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ORIGINAL RESEARCH REPORT

Neoplasms of the appendix: An experience of a tertiary hospital in Southwestern Nigeria

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ABSTRACT

Background: The appendix is a vestigial tube-like organ. Its exact physiological function is unknown. Appendectomies are done usually following a clinical diagnosis of acute appendicitis. Neoplasms can arise from this organ as well. Carcinoids are the most common neoplasms arising commonly at the tips. This retrospective review of neoplasms of the appendix was aimed at identifying the incidence and describing the histological variants of neoplasms of the appendix in our environment. **Materials and Methods:** This study was a 10-year retrospective review of all appendectomy specimens submitted to the Department of Pathology, University College Hospital, Ibadan, Nigeria, from January 1, 2009, to December 31, 2018. Microscopy was done examining the longitudinal sections from the tip to the base of the appendix. The histological diagnosis was extracted from the records in the department and classified using the WHO classification of tumors of the appendix (2019). Patients' biodata such as age and sex were also extracted. The data were analyzed for frequency distribution using SPSS 23. **Results:** The incidence of neoplasms in the appendix was 0.84% of the 1071 appendectomies received in our department over the study period. Low-grade appendiceal mucinous neoplasm (LAMN) was the most common histological variant accounting for 55.5% of neoplasms, followed by metastatic carcinoma at 22.2% and carcinoids at 11.1%. There was a female preponderance of 77.8%. **Conclusion:** Neoplasms of the appendix are rare in our environment, and LAMN was the most common neoplasm of the appendix in our institution. There is a female preponderance among patients with appendiceal neoplasms.

Key words: Appendix, Ibadan, neoplasms, Nigeria

INTRODUCTION

Neoplastic lesions of the appendix are relatively rare and found only in about 2% of all appendectomies.[1,2] Appendectomies are mainly done on account of the clinical diagnosis of appendicitis. Histopathological examination of routine surgical appendix has shown few incidental neoplastic lesions and even negative appendectomies. Hence, most cases of neoplasms of the appendix are only evident after surgical intervention and histological review. The type of neoplasms and their clinical course seen in the appendix vary widely.[3] Patients commonly present with symptoms such as right lower abdominal pain, and vomiting, similar to those of acute appendicitis. There have been reports of appendiceal neoplasm presenting with significant weight loss, fatigue, abdominal mass, and intestinal volvulus.[4,5]

The appendix gives rise to neoplasms with glandular or neuroendocrine differentiation. Epithelial tumors of the appendix range from low grade localized to the mucosal to high-grade invasive tumors.[6] Low-grade appendiceal mucinous neoplasms (LAMNs) are the most common histological type of mucin-producing epithelial neoplasms in a study by Misdraji *et al*.[6] The most common neoplastic lesion of the appendix is the carcinoid tumor, which is usually located at the tip of the appendix.[1,7-9]

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LAMNs include tumors previously known as villous adenoma, cystadenoma, and mucinous tumor of uncertain malignant potential.[6,10] LAMNs are a group of mucinous neoplasm with low-grade cytology. They can present with dissecting of mucin in the appendix wall, and in some cases, mucin or neoplastic cells can be found outside of the appendix.[11] The presence of extraappendiceal neoplastic epithelial cells is a poor prognostic marker as their 5- and 10-year survival rates are 79% and 46%, respectively.[10] Intraappendiceal LAMN or those with just extraappendiceal acellular mucin are usually cured by surgical intervention.[10,12-14]

High-grade appendiceal mucinous neoplasms (HAMNs) are mucinous neoplasms with high-grade cytology present at least focally, but show no infiltrative growth pattern.[11] A diagnosis of HAMN should be made after carefully examining the specimen and excluding mucinous adenocarcinoma. If neoplastic cells are seen outside the appendix or localized area within the peritoneum, a diagnosis of HAMN is excluded, and the most appropriate diagnosis will be a mucinous adenocarcinoma.[11]

Mucinous adenocarcinoma of the appendix is made when there is presence of infiltrative neoplastic cells with high-grade cytology in a mucinous neoplasm.[11] Mucinous adenocarcinoma of the appendix is associated with a dysplastic mucosa; this usually supports a diagnosis of an appendiceal primary in cases that present mainly with pseudomyxoma peritonei.[7] Mucinous adenocarcinomas are clinically aggressive and frequently metastasize to the peritoneum.[11] It has poor prognosis with a 5-year survival rate of 28%.[10,15]

Mucinous signet ring cell carcinoma is a mucinous adenocarcinoma with 50% or more of the tumor containing signet ring cells. Tumors with signet ring morphology <50% are referred to mucinous adenocarcinoma with signet ring cells.[11] Mucinous adenocarcinoma can either be Grade 2 or 3 tumors, whereas mucinous signet ring cell carcinomas are poorly differentiated and thus Grade 3 tumors.[11]

Neuroendocrine tumors are the most common type of tumors in the appendix. It can either be Grade 1, 2, or 3. Well-differentiated neuroendocrine (Grade 1) tumors (carcinoid tumor) is the most frequent neoplasm of neuroendocrine origin.[7] Carcinoid tumors are commonly found at the tip of the appendix. Carcinoid tumors have higher incidence in females and rarely metastasize to the liver.[1] Neuroendocrine tumors can be functional or nonfunctional. If functional, patients will present with the symptoms of carcinoid syndrome.[1]

The aim of this study was to describe the histopathological characteristics of neoplasms of the resected appendix.

MATERIALS AND METHODS

This is a 10-year retrospective review of the histopathology reports of resected vermiform appendix histopathology records of the Department of Pathology, University College Hospital, Ibadan, Nigeria, from January 1, 2009, to December 31, 2018. The requests were made after surgical intervention for the clinical diagnosis of acute appendicitis. Right hemicolectomy specimens with appendix examined were excluded from this study. Age, gender, and histological diagnosis were extracted from the records. Microscopic examination involved examining the tip of the appendix, taken longitudinally and two other circumferential samples taken from the base and mid-portion. The histological diagnosis was classified using the 5th edition of the WHO classification of tumors of the appendix (2019).[16] The descriptive analysis was done using the Statistical Package for the Social Sciences, version 23 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

There were nine cases with neoplastic lesions out of the 1071 appendectomies examined, representing an incidence of 0.84% over the study period. Neoplasms were more common in females who accounted for 77.8% of the cases [Figure 1]. The modal age group was in the fourth decade [Table 1]. LAMN was the most common diagnosis [Table 2]. One of the cases affected the appendix, ovary, and the omentum, and the primary site could not be ascertained. The LAMN did not show significant differences in incidence between males and females [Table 3]. Majority (40%) of the LAMNs occurred in the fourth decade [Table 4].

DISCUSSION

Appendectomies are routine specimens received and evaluated by histopathology laboratories. They are usually performed for the clinical diagnosis of appendicitis. Neoplastic lesions of the appendix are relatively rare

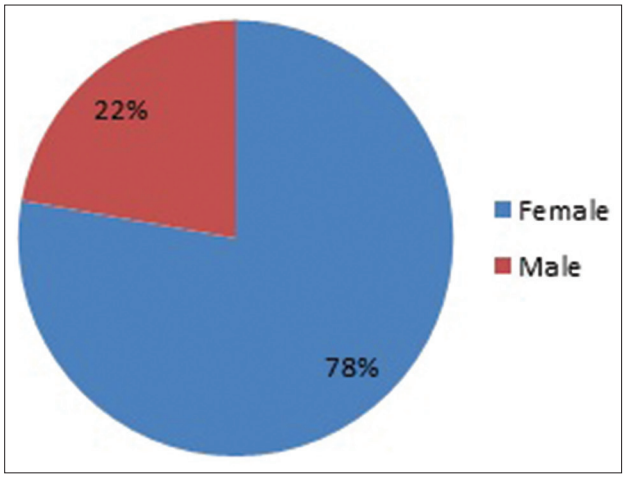

Figure 1: Pie chart showing sex distribution of malignant appendiceal neoplasms

accounting for <2% of all appendectomies.[2,8,13] The 0.84% incidence of neoplastic appendix in this study is very similar to that of Charfi *et al*. who recorded an incidence of 0.7%.[8] There are some reviews from Nigeria and Africa that did not record any neoplastic lesion in their series.[17-19]

LAMN was the most common epithelial neoplasm of the appendix in this study. This differs from the usual pattern of carcinoid tumors being the most common.[1,8] This is interesting as we recorded only one case of carcinoid in our review. Misdraji *et al*. who reviewed epithelial neoplasms of the appendix excluding the carcinoids demonstrated that that LAMN s were the most common.[20] Our findings are also similar to a finding in Bengaluru by Geetha *et al*. who reported that mucocele was the most common neoplasm, followed by carcinoids.[21] Mucocele is a gross descriptive term and not a histopathological diagnosis as it could be as a result of a hyperplastic polyp, LAMN, or even mucinous adenocarcinoma.[6,22,23] Misdraji *et al* and Carr *et al*. in their studies reported equal percentages of adenocarcinomas and carcinoids.[6,24] These tumors have good prognosis when confined to the luminal mucosal without invasion.[6,24] These tumors could rupture and spread to involve the peritoneum and such state is referred to as pseudomyxoma peritonei. LAMN typically occurs in the sixth decade with a wide age range of 20–89 years.[20] In our series, we had modal age of diagnosis to be the fourth decade and had none in the sixth decade. These disparities in histological type and modal age of presentation are likely due to the few numbers of cases seen in this study. LAMN has a varying presentation; it can be suspected during gross examination of the appendectomy specimen with mucin present in the surface or can be grossly unremarkable.[20] About 80% of LAMNs are confined to the appendiceal wall, and 42% of these can have dissection into the muscularis propria.[25,26] In 20% of LAMNs, there is associated perforation or just presence of acellular mucin serosal deposits without a recognizable breach of the muscularis propria.[20,26] LAMNs show frequent mutations in GNAS and KRAS genes.[27] All LAMNs are Grade 1 (well differentiated) tumors.[11] The staging of LAMN is different from how other gastrointestinal tumors are staged. A tumour confined to the appendix is carcinoma in situ or intramucosal carcinoma; Tis (LAMN), even if mucin dissects into the muscularis propria. There are no pT1 and pT2 stages. pT3 is when mucin with or without neoplastic cells is seen within the subserosa, and pT4 is when there is peritoneal deposit.[11]

Table 1: Age group distribution

Age group	Frequency (%)
10-19	1 (11.1)
20-29	1 (11.1)
30-39	3 (33.3)
40-49	1 (11.1)
50-59	2 (22.2)
70-79	1 (11.1)

Table 2: Frequency and percentage distribution of the histological types of tumors of the appendix

Histological diagnosis	Frequency (%)
Carcinoid tumor	1 (11.1)
Low-grade appendiceal mucinous neoplasm	5 (55.5)
Mucinous adenocarcinoma involving the ovary, appendix, adnexa, and omentum	1 (11.1)
Metastatic carcinoma	2 (22.2)

Table 3: Distribution of appendiceal neoplasms within gender

Diagnosis	Sex		Total
	Female (%)	Male (%)	
Carcinoid tumor	1 (100)	0	1
Low-grade appendiceal mucinous neoplasm	3 (60)	2 (40)	5
Mucinous adenocarcinoma involving the ovary, appendix, adnexa, and omentum	1 (100)	0	1
Metastatic carcinoma	2 (100)	0	2
Total	7	2	9

In mucinous adenocarcinoma, the wall of the appendix may appear grossly thickened or encased by tumor, and microscopy commonly shows infiltration of a desmoplastic stroma.[20] Some cases of mucinous adenocarcinoma can be confined to the appendix, although there is usually marked cellular atypia and stromal invasion.[20] Peritoneal carcinomatosis when confined to the abdominal cavity is effectively treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.[28] Early intervention using these treatment modalities improves outcome with a median survival of 27 months compared to 15 months for those who had just chemotherapy.[28]

CONCLUSION

Neoplasms of the appendix are rare in our environment

Table 4: Distribution of neoplasms of the appendix in age decades

Diagnosis	Age group						Total
	10-19	20-29	30-39	40-49	50-59	70-79	
Carcinoid tumor	0	0	1	0	0	0	1
Low-grade appendiceal mucinous neoplasm	1	1	2	1	0	0	5
Mucinous adenocarcinoma involving the ovary, appendix, adnexa, and omentum	0	0	0	0	0	1	1
Metastatic carcinoma	0	0	0	0	2	0	2
Total	1	1	3	1	2	1	9

and are more common in females. LAMN is the most common neoplasm of the appendix in our institution. The result of this study may not be truly representative because of the low number of the neoplasms identified. It is very important to examine all appendectomies done for supposed appendicitis. If a neoplasm is diagnosed and properly staged, it will allow for early referral for appropriate and adequate treatment.

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Conflicts of interest
There are no conflicts of interest.

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