

Chapter 13

Chronic calcific pancreatitis of the tropics with carcinoma

Meenu Hariharan, Subhalal N, Anandakumar M,
Chellam VG, Satheesh Iype

Summary

Background: Carcinoma developing in chronic calcific pancreatitis of the tropics (CCPT) is a well known complication. Early diagnosis is difficult and the overall mortality rate is high. Clinically and pathologically, this malignancy behaves in a different manner compared to denovo pancreatic ductal adenocarcinoma. This paper analyses and compares pancreatic carcinoma occurring along with CCPT and denovo carcinoma.

Methods: One hundred and forty one cases of carcinoma pancreas seen in the Departments of Medical and Surgical gastroenterology, Medical College, Trivandrum, during a 4-year period from January 1993 to December 1996 were retrospectively and prospectively studied. The data were analyzed as 2 groups: Group A – CCPT with malignancy, Group B – patients with denovo pancreatic ducal adenocarcinoma with no CCPT.

Results: There were 23 cases of malignancy in CCPT (Group A) and 118 patients belonged to Group B. Group A patients had a significantly lower age, median age was 38 years (28-61 years) and duration of symptoms ranging from 3 months to 15 years.

Intractable pain, significant loss of weight and worsening of diabetes were the commonest presenting symptoms in cancers with CCPT, noted in 60% of cases. Jaundice, pruritus and loss of weight were the commonest presentation in denovo cancers. The distribution of tumours was similar in Groups A and B with maximum involvement of the pancreatic head.

Hepatic metastases were less common for malignancies developing in CCPT, Group A. In Group A local invasiveness of the tumour was high and overall resectability of the tumour was poor. **Conclusion:** Carcinoma occurs in approximately 25% of cases of CCPT. There is a predilection for involvement of head of pancreas. However, involvement of body and tail of pancreas is higher than denovo pancreatic cancer. Both local infiltration and peritoneal dissemination are higher in CCPT with carcinoma, but liver metastasis is rare.

Introduction

The premalignant nature of CCPT has been established by many prospective and retrospective studies¹⁻⁶. Development of malignancy, at some stage, is seen in less than 1/3rd cases of CCPT in the state of Kerala where CCPT occurs in endemic proportions^{7,8}. Earlier studies from our department had shown that carcinoma arising in patients who have CCPT behave in a different manner clinically and pathologically, compared to denovo pancreatic cancer^{1,3,4}. This retrospective and prospective study tries to analyze and compare carcinoma occurring in CCPT to denovo pancreatic cancer.

Methods

This retrospective and prospective study is based on 141 cases of histologically proven pancreatic carcinoma, 23 of whom had CCPT, that were operated in the Department of Surgical Gastroenterology, Medical College Hospital, Trivandrum, during a period of 4 years from 1993-1996. Standard clinical and radiological criteria were used to diagnose CCPT, which included history of abdominal pain, sonological evidence of dilated pancreatic duct with calculi, ERCP findings and CT scan.

The diagnosis of pancreatic carcinoma was by histopathologic examination of per-operative tru-cut biopsy or resected specimen of the pancreas. For comparison and analysis of data, patients were divided into 2 groups: Group A included CCPT presenting as malignancy and Group B consisted of patients with denovo pancreatic ductal adenocarcinoma and no CCPT. Clinical presentation, morphology and operative findings of these tumours were analyzed.

A total number of 98 cases of CCPT were seen and evaluated in gastroenterology clinic during the study period. Forty three cases underwent various surgical procedures for CCPT and 23 cases (24%) were done for malignancy. Age distribution showed a significant difference of about a decade between each groups, the lowest being in Group A with a median age of 38 years in comparison with Group B (the median age was 54 years). Male preponderance was similar in both groups. Endocrine insufficiency in the form of diabetes mellitus was found in 66% of patients in Group A, but only 19.4% of patients in Group B (Table 1).

Table 1: General features

	Group A	Group B
Total number of cases	23	118
Sex ratio (M:F)	1.6:1	2.19:1
Median age	38 years	54 years
Jaundice and pruritus	70%	86%
Diabetes mellitus	66%	19.4%

Symptoms were analyzed by allotting a scoring system (Table 2 and 3). A score of 5 was observed in 29% of cases belonging to Group A while none of the Group B cases could satisfy the maximum score of 5. The tetrad of jaundice, worsening of diabetes, change in character of pain and significant loss of weight were observed in 60% of cases of Group A. Head of pancreas was the commonest site to be involved in both groups, but there was relatively higher predilection for the body and tail in Group A, when compared with Group B. Distribution of calculi however, was more uniform throughout the gland and no significant relation was found between the location of tumour and calculi.

Table 2: Symptom score

Sl. No.	Symptoms	Score
1	Worsening of diabetes	1
2	Change in character of pain	1
3	Loss of weight	1
4	Jaundice	1
5	Pruritus	1

Table 3: Symptom score in relation to groups

Score	Group A	Group B
0-2	16%	37%
2-4	55%	63%
5	29%	0

Table 4: Location of tumour (Predominant region of cancer involvement)

Location of tumour	Group A	Group B
Head of pancreas	15 (65%)*	106 (90%)
Body of pancreas	4 (17%)**	10 (8.5%)
Tail of pancreas	1 (5%)	2 (1.5%)

* Two cases of CCPT with suspicion of carcinoma of head of pancreas were excluded as peroperatively no tumour was found; however, pathological examination of tissue specimens were positive.

** One case of CCPT with suspected carcinoma of body of pancreas was excluded as preoperatively it was diagnosed as intraductal papillary adenocarcinoma.

Local infiltration to adjacent organs and major vessels were significantly high in Group A. Peritoneal dissemination was higher in Group A as well. Lymph node (LN) metastasis was also slightly higher in Group A (Table 5). Liver metastasis at presentation was significantly more common in Group B compared to Group A. Majority of patients underwent only palliative procedures because of either locally advanced or metastatic disease in Group A.

Table 5: Operative findings

	Group A	Group B
Local infiltration	9 (39%)	24 (20%)
LN metastasis	4 (17%)	12 (10.2%)
Peritoneal metastasis	7 (30.4%)	10 (8.5%)
Liver metastasis	1 (4.3%)	22 (18.6%)

Discussion

Patients with CCPT present with abdominal pain, weight loss, pancreatic calcifications, and glucose intolerance or diabetes mellitus⁷. Kerala, the southwestern state of India has found to be one of the 'hot spots' with

high incidence of CCPT. The etiology of CCPT is largely unknown, and nutritional and environmental factors have been propagated as major causative factors in the etiopathogenesis. Postulated etiologies include a protein-calorie malnourished state, a variety of exogenous food toxins, pancreatic duct anomalies, and a possible genetic predisposition⁷. Chronic cyanide exposure from the diet may contribute to this disease. The cyanogenic glycosides linamarin and lotaustralin are contained in cassava. Cassava, a mainstay of many tropical and subtropical diets, especially in India, reacts with gastric hydrochloric acid, liberating hydrocyanic acid, which is toxic to cells^{10,12}. Duration of exposure to inflammation seems to be the major factor involved in the transition from benign to malignant condition.

CCPT is identified as a premalignant condition and several studies have reported this fact earlier. In our series, CCPT co-existing with pancreatic cancer was 24% of the cases seen in the clinics. Malignancy developed at the prime of their life (median 38 years) in these patients (Group A). It is more than a decade earlier than the development of denovo cancers. An earlier study from this institution had reported pancreatic carcinoma developing in 22 of 240 patients with tropical pancreatitis on a 7-year follow up^{8,9}. Clearly, there is an increased incidence of diabetes mellitus in cases with carcinoma in CCPT. Chari et al. followed 155 patients with TP from Madras, India, for an average of 4.5 years. They found that 25% of the deaths recorded in the group were from carcinoma of the pancreas. The average age for onset of pancreatic cancer was 45 years⁵.

Change in character of pain, development of jaundice, recent worsening of diabetes and significant weight loss are considered predictors of malignancy in CCPT patients³. Jaundice, intractable pain, recent worsening of diabetes and marked weight loss were found in 60% of patients with CCPT presenting with carcinoma.

The distribution of tumours in the pancreatic gland in Group A was similar to that of Group B with a greater predilection for the head, unlike previous studies showing a high incidence of cancer of body and tail of pancreas¹¹. There was a relatively higher involvement of the body than in denovo cancer of pancreas.

Though local aggressiveness of the tumour was found to be more when CCPT coexisted, visceral dissemination was uncommon. Peritoneal dissemination and lymphnode metastasis were found to be higher in CCPT with cancer. The local aggressiveness could be due to the biological features of malignant cell in CCPT and paucity of early visceral metastasis due to excessive fibrosis of the pancreas promoting an early peritoneal dissemination rather than a haematogenous spread. However, early diagnosis of carcinoma in CCPT is a vexing problem to the gastroenterologist because of the inability to localize the tumour precisely in a diffusely fibrotic gland with chronic pancreatitis.

References

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