



Research Article

Incidental Finding of Carcinoid Tumor Post Appendectomy and A Review from GCC Countries

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Abstract

Background: Few types of research in *Gulf Cooperation Council* (GCC) countries address the NETs with a gap in reported cases after appendectomy in Saudi Arabia compared to others.

Objective: This study aimed to describe the experience of a single tertiary care private hospital in the management of incidentally discovered neuroendocrine tumors after appendectomy. Additionally, review the series from nearby countries.

Design: Retrospective case series

Settings: This study was conducted at a single, private tertiary center.

Patients: 458 appendectomies were done for adult patients in Doctor Soliman Fakeeh hospital between January 2016 to December 2018.

Main Outcome Measures: Recurrence rate, survival rate, completion right hemicolectomy

Results: among 458 appendectomies, three appendiceal carcinoid tumors were identified (0.67%). The mean age of 24.3 years, 2 of them were female. All patients present with acute appendicitis and fat stranding on CT images. The carcinoid tumor was not diagnosed preoperatively. The mean diameter of the appendix was 10mm (range: 9 - 12), while the histopathology diameter of the discovered carcinoid was 5mm (range: 4 - 7). There was no postoperative complication. All patients were disease-free for a mean follow-up of 42 months. None of them received reoperation or adjuvant therapy.

Limitations: retrospective review, the low sample size of the case series.

Conclusions: laparoscopic appendectomy is sufficient for a carcinoid tumor size equal to or less than 10 mm with a favorable outcome and 3-years disease-free survival. There is no need for adjuvant therapy in incidentally discovered small-sized carcinoid tumors of the appendix. There is a demand to report the outcome of NETs among GCC countries.

Keywords: Acute appendicitis AA; Appendiceal carcinoid; Case series; *Gulf Cooperation Council* GCC countries; Laparoscopic appendectomy LA; Neuroendocrine tumor NETs; Saudi Arabia

Introduction

The appendiceal NETs has considerable interest to the surgeon in term of the need for right hemicolectomy after incidental pathological finding. It is one of the standard midgut NETs with a variable incidence rate between (0.15% - 1%) [1,2] Since 1907, when the term carcinoid was introduced by Oberndoder [3], Appendiceal NETs have received much attention and case reporting.

Female predominance is notable and explained by an increase in the rate of diagnostic laparoscopy for pelvic disease and concurrent appendectomy. The main presentation is acute abdomen with anorexia, right lower quadrant pain, and leukocytosis. The preoperative diagnosis by images is unusual, and the surgeon might operate for one appendicular NETs for every 100-300 patients [2]. The appendiceal NETs has favorable outcome and prognosis compared to other midgut NETs, which tend to relapse and recur [4]. Recent guidelines consider that a tumor more than 20 mm is a high risk for lymph node metastases and a valuable criterion for selecting patients for right hemicolectomy [4-6]. Midgut NETs witness a rise in management approach, mainly the metastatic diseases, with many therapy options as octreotide long-acting release, interferon, mTOR inhibitors, VEGF inhibitors, peptide receptor radiotherapy, and liver-directed therapy. In the case of locoregional diseases, surgical resection with R0 is still the mainstay of treatment. Few types of research in GCC countries address the NETs with a gap in reported cases after appendectomy in Saudi Arabia compared to others [7-11]. It is an overlooked post appendectomy with either patient left without follow-up or overtreated by hemicolectomy. There is a general agreement that such cases need to be managed in a multidisciplinary approach.

This paper will focus on NETs of the appendix. We reported 3 cases as the first paper from the private sector. In addition, we

review and extend the local experience that discussed the same issue.

Methods

A retrospective data review was done between January 2016 and January 2018 in the surgery department at a single tertiary center, Doctor Soliman Fakeeh Hospital (Jeddah, Saudi Arabia). Four hundred fifty-eight adult patients were included in the review who underwent appendectomies-three patients confirmed by histopathology to have appendiceal carcinoid. Further patient features evaluated include demographic data, clinical presentation, radiology, operative detail, complication, histopathology, follow-up, and survival outcome-the study approved by the Institutional Review Board of Fakeeh College for Medical Science (FCMS).

Results

A total of 458 adult patients underwent appendectomies; three (0.67%) were identified to have carcinoid tumors after histopathology examination, two of them were female. The average patient's age was 24.3 (22 - 27 years), with no comorbidities and an ASA score of 2. The duration of symptoms was less than 48 hours. All three patients present with non-complicated acute appendicitis. There was no significant leukocytosis or neutrophilia. Two patients have an average c-reactive protein level of less than 5mg/l, while the third showed a high level, 77mg/l upon presentation. CT image revealed the average appendix diameter of 10 mm (range 9-12 mm), with fat stranding but no intraperitoneal or pelvic free fluid. The carcinoid tumor was not reported on preoperative workup. The patients underwent laparoscopic appendectomy without conversion to open; the surgeon reported inflammation of the appendix in 2 patients. The average operative time is 56 minutes (30 - 105 minutes). The histopathology reports a carcinoid lesion of mean diameter 5mm (range 4 - 7 mm), at the tip of the appendix, without mesoappendix or lymph nodes. All patients have disease-free survival for three years with no evidence of recurrence on follow-up. None of them required reoperation, readmission, or received adjuvant therapy.

The result is summarized in Table 1.

Incidence rate (%)	0.67% (3 out of 458 patients)
Demographic data	
Sex ratio (male /female)	01:02
Age (mean) (years)	24.3 (22 - 27)
Comorbidities	No
ASA score	2
Symptom's duration (hours)	24 - 48 h
Complicated vs non-complicated appe.	All non-complicated
Laboratory finding preoperative	
WBC (mean) (u/L)	7.5 u/L (10.0 -4.9)
Neutrophil (%)	62.4% (61.2 - 63.9)
C-reactive protein (mean) (mg/l)	27.0 (0.5 - 77)
CT finding preoperative	
Diameter of the appendix (mean)(mm)	10 mm (9 - 12 mm)
Presence of fat stranding	Yes
Free fluid	No
Mass or phlegmon	No
Complicated vs non-complicated	Non-complicated
Operative Detail	
Surgery time (mean) (minutes)	56 minutes (30 - 105)
Approach (laparoscopic vs. open)	All laparoscopic
Stump closure (end loop vs. stapler)	Endoloop
Finding (non-inflamed vs. inflamed)	01:02
Intraoperative/postoperative complication	No
Histopathology	
Tumor type	Classic
Diameter of carcinoid (pathology) (mm)	5mm (4 - 7 mm)
Location (tip vs base)	Tip
Grade	Low
Involve mesentery or lymph node	No
Presence of fecolith	No
PNI / LVI	No
Immunohistochemistry:	

Chromogranin A & synaptophysin	Positive
AJCC / ENETs staging	T1N0M0: T1a (Tumor invades mucosa or submucosa; size ≤ 1cm), no positive node
Follow-up	
30 days morbidity and mortality	No
Disease-free survival (mean) (months)	38 months (30 - 46)
Recurrence	No
Alive	Yes

Table 1: Character of 3 patients with appendiceal carcinoid with average data.

Discussion

The rate of NETs in appendix is variable between (0.15% - 1%) [1,2]. The incidental finding after appendectomy declined in the last few years due to improved diagnosis accuracy, reducing negative appendectomy [12]. The appendix is the second common site of NETs after the small bowel taking into consideration the latter include (duodenum, jejunum, and ileum). Appendiceal carcinoids represent 18.9 % of all other NETs [3], compared to the small bowel, tend to be diagnosed early. Our patient's average age was 24 y. Early life incidence is explained by most acute appendicitis occurring in young. Others justified that by increasing the subepithelial neuroendocrine cells, which peaked in the third decades then declined with age [13]. Nevertheless, the average incidence in the fourth decade is described [3]. Most reviewers have observed female predominance since the high number of pelvic procedures in women; others suggest genetic factors [14-16]. The main clinical presentation is acute appendicitis with or without leukocytosis, as well, the inflammatory marker as CRP might be elevated. The radiological investigation preoperatively is challenging to identify small NETs. Currently, most surgical interventions for acute appendicitis are done by laparoscopy, which has the advantage of examining the entire abdomen for disease spreading, mainly the mesentery and the liver. When in doubt, the surgeon should excise the entire mesoappendix. Our routine practice is to respect the mesoappendix regardless, ensuring enough tissue if the pathology is unfavorable. Further, it helps avoid reoperation for small NETs [17].

In one review, 12 (0.43%) out of 2778 appendectomies were carcinoid. Eight (66.7%) were female, with an average age of 37.5 years. The median tumor size was 7mm with no complicated appendicitis. One patient underwent a right hemicolectomy. The median follow-up was 41.5 months with no recurrences [18]. Another five cases were reported after 1237 appendectomies (0.4%). Four of them were male and mainly present with acute appendicitis. Four out of five did open appendectomy, and one of them was reoperated to complete the excision of the mesoappendix.

All tumors occupy the tip of the appendix with a mean diameter of 0.6 cm (range: 0.3-1.0 cm). No adjuvant therapy was given. All patients were alive and disease-free during a mean follow-up of 33 months [17].

As stated in The European Neuroendocrine Tumor Society (ENETS) and the North American Neuroendocrine Tumor Society (NANETS) guidelines, lymph node metastasis is associated more with a tumor >20 mm, in which the patient will benefit from right hemicolectomy. While tumor with size between 10 - 20 mm at the base with Ki 67 index >3% and lymphovascular invasion might need attention [4-6]. None of our reported cases reach that size. Thus no further surgical resection was offered to the patient. NETs less than 1 cm have almost no risk of recurrence and commonly no need for follow-up [4].

The tip of the appendix is the familiar site of carcinoid compared to the body or base with 70-80%, 15-20%, and 7-8%, respectively. That is explained by the appendage of the subepithelial (neural) neuroendocrine cell toward the tip [3,19,20]. The survival rate and prognosis are excellent for localized disease. All three patients have disease-free survival for three years with no evidence of recurrence on follow-up. The localized carcinoid disease in the appendix is varied between 60- 90 %. Furthermore, localized, regional, and distant metastatic disease has an overall survival of 94%, 84.6%, and 33.7%, respectively [3]. There are various explanations for the favorable 5-years overall survival of appendiceal carcinoid compared to other GIT, 86% vs. 54%, respectively. It could be related to the early presentation or interpreted by the neuroectodermal origin of appendicular NETs in contrast to mucosal origin [3].

An enormous number of reported appendiceal NETs were found in the literature; however, very little was reported in GCC countries. The initial series in Saudi Arabia was reported by Guraya et al. in 2005 [9]. The locally reported series is mentioned in Table 2. The most extensive series came from Abdelaal et al. in 2017 [8]. The total number of cases in GCC was 56 patients

reported from Qatar, Saudi Arabia, and UAE with 32, 15, and 9, respectively [7- 10]. By adding our series, there will be 18 cases from KSA. Three out of 56 underwent a second surgery with right hemicolectomy because of a positive margin-no reported recurrence-one reported case presented with metastatic disease and died without intervention [10]. Even though one local review of 480 appendectomies histopathology between 2011-2014 did not show any carcinoid tumor [11], we reported a series of three patients from 458 specimens. It is the first report from the private sector in Saudi Arabia. Our practice is to routinely discuss the oncology cases in the multidisciplinary approach (tumor board) and achieve agreement on a patient management plan. In conclusion, laparoscopic appendectomy is sufficient for a carcinoid tumor of size equal to or less than 10 mm with a favorable outcome and 3years disease-free survival of 100%, without the need for adjuvant therapy. There is a demand to report the outcome of NETs in GCC countries, mainly for those patients who required a second completion resection either because positive margin or more than 20 mm tumors.

	Guraya et al [9]	Anwar et al. [7]	Abdelaal et al [8]	Albishi et al [10]
Year	2005	2014	2017	2020
country	Saudi Arabia	UAE	Qatar	Saudi Arabia
Series number /total appendectomies	9/1547	9/964	32/13641	6 / 444 (tumor cases)
Incidence rate	0.60%	0.90%	0.23%	NA
Mean age	29.8 y	28.7 y	25.3 ± 7.9 y	NA
	(17 - 51)		(14 - 64)	(19 - 86)
Male: female	01:01.2	02:01	03:01	01:01
Tumors mean size	9.5 mm	3.3 mm	4.86 ± 3.18 mm	(2 - 45 mm)
	(4 - 19)	(1 - 8)	(1.5 - 13)	
2 nd surgery (hemicolectomy)	1 (Positive margin)	0	1 (Positive margin)	1
Median follow up	Seven years (4 - 10 y)	22 months (12-26 m)	2 - 13 years	NA
Recurrence	0	0	0	0
Systemic disease	0	0	0	1 (at presentation, died without intervention)
Overall survival	alive	alive	alive	alive

Table 2: locally reported cases in GCC countries.

References

1. Khan MH, Sultana J, Ahsan T, Ahsan SA (2020) Role of Laparoscopic Appendectomy in the Treatment of Acute Appendicitis and Its Complications. *Mymensingh Med J* 29: 887-894.
2. Griniatsos J, Michail O (2010) Appendiceal neuroendocrine tumors: Recent insights and clinical implications. *World J Gastrointest Oncol* 2: 192-196.
3. Sandor A, Modlin IM (1998) A retrospective analysis of 1570 appendiceal carcinoids. *Am J Gastroenterol* 93: 422-428.
4. Boudreaux JP, Klimstra DS, Hassan MM, Woltering EA, Jensen RT, et al. (2010) The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors: well-differentiated neuroendocrine tumors of the Jejunum, Ileum, Appendix, and Cecum. *Pancreas* 39: 753-766.
5. Ricci C, Ingaldi C, Alberici L, Brighi N, Santini D, et al. (2019) Histopathological diagnosis of appendiceal neuroendocrine neoplasms: when to perform a right hemicolectomy? A systematic review and meta-analysis. *Endocrine* 66: 460-466.
6. Pape UF, Niederle B, Costa F, Gross D, Kelestimur F, et al. (2016) ENETS Consensus Guidelines for Neuroendocrine Neoplasms of the Appendix (Excluding Goblet Cell Carcinomas). *Neuroendocrinology* 103: 144-152.
7. Anwar K, Desai M, Al-Bloushi N, Alam F, Cyprian FS (2014) Prevalence and clinicopathological characteristics of appendiceal carcinoids in Sharjah (United Arab Emirates). *World J Gastrointest Oncol* 6: 253-256.
8. Abdelaal A, El Ansari W, Al-Bozom I, Khawar M, Shahid F, et al. (2017) Frequency, characteristics and outcomes of appendicular neuroendocrine tumors: A cross-sectional study from an academic tertiary care hospital. *Ann Med Surg (Lond)* 21: 20-24.
9. Guraya SY, Khairy GA, Ghallab A, Al-Saigh A (2005) Carcinoid tumors of the appendix. Our experience in a university hospital. *Saudi Med J* 26: 434-437.
10. Albishi AM, Mostafa AMM, Ali HM, Alhagawi YA, Bazeed MF, et al. (2020) Incidence of Gastrointestinal Neuroendocrine Tumor: Case Series, Armed Forces Hospital Southern Region, Hospital-Based Tumor Board Registry. *Case Rep Oncol Med* 2020: 8819392.
11. Jat MA, Al-Swailmi FK, Mehmood Y, Alrowaili M, Alanazi S (2015) Histopathological examination of appendectomy specimens at a district hospital of Saudi Arabia. *Pak J Med Sci* 31: 891-894.
12. Addiss DG, Shaffer N, Fowler BS, Tauxe RV (1990) The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 132: 910-925.
13. Shaw PA (1991) The topographical and age distributions of neuroendocrine cells in the normal human appendix. *J Pathol* 164: 235-239.
14. Moertel CG, Weiland LH, Nagorney DM, Dockerty MB (1987) Carcinoid tumor of the appendix: treatment and prognosis. *N Engl J Med* 317: 1699-1701.
15. Modlin IM, Sandor A (1997) An analysis of 8305 cases of carcinoid tumors. *Cancer* 79: 813-829.
16. Modlin IM, Zucker KA, Zdon MJ, Sussman J, Adrian TE (1988) Characteristics of the spontaneous gastric endocrine tumor of mastomys. *J Surg Res* 44: 205-215.
17. Tchana-Sato V, Detry O, Polus M, Thiry A, Detroz B, et al. (2006) Carcinoid tumor of the appendix: a consecutive series from 1237 appendectomies. *World J Gastroenterol* 12: 6699-6701.
18. Barut B, Gönültaş F (2019) Carcinoid tumors of appendix presenting as acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 25: 510-513.
19. Roggo A, Wood WC, Ottinger LW (1993) Carcinoid tumors of the appendix. *Ann Surg* 217: 385-390.
20. Syracuse DC, Perzin KH, Price JB, Wiedel PD, Mesa-Tejada R (1979) Carcinoid tumors of the appendix. Mesoappendiceal extension and nodal metastases. *Ann Surg* 190: 58-63.