Pediatric Surgery International (2019) 35:1427–1430
https://doi.org/10.1007/s00383-019-04575-1

ORIGINAL ARTICLE

Management of pediatric appendiceal carcinoid: a single institution experience from 5000 appendectomies

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Accepted: 12 September 2019 / Published online: 25 September 2019

Abstract

Aim of the study Appendiceal carcinoid (neuroendocrine tumor or NET) is a rare neuroendocrine neoplasm often found incidentally following appendectomy for appendicitis. Surgery for appendicitis is currently under scrutiny and children are increasingly managed conservatively with antibiotics alone. Herein, we aimed to review our experience with the management of appendiceal carcinoids at our institution.

Methods Following ethical approval, we reviewed the charts of all patients who underwent appendectomy for appendicitis at our institution between 2000 and 2018. The pathology registry was consulted to identify children diagnosed with appendiceal carcinoid. Outcome measures included incidence, demographics, and management.

Main results During the study period, 32 children (23 female) had an appendiceal carcinoid confirmed at pathology. Of these, 13 were initially treated with appendectomy (total of 5,059 appendectomies: 0.3% incidence). The other 19 had an appendectomy elsewhere by an adult general surgeon and were referred to our institution for further management. Overall, the mean age at diagnosis was 13 ± 2.7 years and all patient had a preoperative diagnosis of appendicitis, none of suspected carcinoid. Most children (75%) had acute non-perforated appendicitis. The overall mean size of the lesion was 1 ± 0.9 cm, with a > 2 cm lesion in 3 patients. Following diagnosis, 12 children (38%) underwent an ileocolic resection, due to carcinoid size, invasiveness, and margin clearance.

Conclusions In our cohort, the incidence of appendiceal carcinoid among children with appendicitis is very low. Most carcinoids are small, located at the tip, associated with non-perforated appendicitis, and present in girls. Most were treated with appendectomy alone, with more extensive surgery performed in one third of children.

Keywords Appendicitis · Appendicular carcinoid · Non-operative · Antibiotic · Appendicectomy

Introduction

An appendiceal carcinoid is a rare neuroendocrine tumor, also categorized as gastrointestinal neuroendocrine neoplasia, that represents the most common malignancy of the appendix [1, 2]. It affects children and young adults with a peak during the second and third decade of life and it is typically identified during the post-operative pathology examination of an appendix removed for a diagnosis of acute appendicitis [3, 4]. The preoperative detection of an appendiceal carcinoid is uncommon as shown by a radiology study that reported no carcinoid prospectively identified on preoperative CT scans [5]. This study was conducted in adults, and the authors speculate that small size and location of the lesions made the preoperative detection impossible [5]. This is even more true for children with acute abdominal pain, where ultrasonography is the routine imaging modality, and small lesions may be easily missed.

Appendicitis is the most common surgical condition of the abdomen in the pediatric population and it is diagnosed in 20–30% of children evaluated urgently for abdominal pain [6, 7]. Various aspects of the management of acute appendicitis remain controversial and lack consensus [8]. Surgery has been the standard treatment for acute appendicitis for

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decades, but recently, there has been growing evidence to suggest that antibiotics alone without appendectomy might be an effective alternative. A meta-analysis of five randomized controlled trials in adults showed that antibiotic therapy alone represents a safe and efficacious treatment option for acute uncomplicated appendicitis, and is associated with lower incidence of complications [9]. This experience in adults has been tested also in children and non-operative treatment of acute uncomplicated appendicitis with antibiotics alone has been reported to be a valid alternative to surgery [10–18]. At present, there are randomized controlled trials being conducted to evaluate the effectiveness of this approach in children with acute appendicitis [19–21]. In this context of a possible change of management for these patients, the question on the risk of overlooking a carcinoid tumor arises.

The aim of the present study was to review our institutional experience with carcinoid tumors of the appendix, to establish their incidence and epidemiology, and to review their management in a large volume institution. This study would add to the current debate on antibiotic therapy without surgery for acute appendicitis in children.

Methods

Ethical approval was obtained for this study (REB 1000061801). All pediatric patients (<18 years of age) managed for appendiceal carcinoid at our Institution between 2000 and 2018 were included. For comprehensive patient collection, we searched our institutional operative registry for all patients who underwent appendectomy during the study period as well as the pathology registry for all patients with a postoperative diagnosis of appendiceal carcinoid. Patient data included demographics, pathology, diagnostic investigations, treatment and follow-up. Descriptive statistics were used to analyze perforated and non-perforated appendicitis patients, and to determine patient postoperative outcomes. Data are reported as mean ± SD or median (range) as appropriate.

Results

During the study period, 32 children (female, $n = 23$; 71%) had an appendiceal carcinoid diagnosed at post-operative pathology (Table 1). Of these, 13 patients had surgery at our institution, whereas the other 19 had an appendectomy performed elsewhere by an adult general surgeon and were referred to our institution for post-operative management once the diagnosis of carcinoid was made at histology. At our institution, 5059 appendectomies were performed for acute appendicitis during the study period, so that the incidence of appendiceal carcinoid was 0.3%.

Table 1 Demographics of patients and tumor characteristics

Gender	
Male	9
Female	23
Age	
0–10	5
11–15	21
16–18	6
Pre-operative diagnosis	
Uncomplicated appendicitis	24
Perforated appendicitis	8
Pre-operative imaging	
US	29
CT	3
Surgery	
Appendectomy only	20
IC/RHC	12
Tumor size (cm)	
0–1 cm	20
1.0–2.0 cm	7
> 2 cm	5
Surveillance imaging	
US	0
CT	17
MRI	5

IC Ileocolic resection, *RHC* right hemicolectomy

Overall, the mean age at the time of diagnosis was 13 ± 2.7 years and all patients were preoperatively diagnosed with appendicitis. In no patient, the appendiceal carcinoid was identified preoperatively by ultrasonography and/or CT scan, the imaging studies used to diagnose appendicitis.

Most children with appendiceal carcinoid ($n = 24$, 75%) had a non-perforated appendicitis. The overall mean size of the lesion was 1 ± 0.9 cm, with 3 patients having lesions of > 2 cm size at the pathology analysis. Of the 32 children, 16 (50%) had the tumor at the tip of the appendix. Following diagnosis, 12 children (38%) underwent more extensive surgery (ileocolic resection, $n = 6$; right hemicolectomy, $n = 6$) due to carcinoid size, extent of tumor/invasiveness, and tumor at the resection margin.

Patients were followed up for a median of 6 months (range 1 month to 5 years). None of the patients were followed beyond 5 years, and 2 patients were lost to follow up. Tumor characteristics of patients that were followed varied, however, monitoring imaging modalities were CT scan, and serum 5HIAA and no patient was found to have a recurrence (Table 2).

Table 2 Surveillance data

Surveillance time (*n*)	Carcinoid size (cm)	Surveillance modality
1–6 months (17)	0.3–2.2	CT, 5-HIAA
6 months to 2 years (4)	0.25–1.8	CT, 5-HIAA
2–5 years (11)	0.7–4	CT, 5-HIAA

Discussion

This single center study shows that the risk of an appendiceal carcinoid in children with acute appendicitis is as low as 1 in 300 and that in the majority of cases the appendectomy is sufficient to eradicate the lesion.

Our institutional results are comparable to previous studies. A systematic review and meta-analysis of appendiceal carcinoid tumors in children has reported a similar incidence of carcinoid of 0.3% from 958 appendectomies [22]. Moreover, our study reports a similar female preponderance and age at diagnosis to those reported in the systematic review [22].

None of our patients was diagnosed with appendiceal carcinoid pre- or intra-operatively. This is also in line with most of the reports in the literature [22]. In pediatrics, the routine use of imaging studies to diagnose or exclude appendicitis is variable across countries and not unanimously accepted [8]. Nonetheless, it is widely recognized that in case imaging is required, the standard modality for children with suspected appendicitis is ultrasonography instead of CT [23]. The rationale behind this choice for avoiding CT scans in the pediatric population is the risk of ionizing radiation and efforts have been made to increase the use of ultrasonography [24–26]. This could also be the reason why in pediatric patients the diagnosis of appendiceal carcinoid is not made on preoperative imaging. Interestingly, most patients with appendiceal carcinoids in our series presented with acute appendicitis. This is similar to other series that also reported a lower incidence of carcinoids in patients with perforated appendicitis [3, 22].

The surgical management of appendiceal carcinoid in pediatric population remains controversial and in recent years, we have observed in the literature an inclination to limit extensive resection beyond appendectomy. The North American Neuroendocrine Tumor Society and European Neuroendocrine Tumor Society have recommended a right hemicolectomy for a tumor size > 2 cm, or > 3 mm mesoappendiceal invasion, or for tumors not amenable to R0 resection [27, 28]. A nationwide study based on the database of the National Cancer Institute Surveillance, Epidemiology, and End results analyzed all cases of appendiceal tumors in children in the United States between 1973 and 2011 and concluded that limited appendectomy may be an adequate treatment for pediatric appendiceal tumors [29]. In fact, according to this study, more extensive surgery involving a right hemicolectomy and lymph node sampling based on the presence of aggressive tumor type, greater disease severity and larger tumor size may not increase patient survival, and may instead be associated with a greater operative risk [29]. At our institution, a third of patients underwent more extensive resection than appendectomy alone due to size, invasiveness, and tumor at resection margin. However, examining our series, most of these cases were managed during the first decade of our study period.

Among the malignant tumors that can arise from the appendix, carcinoids have the highest incidence [29]. There is no doubt that the mainstay treatment of an appendiceal carcinoid is surgical resection. However, with the antibiotic treatment alone becoming more popular for uncomplicated appendicitis, the risk of leaving a malignancy untreated has started a debate on how to follow-up patients managed non-operatively. At present, most studies and ongoing trials include a clinic follow-up at different time-points, which is obviously important to assess the efficacy of the non-operative management. Moreover, it is unclear whether patients with appendiceal carcinoids would be identified at a later stage, and whether a delay in treatment would lead to a more extensive resection than appendectomy alone. A Japanese study comparing long-term outcomes between operative and non-operative treatment of uncomplicated appendicitis in children, was designed with an abdominal ultrasound scan for the conservatively treated patients, 1–3 months after successful medical treatment of appendicitis [30]. However, this strategy should be accurately evaluated as it implies costs for follow-up imaging studies and radiological expertise in interpreting the images of an appendix that in many cases would still not be normal. Given the low incidence of appendiceal carcinoid in children and the low risk of lymphovascular or mesenteric involvement in these cases, at present the risk of leaving an unresected carcinoid in situ is considered negligible [21]. The ongoing randomized controlled trial should shed light on this and also inform on whether children that are excluded or unresponsive to the non-operative treatment are the ones with the highest risk of having a malignancy as underlying cause.

Furthermore, review of our institutional data shows that there are no established surveillance guidelines for appendiceal carcinoids. As per our data, patients were followed anywhere from 1 month to 5 years. Tumor characteristics were highly variable, and there was no correlation found between any specific tumor characteristic and surveillance time period. At our institution, CT scan or 5HIAA were used for surveillance. Previous studies have shown the limited value of post-operative surveillance with CT, octreotide scan, or biochemical markers such as serum 5HIAA, and Chromogranin A [22, 28, 31, 32].

We acknowledge that our study is limited as it is a single institution retrospective review with a relatively small cohort compared to multicenter series. Nonetheless, this study confirms the demographics and clinical characteristics of appendiceal carcinoids that have been reported previously and the change in management and surveillance over the years due to the change of protocols and international guidelines.

In conclusion, the incidence of appendiceal carcinoid among children with appendicitis is very low. In our cohort, most carcinoids were small, located at the tip, associated with non-perforated appendicitis, and more commonly found in girls. Appendectomy alone is sufficient in the majority of patients, but the length and modality of follow-up for these patients remain controversial.

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