



Long Term Outcome of Endoscopic Minor Papillotomy in Patients with Symptomatic Pancreas Divisum: Experience from Northern India

Omesh Goyal^{1*}, Arshdeep Singh¹ and Prerna Goyal²

¹*Department of Gastroenterology, Dayanand Medical College and Hospital, Ludhiana, India.*

²*Department of Internal Medicine, RG Stone Hospital, Ludhiana, India.*

Authors' contributions

This work was carried out in collaboration among all authors. Author OG designed the study, performed the endoscopic procedure collected the data and wrote the protocol. Author AS assisted the endoscopic procedure, collected the data and wrote the first draft of the manuscript. Author PG managed the analyses and literature searches of the study. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Pancreas divisum (PD) occurs due to the non-union of dorsal and ventral pancreatic ducts during organogenesis and is the most common developmental anatomic variant of pancreatic duct. Most of the PD cases remain asymptomatic, while others may present with recurrent/chronic abdominal pain. PD is considered an important cause of idiopathic recurrent acute pancreatitis. The diagnosis of PD is challenging and is often delayed. Failure to detect PD may lead to recurrent episodes of pancreatitis and development of chronic pancreatitis. Timely papillotomy of the minor papilla alleviates symptoms in majority of these patients. There is paucity of data on symptomatic pancreas divisum from India. We report a case series of seven patients with symptomatic pancreas divisum, 71.4% of these were females and 57.1% presented with recurrent acute pancreatitis. All the patients had long term symptomatic improvement after endoscopic papillotomy of minor papilla.

*Corresponding author: Email: goyalomesh@yahoo.co.in;

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1. INTRODUCTION

Pancreas divisum (PD), non-union of dorsal and ventral pancreatic ducts during organogenesis, is the most common developmental anatomic variant of pancreatic duct with 5%–14% autopsy prevalence in general population [1]. Usually, <5% patients become symptomatic, common presentations being idiopathic pancreatitis and chronic abdominal pain [2]. Though causative association between pancreas divisum and idiopathic pancreatitis remains controversial, clinical response to surgical/endoscopic sphincterotomy of stenotic minor papilla indicates otherwise [3,4]. There is limited data on prevalence, clinical presentation and management of pancreas divisum from India.

2. METHODS

Prospectively maintained data of all patients of symptomatic PD presenting to the Gastroenterology unit of Dayanand Medical College and Hospital, Ludhiana, India between January 2016 and December 2018 were analysed retrospectively. The long term outcomes of seven patients with symptomatic pancreas divisum who underwent minor papilla sphincterotomy are reported.

3. RESULTS/CASE PRESENTATIONS

3.1 Case 1

A 41 year old non-smoker, non-alcoholic female presented with upper abdominal pain radiating to back since 3 days. There was no history intake of any medications, herbal products or trauma. Abdominal examination revealed mild abdominal distension with epigastric tenderness. Laboratory work-up showed increased levels of amylase [1564 U/L (range 28-100 U/L)] and lipase [2358 U/L (range 13–60 U/L)]. Liver function tests (LFTs) and metabolic profile including serum calcium and triglycerides were within normal limits. There was no evidence of gallstones. Magnetic Resonance Cholangiopancreatography (MRCP) was done subsequently for etiological work-up which revealed pancreas divisum. Endoscopic Retrograde Cholangio-Pancreatography (ERCP) showed dilated dorsal pancreatic duct, and sphincterotomy of minor papilla with stent placement (5 F 12 cm, straight plastic stent) in the pancreatic duct was done. (Fig. 1) The stent was removed after 16 weeks.

She is asymptomatic on 3 years and 6 months follow up.

3.2 Case 2

A 55 year old diabetic female presented with pain upper abdomen since 4 days. This pain was not radiating, aggravated by food intake and relieved only with opioid analgesics. She had an episode of similar pain about 1 year back for which she was admitted to a hospital, diagnosed as idiopathic acute pancreatitis (lipase >3 times upper limit of normal), managed conservatively with intravenous fluids and other supportive care. During the current episode, her liver function tests and metabolic profile including serum calcium and triglycerides were non-contributory. MRCP showed dominant dorsal pancreatic duct and pancreas divisum. (Fig. 2) Sphincterotomy of minor papilla and stenting was performed. The stent was removed after 22 weeks. She is asymptomatic on 3 years follow up.



Fig. 1. Fluoroscopy image during ERCP (after contrast injection) showing dilated dorsal pancreatic duct

3.3 Case 3

A 22 year old female presented to emergency department with history of severe pain epigastrium since 2 days. On investigations, she was diagnosed as acute pancreatitis. Past history was significant for three episodes of mild acute pancreatitis in the past one year, each managed conservatively at local hospital. MRCP done during current admission suggested pancreas divisum. Sphincterotomy of minor

papilla and pancreatic duct stenting was performed. She again developed epigastric discomfort after 8 weeks for which she was evaluated and the pancreatic stent was found blocked. The stent was removed and she has remained asymptomatic till date with a follow up of 2 years and 10 months.



Fig. 2. MRCP image showing dorsal pancreatic duct crossing the CBD and opening above the major papilla

3.4 Case 4

A 24 year old female had complaints of pain upper abdomen for 15 days. She was a non-smoker and teetotaler. She was not under any medication at the time her symptoms appeared. Physical examination revealed mild epigastric tenderness on deep abdominal palpation.

Laboratory tests revealed elevated serum amylase and lipase levels. Metabolic parameters were normal. CECT abdomen showed bulky pancreas with mild peri-pancreatic stranding and dominant dorsal pancreatic duct opening above the level of major papilla suggestive of pancreas divisum. (Fig. 3) Endoscopic sphincterotomy of minor papilla relieved her of symptoms. The pancreatic stent was removed after 12 weeks and she is asymptomatic at 2 years 6 months of follow up.

3.5 Case 5

A 57 year old female got admitted in emergency room with severe epigastric pain since 3 days. There was history of multiple episodes of similar pain in the past 4 years, each diagnosed as mild acute pancreatitis. She had history of hypertension and diabetes mellitus since 8 years. Ultrasound abdomen showed an enlarged and bulky pancreas. There were no dilatations of the pancreatic ducts and there was no evidence of necrotic areas or pancreatic and peri-pancreatic fluid collections. The biliary system, liver and spleen were normal. Metabolic work up was normal. She received standard of care including intravenous fluids (Ringer's lactate), analgesics and nutritional support. MRCP done subsequently showed pancreas divisum. Sphincterotomy of minor papilla and pancreatic duct stenting was done. (Figs. 4 and 5) The stent was removed after 12 weeks. She is asymptomatic on 2 year 4 months follow up.

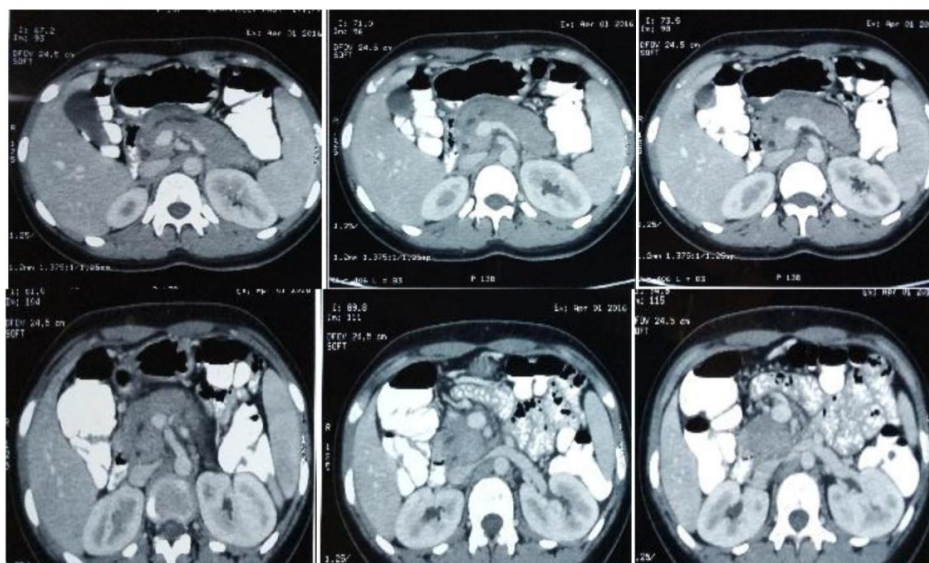


Fig. 3. CECT Abdomen showing dilated dominant dorsal pancreatic duct draining into minor papilla

3.6 Case 6

A 28 year old non-smoker, non-alcoholic male, presented to emergency room with complaints of pain upper abdomen and vomiting since five days. There was no history of trauma, medications or alternative therapies. Laboratory tests revealed elevated serum amylase and lipase levels (greater than 3 times normal). Liver function tests were normal. He did not have hypercalcemia or hypertriglyceridemia. USG abdomen revealed bulky pancreas and normal biliary system. He was managed with intravenous fluids, anti-emetics and analgesics. As there was no evident etiology of acute pancreatitis, MRCP was done which revealed pancreas divisum. Minor papilla sphincterotomy and pancreatic ductal stenting was done. Stent was removed after 24 weeks. He is asymptomatic on 1 year 8 months follow up.

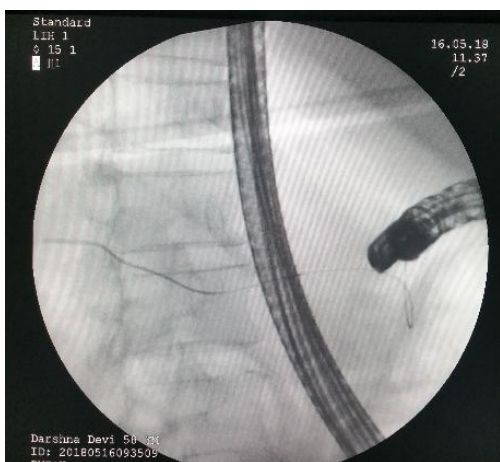


Fig. 4. Fluoroscopy images during ERCP showing guidewire cannuation of dorsal pancreatic duct through minor papilla

3.7 Case 7

A 17 year old male with no co-morbidities and no addictions presented with complaints of severe epigastric pain and vomiting since five days. There was history of multiple similar episodes in past 5 years. Each of the episodes of pain in past were diagnosed as mild acute pancreatitis requiring hospitalization and were managed conservatively with intravenous fluids, analgesics and supportive care. Laboratory and sonographic evaluation confirmed recurrent acute pancreatitis. MRCP done during the current hospitalization suggested pancreas divisum with changes of chronic pancreatitis. Minor papilla

sphincterotomy and pancreatic duct stenting was performed, and the stent was removed after 14 weeks. He is asymptomatic on 1 year 6 months follow up.

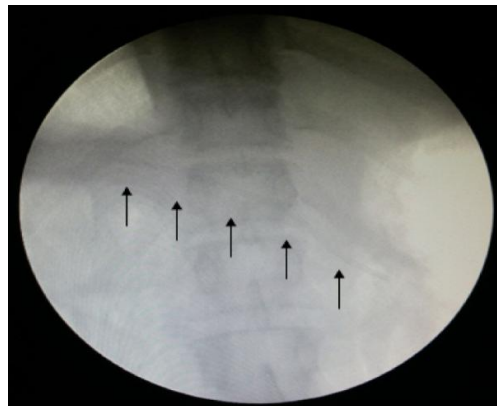


Fig. 5. Fluoroscopy images during ERCP showing plastic stent placed in the dorsal pancreatic duct through minor papilla

4. DISCUSSION

Pancreas divisum is an important cause of recurrent acute pancreatitis (RAP). Despite the controversial causal association, higher frequency of pancreas divisum in patients with RAP than general population, presence of pathological changes confined to the dorsal pancreas in patients with pancreatitis and pancreas divisum, and therapeutic response to sphincterotomy/stenting of minor papilla suggest that the two entities are related [3-6].

We report seven patients with symptomatic pancreas divisum responding to endoscopic sphincterotomy of minor papilla. Five (71.4%) patients were females. Abdominal pain was the most common presenting symptom. Four patients (57.1%) had RAP, while three presented with first episode of AP. All these patients had mild pancreatitis with none of them developing complications like peri-pancreatic collection, pancreatic ascites, pancreatic pleural effusion or organ failure. In fact, three (42.8%) patients did not need hospitalization. Only one patient had concomitant changes of chronic pancreatitis.

In our experience, pancreatic endo-therapy was effective in all (100%) the patients. This response was long lasting (median follow up 2 years 6 months; range 1 year 6 months to 3 years 6 months) in all the patients. None except one patient (patient number 3) had recurrent episode of abdominal pain after the intervention. The

cause of pain in this patient was blockage of the pancreatic stent; and pain settled after removal of the stent. Repeat pancreatic endo-therapy and/or surgical intervention were not required in any of the other patients. None of the patients had immediate procedure related complications or developed post ERCP pancreatitis. Previous studies suggest that best results of endoscopic therapy in patients with pancreas divisum are obtained in patients with RAP [7]. In contrast only 57.1% patients in our case series had RAP, whereas the rest had first episode of AP; but all responded to endoscopic therapy. The established indications for minor papilla sphincterotomy in patients with pancreas divisum include chronic pancreatic pain, recurrent acute pancreatitis, or chronic pancreatitis, while endo-therapy in asymptomatic pancreas divisum is not indicated [8-10]. We performed pancreatic endo-therapy according to these established indications. In addition, pancreatic endo-therapy was also offered to patients presenting with first episode of acute pancreatitis, in whom no other etiology for acute pancreatitis was identified. On long term follow up, none of these patients developed features to suggest chronic pancreatitis. These observations suggest a probable beneficial role of early minor papilla sphincterotomy in patients with symptomatic pancreas divisum, rather than waiting for recurrent episodes of pancreatitis or development of chronic pancreatitis. However, this hypothesis needs corroboration in larger studies.

Gene mutation analysis was not done in the current case series because of unavailability of the facilities and cost limitations. Even though gene mutations are present in only 40% of patients with RAP and pancreas divisum [11], a long term durable response to endotherapy may point towards a less intense association between pancreas divisum and genetics. The sample size in our study is however too small to make a significant derivation. This needs to be evaluated in larger number of patients with symptomatic pancreas divisum.

5. CONCLUSION

To conclude, pancreas divisum should be actively sought as a cause of idiopathic acute pancreatitis, even in patients presenting with first episode of acute pancreatitis. Intensive pancreatic endo-therapy including minor papillotomy results in sustained long term clinical response.

CONSENT

Written informed consent was obtained from all the participants for endoscopic sphincterotomy of minor papilla. The procedures were performed by an experienced endoscopist (OG) and the patients were followed up every 3 months or earlier in case of development of new onset symptoms.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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