were more likely to show potentially resectable tumors than scans performed six months later [25]. Whether higher resectability rates translated into higher cure rates was not addressed.

CT screening of all older subjects with new onset diabetes in order to discover a small number of pancreatic cancers is not feasible. Identification of those features that differentiate pancreatic cancer-associated diabetes from other cases with new-onset diabetes would help direct efforts to the subset of individuals who would most benefit from screening CT, but these factors have not yet been established. Thus, screening CT scans are not warranted in older otherwise asymptomatic adults with new-onset atypical diabetes. At present, screening is only carried out for high-risk individuals who have familial syndromes predisposing them to pancreatic cancer.

## References

- Gullo L, Tomassetti P, Migliori M, Casadei R, Marrano D (2001) Do early symptoms of pancreatic cancer exist that can allow an earlier diagnosis? *Pancreas* 22: 210-213.
- Porta M, Fabregat X, Malats N, et al. (2005) Exocrine pancreatic cancer: symptoms at presentation and their relation to tumour site and stage. *Clin Transl Oncol* 7: 189.
- Holly EA, Chaliha I, Bracci PM, Gautam M (2004) Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area. *Clin Gastroenterol Hepatol* 2: 510.
- Chari ST, Leibson CL, Rabe KG, et al. (2005) Probability of pancreatic cancer following diabetes: a population-based study. *Gastroenterology* 129: 504.
- Aggarwal G, Kamada P, Chari ST (2013) Prevalence of diabetes mellitus in pancreatic cancer compared to common cancers. *Pancreas* 42: 198.
- Huxley R, Ansary-Moghaddam A, Berrington de González A, et al. (2005) Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. *Br J Cancer* 92: 2076.
- Inoue M, Iwasaki M, Otani T, et al. (2006) Diabetes mellitus and the risk of cancer: results from a large-scale population-based cohort study in Japan. *Arch Intern Med* 166: 1871.
- Chow WH, Gridley G, Nyrén O, et al. (1995) Risk of pancreatic cancer following diabetes mellitus: a nationwide cohort study in Sweden. *J Natl Cancer Inst* 87: 930.
- Calle EE, Murphy TK, Rodriguez C, et al. (1998) Diabetes mellitus and pancreatic cancer mortality in a prospective cohort of United States adults. *Cancer Causes Control* 9: 403.
- Wideroff L, Gridley G, Mellekjaer L, et al. (1997) Cancer incidence in a population-based cohort of patients hospitalized with diabetes mellitus in Denmark. *J Natl Cancer Inst* 89: 1360.
- Jee SH, Ohrr H, Sull JW, et al. (2005) Fasting serum glucose level and cancer risk in Korean men and women. *JAMA* 293: 194.
- Bosetti C, Rosato V, Li D, et al. (2014) Diabetes, antidiabetic medications, and pancreatic cancer risk: an analysis from the International Pancreatic Cancer Case-Control Consortium. *Ann Oncol* 25: 2065.
- Batabyal P, Vander Hoorn S, Christophi C, Nikfarjam M (2014) Association of diabetes mellitus and pancreatic adenocarcinoma: a meta-analysis of 88 studies. *Ann Surg Oncol* 21: 2453.
- Gullo L, Pezzilli R, Morselli-Labate AM, Italian Pancreatic Cancer Study Group (1994) Diabetes and the risk of pancreatic cancer. *N Engl J Med* 331: 81.
- Chari ST, Leibson CL, Rabe KG, et al. (2008) Pancreatic cancer-associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. *Gastroenterology* 134: 95.
- Pannala R, Leirness JB, Bamlet WR, et al. (2008) Prevalence and clinical profile of pancreatic cancer-associated diabetes mellitus. *Gastroenterology* 134: 981.
- Wong HK, Tang F, Cheung TT, Cheung BM (2014) Adrenomedullin and diabetes. *World J Diabetes* 5: 364.
- Javeed N, Sagar G, Dutta SK, et al. (2015) Pancreatic Cancer-Derived Exosomes Cause Paraneoplastic  $\beta$ -cell Dysfunction. *Clin Cancer Res* 21: 1722.
- Gapstur SM, Gann PH, Lowe W, et al. (2000) Abnormal glucose metabolism and pancreatic cancer mortality. *JAMA* 283: 2552.
- Stolzenberg-Solomon RZ, Graubard BI, Chari S, et al. (2005) Insulin, glucose, insulin resistance, and pancreatic cancer in male smokers. *JAMA* 294: 2872.
- Michaud DS, Liu S, Giovannucci E, et al. (2002) Dietary sugar, glycemic load, and pancreatic cancer risk in a prospective study. *J Natl Cancer Inst* 94: 1293.
- Wolpin BM, Bao Y, Qian ZR, et al. (2013) Hyperglycemia, insulin resistance, impaired pancreatic  $\beta$ -cell function, and risk of pancreatic cancer. *J Natl Cancer Inst* 105: 1027.

23. Carreras-Torres R, Johansson M, Gaborieau V, et al. (2017) The Role of Obesity, Type 2 Diabetes, and Metabolic Factors in Pancreatic Cancer: A Mendelian Randomization Study. *J Natl Cancer Inst* 109.
24. Bao Y, Giovannucci EL, Kraft P, et al. (2013) A prospective study of plasma adiponectin and pancreatic cancer risk in five US cohorts. *J Natl Cancer Inst* 105: 95.
25. Pelaez-Luna M, Takahashi N, Fletcher JG, Chari ST (2007) Resectability of presymptomatic pancreatic cancer and its relationship to onset of diabetes: a retrospective review of CT scans and fasting glucose values prior to diagnosis. *Am J Gastroenterol* 102: 2157.