ORIGINAL RESEARCH

Histopathological Spectrum of Periampullary Tumours with Special Emphasis on Immunohistochemistry

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ABSTRACT

Background:Periampullary tumours are one of the most common cause of cancer related deaths. They have least survival rates. As most of the periampullary tumours are malignat tumours, early diagnosis and management improves the survival. Ampullary adenocarcinomas shows distinct morphologies with specific immunohistochemistry profile.

Materials and Methods: This study was done over a period of three years in the department of pathology. Rsectedspecimens (Whipple's procedure and excision biopsies) received in the department were adequately grossed, sectioned and stained with H&E. CK20 and MUC 1 immunohistochemistry markers were applied for ampullary adenocarcinomas.

Results: Out of 26 cases, 15 were of ampullary adenocarcinomas. Out of ampullary adenocarcinomas, eight were intestinal type, five were pancreaticobiliary type and two were mixed type. On IHC with CK20 and MUC1,four cases came out to be intestinal type adenocarcinomas. Follow up was done in some of these cases to assess the survival rates.

Conclusion: Prognosis varies among tumour subtypes. Histological subclassification still holds good for assessing the prognosis in periampullary tumours.

Keywords: Periampullary tumours, Intestinal type, pancreaticobiliary type, Immunohistochemistry.

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INTRODUCTION

Periampullary region encircles a radius of 2cm diameter around ampulla of vater, which includes pancreatic head and uncus, lower end of common bile duct, ampulla of Vater and periampullary duodenum.[1]Pancreatic adenocarcinoma is the most common malignant neoplasm arising from this region. It is the 4thmost common cause of cancer-related deaths, with the least survival rates.[2] Malignant lesions are more common in this region than their benign counterparts. So, early diagnosis and management improves survival.

The ampullary carcinomas may arise from two different types of mucosa because ampullary papilla is lined by intestinal epithelium while the other parts are lined by pancreatico biliary type of epithelium, which thus reflect the broad histomorphological spectrum of these

tumors.[3] These are intestinal type, pancreaticobiliary type& mixed type, having both the morphologies.[4,5]

On immunohistochemistry, most of the intestinal type adenocarcinomas are positive for cytokeratin 20 (CK20) and only 50% are positive for cytokeratin 7 (CK7). Most of thepancreaticobiliary type adenocarcinomas are cytokeratin 7 positive and cytokeratin 20 negative. The markers of intestinal phenotype such as CDX2 and MUC2 are positive in intestinal type adenocarcinomas, but are negative in those with a pancreatobiliary phenotype. The latter are positive for MUC1 (EMA).[5]

Aims and objectives

- To analyze the histopathological spectrum of periampullary tumours.
- To subcategorize ampullary adenocarcinomas based on the 2019 WHO classification.
- To evaluate the diagnostic utility of immunohistochemical markers like CK-20 and MUC-1 in ampullary tumours.

MATERIALS & METHODS

The present study is an observational study, conducted in the Department of Pathology, Rangaraya Medical College, Kakinada, Andhra Pradesh over a period of 3 years (from June 2015 to May 2018). A total of 26 cases were encountered. Clinical details like age, sex, biochemical & radiological findings and clinical diagnosis were obtained from the hospital records. Specimens received in the department of pathology after the surgeries likeWhipple's procedureand excision biopsy were included in this study. Specimens were grossed according to the Royal College of Pathology protocols and processed. Sections of 4µ thickness were obtained paraffin blocks and stained with hematoxylin and eosin(H&E) stain. Tumours were classified according to the 2019 WHO classification. The periampullary carcinomas were further subclassified based on histomorphology and were correlated with immuno histochemical markers CK20 and MUC1.

RESULTS

Table 1: Age distribution of periampullary tumours

Age group (in years)	Number of cases (n=26)
21-30	2
31-40	5
41-50	5
51-60	9
61-70	5

In the present study most of the periampullary tumours were in the age group of 51-60 years [Table 1]. Males are commonly effected with male to female ratio of 3.3:1.

In the present study of periampullary tumours, ampulla of vater was the common site involved followed by head of pancreas [Figure 1].

In the present study, all the periampullary lesions turned out to be malignant tumours. They were histologically classified based on WHO classification of tumours of GIT. Out of 26 tumours, 15 (57.69%) cases were ampullary adenocarcinoma, 8 (30.77%) cases were pancreatic ductal adenocarcinoma, two (7.69%) cases were mucinous adenocarcinoma and one (3.85%) case was invasive papillary adenocarcinoma [Figure 2].

Based on histomorphology, ampullary adenocarcinomas were further sub-classified into intestinal type, pancreaticobiliary type and mixed type [Table 2].

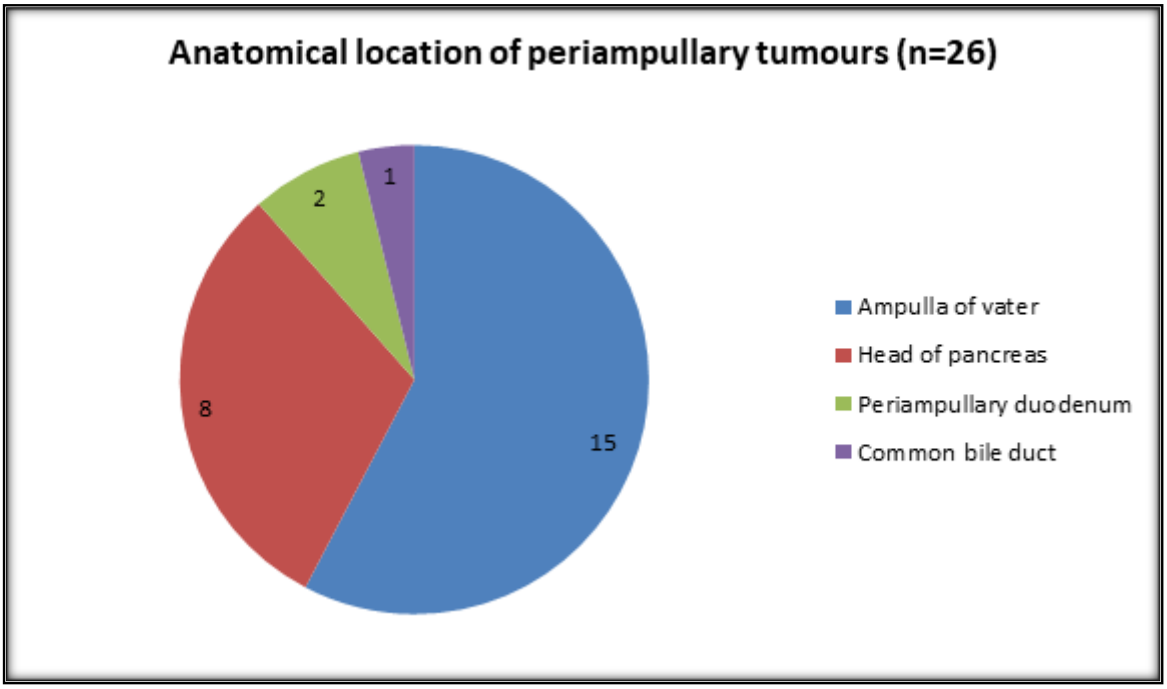

Figure 1: Anatomical location of periampullary tumours

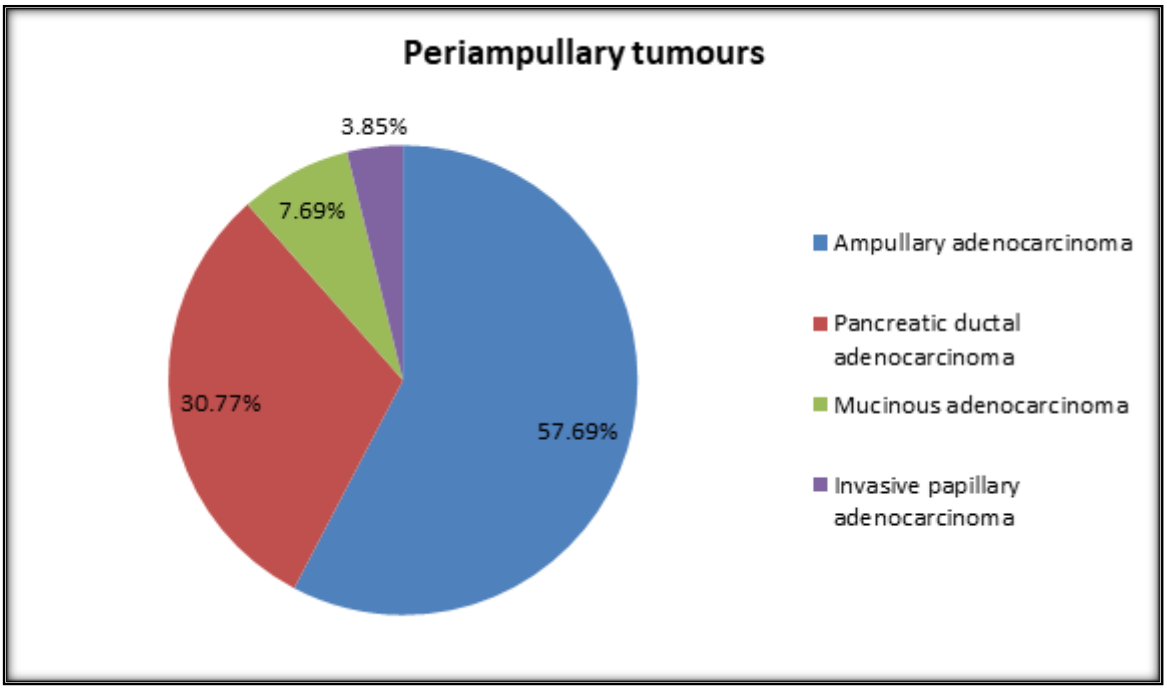

Figure 2: Histopathological spectrum of periampullary tumours

Table 2: Histological subtypes of ampullary adenocarcinomas

Histological subtype	**No.of cases (n=15)**
Intestinal type	8
Pancreaticobiliary type	5
Mixed type	2

Out of 15ampullaryadenocarcinomas, 8 cases were diagnosed as intestinal type of carcinoma, five cases as pancreaticobiliary type and two cases were reported as mixed type based on histomorphology.

Immunohistochemistrywas done for six selected cases of ampullary adenocarcinomas with markers such as MUC1 (EMA) and CK20. Surprisingly, IHC showed positive MUC1 and negative CK20 staining in all the cases of intestinal type, which were diagnosed on histomorphology. Pancreaticobiliary type of carcinoma showed MUC1 positive and CK20 negative.Mixed type showed focal positivitywith CK20 and diffuse positivity with MUC1 [Table 3].

Table 3: Immunohistochemistry of ampullary tumours

Subtype	On H&E (n=6)	On IHC (n=6)
Intestinal type (CK20+/MUC1-)	4	0
Pancreaticobiliary type (CK20-/MUC1+)	1	5
Mixed type (CK20-, MUC1-/CK20+,MUC1+)	1	1

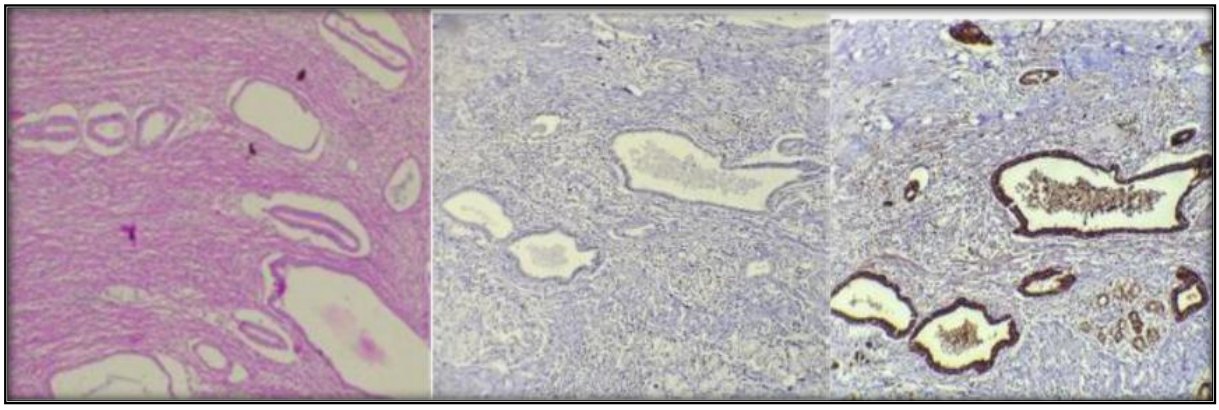

Figure 3: Pancreatico biliary type ampullary adenocarcinoma (a); Negative staining with CK20(b); Positive staining with MUC1 (c).

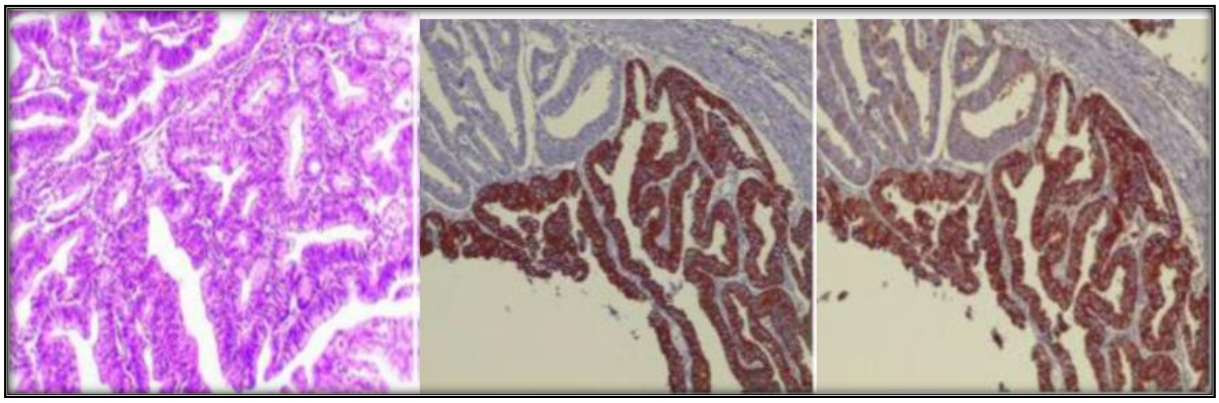

Figure 4: Mixed type adenocarcinoma (a); Positive staining with CK20 (b); Positive staining with MUC1 (c).

Table 4: Follow up of periampullary tumours

Histological type	Survival in months			
	<6	<6-12	<12-18	>18
Intestinal type	1			3
Pancreaticobiliary type	2			
Mucinous adenocarcinoma			1	
Pancreatic ductal adenocarcinoma	2			
Invasive papillary adenocarcinoma				1

On follow up, one case of intestinal type ampullary adenocarcinoma and two cases each of pancreatic ductal adenocarcinoma and pancreatico biliary type ampullary adenocarcinoma died below 6 months after diagnosis. One case of mucinous adenocarcinoma died at 15 months of diagnosis. One case of invasive papillary adenocarcinoma died after 18 months of diagnosis [Table 4].

DISCUSSION

In the present study of periampullary tumours, male to female ratio was 3.3:1 which was similar to the studies done by Aarthi et al,[6] Chang KJ et al,[7] Kimura et al andMichelle et al.
Mean age was 56 years in the present study which was lesser than the studies of Kimura et al,[8] and Michelle et al, but similar to the studies done by Aarthi et al and Chang KJ et al.
Present study revealed intestinal type of adenocarcinoma to be the most common histological type in contrast to other studies, which showed pancreaticobiliary type as the most common type.
In the present study, common site of periampullary carcinomas was ampulla of vater(57.69%) followed by head of pancreas, ampullary duodenum and common bile duct, in contrast to study done by Piorkowski et al,[9] where majority of tumours are arising from the pancreas (58%), followed by common bile duct (16%), ampulla of vater (11%) and duodenum (7.5%).
In the present study, all the tumours with intestinal type morphology turned out to be pancreaticobiliary type adenocarcinoma on immunohistochemistry (positive MUC1staining and negative CK20 staining).
Histopathologically diagnosed pancreaticobiliary type of adenocarcinoma showed concordance with immunohistochemistry staining pattern with MUC1 positivity and CK20 negativity.
Tumours with mixed type adenocarcinoma morphology showed concordance with immunohistochemistry.
Similar studies were done by Yasunariet al,[10] and Hui Zhou et al, who also found discordancebetween the histological diagnosis and IHC staining pattern.
In the present study, follow up of 10 cases revealed intestinal type adenocarcinoma (histological diagnosis) with higher survival rate (beyond 18 months) when compared to pancreaticobiliary type of ampullary carcinoma and pancreatic ductal adenocarcinoma. Out of four cases of intestinaltype of ampullary adenocarcinoma, one case succumbed within 6 months after surgery due to an associated cardiac disease, and the rest of the three cases showed a mean survival rate of more than 18 months.
In the cases withpancreaticobiliary type, the survival period after surgery was less than six months. Pancreatic ductal adenocarcinoma also showed a survival rate of less than six months. Mucinous adenocarcinoma showed a survival period of 16 months and invasive papillary adenocarcinoma showed more than 18 months survival period after surgery. The survival rates of patients with the histological diagnosis comparable with other studies.
This conflicting variation between the histopathological and IHC studies is mainly due to the low specificity of expression of MUC1 in some intestinal-type tumors.[11]In the present study, the mean survival rate of different entities was correlated well with the study done by Kimura et al.

CONCLUSION

This study necessitates the classification of periampullary carcinomas based on the histomorphology as prognosis varies among tumour subtypes. Histological subclassification still holds good for assessing the prognosis in periampullary tumours rather than with immunohistochemistry.

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