ADENOCARCINOMA OF APPENDIX. A TWELVE YEAR EXPERIENCE FROM A CANCER HOSPITAL IN PAKISTAN

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ABSTRACT

Objective: To study the surgical and oncological outcome of all the patients presenting with a diagnosis of the appendix’s carcinoma at SKMCH & RC. Methodology: From 2006 to 2017, all patients diagnosed with carcinoma of the appendix were included in the study. Demographic variables were collected. Surgical outcomes in terms of operation performed and its complications were recorded. Short and long term oncological outcomes were recorded. All data were entered and analyzed in SPSS version 21. Results: A total of 19 patients were included in the study. The median age was 54.8 +/- 2.9 years. There were seven male and 12 female patients. The most common presentation was pain RIF in 16 patients, followed by altered bowel habits in 3 patients. 15 patients were diagnosed after they had their operation. 13 had an open appendectomy, and 2 had a TAH BSO with appendectomy. Open appendectomy was performed in 68.4% (n=13) of the patients, right hemicolectomy in 21.1% (n=4) patients. Two patient had a TAH BSO + appendectomy. Twelve patients received adjuvant chemotherapy. Six patients had a disease recurrence. All patients had a median survival of 50 months. Conclusion: Cancer of the appendix is rare and needs to be managed aggressively. All patients are best treated with a formal right hemicolecctiony with adjuvant chemotherapy.

KEYWORDS Carcinoma Appendix, appendicular cancer, adenocarcinoma, neuroendocrine cancer, lower-middle-income country

Introduction

The appendix was first described by Jacopo Berengario da Carpi in 1552 [1,2]. Appendiceal tumours constitute less than 0.5% of all gastrointestinal tumours [3]. The phenotype of appendiceal tumours are like that of colonic tumours [4,5], but appendiceal mucinous neoplasms are more frequently encountered5. The mean age of presentation of appendiceal neoplasm is in the sixth decades of life [6,7]. The disease is more prevalent among men than women. Right iliac fossa pain is the most common symptom[8].

The first appendectomy was performed in 1735. In America, nearly 300,000 are performed yearly [9,10]. It is difficult to diagnose carcinoma of the appendix preoperatively, and it is usually made on the histopathology specimen and intra-operatively on the bases of operative findings. Of all appendectomy specimens sent for histo-pathological analyses, less than 1% of the specimen revealed neoplasm[11,12]. About 74% of appendiceal cancers have already been spread, and at least one-third present as metastatic due to ignorance. Surgery remains the mainstay of treatment[14]. Appendectomy alone can be used for biopsy purposes in premalignant lesions, such as adenomatous polyps, adenocarcinoma in situ, or non-perforated low-grade mucinous tumours with R0 margins[14]. In case of advanced disease, right hemicolecctiony is the procedure of choice. Patients with nodal metastases and metastatic disease need adjuvant chemotherapy [14]. Prognosis of this neoplasm is dependent on tumour characteristic, aetiology and stage of the tumour, as the 5-year disease-specific survival varies from 27-93% [15].
The rationale of this study is to understand the clinicopathological factors, diagnostic measures and prognosis of the disease. Carcinoma of the appendix is a rare neoplasm due to which there is a paucity of data from this part of the world. This study will enlighten the world and add the information in the literature about carcinoma of the appendix and its management.

**Methodology**

It is a retrospective descriptive case study with convenient sampling. The ethical approval was sought from the Institutional Review Board (IRB) of Shaukat Khanum Memorial Cancer Hospital & Research Centre, Pakistan. Informed consent was taken prior to the collection of data. All patients diagnosed with primary adenocarcinoma of the appendix at Shaukat Khanum Memorial Cancer Hospital and Research Centre are included. Patient with secondary malignancies is excluded. Data was collected through HIS (Electronic data) at Shaukat Khanum Memorial Cancer Hospital and Research Centre. Calculations were performed with Statistical Package for the Social Sciences (SPSS 20) for Windows version 20. Median values with minimum and maximum value are described for skewly distributed quantitative variables. For categorical variables, a number of observations and percentages are reported. Outcomes were assessed are age, management, overall survival, disease-free survival, recurrence and site of metastases.

**Results**

A total of 19 patients were included in the study. The mean age of presentation is 54.9 +/- 2.9 years. The study includes a range of patient from 32 to 69 years of age. 63.2% (n=7) were female and 36.8% (n=7) were male. Most of our cases were diagnosed after undergoing an operation for appendicitis. 2 patients had undergone TAH BSO for an ovarian pathology. Only four patients were diagnosed preoperatively and underwent a formal right hemicolectomy. Cases operated outside had positive margins in 7 patients and required additional surgery and chemotherapy. 10 (52.6) patients underwent completion of right hemicolectomy after appendectomy. Only 12 patients had cleared margins and were not given any adjuvant therapy and kept on follow-up. Pain in the right iliac fossa was the commonest symptom in 84.2% (n=16) of the patients, followed by altered bowel habits in 15.8% of the patients—the majority of the patients presented within one year after becoming symptomatic.

Mucinous adenocarcinoma is the commonest among all histological sub types i.e. 78.9% (n=15), followed by neuroendocrine carcinoma i.e. 2 (10.5%), signet and adenocarcinoma constituting 5.3% each (n=1) 84.2% (n=16) had well differentiated carcinoma and 15.8% (n=3) had moderately differentiated carcinoma.

Pathological staging T4 is the most common presentation, constituting 36%, followed by T3 and T2 in 15.8% of the patients. Two patient had T2, and one had T1, data of three patients histopathology was missing. In over 50% of the patients, either lymph nodes were not present or cannot be assessed; 31.6% (n=6) had N1 lymph nodes. Open appendectomy was performed in 68.4% (n=13) of the patients, right hemicolectomy in 21.1% (n=4) patients and 10.5% (n=2) underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy and omentectomy. After analyses of the specimen, 63.2% (n=12) patients had clear margins. Those who had positive margins were given chemotherapy in an adjuvant setting and followed up. 68.5% (n=13) patients received adjuvant chemotherapy. 31.6% (n=6) patients developed pseudomyxoma peritonei. Recurrence was seen in 6 patients (31.6%). All of the patients had local recurrence. Among five patients, a CT scan was the modality of choice, and one patient underwent MRI for the diagnoses. Surgery with chemotherapy was performed among three patient while one patient underwent surgery, 1 had chemotherapy for curative intent, and 1 had palliative chemotherapy. Five patients developed metastases, 2 had hepatic, and 2 had the peritoneal disease. Surgery was performed. Surgery was performed in 2 patients, while two patient underwent surgery and chemotherapy, and 1 had palliative chemotherapy. 17 (89.5%) patients are alive at present after the management. Median survival after treatment is 50 months (10-120 months).

**Discussion**

Carcinoma of the appendix is a rare entity with only a few hundred cases have been reported. Most of the studies are either case reports or case study. Rokitansky first described appendiceal mucocele in 1842[16]. Mucocele is a term defining the dilation of the appendiceal lumen with a mucus collection, and it can be due to benign or malignant causes. This study will discuss the management and survival of the disease.

Due to the rarity of this cancer, only 19 patients have been treated in our hospital, as previous studies showed that these cancers are present in only 0.1-0.2% of all appendectomy specimen[17,8,19]. The mean age of the disease was 54.39 years, suggesting it affects the second half of life which is comparable to other studies in which the mean age was 52 years[20]. This study demonstrates that carcinoma of the appendix is more predominant among women.

The most common manifestation in this study is a pain in the right iliac fossa which is an indication of acute appendicitis. Gomez C.A. et al. published that in 18-24% of the cases, carcinoma of the appendix presents as acute appendicitis[21]. De Moerloose and Reverdin reviewed the literature and revealed that out of 145 cases of appendix’s carcinoma, the most common presentation was acute appendicitis followed by mass in the abdomen and ileus[22].

In our study, pseudomyxoma peritonei is seen in 31.6% of the patients. It is a known and fearsome complication after appendiceal perforation, either spontaneous or during surgery [23,24,25]. It can occur both in benign and malignant with a 5-year survival rate of 53-75%.

Due to the limited resources availability and low socioeconomic status, patients present late. These are the reasons behind pathological T4 being the most common presentation. Upfront surgery is the treatment of choice in the resectable disease with adjuvant therapy such as chemotherapy. The surgical approach is still controversial (laparoscopy vs laparotomy and appendectomy vs right hemicolectomy)[21]. Most of our patients underwent open appendectomy as patients presented with right iliac fossa pain. Some had involved margins for which right hemicolectomy was performed. Gonzalez Moreno et al. stated that appendectomy with good resection margins is standard of care unless lymph node involvement[26,27]. Right hemicolectomy should not be performed intraoperatively on suspicion of carcinoma of the appendix. However, if there is a presumptive diagnosis of carcinoma or intraoperative frozen section proven carcinoma, then right hemicolectomy can be performed [26,28].

In our study, recurrence was seen in 31.6%, which is high compared to the study performed by Nash et al. [17]. Some studies have shown the survival after an appendectomy or right
hemicolectomy is 60% after five years[29]. In our study, the median survival was 50 months which is comparable. The study’s limitation is due to the rarity of the disease, as only a few cases have been presented to Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH an RC). SKMCH and RC is the only tertiary care cancer centre in Pakistan, so we cannot comment on the incidence of the disease. The majority of the patients presented to us with appendectomies already performed, so not a lot is known about the surgical procedure, and thus, histopathological analyses is not satisfactory. Our hospital is not equipped to perform HIPEC and peritonectomy, which is a limiting factor in addressing the management of carcinoma of the appendix. As such, there are no existing data that describe clinicopathological features of carcinoma of the appendix in Pakistan, nor are there any studies that identify potential risk factors specific to our population. This is the first study to perform a comprehensive review of clinicopathological characteristics and survival analyses of the appendix’s carcinoma in Pakistan.

**Conclusion**

Carcinoma of the appendix is a rare entity with few published studies. Pain in the right iliac fossa mimicking acute appendicitis is the most common symptoms. The majority of the patients present late as a result of a lack of facilities. Surgery remains the treatment of choice, with appendectomy the commonest procedure. Prognosis is the disease is better if appropriate treatment is provided.

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**Conflict of interest**

There are no conflicts of interest to declare by any of the authors of this study.

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