COMPARISON BETWEEN PREOPERATIVE IMAGE GUIDED BIOPSY AND OPEN BIOPSY IN CLINICALLY LABELED "UNRESECTABLE CARCINOMA PANCREAS"

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Summary

Although clinical findings along with modern laboratory investigations and imaging can help to diagnose pancreatic cancer and label them resectable or unresecable, tissue diagnosis is essential to confirm the diagnosis and proper management. This retrospective review was done form July 2004 to June 2006 in BIRDEM hospital, Dhaka, Bangladesh, in patient with clinically labeled 'unresectable carcinoma pancreas' to evaluate the preoperative and postoperative biopsy pattern with their histopathological diagnosis. Forty (40) patients were clinically labeled as 'unresectable carcinoma pancreas'. Preoperatie image guided biopsy was taken in 25 patients. Methods of preoperative tissue diagnosis with their histopathology reports were noted. In forty (40) patients it was planned to take open biopsy along with other palliative surgical procedures. In 38 patients tumours found unresectable and biopsy were taken from the lesion, involved organ or lymph node. In 2 patients curative resection were done and whole specimens were sent for histopathology. Histopathology report of post surgical specimen was compared with preoperative histopathology report. Preoperative biopsies were done by ERCP in 12 patients. Ten (10) image (ultrasonography, computed tomography scan) assisted fine needle aspiration biopsy were taken from the pancreatic lesion. Preoperative imaging failed to detect any pancreatic mass in the rest 3 patients but showed suspected liver metastasis. Image (computed tomography scan) assisted 03 fine needle aspiration biopsies were taken from 3 hepatic metastasis. Histopathological report showed pancreatic duct cell carcinoma in 19 (76%) patients, 1(4%) patients had chronic pancreatitis. Biopsy report was not conclusive in 2 (8%) patients. All 3 biopsies from liver focus were metastatic pancreatic cancer (12%). Histopathology report of laparotomy samples revealed that 35 patients (87.5%) had pancreatic duct cell carcinoma. Out of the rest 5 patients 2 patients (5%) were chronic pancreatitis, non Hodgkin's lymphoma 01 patients (2.5%), tuberculosis 01patients (2.5%) and metastatic renal cell carcinoma 01 patient (2.5%). Open biopsy has a greater diagnostic accuracy than preoperative biopsy in diagnosing unresectable pancreatic carcinoma and to exclude other pancreatic mass lesions labeled clinically as 'unresectable carcinoma pancreas'. Open biopsy is recommended in clinically labeled 'unresectable carcinoma pancreas'.

Key words

Pancretic carcinoma; unresectable; histopathology

Introduction

Cancer pancreas is the 4th leading cause of all cancer death. The peak incidence is in 5th and 6th decades of life [1]. The term pancreatic cancer is sometimes loosely used to include all types of malignant neoplasm of the non endocrine pancreas as well as malignant islet cell tumour. In clinical practice, pancreatice cancer is synonymous with pancreatic ductual adenocarcinoma which constitute 90% of all the malignant tumour of the gland [2]. Other lesions are chronic pancreatitis (3.73%), primary pancreatic neuroendocrine tumour (3.73%), metastatic renal cell carcinoma (0.93%), Lymphoma (0.93%) etc [3]. It arises most frequently from the pancreatic ducts & most commonly in the head of the pancreas. The incidence is 70% in the head & 30% in the body and tail of the pancreas [4]. Pancreatic cancer are diagnosed on the basis of clinical presentation, laboratory investigations including tumour markers, imaging studies & some endoscopic procedures [1]. Unfortunately at the time of presentation 90-95% patients are unsuitable for curative resection [3]. Findings contraindicate for curative resection are liver meatastasis, celiac lymph node involvement, peritoneal implant, invasion of transverse colon and hepatic hilar lymph node involvement. These lesions are labeled as 'unresectable carcinoma pancreas [5].

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Despite modern imaging, it is mandatory to have a histological proof before the lesion is labeled as cancer pancreas because many benign conditions or treatable malignant condition (e g. Lymphoma) simulate the features of cancer. Benign conditions need different management policy & have a significantly better prognostic value. Histological diagnosis is also essential for planning post operative chemotherapy as newer chemotherapeutic agents are producing satisfactory response in some pancreatic cancer [6].

Biopsy is the only way to make a definitive diagnosis of pancreatic cancer. Biopsies of the pancreas & bile duct can be performed in several ways as image guided fine needle aspiration cytology (FNAC), endoscopic retrograde cholangio-pancreaticography (ERCP) & biopsy, brush cytology and by laparoscopic or open surgical procedures [7]. Meyer also reported that laparoscopic biopsy is possible [8].

Computed tomography (CT) scan and ultrasonography (US) are commonly used image to evaluate and characterize pancreatic masses and to guide percutaneous pancreatic biopsy. Endoscopic sonography also used to obtain biopsy [3].

In our country we still depend mostly on US as in a few centers CT scan, ERCP, magnetic resonance imaging (MRI) mangnetic resonant cholangio-pancreaticography (MRCP) and laparoscopy are available. Due to the scarcity of specialized centers and investigations facilities, quite a considerable number of patients remain undiagnosed & untreated, diagnosed at the advanced stage of the disease and may be maltreated. Benign conditions like chronic pancreatitis may be treated as malignant condition of pancreas even may simulate with inoperable pancreatic cancer.

Present study was carried out in Bangladesh Institute for Research & Rehabilitation in Diabetic Endocrine & Metabolic Disorders (BIRDEM) hospital to see how biopsies were taken from such patient before laparotomy and their histopathological diagnosis. The preoperative tissue diagnosis was compared with the histopathology of post laparotomy specimen.

Materials and methods

This retrospective study was carried out form July 2004 to June 2006 (study period 2 years) in the department of Hepato-Biliary-Pancreatic Surgery in BIRDEM hospital, Dhaka, Bangladesh. Hospital records were evaluated but inadequate incomplete patients files were not considered further.

After careful scrutiny of clinical, laboratory and imaging studies, it was found that, fifty (50) patients were labeled as 'unresectable carcinoma pancreas'. It was noted that union international contra Le cancer (UICC) staging system were adopted for staging of pancreatic cancer staging (stage I- IV).
Among the 50 patients it was decided not to carry out any surgical intervention in 10 preoperative biopsy proved pancreatic cancer patients as there was distant metastasis in 4 (08%) patients, locally advance disease in 3 (06%) patients and 3 (06%) patient had very poor general condition to withstand surgery. Laparotomy was carried out in the rest 40 patients with the plan to take open biopsy along with some surgical palliation. Out of these 40 patients, 25 patients had previous image assisted preoperative tissue diagnosis for 'unresectable carcinoma pancreas'. So, twenty five (n_1=25) patients had preoperative tissue diagnosis and were included for the study. Forty (n_2= 40) patients having postoperative tissue diagnosis also included for the study. As 10 patients had not been undergone laparotomy and open biopsy, were excluded from the study. It was noted how preoperative tissue diagnosis was made and what imaging modality was used preoperatively in these patients. Histopathology reports of these patients were assessed. After abdominal exploration it was recorded that pancreas was palpated for the site of the lesion and its mobility assessed. Location of the tumour with fixity, local extension, contagious organ involvement, vascular invasion, liver involvement, nodal involvement, peritoneal involvement, mesenteric invasion etc. assessed and biopsy was taken from the lesion and the involved structures. It was seen that excision of the involved lymph nodes were also carried out for histological diagnosis. In 36 patients biopsy and palliative surgery were done. In 2 patients tumor were resectable (Whipple's procedure done) and whole specimen were sent for histopathology. In a 2 very grossly advanced disease it was possible only to take biopsy, no palliative surgical procedure was attempted. Histopathology report of post surgical specimen was compared with preoperative histopathology report. The frequency of preoperative biopsy to diagnose pancreatic duct cell carcinoma, other lesion, inconclusive result or missed diagnosis were checked and compared to post laparotomy histopathological diagnosis. In our study it was noted that no biopsy was taken by laparoscopy. Patients having preoperative FNAC or brush cytology for diagnosis was not included for study. Data were processed and analyzed. Chi-square (α^2) test was applied to show the significance in difference between observed & expected value (qualitative) p-value < 0.01 was taken as significant.

Results

Sex distribution

Among 40 patients male were 23 & female were 17. Male female ratio was 1.35:1.

Age distribution

Patients most commonly presented between the ages of 56-60 years (13 patients 32.5%).Two patients (5%) presented between 45-50 years of age. This is the least common age of presentation. Overall common age of presentation is in between 51 to 70 years of age (77.5%). No patient presented before 45 years of age (Table I).

Procedures of preoperative biopsy (n_2=25)

Preoperative biopsy was taken in 25 patients (62.5% of the total patients). ERCP & biopsy was the commonest (12 patients 48%). Image assisted fine needle aspiration biopsy were taken from the lesion (10 biopsy 40%) & hepatic metastasis (3 biopsy 12%). US was used as imaging modality in 06 patient (24%) with pancreatic lesion. CT guided biopsy were taken from 04 (16%) pancreatic lesions and all 03 (12%) liver metastasis (Table II).

It was noted that (Table III), Whipple's operations were performed in 2 patients and the specimen sent for histopathological examination. Biopsy was taken from the lesion, contagious organ involved, vascular invasion, liver involvement, nodal involvement, peritoneal involvement and mesenteric invasion. In some patient multiple biopsies were taken, so, total numbers of biopsies are more than patients underwent laparotomy.

Histopathological report of preoperative biopsy as showed in table-IV are, pancreatic duct cell carcinoma in 19 (76%) patients, 1(4%) patients had chronic pancreatitis. Biopsy report was inconclusive in 2 (8%) patients. All 3 biopsies from liver focus were metastatic pancreatic cancer (12%). Histopathological report of the post laparotomy collected specimen (Table IV) had revealed that, pancreatic duct cell carcinoma is the commonest lesion (35, 87.5%) of clinically labeled unresectable carcinoma pancreas. All the biopsies from local involved organ, involed lymph nodes and liver involvement etc. reported as pancreatic carcinoma. But five (05, 12.5%) clinically labeled 'unresectable carcinoma pancreas' patients were histopathologically reported as, chronic pancreatitis (02, 05%), non Hodgkin's lymphoma (01, 2.5%), tuberculosis (01, 2.5%) and metastatic renal cell carcinoma (01, 2.5%).

Table I : Age distribution of patients (n_2=40)

Age (Year)	Patient	Percentage (%)
< 45	0	0%
45-50	2	5%
51-55	3	7.5%
56-60	13	32.5%
61-65	10	25%
66-70	5	12.5%
71-75	6	15%
> 75	1	2.5%

Table II : Imaging used to collect preoperative biopsy specimen.

Imaging used	Biopsy taken from	Patients	Percentage (%)
ERCP	Pancreas	12	48%
US	Pancreas	6	24%
CT	Pancreas	4	16%
	Hepatic metastasis	3	12%

Table III : Peroperative biopsy specimen (n_2=40)

Open biopsy were taken from	40 (100%)
Pancreatic lesion (incision biopsy)	38 (95%)
Resected specimen (Whipple's procedure)	02 (05%)
Local involved organs	13 (32.5%)
Involved lymph node	12 (30%)
Mesentery	05 (12.5%)
Liver involvement	05 (12.5%)
Vascular invasion	05 (12.5%)
Peritoneal seedling	08 (20%)

** Only biopsy was taken from 2 grossly advanced disease as no palliative surgical procedure was possible**

Table IV : Histopathological diagnosis of preoperative and post laparotomy collected specimen.

Histopathological diagnosis	Preoperative biopsy (n_1=25)	Postoperative biopsy (n_2=40)
Pancreatic duct cell carcinoma	19 (76%)	35 (87.5%)
Chronic pancreatitis	01 (04)	02 (05%)
Non Hodgkin's lymphoma	-	01 (2.5%)
Tuberculosis	-	01 (2.5%)
Metastatic renal cell carcinoma	-	01 (2.5%)
Metastatic pancreatic cancer to liver	03 (12%)	-
Inconclusive	02(08%)	-

Discussion

The incidence of pancreatic cancer has back tripled over the last 40 years through out the west [2]. The incidence of pancreatic cancer is 10 per 100,000 per year [4]. Unfortunately at the time of presentation 90-95% patients are unsuitable for curative resection because of local spread, involvement of the mesenteric lymph nodes, hepatic or distant metastasis [4].

According to Russel pancreatic cancer affects male and female to the same degree. Male to female ratio has been decreased in the recent years suggesting that more women are now being diagnosed with this cancer [4]. Present study showed that male (23 patients) are affected more than the female (17 patients) and male to female ratio was found 1.35:1. Yeo and Cameron also noted male sex is more vulnerable to pancreatic cancer [6].

Pancreatic cancer is a disease of aging [4]. Out of 40 studied patients, 31 patients (77.5%) presented between 51-70 years age. Two patients (5%) were diagnosed between 45-50 years of age and it is the least common age of presentation. No patient was diagnosed before 45 years of age. It implies that before 45 years of age pancreatic cancer is rare in clinical practice. Doherty and Way has shown that the peak incidence is 5th and 6th decades [1]. Present study also supports it.

In the absence of pancreatic mass ERCP is indicated. It is most sensitive test (95%) for detecting pancreatic cancer. It is also helpful in taking biopsy specimen [1]. ERCP safely and precisely locate the biopsy site for cytological diagnosis of unresectable pancreatic cancer in 93% case [9]. In our study 12 biopsies were taken by ERCP and no complication was observed.

CT guided fine needle aspiration biopsy (FNAB) is a safe procedure with 83% sensitivity and low rate (10%) of minor complication such as haematoma or abdominal pain [10]. In the present study 7 patients underwent CT guided FNAB and only one patient had abdominal discomfort.

CT guided FNA is 62% sensitive in detecting pancreatic cancer. US guided FNA is 62% sensitive in detecting pancreatic cancer. Endoscopic ultrsound (EUS) guided FNA IS 84% sensitive and is superior to CT/US guided FNA [11]. This study has shown that US guided FNAB were done in 6 patients but no patient undergone EUS guided biopsy.

Preopeartive cytological diagnosis by FNA is not recommended for pancreatic cancer where curative resection seems to be possible. For the unresectable disease FNA is advised to have a cytological proof. FNA is highly specific (99%) and rate of complication like pancreatitis or peritoneal seedling is very low (< 1%) [12]. In our study 2 patients underwent curative resections where previous FNAB were carried out.

They evaluated CT guided FNAB in 29 patients of pancreatic mass. Diagnosis was confirmed in 22 patients in first samples [10].

In the rest suspicious cases during close follow up, CT guided FNAB were carried out in 05 patients and EUS guided FNAB were done 2 patients. They found pancreatic ductual adenocarcinoma in 19 (65.51%) patients, metastatic carcinoma in 06 (20.68%) patients, benign cyst in 2 (6.89%) patients, acute on chronic pancreatitis 1 patients (3.44%) and neuroendocrine tumour in the rest one (3.44%). Metastatic cancer were prostatic carcinoma (1patients 3.44%), hepatocellular carcinoma (1 patients 3.44%), lung cancer(1 patients 3.44%), renal cell carcinoma(1 patients 3.44%), gastric carcinoma(1 patients 3.44%) and unknown cancer (1 patients 3.44%) [10]. Our study differs from them in terms of diagnosis of pancreatic duct cell carcinoma (76% versus 65.51%). In our study 8% sample was inconclusive but their sample had given some diagnosis.

In the pancreas a variety of non-neoplastic conditions may form solid masses that mimic cancer. Up to 5% of pancreatectomies performed with the preoperative diagnosis of carcinoma will prove to be non neoplastic by pathological examination. These are pancreatitis, adenomyomatous hyperplasia of the ampula of vater, lipomatous hypertrophy, haemartoma, tuberculosis etc [13].

Histopathological report of the post laparotomy collected specimen was very interesting. Five (12.5%) patients were not pancreatic caner as thought before as ‘unresectable pancreatic cancer’. Even 3 (7.5%) patients had non neoplastic mass lesion as chronic pancreatitis 2 patients (5%) tuberculosis1 patients (2.5%) mimicking ‘unresectable pancreatic cancer’.

Accuracy of postoperative biopsy (35 patients, 87.5%) in diagnosing pancreatic duct cell carcinoma is significantly higher (p value>0.01) than preoperative biopsy (19 patients 76%). Efficacy of preoperative (1 patient 4%) and postoperative (2 patients 5%) biopsy, to diagnose chronic pancreatitis are almost equal. But, preoperative biopsy may miss 7.5% lesion (e.g. tuberculosis, lymphoma, metastatic renal cell carcinoma etc.). Preoperatively inconclusive 2 patients were diagnosed as pancreatic duct cell carcinoma on post operative biopsy. So it is clear that open biopsy is a better option than biopsy by other means.

Conclusion

Tissue or histological proof is essential to confirm the diagnosis of pancreatic cancer. ERCP or image guided preoperative pancreatic biopsy is good to have adequate tissue. US and CT scan are good imaging modalities to help biopsy sample. Open biopsy has a greater diagnostic accuracy than preoperative biopsy hence recommended where possible.

Disclosure

All the authors declared no competing interestes.

References

1. Doherty GM, Way LW. Pancreas. In:Way LW, Doherty GM, editors. Current surgical diagnosis and treatment.New York: Lange Medical books; 2003;602-612.

2. Moosa AR, Mouvet M, Gmagami RA. Disorder of pancreas. In: Cuschieri SA, Stelle RJC, Moosa AR, editors. Essential surgical practice. London: Arnold; 2002;477-576.

3. Paulsen SD, Nghiem HV, Negussie E et al. Evaluation of image guided core biopsy of pancreatic mass. AJR 2006; 187(3): 769-772.

4. Russel RCG. The pancreas. In: Russl RCG, William N, Bulstrode CJK, editors. Short practice of surgery. London: Arnold; 2004;1114-1132.

5. Fisher W E, Anderson D K, Bell R H et al. Panceas. In: Brunicardi F C, Anderson D K, Billiar T K et al., editors. Schwartz's principles of surgery. New York: McGraw-Hill Medical Publishing division; 2005; 1221-1296.

6. Yeo CJ, Cameron JL. Exocrine pancreas. In: Townsend CM, Beauschamp RD, Evers BM, Mottok KL, editors. Sabiston textbook of surgery, the biological basis of modern surgical practice. Philadelphia: Saunders; 2001;1112-1141.

7. Mayo clinic (US). Pancreatic cancer. New York : The institute; 2007.

8. Meyers WC, Schauer PR. Pancreatic cancer: palliative . In: Carter D, Russel RCG, Pitt H A, Bismuth H, editors. Rob and Smith's operative surgery, hepatobiliary and pancreatic surgery. London, New York: Chapman and Hall Medical; 1996;585-593.

9. Kidd R, Patrik CF and Ball TJ. ERCP guided percutaneous fine-needle aspiration pancreatic biopsy. West J Med 1980; 132(4): 283-287.

10. Gupta S, Ahrar K, Morello, Wallace and Hicks MJ. Mass in and around the pancreatic head: CT guided coaxial FNAB with a posterior transcaval approach. Radiology 2002; 222(1): 63-69.

11. Horwhat JD, Paulson EK, McGrath K et al. A randomized comparison of EUS guided FNA versus CT or US guided FNA for the evaluation of pancreatic mass lesion. Gastrointest Endosc. 2006; 63(7):966-975.

12. Hirshberg foundation of pancreatic cancer research (US). Diagnosis of pancreatic cancer. Los Angeles: The institute; 2007.

13. Adsay NV, Basturk O, Klimstra DS and Kloppel G. Pancreatic Pseudotumour: non-neoplastic lesion of the pancreas that clinically mimic pancreas cancer. Seminar in diagnostic pathology. 2004; 21(4): 260-267.