 DOI: 10.18231/2394-6792.2017.0086

Clinico- morphological study of pancreatic neoplasms

Preethamol S[1,*], Prasanth PS[2]

[1]Assistant Professor, Dept. of Pathology, Govt. Medical College, Thiruvananthapuram, [2]Assistant Professor, Dept. of Radiodiagnosis, Sree Uthradom Thirunal Academy of Medical Sciences, Thiruvananthapuram

***Corresponding Author:**
Email: drpreetha80@yahoo.co.in

Abstract

Pancreatic malignancy is the second leading cause of digestive cancer related death after colon cancer. Pancreatic neoplasms can be divided into Ductal adenocarcinoma, neuroendocrine tumors and cystic neoplasms. Our objective was to study the unususal lesions of pancreas with immunohistochemical expression. From this we reached a conclusion that the variants of pancreatic neoplasms are rare and high index of suspicion, careful search for characteristic histological features and supportive immunohistochemical studies are required for correct diagnosis and appropriate treatment.

Keywords: Pancreatitis, Pancreatic cancer, Endocrine tumors, Exocrine tumors, Cystic neoplasms, Whipples resection.

Manuscript Received: 11th January, 2017 **Manuscript Accept:** 13th April, 2017

Introduction

Pancreatic malignancy is one of the most lethal human cancer with less than 5% survival has been reported.(1) It is the fourth and fifth most common cancer in men and women respectively. According to 1995 National Cancer Data Base Report on Pancreatic cancer, including 17,490 patients with pancreatic cancer, 52% had stage 4 disease at diagnosis and the overall curative resection rate was only 14%.(2)

An increase in risk is also associated with hereditary pancreatitis but additional etiological factors remain to be identified.(3)

Ductal adenocarcinoma and it's variants are the most common malignancy of pancreas representing 85-90% of all pancreatic neoplasms.(4,5,6)

Although relating grade of histologic differentiation to prognosis is attractive, so far it has not been very helpful in practice.(7)

This study is undertaken to identify the incidence of different pancreatic neoplasms (exocrine & endocrine), both benign and malignant. Morphological study of each neoplasm and its association with chronic pancreatitis was done. Grading and Staging of exocrine tumors was also done. Immunohistochemical studies which were available in our Department was done in poorly differentiated exocrine and endocrine tumors.

Materials and Method

This study was conducted in the Department of Pathology, Govt. Medical College Hospital, Thiruvananthapuram and materials were obtained from The Department of Surgical Gastroenterology, Govt. Medical College Hospital, Thiruvananthapuram. The ethical clearance from the institute was taken to conduct the study.

The study population included the patients admitted with signs and symptoms of jaundice and abdominal mass with abnormal biochemical parameters, who showed relevant CT and MRI findings and underwent surgical resection.

The specimens we received included trucut biopsies from the tumor, distal pancreatectomy and whipples resection. These tissues were fixed in 10% formalin, samples from representative areas were processed, stained with Hematoxylin and Eosin and studied under light microscope.

The various patterns of specific lesions are studied according to WHO Classification. Changes in adjacent pancreatic parenchyma was also noted. Special staining with PAS was done in mucinous neoplasms and Immunohistochemistry, which were available in our department was done in poorly differentiated exocrine and endocrine neoplasms.

In this study grading of exocrine pancreatic neoplasms was done using WHO grading system and staging using AJCC/UICC staging system.

Observations and Results

A total of 60 cases of pancreatic tumors were studied for their morphological and histopathological correlation. Assessment of its association with chronic pancreatitis was also done.

Samples we received was either Trucut biopsy (in case of inoperable lesions), distal pancreatectomy or Whipples resection. Five patients (8.33%) underwent Trucut biopsy, 12 (20%) underwent distal pancreatectomy, 43 (71.67%) had Whipples resection.

The neoplasms was either solid, cystic and solid-cystic. 45 cases were solid tumors accounting for 75%, including three endocrine tumors (**Table 1).**

Among the age group which was studied range from 17-77 yrs.

The maximum cases of solid neoplasms ranged 40-49 yrs and that of cystic neoplasms is from 30-39yrs. (**Table 2)**

In our study a male preponderance was noted with solid neoplasms (51.11%).

Cystic and Solid cystic neoplasms were entirely seen in females.

Most common site of tumor was head of pancreas in 42 cases accounting for 70%, followed by tail of pancreas in 11 cases.

The common clinical symptoms which were assessed include jaundice, abdominal pain and mass abdomen.

80% of the patients presented with jaundice and 12% presented with abdominal pain. Cystic neoplasms mainly presented as abdominal mass.

57 cases were exocrine accounting for 95% which originates from ductal epithelial cells.

Out of the 55 cases evidence of pancreatitis was present in 14 cases accounting for 25.45%, after excluding 5 trucut biopsy cases.

Evidence of pancreatitis was seen exclusively in exocrine neoplasms.

Parameter which was concentrated on microscopy was the different patterns of neoplasm. Most common pattern in solid neoplasm was glandular or adenomatous pattern, which was found in 39 cases (86.67%).

Of the 13 cystic neoplasms 8 were mucinous which accounts for 61.54% and 5 were serous cystic neoplasms (38.46%).

Among 8 mucinous cystic neoplasms 2 cases were mucinous cystadenocarcinoma and 2 were borderline cystic neoplasms and 4 were mucinous cystadenomas.

Apical mucin positivity was there in all mucinous cystic neoplasms and mucin producing adenocarcinomas.

Immunohistochemical study was done in 6 cases of poorly differentiated exocrine and 3 cases of endocrine neoplasms**.**

All endocrine tumors were positive for chromogranin, synaptophysin and NSE.

Grading was done for exocrine neoplasms based on WHO grading system. (**Table 2)**

According to this, of the 57 cases of exocrine neoplasms, one case was papillary hyperplasia with atypia which comes below grade I, hence mentioned as grade x.

Staging was done for exocrine neoplasms based on AJCC /UICC staging system. According to this, of the 52 cases (after excluding endocrine and trucut biopsies) 11 were under stage IV (21.57%) with distant metastasis,6 were under stage III (11.76%) depending on the involvement of node and extension into superior mesenteric artery, 15 were under stage II (29.41%) and 19 case were stage I (37.26%) without any demonstrable nodal involvement. Staging was not done in one case, which comes below stage of Tis. (**Fig. 2)**

Table 1: Dominant site of involvement varies with the nature of neoplasms

	Solid	Cystic	Solid-cystic	Endocrine
Head	33 (78.57%)	5 (38.46%)	1 (50%)	1 (33.33%)
Body	7 (16.67%)	2 (15.59%)	1 (50%)	1 (33.33%)
Tail	2 (4.76%)	6 (46.15%)	0	1 (33.33%)

Table 2: Grading of exocrine neoplasms

	Number	Percent
Grade I	23	40.35
Grade II	22	38.60
Grade III	11	19.30
Total	56	

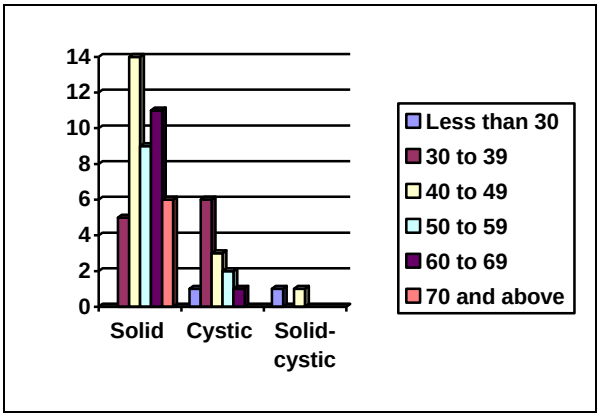

Fig. 1: Age range varies with the nature of neoplasms

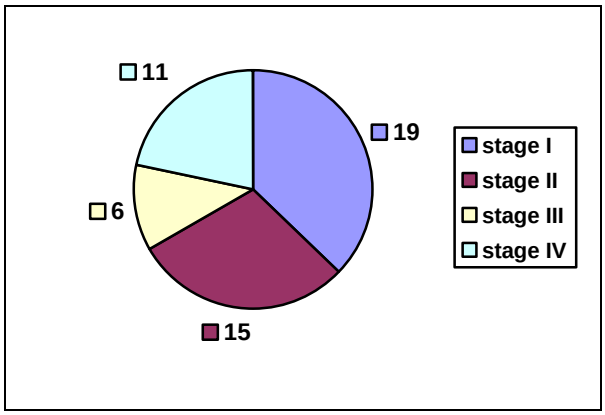

Fig. 2: Staging of exocrine neoplasm

Discussion

Pancreatic carcinoma is one of the most common cancers worldwide with highest incidence in industrialized countries. 61% of pancreatic malignancies occur in European countries and the incidence is lowest in Asia.

According to Ahlgren JD et al,[8] more than 95% of malignant tumors of the pancreas are exocrine and endocrine pancreatic tumors (EPTs) are uncommon.

In our present study the data was comparable with 95% of neoplasms being exocrine and 5% being endocrine in origin.

Ductal adenocarcinoma and its variants are the most common neoplasms in the pancreas, representing 85-90% of all pancreatic neoplasms[4,5,6] serous tumors representing approximately 2-5% of all exocrine pancreatic tumours.[6]

Solid-pseudopapillary neoplasm accounts for approximately 1-2% of all exocrine pancreatic tumours.[4,5]

In our present study solid neoplasms accounted for 75% of tumors, cystic neoplasms accounted for 21.67% and solid-cystic tumors were 3.33%.

According to Lowenfels et al,[3] the median age of diagnosis for solid neoplasms was around 50yrs and according to Sternberg's Diagnostic Surgical Pathology[7] most common age group is in the 6^{th}-7^{th} decade of life, whereas cystic neoplasms are common in middle age group.

In our present study the age group was comparable with the above data most common age group for solid neoplasms was between 40-49 yrs with a median age of 44 yrs while 2^{nd} commonest was between 60-69yrs. Cystic neoplasms were common in the middle age group between 30-39yrs.

In a study by Hammel et al,[9] pancreatic ductal carcinoma was more common in males with M:F ratio of 1.5-2:1. According to MacMahon,[10] sex ratio is 1.6:1.According to Campell et al,[22] cystic neoplasms have got female preponderance.

In our study ductal carcinoma has got a sex ratio of 1.04:1 which indicates an increasing incidence in females. Cystic neoplasms were exclusively seen in females.

According to Greene et al,[11] the most common site of carcinoma was head of pancreas. According to Cubilla AL,[12] most common location was head of pancreas in 70% of cases, second commonest being the body. Cystic neoplasms were commonly seen in tail.

In our study most common location of solid neoplasms was head which accounted for 78.57% followed by body 16.67%. 46.15% of cystic neoplasms were located in the tail of pancreas. This observation was comparable with the above data.

According to Warshaw A, Sahani D et al,[12] most patients with pancreatic cancer initially presented with complaints of jaundice. According to Gold et al[5] 85% of patients presented with progressive jaundice and pain.

In our study 80% of the patients presented with jaundice and 12% presented with abdominal pain. Cystic neoplasms mainly presented as abdominal mass.

According to Bansal PL et al,[15] chronic pancreatitis, which is most commonly related to alcoholism, has been associated with an increased risk whereas Chow et al,[16] suggest that an increased risk is observed only when the diagnosis of chronic pancreatitis precedes the diagnosis of cancer by less than 10 years.[7]

In our present study evidence of pancreatitis was present in a significant percent (25.45%) of exocrine neoplasms and was absent in endocrine neoplasms.

Pancreatic neoplasms were classified based on the scheme proposed by WHO. Gross consistency and microscopic pattern were the most important parameters which were assessed for grouping these tumors into specific categories.

In our study majority of patients that is 42 cases (70%) were solid exocrine neoplasms and 13 cases (21.67%) were cystic exocrine neoplasms, 3 cases were endocrine neoplasms (5%) and 2 (3.33%) were solid – cystic neoplasms.

Staging was done for exocrine neoplasms based on AJCC /UICC staging system. According to this, of the 52 cases (after excluding endocrine and trucut biopsies) 11cases were under stage IV (21.57%) 6 cases were under stage III (11.76%) 15 cases were under stage II (29.41%) and 19 cases were stage I (37.26%). Staging was not done in one case, which comes below stage of Tis.

Grading was done for exocrine neoplasms based on WHO grading system. According to this, of the 57 cases, 23 cases were under grade I (40.35%), 22 cases were under grade II (38.60%), 11 cases were under grade III (19.30%) and one case was papillary hyperplasia with atypia which comes below grade I, hence mentioned as grade x.

Tumors with no differentiation or minimal differentiation that is discernible only in rare, tiny foci (undifferentiated carcinomas by WHO classification) are categorized as grade 4. For pancreatic ductal carcinoma, histologic grade has been shown to have prognostic significance, with high grade (grades 3 and 4) being an unfavorable prognostic factor.[14,17] In comparisons between the Klöppel grading system and the TNM grading system, no differences in predictive value have been demonstrated.[18]

Among the 13 cystic neoplasms 2 cases were malignant, 2 were borderline and 9 were benign.

Since there is no staging system commonly in use for Pancreatic Endocrine Tumors, and the grading system remains controversial, staging and grading was not done in endocrine neoplasms.[19-21]

Conclusions

- Pancreatic ductal carcinomas and its variants are more commonly seen in elderly age group. Cystic and endocrine neoplasms are in the middle age group.
- There is a slight increased incidence of solid pancreatic adenocarcinomas in males compared to

females and cystic neoplasms are common in females.
- Majority were exocrine pancreatic adenocarcinomas.
- Study of adjacent pancreas showed evidence of chronic pancreatitis in significant number of cases.
- Immunohistochemistry has got a valuable role in case of poorly differentiated exocrine and endocrine neoplasms.
- On follow up, high grade neoplasms has got a poor prognosis.

References

1. Coleman, M.P, Gatt G, Verdecehia, A, Esteve, J. Sant, M, Storm, H, Allemani C. Ciccolallo,L. Santaquilani, M, and Berrino, F. EUROCARE-3 Summary: Cancer survival in Europe at the end of 20th century. Ann oncol, 14 Suppl 5: v 128-149,2003.
2. Niredeerhuber JE, Bermann MF, Menck HR. The National Cancer Data Base report on Pancreatic cancer. Cancer, 1995,76(9):1671-1677.
3. Lowenfels AB, Maisonneuve P, Dimagno EP, Elitsur Y, Gates-LK J, Perrault J, Whitcomb DC (1997). Hereditary pancreatitis and the risk of pancreatic cancer. International Hereditary Pancreatitis Study Group. J Natl Cancer Inst 89:442-446.
4. Cubilla AL, Fitzgerald PJ (1984).Tumours of the Exocrine Pancreas. AFIP: Washington, D.C.
5. Kloppel G (1994). Pancreatic, nonendocrine tumours. In: Pancreatic Pathology, Kloppel G, Heitz PU (eds), Churchill Livingstone: Edinburgh.
6. Solcia E, Capella C, Kloppel G (1997).Tumours of the Pancreas. AFIP: Washington, D.C.
7. Stephen S. Sternberg. Diagnostic Surgical Pathology,4th edition.
8. Ahlgren JD (1996). Epidemiology and risk factors in pancreatic cancer. Semin Oncol 23:241-250.
9. Perez-Ordonez B, Naseem A, Lieberman PH, Klimstra DS. Solid serous adenoma of the pancreas. The solid variant of serous cystadenoma? Am. J. Surg. Pathol. 1996;20;1401-1405.
10. Mahon B. Risk factors for cancer of the pancreas. Cancer 1982,50:2676-2680.
11. Greene FL, Page DL, Fleming ID, et al. eds. *AJCC Cancer Staging Manual*. 6th ed. New York: Springer; 2002.
12. Tseng J, Warshaw A, Sahani D et al. Serous cystadenoma of the pancreas: tumour growth rates and recommendations for treatment.Ann.Surg.2005;242;413-421.
13. Kosmahl M, Wagner J, Peters K et al. Serous cystic neoplasms of pancreas; an immunohistochemical analysis revealing alpha- inhibin, neuron specific enolase and MUC6 as new markers. Am. J. Surg. Pathol.2004:28:339-346.
14. Gold EB, Goldin SB (1998). Epidemiology of and risk factors for pancreatic cancer. Surg Oncol Clin N Am 7:67-91.
15. Bansal, P., and Sonnenberg, A.: Pancreatitis is a risk factor for pancreatic cancer. Gastroenterology, *109:*247, 1995.
16. Chow, H-W., Gridley, G., Nyren, O., et al.: Risk of pancreatic cancer following diabetes mellitus: A nation-wide cohort study in Sweden. J. Natl. Cancer Inst., *87:*930, 1995.
17. Klöppel G, Lindenthal G, von Bülow M, Kern HF. Histological and fine structural features of pancreatic ductal adenocarcinoma in relation to growth and prognosis: studies in xenografted tumours and clinico-histopathological correlation in a series of 75 cases. *Histopathology*. 1985;9:841-856.
18. Giulianotti PC, Boggi U, Fornaciari G, et al. Prognostic value of histological grading in ductal adenocarcinoma of the pancreas: Klöppel vs TNM grading. *Int J Pancreatol*. 1995;17:279-289.
19. Kloppel G, Heitz PU. Tumors of the endocrine pancreas. In: Fletcher CD, ed. *Diagnostic Histopathology of Tumors.* 2nd ed. London, England: Churchill Livingstone; 2000:1083–1098.
20. Perez-Montiel MD, Frankel WL, Suster S. Neuroendocrine carcinomas of the pancreas with 'rhabdoid' features. *Am J Surg Pathol.* 2003;27:642–649.
21. Capella C, Heitz PU, Hofler H, Solcia E, Kloppel G. Revised classification of neuroendocrine tumours of the lung, pancreas, and gut. *Virchows Arch.* 1995;425:547–560.
22. F Campbell and B Azadeh: Review - Cystic neoplasms of exocrine pancreas. Histopathology 2008:52.539-551.