

BRIEF ARTICLES

## Primary epithelial tumours of the appendix in a black population: A review of cases

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rare in our experience, and are represented principally by carcinoid tumours and adenomas. Carcinoid tumours occurred in younger patients but were slightly more common in men than women. Tumours were not suspected clinically and were diagnosed incidentally in specimens submitted for acute appendicitis supporting the need for histological evaluation in all resection specimens.

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### Abstract

**AIM:** To determine the prevalence, histologic types and clinical features of primary epithelial tumours of the vermiform appendix in a predominantly black population.

**METHODS:** All cases of primary tumours of the appendix identified by review of the histopathology records at the University of the West Indies between January 1987 and June 2007 were selected. Relevant pathologic and clinical data were extracted with supplementation from patient charts where available. Non-epithelial tumours were excluded. The total number of appendectomy specimens over the period was also ascertained.

**RESULTS:** Forty-two primary epithelial tumours were identified out of 6 824 appendectomies yielding a prevalence rate of approximately 0.62%. Well-differentiated neuroendocrine cell tumours (carcinoids, 47.6%) and benign non-endocrine cell tumours (adenomas, 45.2%) were most common with nearly equal frequency. The median age was 43 years, with no sex predilection. Carcinoid tumours occurred in younger patients (mean age 32 years), with a male-to-female ratio of 1.2:1. A clinical diagnosis of acute appendicitis was the most common reason for appendectomy (57.1%) and was histologically confirmed in 75% (18 of 24) of cases. In total, 16.7% of cases were diagnosed after incidental appendectomy.

**CONCLUSION:** Appendiceal epithelial tumours are

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### INTRODUCTION

Primary appendiceal tumours are uncommon. They are often diagnosed incidentally after histopathological examination of the vermiform appendix submitted in the course of the management of another clinical diagnosis. This paper reviews the primary appendiceal tumours diagnosed at the University Hospital of the West Indies during the period from January 1987 to June 2007, and to our knowledge represents the first such analysis in a predominantly black population.

### MATERIALS AND METHODS

The surgical pathology records of the Department of Pathology at the University of the West Indies were retrospectively reviewed over the time period January 1987-June 2007 and all cases of primary neoplasms of the appendix were selected. Non-epithelial tumours were excluded from the study population because of diagnostic controversy in the absence of immunohistochemical

Table 1 Demographic data and histologic types

Tumour type	Age range (yr)	Mean age (yr)	Median age (yr)
Carcinoid	18-70	32 ± 20.3	35.8
Adenoma	29-87	59 ± 15.2	58.6
Adenocarcinoma	36-74	55 ± 19.0	55

evaluation. The parameters examined included patient age, sex, the clinical history, the surgical procedure, the gross description of the specimen submitted and the histopathological diagnosis. Patient charts were retrieved where possible, for additional clinical information. The total number of appendectomies over the time period was also ascertained.

## RESULTS

In the period under study, 6824 appendices were submitted for pathologic evaluation. Forty-two primary epithelial tumours of the appendix were identified, yielding a prevalence rate of approximately 0.62%.

The overall age range of patients was 18-87 years with a mean age of  $45.9 \pm 19.3$  years and a median age of 43 years. The male-to-female ratio for all tumours was 1:1. Table 1 illustrates the demographic data with respect to each tumour type.

Of the 42 epithelial tumours identified, 20 (47.6%) were carcinoids, including 1 insular and 3 goblet cell carcinoids. Of the 19 (45.2%) adenomas, we identified 15 villous adenomas, the majority of which (11, 26.2%) were morphologically mucinous cystadenomas, as well as 1 tubular and 3 tubulovillous adenomas. All 3 cases of adenocarcinoma were of the mucinous type. Interestingly no cases of serrated adenomas were found in the records.

Only in 3 cases of carcinoid and 1 case of mucinous cystadenocarcinoma was the lesion identified grossly. Measurements were recorded for 2 out of 3 cases of carcinoid measuring 1.3 and 1 cm in maximum dimension.

In 26 of the cases the clinical diagnosis was acute appendicitis, appendiceal abscess in 3, appendix mass, caecal carcinoma, primary peritonitis and an appendiceal tumour in 1 case each. In a further 7 cases, the vermiform appendix was removed incidentally. No clinical diagnosis was submitted in 2 cases.

Of the 42 cases, only 7 patient charts were retrievable; review of the clinical notes revealed aggressive behaviour in one case of carcinoid tumour (goblet cell variant) with hepatic metastases, in a 50-year-old female, who presented with perforated appendicitis. The tumour was not identified grossly in this case.

In 4 of 42 cases there were synchronous colonic neoplasms giving a prevalence rate of 9.5%. Two of these 4, were cases of solitary synchronous caecal carcinoma accompanying a mucinous cystadenoma of the appendix in 1 case and an adenocarcinoma of the appendix in the other. In the other 2 cases, there was a single case of a caecal carcinoma and 2 tubulovillous and 1 villous colonic adenomas coexistent with an appendiceal tubulovillous adenoma in a right hemicolectomy specimen. The other case was that of a caecal carcinoma and 2 tubulovillous colonic adenomas coexistent with a mucinous cysta-

denoma of the appendix in a right hemicolectomy specimen. The carcinoma was diagnosed pre-operatively in 3 of the cases with no pre-operative diagnosis proffered in the other case. In none of these 4 cases was an appendiceal tumour suspected, nor was there evidence of any inherited syndromes in any of the cases.

No metachronous colorectal lesions were diagnosed up to June 2007. This search was limited by the retrieval of only 7 patient charts.

Pseudomyxoma peritonei was rare, with 1 such case diagnosed in a patient with a mucinous cystadenoma. Acute appendicitis was found to complicate a neoplasm in 54.8% of cases. Incidental appendectomy contributed to 16.7% of the neoplasms diagnosed.

## DISCUSSION

Tumours of the appendix are uncommon. Our prevalence of 0.62% is comparable to the prevalence rate of 0.5%-0.9% found in other studies in New Zealand and the United Kingdom<sup>[1-3]</sup>. No published reports are available for other predominantly black populations. The clinical picture was most frequently that of acute appendicitis (24 of 42) with histologic confirmation in 75% of these cases. Of note, incidental appendectomy provided 7 cases (16.7%). This highlights the utility of routine histopathologic examination of appendiceal specimens because the diagnosis is often made without antecedent clinical suspicion and these diagnoses can potentially alter patient management<sup>[4]</sup>.

Importantly, the index of suspicion of appendiceal tumours should be raised in cases clinically suggestive of acute appendicitis in the middle aged and elderly, given the median age of 43 at diagnosis of these tumours in our experience.

Carcinoid tumours show epithelial and neuroendocrine differentiation, and may arise in many sites, but most commonly in the gastrointestinal tract<sup>[5]</sup>. These tumours frequently arise at the tip of the appendix<sup>[6]</sup> and are reportedly the most common tumours of the appendix<sup>[2,7]</sup>. Gaskin *et al*<sup>[8]</sup> in a previous study of carcinoids of the gastrointestinal tract from our institution reported that the appendix was the most common location with a similar mean age to that documented in this study. In our study, there were almost equal numbers of carcinoids and adenomas, but patients with carcinoids were younger than those with adenomas and adenocarcinomas. There is a paucity of literature with regards to neuroendocrine tumours in black populations, however, in one study the incidence of carcinoid tumours in all sites was found to be highest in African-American males<sup>[9]</sup>. Other studies, including those from the SEER data (1973-2001) report that appendiceal neuroendocrine tumours are more common in females<sup>[8,10,11]</sup>, in contrast to our data, which revealed a slight male predilection. This may be due in part to the small size of the study population.

While the overall behaviour of carcinoids is unpredictable, appendiceal carcinoids have an excellent prognosis<sup>[5,11]</sup>. Importantly, where lesions are identified in the gross assessment of the specimen, they should be measured. Appendectomy is appropriate for lesions

< 1 cm but for lesions over 2 cm in diameter there is a significant increase in metastatic spread and thus right hemicolectomy is required in such cases<sup>[3,6]</sup>. There remains controversy around what is the appropriate treatment for lesions between 1-2 cm. Authors have suggested that additional criteria be examined in such cases. These criteria include proliferation markers, mitotic activity, vascular and mesoappendiceal invasion<sup>[6,12]</sup>. Unfortunately, there was one case of an unmeasured grossly visible lesion in our review. This potentially exposed the patient to not receiving further surgery which may have been necessary.

After diagnosis of an epithelial non-endocrine neoplasm of the appendix, the entire colorectum should be examined for synchronous lesions<sup>[13,14]</sup>. In this series, appendiceal adenomas were associated with synchronous colonic tumours in 9.5% of cases, further underscoring the need for colorectal examination and surveillance post diagnosis of appendiceal adenoma. The relative unavailability of colonoscopy in our population over the period and the small sample size may be responsible for such a high rate when compared to Khan *et al*<sup>[14]</sup>. The absence of cases of serrated adenomas may reflect past alternative classification of these lesions, or a lack of reporter awareness or it may be highlighting a lesser contribution by the serrated pathway to colorectal carcinoma in our population. This area requires further study. Based on the available records, there were no cases of colorectal carcinoma syndromes with appendiceal involvement diagnosed during the period. Pseudomyxoma peritonei, a term best avoided for diagnostic purposes, was extremely rare.

## COMMENTS

### Background

Primary appendiceal tumours are uncommon. They are often diagnosed incidentally after histopathological examination of the vermiform appendix submitted in the course of the management of another clinical diagnosis. No previous research has been done in a predominantly black population to determine the prevalence or histologic types of primary epithelial tumours of the appendix.

### Research frontiers

Carcinoids (neuroendocrine tumours) are considered the most common primary appendiceal neoplasm and there is some evidence that African-American males have the highest incidence of carcinoids in all sites. However, several articles including the SEER database identified carcinoids more frequently in females. The roles of gender and ethnicity, if any, are unclear and require further investigation. The serrated pathway to colorectal carcinoma has been well described but the absence of such lesions in this study may reflect inappropriate classification or lack of reporter awareness. Further specific research into the serrated pathway to colorectal carcinoma in predominantly black populations is required.

### Innovations and breakthroughs

This and other articles have validated the use of routine histologic examination of appendectomy specimens given the frequency of diagnosis of incidental tumours which potentially require specific management. Generally carcinoid tumours portend a favourable prognosis but in some cases these tumours behave aggressively. Several criteria including proliferative markers, mitotic activity, vascular and mesoappendiceal invasion are being examined to determine their utility in predicting the behaviour of carcinoid tumours. The gross documentation of tumour size is important in determining if further management is required. While carcinoids are generally thought to be the most common tumour of the appendix, in this study an almost equal number of

adenomas were diagnosed. The published description of the sessile serrated adenoma and its recognition as a precursor to adenocarcinoma of the colon and rectum opened a new paradigm of research into colorectal carcinoma. It also highlighted that these lesions may have been previously misdiagnosed as hyperplastic polyps.

### Applications

Routine histopathological examination of appendectomy specimens is justified given the not infrequent incidental finding of appendiceal tumours. In cases of appendicitis in the elderly, the index of suspicion for epithelial tumours of the appendix should be raised. Moreover, once the diagnosis of an adenomatous lesion is made, colonoscopic examination of the entire large bowel is mandatory given the frequency of synchronous colorectal neoplasia in our population.

### Terminology

The term carcinoid refers to tumours which show epithelial, endocrine and neural characteristics which have been identified by light microscopic, ultrastructural and immunohistochemical means. The term serrated pathway of colorectal carcinoma refers to those lesions which arise from precursors with a peculiar hyperplastic morphology associated with architectural dysplasia but no cytologic abnormalities. These tumours have specific mutations which further distinguish them from the adenomatous and the hereditary nonpolyposis colorectal cancer (HNPCC) pathway.

### Peer review

This retrospective brief report is the first publication describing the prevalence and types of primary epithelial tumours of the appendix in a predominantly black population. It also describes the rate of synchronous neoplasia and highlights the need for routine histopathology. Thus, it is of reference value to the international scientific medical community.

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