Original Article

Carcinoid/Neuro endocrine tumors – A clinicopathological spectrum

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Abstract

Carcinoid tumor is the generic term traditionally applied to low grade malignant neoplasms originating from the diffuse endocrine system, exclusive of the pancreas and the thyroid C- cell. This term is being progressively replaced by well differentiated neuro endocrine tumor/ carcinoma. It is now acknowledged that they represent a group of related neoplasms rather than a single pathologic entity. The digestive tract contains a large number of endocrine types, any of which can be represented in these neoplasms singly or in combination. Carcinoid tumors are located throughout the GIT, the other sites in our study being bronchus and ovary. The recent WHO classification categorizes these lesions into well differentiated Neuro endocrine tumors (WNET) or poorly differentiated neuro endocrine carcinomas, the degree of differentiation, depending on the extent to which the neoplastic cells, resemble their non neoplastic counterparts. These tumors present a varied histomorphological pattern. Our study has included the different patterns, the typical and malignant carcinoids.

Key words: Carcinoid tumors, neuro endocrine, malignant.

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INTRODUCTION

Carcinoid tumours/ are rare tumours which have long been a source of clinical and pathological interest. The fundamental biology of these neoplasms still eludes precise delineation. The term "Karzinoid" was first utilized by Obendorfer in 1907 to define a tumour, that, although resembling an adenocarcinoma, behaved in a more benign fashion[1]. Williams and Sandler proposed that Carcinoid tumours could be divided according to an embryologic classification into foregut, midgut and hindgut carcinoids, and that these subdivisions correlated with morphologic patterns, silver affinity, and clinical behaviour[2]. The histological spectrum of neuroendocrine/carcinoid tumours has been expanded to include classic carcinoid tumours, atypical carcinoid tumours and composite tumours. The classic carcinoid tumour consists of a monotonous population of small cells arranged in solid nests, in insular, trabecular, rosettes, or in microglandular patterns[3].Although the term carcinoid tumour has been broadly used to refer to many neoplasms derived from the dispersed diffuse neuroendocrine system (DNS), the WHO recommends that the term be used only for those neoplasms of the DNS with the recognized histologic patterns of intestinal carcinoids[4].The International Classification of Diseases has changed the definition of "Carcinoid" in each version, and since 1986, these tumours, except those of the appendix have generally been considered malignant as was originally thought in classic histologic terminology. Unfortunately, the criteria for establishing the degree of malignancy are not clear in this class of neoplasia,

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histology fails to precisely distinguish the likelihood of aggressive or metastatic potential[1].

MATERIAL AND METHODS

All cases of carcinoid tumours reported in the Department of Pathology, in two institutions over10 years were included in the present study. The clinical details were recorded and slides were reviewed. The sections studied were from paraffin embedded blocks stained with haematoxylin and eosin.

RESULTS

Details of the various carcinoids in our study are shown in Table 1.

Gastrointestinal (GI) Carcinoids: 18 cases were recorded, involving the appendix, small intestine, rectum, caecum, transverse colon, stomach.

Appendix: Carcinoids of the appendix were the most common (8 cases) in this group and among all the cases studied. The most common presentation was acute appendicitis. The patients were in the age group 18-50 years, with a male to female ratio of 2:3. histologically insular and mixed patterns were most common.

Rectum: There were two cases, one in a 50 year old man who presented with bleeding per rectum and the other in a 43 year old man who presented with history of alternate diarrhea and constipation. The second case was a malignant carcinoid with metastasis in the lymph nodes.

Colon: Two cases were encountered in 62 year old man who presented with perforation of the colon and 74 year old man who presented with a mass in the right lower abdomen. On histological examination, the transverse colon showed a carcinoid with mixed pattern..

Stomach: A 42 year old female was operated for calculous cholecystitis. A nodule was found on the greater curvature of the stomach. Histology showed a classic carcinoid with insular pattern.

Bronchial carcinoids: There were3 cases forming the second largest group in our study. The patients were in the age group 30 to 40 years with a male to female ratio of 1:1. Patients presented with fever and respiratory symptoms like cough with expectoration, dyspnoea and one case also had recurrent haemoptysis. The predominant histological patterns were insular and trabecular.

Ovary: Two cases, one in a 44 year old and another in an 60 year old female were encountered. Both patients presented with bilateral pelvic masses and ascites. One patient had a dermoid cyst in the other ovary. The second case was a malignant strumal carcinoid with metastasis in the contralateral ovary, myometrium and lungs.

Table 1: Details of the carcinoid tumours in our series

Site	Number	Presentation	Age (yr)	Predominant pattern
Appendix	8	Acute appendicitis -2 Incidental -1 Recurrentappendicitis-3	18-50	Mixed -Insular
Bronchus	3	Fever, cough, dyspnoea Recurrent haemoptysis	30 -40	Insular Trabecular
Rectum	2	Bleeding Alternate diarrhoea & constipation	43,50	Insular Malignant
Ovary	2	Bilateral pelvic masses with ascites	44,60	strumal carcinoid
Colon	2	Mass	62,74	Trabecular, Malignant
Stomach	1	Incidental (duringcholecystectomy)		insular
Small intestine	4	Mass	30-50	insular, mixed

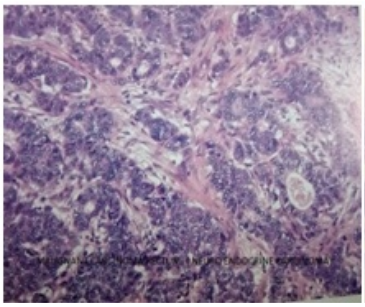
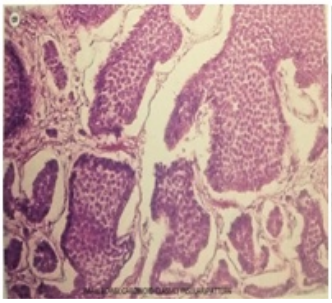


Figure 1:



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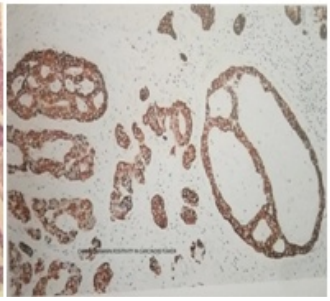

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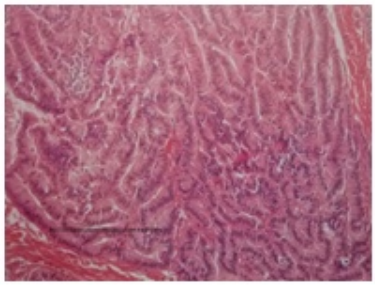

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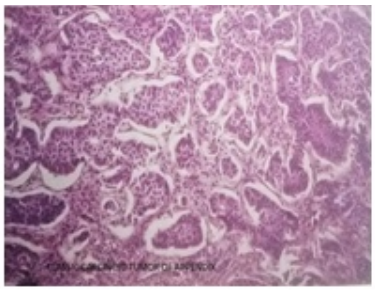

Figure 5:

Legend

Figure 1: Malignant carcinoma rectum- (Neuro Endocrine Carcinoma); **Figure 2:** Small bowel carcinoid-classic (insular) pattern; **Figure 3:** Chromogranin positivity in carcinoid tumor; **Figure 4:** Rectal carcinoid trabecular pattern; **Figure 5:** Classic circanoid tumor of appendix.

DISCUSSION

Patients with carcinoid tumours can present with diverse and nonspecific clinical features as also seen in our study. Hence, unless the patient has carcinoid syndrome it is not possible to diagnose these tumours clinically. The commonest site of origin of carcinoids varies from series to series. GI carcinoids are the most commmon[1,5,6] of which appendiceal carcinoids were the most common in one study[6] while small intestinal carcinoids were the commonest in two other studies[1,5]. In our study carcinoids of the appendix formed the largest group. Appendiceal carcinoids form 85% of all appendiceal neoplasms[7]. Most carcinoids are found in appendices removed incidentally at laparotomy for some unrelated condition, or in specimens removed for acute appendicitis. The association with appendicitis is commonly thought to be coincidental[7]. However it is possible that chronic infection may play a role[8]. These tumours occur at all ages and are somewhat more common in females. Most are small, measuring less than 1 cm. in diameter. About 70% occur in the tip, 22% in the body and less than 10% at the base. Adenocarcinoid is also variously known as mucinous carcinoid, goblet cell carcinoid and crypt cell carcinoid, most commonly seen in the appendix (usually at the tip[9]), although it can occur in other sites. The tumour seems to hold an intermediate place between carcinoid and adenocarcinoma. The overall clinical behaviour suggests a more aggressive neoplasm. We came across a case of adenocarcinoid in a 25 year old female. The appendix was dilated at the distal end and was filled with thick mucinous material. Colonic carcinoids are relatively uncommon, the site of predilection being the caecum and rectum. They are often large. 50% of the cases have metastasis at the time of diagnosis[9]. We encountered two cases of rectal carcinoids and one case of caecal carcinoid. In an earlier study the incidence of rectal carcinoids was 12.6%[1] and in another study rectal and carcinoids were found in 12% and 13% of the cases respectively[5]. In yet another study of 84 colonic carcinoids 99% were found in the rectum and 1% in the distal colon[10]. Gastric carcinoids comprise 4-5% of the total GI carcinoids[5,9]. They are commonly polypoid and most occur in the antrum[9]. We could record one case of gastric carcinoid which was found incidentally. Meckel's Diverticulum-- Carcinoids in this site are rare. They resemble appendiceal carcinoids to the extent that they are small, single and asymptomatic and have a favourable prognosis. The first carcinoid in this location was reported in 1907, and it is thought that 11% of resected Meckel's diverticula have carcinoids[11]. A study which analysed the largest series of carcinoids to date, reports that only 109 cases of carcinoids in this site have been encountered so far[1]. The propensity of such lesions to occur in diverticula suggests that alterations in luminal content may be of significance[1]. Bronchial carcinoids form 1-2% of all primary lung neoplasms,90% of which are central and endobronchial and 10% are peripheral[12]. We found 3 carcinoids located in the bronchus. Bronchial carcinoids are considered true malignancies belonging to the neuroendocrine tumour family, because their potential to metastasize has been recognised[13]. Typical carcinoids are considered as Grade I tumours[6]. WHO has included these tumours under the spectrum of neuroendocrine (the most malignant of which is small cell lung carcinoma) but retained the term carcinoid for a number of reasons[14],

- They morphologically look like carcinoids found at other body sites,
- Patients are younger than those getting other tumours in this group,
- 20-40% of the patients are non-smokers,
- These can occur in multiple endocrine neoplasia,
- Teuroendocrine cell hyperplasia is relatively frequent,
- These tumours are readily diagnosed by light microscopy.

Ovarian carcinoids are uncommon (1% primary)[15] ovarian neoplasms that classified as monodermal teratomas, since most are associated with a teratomatous element(strumal carcinoid). A pure ovarian carcinoid has most likely overgrown the teratoma in which it originated, but alternate possibilities of origin from neuroendocrine cells/non endocrine cells by neometaplasia have been suggested[7].Primary ovarian carcinoids are practically always unilateral, although they may be associated with a benign cystic teratoma in the contralateral ovary[16]. This feature was seen in one of our cases. Strumal carcinoid of the ovary usually has a benign clinical course. Cutaneous carcinoids are usually thought to be secondary from a primary in the digestive or pulmonary tumours. Only few cases of primary cutaneous carcinoids have been published so far, and their existence remains controversial[18]. At the histochemical level, the classic carcinoid tumor is argentaffin (and therefore also argyrophylic) positive for the diazo reaction. Electron microscopy demonstrates dense core secretory granules. Immunohistochemically, there is a reactivity indicative of epithelial, intestinal and neuroendocrine differentiation as manifested by epithelial (keratin-CK7andCK20, CEA), intestinal (cdx-2) and neuroendocrine (neuronspecificenolase, (NSE) chromogranin and synaptophysin. The pathobiology and site specific behaviour of these ill-understood lesions have remained a source of considerable pathologic and clinical debate. More recently, considerable change has occurred in regard to their cell of origin, biologic products, markers of proliferative activity and the production of diverse growth factors[1].

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