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Fibrocalculous Pancreatic Diabetes - a Unique Differential among Diabetic

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ABSTRACT

Fibrocalculous pancreatic diabetes is a unique variant of diabetes mellitus and also known as type 3c diabetes mellitus. It is related to the patient who is young, non-alcoholic and belonging predominantly from the tropical region. It is a severe form of diabetes which can also be linked to the fact that it predisposes to malignancy.[1] Among the variants of diabetes that we commonly encounter, fibrocalculous pancreatic diabetes has been rarely diagnosed in the developing countries. With the advancement of diagnostic capacity, it can be identified clinically and managed efficiently. It should be considered in patients with typical features of diabetes, abdominal pain, and pancreatic calculi. There is limited reporting of this case in Nepal because of misdiagnosis, so we are reporting a 40 years male who presented with recurrent episodes of abdominal pain with mucus mixed stool for the last 28 years and was diagnosed as fibrocalculous pancreatic diabetes.

Keywords: Blood glucose; eastern Nepal; fibrocalculous pancreatic diabetes; pancreas.

INTRODUCTION

The prevalence of diabetes mellitus was 8.5% according to a recent survey conducted in Nepal.[1-2] Type 1 and type 2 diabetes are commonly diagnosed, but a rare type 3c diabetes is often misdiagnosed as type 2 diabetes. Type 3c diabetes occurs due to pancreatic failure or inability of the pancreas to produce enough insulin for regulating glucose.[3] The symptoms making a classical triad of FCPD included diabetes, pain abdomen and steatorrhoea.[4] Although this disease is prevalent in the tropical and subtropical regions, this is the first diagnosed case of FCPD in our center with a typical clinical presentation who had misdiagnosis for the last 28 years.

CASE REPORT

A 40 year male from eastern Nepal, presented to the outpatient department of General Medicine of Birat Medical College Teaching Hospital (BMCTH) on 13 December 2019 with complaints of recurrent upper abdominal pain which was gradual onset, intermittent, burning, radiating to the back, progressive,associated with the passage of greasy stool, and intermittent discomfort in the upper abdomen for the last 28 years. He was non-vegetarian, non-alcoholic, and non-smoker. After finding pancreatic calcification on ultrasonography of the abdomen done outside our center, the patient arrived to the General Surgery department of Birat Medical College and Teaching Hospital (BMCTH), where he was advised for Contrast-Enhanced Computed Tomography (CECT)-abdomen, blood glucose profile, and renal function test. He was then referred to the Department of Medicine for further evaluation. His BMI (Body Mass Index) was 18.1kg/m^2 and abdominal examination was normal. He had elevated fasting plasma glucose level (169 mg/dl), 2 hours plasma glucose level after 75-gram glucose load (297 mg/dl), and glycated hemoglobin (HbA1c) (8.6%). He was diagnosed with diabetes mellitus.Ultrasonography findings revealed multiple intraductal calculi in the pancreas. Further, CECT found dilated main pancreatic duct suggesting chronic pancreatitis with intraductal calcific foci, Figure 1. He was managed with oral hypoglycemic agents and proton pump inhibitors.

On follow-up, he had similar complaints despite having current medical intervention. After further investigation, his hemoglobin (13.1 g/dl), thyroid-

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stimulating hormone (3.815 micIU/ml), serum amylase (54 u/L), and carbohydrate antigen (CA19-9: 10.2 U/ml) were found within normal limits. The lipid profile showed hypertriglyceridemia and low HDL-cholesterol, and low Vitamin D3 (17.81 ng/ml). On X-ray of the abdomen , the pancreatic duct was diffusely calcified, Figure 2. After all the evaluation, provisional diagnosis of FCPD was made. The treatment was based on avoidance of fatty foods, frequent small carbohydrates and protein diet, management of pain, and supplementation of the pancreatic enzyme. On follow-up, the patient showed clinical improvement with a BMI of 20.8 kg/m^2, good glycaemic control, and minimal episodes of pain in the abdomen. He was prescribed Gliclazide 30 mg once daily before meal, Pancreatic enzyme 30,000 IU supplement with meal, and Metformin hydrochloride 850 mg twice a day after meal.

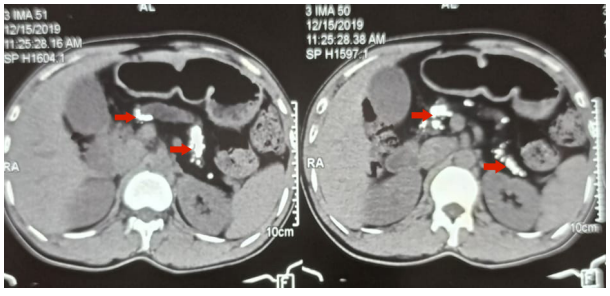

Figure 1. Axial section of CT Scan showing hyperdense opacities in the pancreas itself suggesting multiple calculi.

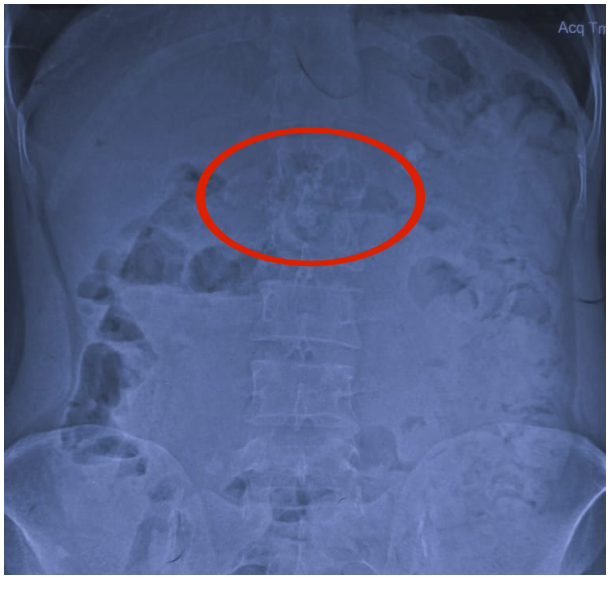

Figure 2. X-Ray abdomen showing presence of radio-opaque shadows around the thoraco-lumbar vertebral region, possibly pancreatic calcification.

The patient was treated with conservative management along with oral hypoglycemic agents and pancreatin supplements. Since last one year of follow-up, his fasting and 2 hours postprandial plasma glucose level has significantly improved from 157 mg/dL to 70 mg/dL and 419 mg/dL to 146 mg/dL respectively (Figure 3). He is on constant follow-up for appropriate tests and clinical assessment.

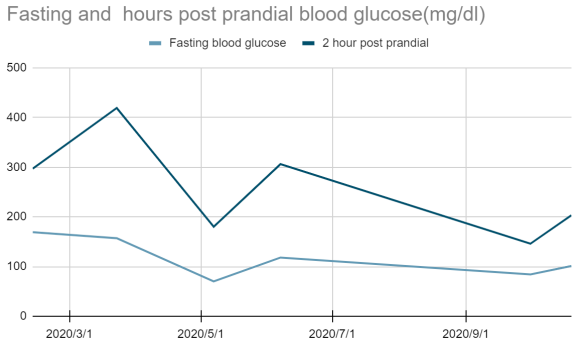

Figure 3. Fasting and 2-hour postprandial plasma glucose level of last one year.

DISCUSSION

We reported the case of FCPD from eastern Nepal. There are very limited scientific studies conducted about this disease in Nepal. However, a retrospective study conducted in 55 participants in a tertiary hospital in Nepal concluded that 68% participants with chronic pancreatitis had accompanying diabetes.[5] Chronic pancreatitis in itself means a state of progressive inflammatory and fibrotic change in the pancreas that results in permanent structural damage which causes exocrine and endocrine insufficiency. The most common cause of chronic pancreatitis mostly is idiopathic in contrast to fibrocalculous pancreatic diabetes the cause of pancreatic insult becomes a chronic inflammation due to pancreatic calculi.Prior to occurrence of diabetes in FCPD there is a pre-diabetic phase which is found mostly associated with people in tropical region calling it as tropical chronic pancreatitis.[1] The diagnostic criteria for FCPD are: (i) tropical/subtropical predilection, (ii) diabetes confirmed on standard Oral Glucose Tolerance Test (OGTT),(iii) presence of chronic pancreatitis confirmed by x-ray findings showing pancreatic calcification and absence of other causes of pancreatitis like alcoholism, hyper-parathyroidism, gallstone and hepatobiliary disease.[6] Hyperglycemia due to pancreatic dysfunction has been called pancreatogenic type 3c diabetes.[7] Diverse set of etiologies include malnutrition, toxins in diet like cassava, genetic

predisposition, serine protease inhibitor kazal type 1 (SPINK1) mutations, oxidative stress,auto-immune factors,and micronutrient deficiency like vitamin C and vitamin D.[8] A two hit theory that has been postulated where a first hit states mutations in the genes involved in FCPD causing formation of super trypsin in the acinar cells of pancreas and the second hit explaining that the unidentified genes resulting in one or more phenotypes like stone formation, fibrosis and diabetes.[1] In this case, the patient presented with vague symptoms of upper gastrointestinal discomfort and was being treated for acid peptic disease. Investigations like X-ray of abdomen, ultrasonography of abdomen and pelvis, and computed tomography scan of the abdomen along with the history helped prove diabetes as a different entity namely Fibrocalculous Pancreatic Diabetes. He had a typical feature presenting with calculus in the pancreatic duct, steatorrhoea, and diabetes which fits into the criteria of fibrocalculous pancreatic diabetes. Two case reports in China reveal that two clinical scenarios of FCPD were managed with intensive insulin therapy, Calcium, and Vitamin D3.[9] Similarly, another case report in Srilanka show that a case of FCPD was managed with glycemic control using oral hypoglycemic drugs and insulin, management of pain, exocrine and endocrine functions of the pancreas.[6] In contrast, this case has been managed based on glycaemic control using oral hypoglycaemic drugs only, management of pain, and supplementation of the pancreatic enzymes. We could solely diagnose our case with history, examination, and supportive tests. However, the limitations encountered were a lack of genetic testing (Human leukocyte antigen -DQB1 typing) and testing for Tumor necrosis factor-lymphotoxin microsatellite markers (Tumor necrosis factor alpha, Tumor necrosis factor c and Tumor necrosis factor d).[10] specific testing methods and the genes involved like SPINK 1 mutation which is a trypsin inhibitor gene and some auto-immune factors which are also implicated in the cause of FCPD.[11] The patients of FCPD are at about 100 times more risk of developing Pancreatic cancer as compared to other forms of pancreatitis.[12] Therefore, routine follow up is mandatory to monitor the development of cancer in these patients.[9]

CONCLUSIONS

The presentation of diabetes in the form of Fibrocalculous Pancreatic Diabetes (FCPD) has been least studied in our country. Currently it stands out as a secondary form of diabetes with etiologies yet to be discovered. Being a resource limited country, we had limitations with genetic testing (HLA-DQB1 typing), Spink 1 gene mutation, TNF-LT microsatellite markers (TNFa, TNFc and TNFd) for proper diagnosis of the case. The management includes lifestyle modifications and medications, along with insulin therapy. Insulin therapy has been found ideal in treating other known cases of FCPD in contrast to which our patient did not require any insulin supplementation.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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