SCIENTIFIC ARTICLE

Neoplasms of the appendix: a retrospective analysis of 5-year data on histopathology of appendicectomy specimens in a tertiary care hospital

Halgaha Withanage Thushara Dananjaya Wijayaratne[1], Shanika Madonna Fernandopulle[2]
[1]Postgraduate Institute of Medicine, University of Colombo, Sri Lanka
[2]North Colombo Teaching Hospital, Sri lanka

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Abstract

Introduction

Right iliac fossa pain due to appendicular disease is a common clinical presentation to a surgical casualty ward. Neoplasms of the appendix are rare but sometimes they present with acute symptoms similar to acute appendicitis. Studies on neoplasms of appendicectomy are sparse in Sri Lanka. Our objective is to study the epidemiological, demographic characteristics and histopathological data on appendicectomy specimens.

Method

A retrospective descriptive study using the database on appendicectomy specimens in the pathology department of Colombo North teaching hospital, Ragama from January 2015 to December 2019.

Results

Neoplastic lesions were noted in 16[0.82%] among 1939 appendicectomy specimens. All [n=16, 100%] were primary neoplasms and the male to female ratio was 5:11. The percentage of neoplasms was higher in the elderly population compared to the young. Six of the 16 specimens [37.5%] had associated features of acute appendicitis. The commonest neoplasm was neuroendocrine neoplasm [including goblet cell carcinoid tumour] [n=9, 56.25%]. The mean age was 33 years and comprised 0.46% of the population. Mucinous neoplasms were noted in 6 [37.5%] and comprised 0.3% of the population. The median age was 59 years. The resection margin was well away from the tumour in all [n=9] Neuroendocrine neoplasms while the tumour had involved the resection margin in 4 out of 6 [66.6%] of mucinous neoplasms.

Conclusion

Appendicular neoplasms are rare but higher in the elderly population compared to the young. Neuroendocrine neoplasms are the commonest incidental tumours and they are less aggressive at the time of diagnosis. Meticulous dissection is important with a good clearance of the resection margin in suspected mucinous appendiceal neoplasms.

Correspondence: Thushara Dananjaya Wijayaratne
E-mail: thusharawijayaratne@gmail.com
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Introduction

Right iliac fossa [RIF] pain is a common presenting symptom among many admissions to a surgical casualty unit. Underlying pathology may vary and common differential diagnoses include inflammatory conditions like acute appendicitis, diverticulitis and pelvic inflammatory disease [PID].

Acute appendicitis is commoner than the other differential diagnoses. The aetiology of acute appendicitis is unclear but it is believed that the obstruction of the lumen with a faecolith or a foreign material leads to acute inflammation [1]. However, underlying neoplasms in the appendix should also be considered in the middle-aged and elderly population when they present with features suggestive of acute appendicitis [2]. The incidence of primary neoplastic lesions is about 0.7-1.7% of appendicectomy samples[3] and an increased incidence has been observed [4].

The neoplastic histology of the appendix varies from benign to malignant. Origin of primary neoplasms of the appendix is from epithelial, mesenchymal or lymphoid tissues. Epithelial and mesenchymal neoplasms are the commonest and the incidence of other tumours are less[5]. Secondary deposits are also found in the appendix of which the primary site is a different organ. It is found that the commonest neoplasm is the neuroendocrine tumour/ carcinoid tumour of the appendix [2]. The commonest malignant neoplasm is mucinous adenocarcinoma of the appendix. [6]. These figures are mainly from western countries and regional or local studies are sparse.

The WHO Classification of Tumours of the Digestive System is used to classify the tumours of the appendix. The 4th edition of WHO Classification of Tumours of the Digestive System [7] was used at our institution during the study period.

However, currently, the neoplasms of the appendix are classified using the 5th edition of it which was published in June 2019 [5]. There are several changes noticed in the new

edition. The epithelial tumours are classified broadly into serrated lesions and polyps, mucinous neoplasms, adenocarcinomas and neuroendocrine neoplasms. Goblet cell carcinoid which was considered as a neuroendocrine neoplasm is now renamed as goblet cell adenocarcinoma and considered as an adenocarcinoma. Depending on the pattern of invasion, Low grade appendiceal mucinous neoplasms [LAMN] and High grade mucinous appendiceal neoplasms [HAMN] are categorised under mucinous neoplasms and mucinous adenocarcinoma is categorised under Adenocarcinoma. Neuroendocrine tumour nomenclature remains mostly unchanged.

It is important to study the incidental neoplastic lesions in appendicectomy specimens to critically analyse the stages of each tumour at presentation/surgery and adequacy of resection. A mucinous appendiceal lesion such as low-grade appendiceal neoplasm or mucinous adenocarcinoma may progress into pseudomyxoma peritonei [PMP]. So proper workup and treatment reduce the disease morbidity and mortality.

This study will provide a better understanding of the incidental neoplasms in the appendix in the Sri Lankan context and lay a foundation to carry out further studies. Epidemiological data such as incidence and demographic data aids in taking proper clinical judgement and selecting the patients to perform pre-operative workup like CECT. Also, it helps to set forth consensus on management at the national level.

Our objective of the study was to provide epidemiological and demographical data on appendiceal neoplastic lesions and describe the pathological staging and resection margins of the neoplasms following the surgery.

Materials and methodology

A retrospective cross-sectional descriptive study was carried out using the database of appendicectomy histopathology reports in the department of pathology, North Colombo Teaching Hospital [NCTH], Ragama.

The database consists of data on all appendicectomy specimen received to the department of pathology, NCTH since 2015. This included data on gender, age, histological type of the lesion and TNM classification of received samples.

Histology of tumours was classified according to the 4th edition of WHO digestive system tumour classification [2010] [7]. TNM staging was done using the 7th edition of the American Joint Commission on Cancer [AJCC] staging system.

Inclusion criteria

All appendicectomy samples received to the pathology lab from the year 2015- 2019 were analysed. Appendixes of right hemicolectomy samples were not included in the study as the objective of the study is to analyse the proportions of neoplasms among samples that were clinically diagnosed as acute appendicitis. A 5-year data were collected from 2015-2019.

Histologically proven neoplasms were selected and detailed histology reports of selected cases were analysed from the anonymized database. Relevant data were extracted from the reports to a separate data extraction sheet. Data was stored in a confidential database accessible only to the investigators.

Frequency and percentages were used in categorical data. Continuous data such as age, size of tumours were reported using median and standard deviation. Collected data were analysed using SPSS v 23.0

Results

We analysed histology reports of 1939 appendicectomy specimens collected over a 5-year duration from 2015- 2019. The mean age of the study population was 26 years [SD- 14]. The age of the population ranged from 4 years to 84 years.

The commonest diagnosis was acute appendicitis [n=1415 [72.97%]]. Incidental neoplasms were found in 16 [0.82%] specimens of the study population [n=1939] [Table 1]. The mean age of the patients with incidental neoplasms in the appendices was 44 years [SD-19, IQR-27].

Six of the 16 specimens [37.5%] had associated features of acute appendicitis. Microscopy of all 6 specimens revealed to be neuroendocrine tumours including goblet cell carcinoid tumours.

There was a single specimen with hyperplastic polyp without dysplasia. Neoplastic lesions included both benign and malignant pathologies. All neoplasms [100%] were primary appendiceal neoplasms and arises from epithelial cells. The male, the female ratio was 5:11. The commonest type of neoplasm was the neuroendocrine neoplasm [Table 2].

The population was grouped into 3 categories according to age to analyse the proportions of neoplasms among each category [Table 3].

The percentages of neoplastic lesions were different between age categories. A higher proportion of neoplasms was noted in the elder population [Age>60 years].

There were 4 neoplastic lesions in the category of >60 years of age. Two specimens were invasive mucinous adenocarcinomas. One was a low grade mucinous append-iceal neoplasm and the TNM staging was T4a. The other specimen was a grade 2 neuroendocrine tumour.

The commonest incidental neoplasms were neuroendocrine neoplasms [n=9, 56.25%]. The proportion of neuroendocrine neoplasms out of the whole population was 0.46%. The mean age was 33 years. The male to female ratio was 1:2. According to the WHO classification of the digestive tumours 4th edition, the goblet cell carcinoid tumour of the appendix was also included in the neuroendocrine neoplasms [7].

Table 4 explains the AJCC TNM staging of neuroendocrine neoplasms found in our population. This means the staging of the neoplasm at the time of symptom occurrence. Most NETs showed symptoms at the T1a stage.

Tumour size was measured in 6/7 NET grade 1 and 2 tumours. In one specimen, the size was too small to measure and it was disregarded. From the 6 specimens, the mean size of the tumour was 4.66mm [range – 2mm-7mm], All the NET grade 1 and 2 tumours were less than 10 mm. Of the Goblet cell carcinoid tumours, the size measured was 6.6mm and 25mm in diameter respectively. Compared to Neuroendocrine tumour grades 1 and 2, Goblet cell carcinoid tumour size was larger in the appendicectomy specimen.

Resection margins were well away from the tumour in all cases [100%]. 1/9 [11%] had a macroscopic abnormality of which the appendix tip was dilated. The microscopy of the specimen with dilated tip was a goblet cell carcinoid tumour.

Mucinous neoplasms included 3 low-grade appendiceal mucinous neoplasms [LAMN] and 3 invasive mucinous adenocarcinomas [Table 5].

The proportion of mucinous neoplasms in the study population was 0.3%. The mean age of the mucinous neoplasms was 59 years. The male to female ratio was 1:2. Mucinous neoplasms included low-grade appendiceal neoplasms [LAMN] and invasive mucinous adenocarcinomas. The mean age of Invasive mucinous appendiceal carcinoma was 59.3 years and the mean age of LAMN was 58.6 years. The number of cases and TNM staging is presented in table 4. The tumours had involved the resection margins in 4 specimens [66.6%].

Mucocele is a cystically dilated appendix that contains mucin. Two specimens [33.3%] of mucinous neoplasms were macroscopically identifiable during the surgery and had features of a mucocele. Altogether there were 5 mucoceles in our population. Three specimens out of 5 [60%] of mucoceles were histologically diagnosed as retention cysts and, 2/5 [40%] mucoceles had an underlying mucinous neoplasm.

In one specimen of mucinous lesions, the histology of the resection margin was composed of a fibrofatty tissue fragment without appendiceal tissue with mucinous adenocarcinoma. The resection margin of this specimen was considered positive for the tumour. However, the staging was not given in this case.

There was a single specimen with histology of villous adenoma. It consisted of columnar epithelium with low-grade dysplasia. Lamina propria and muscle wall were preserved.

Discussion

According to the results of the study and considering the worldwide figures, appendiceal neoplasms are rare. The proportions of neoplasms in appendicectomy specimens [0.82%] is similar to the other published series in Europe and Asia [Table 6] [2,8- 9]. A female preponderance was noted in neoplastic appendicular lesions [Male: Female= 5:11].

Although the appendiceal neoplasms are rare, there is a noticeable difference in the proportions of appendiceal neoplasms between age groups. It is observed that the proportion of incidental neoplastic lesions is higher in the middle age and elder population. The chi-square test or fisher's exact test was not applied to assess the significance as the number of samples were low and are not fulfilling the criteria [table 3]. However, this percentage difference indicates that an underlying neoplasm should also be considered when a patient of middle age or old age presents with features of acute appendicitis. A high level of suspicion is necessary to consider further imaging studies before surgery.

The results of our study show that neuroendocrine neoplasms are the commonest among appendiceal neoplasms even in the current study [2]. The mean age of neuroendocrine neoplasm was 33 years which represent the middle age category. Our results showed 6/9 [66.67%] neuroendocrine neoplasms had features of acute inflammation in the wall of the appendix. This implicates that the neuroendocrine neoplasm is a possible reason to obstruct the lumen which triggers acute inflammation. Though it is common in middle age people, except for goblet cell carcinoid, most of the tumours were of T1a staging and resection margins are well away. Neuroendocrine tumours [NET] are less invasive when compared to other types of tumours at the time of diagnosis. According to the ENETS consensus guidelines for neuroendocrine neoplasms of the appendix [excluding goblet cell carcinoids], tumours <2cm can be adequately managed with appendicectomy alone provided that the margins are clear of tumour. This means even if the histology of the appendix shows incidental NETS in the young patients who presented with features of appendicitis, most NETS would be

Table 1. Histological diagnosis of specimens of the study population

Histology of the appendix	No. of cases	Percentage
Acute appendicitis	1415	72.97%
Nonspecific changes	282	14.54%
Submucosal Lympho-follicular hyperplasia	198	10.21%
Neoplasms	16	0.82%
Fibrous occlusion of appendix	14	0.72%
Parasitic infestations	5	0.25%
Retention cysts	3	0.15%
Extrauterine endometriosis	2	0.10%
Infarcted tissue	2	0.10%
Xanthogranulomatous inflammation	1	0.05%
Hyperplastic polyp	1	0.05%

Table 2. Distribution of neoplasms of appendix in the study population

Neoplasm	No. of specimens	Percentage
Neuroendocrine neoplasms	9	56.25%
Low-grade Appendiceal mucinous neoplasms	3	18.75%
Invasive Appendiceal mucinous adenocarcinoma	3	18.76%
villous adenoma	1	6.25%

Table 3. Age groups and the percentage of neoplasms in each age category

Age groups [years]	No. of specimen and Percentage population	Neoplastic lesions in each group	Percentage of neoplasms in each category
0 – 29	1286 [66.3%]	3	0.23%
30-59	589 [30.4%]	9	1.52%
>60	64 [3.3%]	4	6.25%

Table 4. Tumour staging of the neuroendocrine neoplasms [7th edition of AJCC TNM classification]

Type of Neuroendocrine neoplasm	No. of cases	Staging	No. of cases
Neuroendocrine tumour [NET] grade 1	6	T1a	5
		T3	1
Neuroendocrine tumour [NET] grade 2	1	T1a	1
Goblet cell carcinoid tumour.	2	T3	1
		T4	1

Table 5. Tumour staging of the mucinous neoplasms [7th edition of AJCC TNM classification]

Type of mucinous neoplasm	No. of cases	Staging	No. of cases	Involvement of tumour in resection margin
Low grade appendiceal mucinous neoplasm [LAMN]	3	Tis	1	Yes
		T3	1	Yes
		T4a	1	No
Invasive appendiceal mucinous adenocarcinoma.	3	T3	1	Yes
		T4a	1	No
		Staging not done	1	Yes

Table 6. Comparison of studies on neoplasms of appendicectomy specimen

Author and the country	Year	Number of patients	Number of neoplasms	Percentage of neoplasms observed among routine appendicectomy specimen
Connor - UK	1979-1994	7970	74	0.9%
Lee -South Korea	2000-2005	3744	28	0.7%
Kunduz- Turkey	2011-2017	3554	28	0.78%
Current study- A single tertiary care centre in Sri Lanka.	2015-2019	1939	16	0.82%

in the early stage and would not need a second surgery to complete management.

Goblet cell carcinoid is now classified as a separate group of tumours according to the updated WHO classification of tumours of appendix published in 2019 [5]. The mean age of the patients diagnosed with appendiceal mucinous neoplasm is 59 years. Seventy-five per cent of neoplasms found in patients over 60 years of age were mucinous neoplasms. So, it is clear that even in the Sri Lankan context, mucinous neoplasms are common among the elderly population.

Mucinous neoplasms of the appendix are associated with pseudo myxoma peritonei[PMP]. It is characterised by the growth of mucinous neoplasm within the peritoneal cavity producing peritoneal deposits and mucinous ascites which has a poor prognosis [10,11]. Even though PMP is an indolent tumour, it evolves with time and causes morbidity which needs complete cytoreductive surgery plus hyperthermic Intra-peritoneal chemotherapy later in a specialized oncosurgical unit [11]. According to our study, 33.3% of the appendiceal mucinous neoplasms are macroscopically identifiable as a mucocele and 40% of mucoceles are having underlying mucinous neoplasm [12]. Also, the tumour had involved the resection margin in 66.6% of cases of mucinous neoplasms of the appendix. It is important to be vigilant and perform a meticulous dissection when a macroscopically suspicious lesion in the appendix is noticed during the surgery to prevent the rupture of such lesion and contamination of the peritoneal cavity to avoid the development of PMP. Also, assistance from an experienced surgeon would be beneficial in these situations.

Diagnosis of appendiceal neoplasms can be done by performing imaging studies, especially mucinous type neoplasms of the appendix when it is associated with the gross appearance of a mucocele[13]. It is possible to differentiate a benign mucocele from a malignant mucocele using the contrast-enhanced CT [CECT] abdomen finding of the appendix [14]. According to this study, the elderly population is more prone to get mucinous appendiceal lesions. Hence, when an elderly patient presents with features of acute appendicitis it would be beneficial to perform a CECT abdomen. This aids a pre-operative diagnosis which helps us to offer proper management.

Unavailability of data on presenting complaints in the early years [2015-2016] was one of the limitations of the study. So, the analysis on presenting complaints was not included in the study. It is found that most of the appendicular neoplasms present with features of appendicitis or right iliac fossa pain [2]. Considering the above finding and the fact that appendicectomy is done for the patients with features of acute appendicitis and RIF pain, we assumed that all specimens we received are clinically diagnosed as acute appendicitis. It is beneficial to gather data on specific presenting complaints with imaging studies when future studies are done on this topic.

Conclusion

Appendicular neoplasms are rare. Appendicular neoplasms [malignant] should be suspected in the elderly population. A female preponderance was noted in neoplastic lesions. Neuroendocrine neoplasms are the commonest incidental tumours and they are less aggressive at the time of diagnosis. Meticulous dissection is important to achieve negative resection margins in mucinous appendiceal neoplasms to prevent future complications.

complications.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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