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Clinicopathological Spectrum Of Non Adenocarcinomatous Tumors Of Pancre As Benign As Well As Malignant

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Abstract: ***Background****:Although adenocarcinomas are the most common tumors of pancreas the incidence of non adenocarcinomatous tumors e.g. neuroendocrine neoplasms, solid pseudopapillary neoplasms is rising partly due to advancement in diagnostic methods.*
AIMS and Objectives *:To study the histopathological patterns of non adenocarcinomatous tumours of pancreas (Benign as well as Malignant) and to study the clinical profile of the patients related to age, gender, symptoms, radiological findings.*
Subjects and Methods:*The study was conducted at Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir in the department of Pathology. It was a prospective study for a period of one and a half years(1.5 yrs) from July 2013 to December 2014 and retrospective for a period of 19 years from July 1994 to June 2013.The study included all the cases of non adenocarcinomatous tumors of pancreas (benign as well as malignant) .*
Results:*Well differentiated neuroendocrine carcinoma was the most common single neoplasm accounting for 34.14% of the cases. Second most frequent neoplasm was mucinous cystadenoma comprising 19.51% of the cases. Serous cystadenomas were the third most frequent neoplasms constituting 17.07% of the cases. Four (9.75%) cases of solid pseudopapillary neoplasms were seen. Two (4.87%) well differentiated neuroendocrine tumors were seen. One case each of cavernous hemangioma, lymphangioma, intraductal papillary mucinous neoplasm with invasion, without invasion, gastrointestinal stromal tumor and pancreatic intraepithelial neoplasia was seen. There was a strong female predominance with 76% of the cases seen in females.*
Conclusion: *Most of the cases in our study have been diagnosed in the last decade only which clearly shows that improvement in diagnostic modalities and knowledge about these tumors have helped in diagnosing more of these tumours correctly and early.*

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I. Introduction

Ductal adenocarcinomas and its variants are the most common neoplasms in the pancreas, representing 85-90% of all pancreatic neoplasms[(12,3)].The non adenocarcinomatous tumours are very rare and constitute 10-15 percent of all pancreatic tumours. Accordingly the primary epithelial tumours of pancreas includes the exocrine and the endocrine tumours[(4)]

Materials and Methods: Patients who underwent Whipples procedure were included in study. Sections were taken from growth and were processed and stained with Hematoxylin and Eosin stain. The diagnosis was mainly done on morphology and immunohistochemistry was performed, wherever required.

Aims and objectives: to study the histopathological patterns of non adenocarcinomatous tumours of pancreas (Benign as well as Malignant) and to study the clinical profile of the patients related to age, gender, symptoms and radiological findings.

II. Results

The present study includes 41 cases of non-adenocarcinomatous tumors of pancreas reported in the Department of Pathology at Sher –I –Kashmir institute of Medical Sciences (SKIMS) Srinagar Kashmir. The observations made are as follows.

Microscopy	**Frequency**	**%age**
Well differentiated neuroendocrine tumor	2	4.87%
Well differentiated neuroendocrine carcinoma	14	34.14%
Mucinous cystadenoma	8	19.51%
Serous cystadenoma	7	17.07%
Solid pseudopapillary neoplasm	4	9.75%

Cavernous hemangioma	1	2.43%
Lymphangioma	1	2.43%
Gastrointestinal stromal tumor (GIST)	1	2.43%
I.P.M.N with invasion	1	2.43%
Pan in 1a	1	2.43%
I.P.M.N without invasion	1	2.43%
Total	41	100 %

Table1: Distribution of cases according to Histopathology

Site	**Frequency**	**%age**
Head	25	61%
Neck	3	7.3%
Body	2	4.9%
Tail	9	22%
Body and tail	2	4.9%
Total	41	100%

Table 2: Distribution of cases according to site

Radiology	**frequency**	**%age**
Unilocular cyst	9	21.95%
Multiseptate cyst	7	17.07%
Multiseptate cyst with calcification	1	2.4%
Contrast enhacing solid mass	17	41.5%
Solid cystic mass	2	4.9%
Hypodense mass with calcification	2	4.9%
Cystic mass with dilated M.P.D	1	2.4%
Cystic mass with mural nodule with dilated M.P.D	1	2.4%
Multiple calculi in dilated M.P.D	1	2.4%
Total	41	100%

Table 3: Distribution of cases according to radiology

Gross morphology	**Frequency**	**%age**
Solid	19	46.3%
Multilocular cystic	9	21.95%
Unilocular cystic	9	21.95%
Solid cystic	4	9.75%
Total	41	100%

Table 4: Distribution of cases according to gross

Behaviour	**Frequency**	**%age**
Benign	18	43.90%
Borderline	5	12.19%
Malignant	17	41.46%
Premalignant	1	2.43%
Total	41	100 %

Table5: Distribution of cases according to behaviour

Out of two well differentiated neuroendocrine tumors (figure 1) both were seen in males.There were 14 cases of well differentiated neuroendocrine carcinomas .Out of which 11(78.57%) were females and 3(21.42%) were males.There were 8 cases of mucinous cystadenomas and were seen exclusively in females.Out of 7 cases of serous cystadenomas 5(71.42%) were females and 2 (28.57) were males. 4 cases of solid pseudopapillary neoplasm (figure 2) were all females

One case of cavernous hemangioma,lymphangioma,gastrointestinal stromal tumor (figure 3) was seen. All were present in females. 2 cases of intraductal papillary mucinous neoplasm were seen one with invasion and other without invasion.Both of them were males.

Fig1: Neuroendocrine tumor (10x,H&E

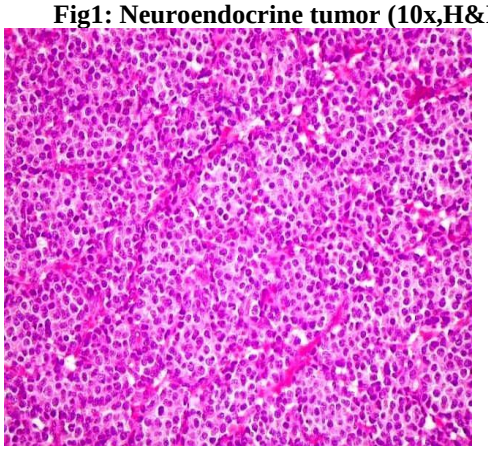
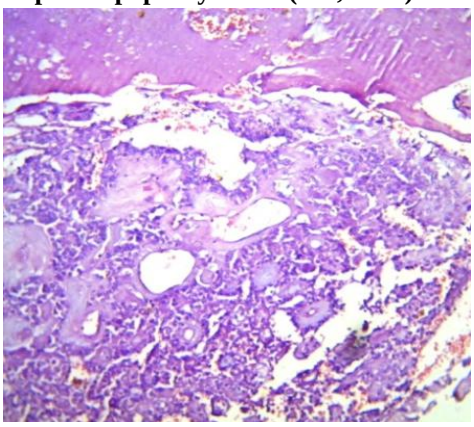


Fig 2:Solidpseudopapilary tumor(10x,H&E)



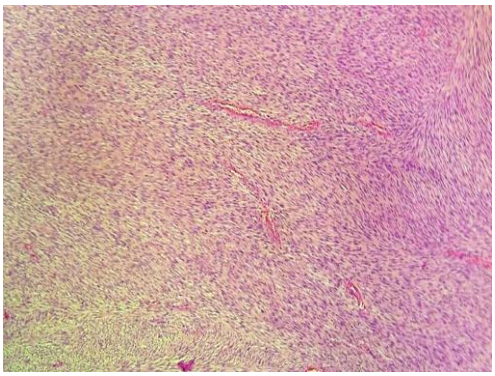


Fig 3:GIST with spindle cells (10x)

Fig 4:Gross showingTumor in head of Pancreas

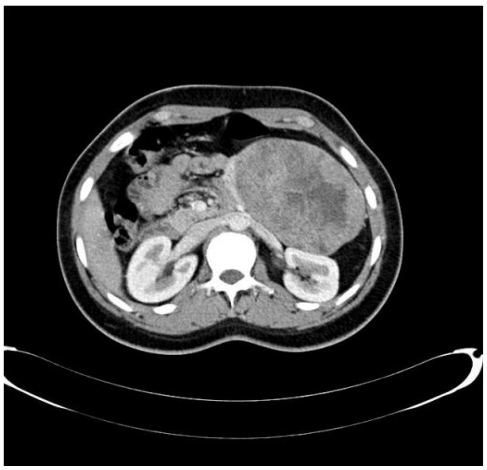


Fig 5:CECT showing solid mass in

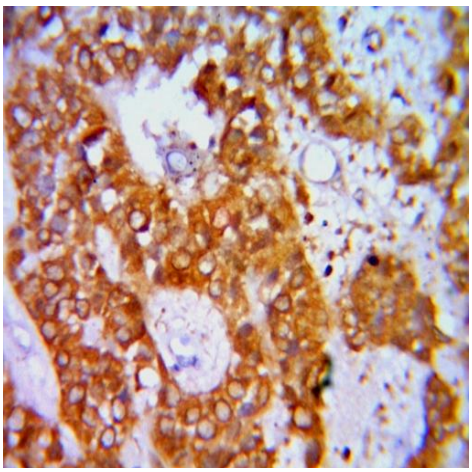


Fig 6: ChromagraninA positivity tail of pancreas

One case of Pan IN 1a was seen in association with chronic pancreatitis. The patient was a male.The predominance of non adenocarcinomatous tumors were seen in females. In our study 31-40 years age group was the most common. The most frequent symptom was pain abdomen present in 28(68.3%). The most common site for tumors in the study was head of pancreas (figure 4) seen in 25(61%) cases followed by 9 (22%) cases in tail of pancreas as shown in table 2 . Size of the tumors ranged from less than 1 cm to 11 cm with most of the tumors falling in the size range of 3-4 cm . Most common radiological presentation was a contrast enhancing solid mass (17 patients) followed by uniloculated and multiseptate cystic masses as shown in table 3. Contrast

enhanced CT (CECT) (figure 5) abdomen was the main modality used in all the patients for radiological assessment. On the basis of gross appearance tumors were divided into solid, solid,cystic, multilocular and unilocular cysts. Most of the tumors were in the solid category which included 19 (46.3%) cases as shown in table 4.

Behaviourally most of the tumors belonged to the benign category.18 tumors were included in this category.Second most common group was of malignant tumors as shown in table 5.Out of 16 cases of neuroendocrine neoplasms in our study 3 showed syndromic association. All three patients had neurofibromatosis type 1.

2 (100%) out of 2 patients with well differentiated neuroendocrine tumor were functional and had raised insulin levels in blood. Out of 14 patients of well differentiated neuroendocrine carcinoma only 3(21.42%) were functional and all three of them were insulinomas. 11(78.57%) patients had non functional tumors. Thus there were 5(31.25%) functional tumors. Out of total of 16 neuroendocrine neoplasms and all were insulinomas 19.15(93.75%) out of 16 neuroendocrine neoplasms showed reactivity for synaptophysin as with neuron specific enolase. Chromogranin A(figure 6) had a decreased sensitivity and was positive in 10 (62.5%) cases.out of 16 tumors. Cytoplasmic positivity was seen in all the three markers. When the nodal status was assessed in neuroendocrine neoplasms, Peripancreatic nodes were involved in 3 (18.75%) out of 16 tumors .

The TNM staging of tumors was done as per the latest TNM guidelines for pancreatic cancers. There were 2 cases of well differentiated neuroendocrine tumor and both (100%) were in T1 stage. 5(35.71%) out of 14 well differentiated neuroendocrine carcinomas were in T2 stage and remaining 9(64.28%) were in T3.Out of 16 neuroendocrine neoplasms only 2 (12.5%) showed evidence of distant metastasis. In both the cases liver was the site of metastasis. 14(87.5%) patients showed no evidence of distant metastasis .

Both (100%) well differentiated neuroendocrine tumors were in stage 1.Out of 14 well differentiated neuroendocrine carcinomas 2(12.5%) had stage1 disease, 12(75%) had stage 2 disease and 2 (14.28%) had stage 4 disease . No nodal metastasis was seen in any of the cases of solid pseudopapillary neoplasm .One (25%) out of 4 cases of solid pseudopapillary neoplasm showed liver metastasis Only 1 (25%) patient had Stage 4 disease due to liver metastasis. All other patients were in stage 1.All 4 solid pseudopapillary neoplasms showed positivity for progesterone receptors but were all negative for estrogen receptors .

III. Discussion

Glenn K Bonney et al also found the mean age at diagnosis in pancreatic neuroendocrine neoplasms to be 54 years which is higher than our study[5]. **Schurmann G et al (1990)** who found that chromogranin A stained a much higher proportion of neuroendocrine tumor cells in tumors with hormonal activity than in hormonally inactive tumors[6]. The mean age in other studies was slighter higher than our study. One possible reason may be a stronger syndromic association in our study as we had 3 patients of neurofibromatosis 1 with associated neuroendocrine neoplasms Most common radiological presentation in our patients was a solid mass with marked contrast enhancement which was present in 17(41.5%) patients .This was primarily because neuroendocrine neoplasms were the most common neoplasms in our study.

M .E Abreu et al conducted a study on neuroendocrine neoplasms of pancreas .CECT done on 19 cases showed a solid lesion with homogenous contrast enhancement in 6 patients and heterogeneous enhancement in 13 while as cystic change was seen in 5 cases. The mean size of homogenous solid lesions was 20mm and in heterogeneous solid lesions was 54 mm [7].

Chhaya J Bhatt et al who conducted a study on computerised tomographic features of uncommon pancreatic masses and found that 3 out of 3 serous cystadenomas were multiseptate cystic masses and 2 out of them showed central calcification[8] **Tak Geun Oh et al (2012)** who found that 25(68%) of the neuroendocrine neoplasms out of a total of 37 cases were present in the head of pancreas[9]. In our study head of pancreas was the most common site .61 % of the tumors were present in the head, followed by tail (22%), neck (7.3%), body (4.9%) and body and tail (4.9%).

Kosuke Okuwaki et al (2013) found that liver was the site of distant metastasis and was present in 19 out of 79 pancreatic neuroendocrine neoplasms[10] where as in present study only 2/16 (12.5%) out of 16 neuroendocrine neoplasms showed distant metastasis. Liver was the site of metastasis in both the tumors

Immunohistochemistry.

Our findings are consistent with **Neda Nozari et al (2014)** who found that synaptophysin was positive in 100% patients and chromogranin A in only 60.7% patients of non functional neuroendocrine tumors[11]. Only 3(18.75%) out of 16 cases showed evidence of nodal metastasis on histopathology..

IV. Conclusion

The study was focussed on non adenocarcinomatous tumors of pancreas which were once considered as rare tumors of pancreas but their number has increased in last couple of decades. Ours was a study of 20 years but most of the cases in our study have been diagnosed in the last decade only which clearly shows that

improvement in diagnostic modalities and knowledge about these tumors have helped in diagnosing more of these tumours correctly and early**.**

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Abbreviations

SSPT	Solid Pseudopapillary Tumor
CH	Cavernous Hemangioma
LYM	Lymphangioma
GIST	Gastrointestinal Stromal Tumor
IPMNI	Intraductal Papillary Mucinous Neoplasm with Invasion
IPMN	Intraductal Papillary Mucinous Neoplasm
Pan IN 1a	Pancreatic Intraepithelial Neoplasia 1a
U.C	Unilocular Cystic Mass
Pan IN 1a	Pancreatic Intraepithelial Neoplasia 1a

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