



Frequency, characteristics and outcomes of appendicular neuroendocrine tumors: A cross-sectional study from an academic tertiary care hospital



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ARTICLE INFO

Article history:

Received 17 May 2017

Received in revised form

16 July 2017

Accepted 17 July 2017

Keywords:

Carcinoid

Appendectomy

Appendix

Neuroendocrine tumor

ABSTRACT

Background: Appendicular neuroendocrine tumors (NET, Carcinoid tumors) of the appendix are rare and mostly diagnosed incidentally on the post-operative histopathological examination. NET are usually associated with good 5-year survival rates. We aimed to assess our experience for the diagnosis and management of NET over 11 years.

Method: It is a retrospective chart review of all clinically suspected patients with acute appendicitis who underwent emergent appendectomy with intention to treat between January 2004–December 2014, and were clinically followed up until 2016.

Results: During the study period, a total of 13641 patients underwent emergency appendectomy, of which 32 were histologically confirmed NET. The mean age of the NET cases was 25.3 ± 7.9 years; 78% were males and all were clinically presented with acute appendicitis. The mean leucocyte was $15 \pm 14 \times 10^9$ per Liter, and mean tumor size was 4.86 ± 3.18 (ranged 1.5–13) mm. The median length of hospital stay was 4 (2–15) days. One patient had right hemicolectomy; diagnosed with right colonic cancer with NET being an incidental finding as part of histopathological assessment. Another patient required a second stage procedure; he was diagnosed as goblet cell carcinoid with positive margin. None of the patients died 30-day postoperatively and all of them survived on clinical follow-up that ranged between 2 and 13 years.

Conclusion: Carcinoid tumors of the appendix are rare and typically diagnosed incidentally. Detailed examination of routine appendectomy specimens is the key for diagnosis. Simple appendectomy suffices for tumors <2 cm for adequate clearance. Appendicular carcinoid tumors are associated with good long-term outcomes.

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1. Introduction

Appendicular Neuroendocrine tumors (NET) are neoplasms of the appendicular sub-epithelial neuroendocrine cells [1]; the majority of which are benign and rarely metastasize. NET comprises the most common neoplasm of the appendix [2]. Nevertheless, NET are rare neuroendocrine neoplasms that are encountered incidentally in 1 out of 200–300 appendectomies [3]. The scarcity of NET has been demonstrated globally for instance 0% incidence in Saudi

Arabia (2011–2014) [4]; 0.48% in Tunisia (1995–2001) [5]; and 0.45% in Turkey [6].

NET demonstrate no specific clinical presentation [2], being generally asymptomatic; or present as acute appendicitis, where NET are diagnosed incidentally after appendectomy [7,8]. Most NET are located at the tip of the appendix. They are usually minute, measuring <1 cm, and rarely grow >2 cm in diameter [9]. Whilst NET customarily behaves as benign, they have the prospect for malignancy [10]. Still, the long-term prognosis of incidental NET is good [11], with very low evidence of recurrent disease [12].

Still the published literature reveals gaps about the prevalence of NET. First, much of the literature represents single case reports [2,3]. However, some investigators analyze rather modest numbers

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of appendectomy cases, ranging from 480 [4] or 964 appendectomies [13] to <10000 appendectomies (e.g. 2197, Saylam et al., 2011 [6]; 6777, Coşkun et al., 2006 [14]; 9584 Beyrouti et al., 2004) [5]). Interestingly, the current study bridged this gap and appraised a much larger sample of appendectomies ($n = 13641$). Secondly, in terms of geographical distribution, there exists few published reports on NET from the Eastern Mediterranean Region such as Turkey [6,14], and Tunisia [5]. However, only few published studies on NET are available from the Arab Middle Eastern region including Saudi Arabia [4] and United Arab Emirates [13]. The incidence of NET varies across different studies, and the current study is seminal in detailing the frequency of these tumors in our region. Given that the appendix is one of the most common gastrointestinal tract sites for carcinoids [15], it is important to assess the occurrence and clinico-pathological profile of NET in our population. Herein, we assessed the frequency, clinical, ultrasound, computerized tomography (CT) and histopathology characteristics of NET in the State of Qatar.

2. Methods

It is a retrospective chart review of all clinically suspected patients with acute appendicitis who underwent emergent appendectomy with intention to treat between January 2004 and December 2014 and was clinically followed up until 2016 in some cases. Histopathological records of 13641 patients who underwent appendectomy at our institution were retrieved and reviewed to determine the prevalence rate of NET based on histopathological findings. The medical records of patients histologically confirmed to have NET were comprehensively assessed for the pre-operative clinical presentation, operative and postoperative findings. These clinico-pathological data included demographics, clinical presentation such as symptoms and elicited signs, modality of diagnosis (ultrasonography, CT scan and histological findings), hospital length of stay, treatment and post-operative complications. For all patients, the pathology from the initial resection was utilized to characterize the tumor pathology i.e. tumor location, tumor size, proximal and mesenteric circumferential margin, lymph node involvement and tumor differentiation in line with others [8]. Patients without clinical or pathologic evidence of lymph node involvement were considered to be negative for lymphovascular and/or perineural infiltration [8]. The histopathological categorization of these tumors was based on the AJCC Cancer Staging Manual, 7th Edition [16]. Ethical approval was obtained from the Institutional Review Board, Medical Research Center (IRB# 14516/14) at Hamad Medical Corporation, Qatar. Data were presented as proportions, mean \pm standard deviation or median and range. Data analysis was carried out using the Statistical Package for Social Sciences version 20 (SPSS Inc., Chicago, IL, USA).

3. Results

Of the total 13641 resected appendices, 32 cases were diagnosed with carcinoids, generating an incidence of 0.23%. Table 1 depicts the demographic and clinical characteristics of the patients. The mean age of the cases was 25.3 ± 7.9 years (range 14–64); 78% were male with male to female ratio of 3:1. There observed equal distribution of NET among non-Arab (59.4%) and Arab (40.6%) nationalities. The most frequent presenting symptom was localized pain (90.6%), followed by shifting pain (53%) and other symptoms (such as nausea, vomiting, rectal bleeding and anorexia) were found in 75% patients. The common signs were localized tenderness (90.6%), fever (25%), generalized tenderness (6.3%), and abdominal distension (6.3%). Laparoscopic appendectomy was the most common procedure undertaken (62.5%) followed by open

Table 1
Demographic and Clinical Characteristics of the sample ($n = 32$).

Variables	n (%)
Patient Characteristics	
Demographic	
Males	25 (78.1%)
Age (years, mean \pm SD)	25.3 ± 7.9
Nationality	
Arabs ^a	13 (40.6%)
Non-Arabs ^b	19 (59.4%)
Clinical features	
Symptoms	
Localized pain	29 (90.6%)
Shifting pain	17 (53.1%)
Other Symptoms ^c	24 (75.0%)
Signs	
Localized tenderness	29 (90.6%)
Generalized tenderness	2 (6.3%)
Palpable mass in right iliac fossa	1 (3.1%)
Fever	8 (25.0%)
Abdominal distension	2 (6.3%)
Types of surgical procedures	
Open Appendectomy	10 (31.2%)
Laparoscopic Appendectomy	20 (62.5%)
Laparoscopic Procedure converted to Open	1 (3.1%)
Formal Right Hemicolectomy	1 (3.1%)
Length of hospital stay (days, median&range)	4 (2-15)

^a Qatar, Egypt, Jordan, Sudan, Palestine, Iran, Lebanon, India.

^b Pakistan, Nepal, Bangladesh, Sri Lanka, Philippines.

^c Nausea, vomiting, rectal bleeding, anorexia.

appendectomy (31.2%). One case had a midline laparotomy, and another case required a formal right hemicolectomy (patient was diagnosed as adenocarcinoma of the right ascending colon, where NET was incidentally discovered). Only one case underwent second stage procedure, as this patient was diagnosed for goblet cell carcinoid with positive proximal and mesenteric circumferential margins (hence was re-operated upon, where right hemicolectomy was undertaken). The median length of hospital stay was 4 (2–15) days.

Table 2 shows the findings of the laboratory investigations as well as imaging characteristics of the patients. NET patients exhibited mild leukocytosis and normal bilirubin levels. About half of the cases (43.8%) required preoperative abdominal ultrasonography for definitive diagnosis, where 71.4% had ultrasound features of appendicitis, 64.3% cases had free fluid, and only one (7.1%) case had appendicular mass. Preoperative abdominal CT scan was undertaken for five patients, of which all had minute pockets free air, while 2 cases had other findings (e.g. thickening of ceecal wall or terminal ileum).

Table 3 demonstrates the histopathologic characteristics of the

Table 2
Investigations and imaging characteristics of the sample ($n = 32$).

Investigations	
Laboratory	
WBC (10^9 per Litre) (mean \pm SD)	15 ± 14
Bilirubin (mg/dl) (mean \pm SD)	12.8 ± 10
Preoperative abdominal Ultrasound	
Features of appendicitis	10 (71.4%)
Free fluid	9 (64.3%)
Appendicular mass	1 (7.1%)
Preoperative abdominal CT scan	
Features of appendicitis	5 (15.6%)
Appendicular mass	3 (60.0%)
Free fluid	5 (100.0%)
Free air	1 (20.0%)
Other findings (thickening of ceecal wall or terminal ileum)	5 (100.0%)
	2 (40.0%)

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