



PREVALENCE OF APPENDICULAR CARCINOID TUMOUR IN NORTH WEST RAJASTHAN: A TWO YEARS RETROSPECTIVE STUDY AT OUR INSTITUTE

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Abstract

Background: Carcinoid tumours are rare incidental finding in appendectomy specimens. Appendiceal carcinoid tumours are found in 0.3–0.9 per cent of patients undergoing appendectomy.

Methods: The medical records of all the patients who underwent consecutive appendectomies and the specimen sent to pathology department for biopsy in Sardar Patel Medical College, Bikaner, were retrospectively analysed. Detailed medical history was noted age, gender, indication for surgery, surgical procedure, tumour localization in the appendix, diameter of the lesion after fixation with formaldehyde, and overall incidence of tumour reviewed in detail

Results: Out of the total 1382 patients, 2 (0.15%) were found to have histological evidence of carcinoid tumour of the appendix. Both were male patients with a mean age of 26.5 years (range: 13-40 years). Acute appendicitis was the clinical presentation for both patients. Open appendectomy was performed in one and laparoscopic in other one. Histologically, all tumours were located at the tip of the appendix with a mean diameter of 0.7cm (range: 0.6-0.8 cm).

Conclusion: Carcinoid tumours of the appendix are extremely rare and invariably remain asymptomatic and are mostly discovered incidentally for appendectomy done for other reasons, mostly acute abdomen. Carcinoid Tumour was diagnosed on histological examination of the removed appendix. The site and the size of the tumours rather than the depth are used for the assessment of the CT.

Keywords: Carcinoid Tumour, Acute Appendicitis, Neuroendocrine Tumours

Introduction:

The most common cause for acute abdomen in all age groups is appendicitis and an appendectomy is one of the most frequently performed surgical procedure worldwide. ^[1] Declining rates of acute appendicitis have been reported in the United States and Europe. ^[2] In developing countries, the incidence is increasing in most urban centres, probably due to adoption of western diet. ^[3]

Though non-neoplastic lesions outnumber the neoplastic counter parts, appendiceal neoplasms are also frequently encountered and these may be a primary or secondary neoplasm involving the appendix. Neoplasms of the appendix are rare, with an incidence of approximately 1.2 cases per 100,000

inhabitants in the United States. ^[4] Increased appendectomy may contribute to the increased incidence of appendix tumours. Tumours of the appendix can be divided into epithelial and non-epithelial tumours. Epithelial tumours are adenocarcinomas and may or may not be mucin-producing. The major non-epithelial tumours are Neuroendocrine Tumours (NETs) and lymphomas. ^[5]

Carcinoid are neuroendocrine tumours derived chiefly from enterochromaffin cells or *kulschitsky* cells. They are capable of amine precursor uptake and decarboxylation (APUD cells) ^[6]. Carcinoid tumours were first reported by Otto Lubarsch in 1888 ^[7]. “Kazinoïd” is a word was first used by Obemdorfer in 1907 to explain a tumour behaving in a fashion that is more benign than Malignant. ^[8] Neuroendocrine

tumours (NETs) can affect several organs. Two-thirds of the neuroendocrine tumours are found in the gastrointestinal tract (54.5%), with the small intestine being the most affected (44.7%), followed by the rectum (19.6%), appendix (16.7%), colon (10.6%), and at last, by the stomach (7.2%).^[9]

The most common clinical presentation of carcinoid tumour is acute appendicitis. These tumours can invade regionally and/or metastasize at a distance. They have a 5-year survival of more than 90%. Appendiceal NENs arise from subepithelial NE cells that are present in the lamina propria and submucosa of the appendix wall (Shaw 1991).^[10] Masson first identified the subepithelial cells as the origin of aNENs and demonstrated that these neurosecretory cells exhibit both endocrine and neural characteristics as integral parts of the subepithelial nervous plexus (Masson 1928, Sandor & Modlin 1998).^[11] These cells are more numerous at the tip of the appendix, as opposed to epithelial NE cells, which are equally distributed at all sites within the appendix. Morphologically, the vast majority of appendiceal NETs are serotonin-producing enterochromaffin (EC) cell tumors, similar to their counterparts in the jejunoleum. Previously, these tumors have been known as "classic" carcinoid tumors. Microscopically EC cell tumors are composed of unencapsulated, tightly packed solid nests ("insulae") of small monotonous cells with occasional acini [Picture 1] which harbor luminal material that is positive for periodic acid–Schiff stain, but do not contain mucin. Tumor cells contain abundant amphophilic, often granular, cytoplasm. The nuclei are typically round with coarse "salt and pepper" chromatin and small nucleoli; mitotic figures are rare. Occasional tumours display degenerative-type nuclear atypia with hyperchromasia and multinucleation, which has no bearing on behaviour. A retraction of the tumor periphery from the stroma is usually evident and sometimes prominent. Invasion of the appendiceal muscle wall and lymph vessels is the rule, and spread to the peritoneal surface is not rare.^[12]

The prevalence of appendiceal NENs (carcinoid tumours) among primary malignant lesions of the appendix ranges between 32 and 57%.^[13, 16] Carcinoids of the appendix are rare occurring in approximately 0.3 to 0.9% of specimens from appendectomy.^[14] They are commonly seen in the third to fifth decade.^[15] Appendiceal carcinoid tumour lacks specific clinical features and its clinical presentation may not differ from that of acute

appendicitis. It is usually diagnosed incidentally during surgery for acute appendicitis and occasionally during other abdominal procedures (colectomy, cholecystectomy, salpingectomy). Carcinoid tumours can lead to a carcinoid syndrome characterized by flushing, bronchoconstriction, diarrhoea, and right valve disease caused by release of vasoactive substances.

Aims and objectives

- To determine the prevalence of appendicular neuroendocrine tumours (carcinoid tumour) at Sardar Patel Medical college and associated groups of hospitals.
- To compare the prevalence in our region with global and national literature.

Methods

This study is a retrospective study conducted at the Department of Pathology, Sardar Patel Medical College and associate group of hospitals, Bikaner, Rajasthan over the period of two years from September 2017 to September 2019. PBM and associated hospitals is the largest tertiary care teaching hospital in Bikaner region of North West Rajasthan, and the department of Pathology receive tissue samples from PBM hospital and other government and private hospitals in the zone. We report here the incidence of carcinoid tumours of appendix at a single centre and compared the experience with the recent available literature on this subject.

All appendectomy specimens received at the department of pathology during the study period were included in the study. Samples which were not satisfactory or tissue other than appendix is excluded. The clinical and other relevant data was recorded from the requisition form. Gross examination was done and findings recorded. All the appendectomy specimens were fixed in 10% formalin. Three sections were taken from each of the appendectomy specimen – comprising of one section from the tip, one each from proximal and mid one third. All sections were stained with hematoxylin and eosin and examined under the light microscope. Special staining was done whenever required.

Results

We received a total of 1382 appendectomy specimens during the study period. Out of these 1382 patients, 2 patients (0.15%) [Table 1] were found to

have histological evidence of carcinoid tumor of the appendix. Both patients were male with a mean age of 26.5 years (13 years and 40 years). Both the patients presented with the symptoms of pain in lower abdomen with nausea and vomiting, acute appendicitis was the clinical presentation for both patients. Symptoms of carcinoid syndrome (flushing or diarrhea) or Cushing's syndrome were not described in any of these patients. Open appendectomy was performed in one and

laparoscopic appendectomy in the other case. Histologically, all tumors were located at the tip of the appendix with a mean diameter of 0.7 cm (range: 0.6 - 0.8 cm). The clinicopathological data in relation to carcinoids are shown in Table 2. [Table 2] The histopathological features of carcinoid are shown in images, first image is high power view (x400) showing sheets of tumour cells [Figure. 1] and second is low power scanner (x40) view showing invasion of tumour till muscular layer. [Figure. 2]

Table 1: Summary of present study showing prevalence of carcinoid tumour of appendix at our institute.

Study Period	Total cases studied	No. of Carcinoid tumour	Prevalence
September 2017 to September 2019	1382	2	0.15%

Table 2: Clinicopathological characteristics of patients with appendiceal carcinoids

Patient No.	Age (years)	Gender	Presenting Complaints	Tumour size	Tumour location	Tumour extent (histopathological)
1	13	Male	Pain lower abdomen, nausea	0.6 cm	Tip of appendix	Muscular layer
2	40	Male	Pain abdomen, dyspepsia, loss of appetite	0.8 cm	Tip of appendix	Muscular layer

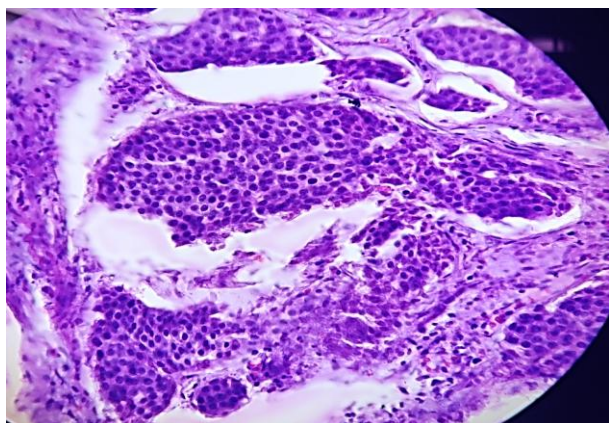


Figure 1: High power view (40x) of carcinoid tumour of appendix showing sheets of tumour cells.

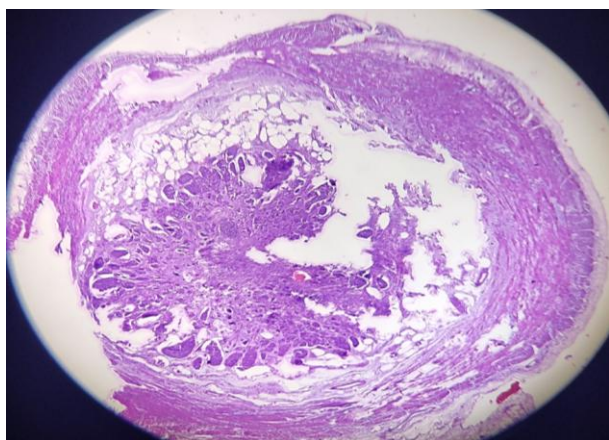


Figure 2: Low magnification view (4x) showing invasion of carcinoid tumour till muscular layer.

Discussion

Carcinoid tumours are considered as the most challenging tumors in clinical practice as they remain typically undiagnosed preoperatively, and are only discovered incidentally on histopathological examination. Most pathologists encounter this tumour only once in their career. Due to significantly low incidence of this tumour, we are of the view that even this small series will be a useful aid for determining incidence of carcinoid of appendix in North West Rajasthan. This observation is consistent with the results of our study where during appendectomy, in none of the patients, the suspicion of appendicular tumour was raised. All the detected cases were incidentally discovered and confirmed during histological analysis of appendisectomy cases. [13]

It accounts for 32%-57% of all appendiceal tumors [16] in patients with a reported mean age of 42 years [17] with slightly higher incidence in female patients. [18] The prevalence of carcinoid tumour in patients undergoing appendectomy in our database is 0.2%, which is slightly lower than the available international literature; Unusual is the predominance of male patients in our series with mean age of 26.5 years, a finding probably due to small series.

Seventy to ninety per cent of all appendiceal carcinoids are < 1 cm in diameter, 4-25% are 1-2 cm,

and few are 2 cm.^[19] Appendiceal carcinoid tumour exhibits little metastatic potential and therefore rarely presents with metastases.^[14, 19] Characteristics of the tumour predicting aggressive behaviour include size, histological subtype and mesoappendiceal involvement.^[20] In the present study, all the tumours were less than 1cm (mean diameter of 0.7 cm) and localized at the tip of the appendix with no evidence of regional or distant metastases.

Carcinoid syndrome occurs in less than 10% of patients with carcinoid tumour.^[20] These are caused by vasoactive substances such as 5-hydroxytryptophan (5-HIAA), histamine, bradykinin and serotonin that are produced by tumour cells. Because these substances are metabolized during their first passage

through the liver, gastrointestinal carcinoids do not cause carcinoid syndrome unless they are metastatic to the liver and ovary.^[21] None of the patients in this series show features of carcinoid syndrome.

We compared the findings of this study with the available literature from other parts of India and South East Asia. The prevalence of carcinoid tumour of appendix reported between 0.1% to 0.64% of all appendicectomies done in different studies conducted in different institutes in India.^[22, 23, 24, 25] The findings of different studies are summarized in Table 3. [Table 2] We reported the incidence of 0.2 % of all appendicectomy done at our institute, the finding consistent with other studies done in India with result towards the lower end.

Table 3: Summary of different studies done in India and their findings.

S. No.	Study	Study period	Total appendicectomy cases	No. of Carcinoid	Incidence
1	S.C. Gupta et al. [22]	25 years from 1989	2921	4	0.1 %
2	Upadhyaya et al. [23]	Jan 2006 – Aug 2007	515	3	0.58 %
3	Shaik S, Jayakumar NM et al. [24]	Jan 2015 – Dec 2016	175	1	0.64 %
4	Kokila K et al. [25]	Jan 2017 – Dec 2017	1100	2	0.2 %
5	Present Study	Sep 2017 – Sep 2019	1382	2	0.15%

Conclusion

Carcinoid tumours of the appendix are extremely rare and invariably remain asymptomatic and are mostly discovered incidentally for appendicectomy done for other reasons, mostly acute abdomen. Carcinoid Tumour was diagnosed on histological examination of the removed appendix. The site and the size of the tumours rather than the depth are used for the assessment of the CT.

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