

Hidden hazard in appendix in children: Carcinoid tumors

Yusuf Atakan Baltrak¹, Onursal Varlikli²

From Specialist Pediatric Surgery, Departments of Pediatric Surgery, ¹Kocaeli Derince Education and Research Hospital, Derince, Kocaeli, ²Sakarya Education and Research Hospital, Sakarya, Turkey

Correspondence to: Yusuf Atakan Baltrak, Department of Pediatric Surgery, Kocaeli Derince Education and Research Hospital, Derince, Kocaeli, Turkey. E-mail: dratakanbaltrak@gmail.com

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ABSTRACT

Introduction: Carcinoid tumors (CT) are the most common tumors of the appendix. The incidence of CT of the appendix is generally 1–2 in every 1000 appendectomy material. **Objectives:** The objectives of the study were to discuss the follow-up and treatment of CT of the appendix in the specimen of patients who underwent an appendectomy. **Materials and Methods:** This retrospective study enrolled the patients who were diagnosed with CT of the appendix as a result of an examination of the appendix specimen after the patients underwent an appendectomy. All the patients, who underwent appendectomy in the pediatric surgery clinic of our hospital between November 2015 and November 2018, were included in the study. Patients' demographic characteristics, clinical findings, pre-operative laboratory and imaging results, location, diameter and size of the tumor, mesoappendix invasion status, mitotic index and Ki-67 elevation, hospital stay duration, surgical types and complications, and results of laboratory and imaging tests were evaluated. **Findings:** Eight of the 621 patients (1.2%) who underwent an appendectomy were diagnosed with CT of the appendix. The median age of the patients was 13 years (range, 11–16 years). Of the eight patients, five (62.5%) were female and three (37.5%) were male. All patients presented to our clinic with abdominal pain. No surgical complications were observed during the operation and in the early post-operative period. The mean hospital stay was 2.7 days (2–5 days). In all the patients, the tumor size was <2 cm, the surgical margins were clean, the mitotic index was <2%, the Ki-67 index was below 1%, and the tumor had not spread to the mesoappendix. Only in one of the patients, the CT was located in the appendix radix; in the other seven patients, the tumor was in the middle and end of the appendix. **Conclusion:** CT of the appendix are clinically similar to acute appendicitis but may be found incidentally during other surgical procedures other than an appendectomy. Diagnosis is made after the pathological specimen diagnosed with CT is histopathologically evaluated. The size, diameter, and depth of the tumor, mesoappendix invasion, mitotic index, and Ki-67 elevation are used in the evaluation and treatment of the tumor.

Key words: Appendix, Carcinoid Tumor, Children

Carcinoid tumors (CT) are the most common tumors of the appendix [1,2]. The incidence of CT of the appendix is generally 1–2 in every 1,000 appendectomy material [3]. CTs are detected by a pathological examination after another procedure (appendectomy). The diameter of CT in children is usually <2 cm [4]. Similar to acute appendicitis, CT of the appendix may cause pain in the lower abdominal quadrant. The diagnosis should be confirmed histologically. The present study aims to discuss the follow-up and treatment of CT of the appendix in the specimen of patients who underwent appendectomy due to acute appendicitis.

MATERIALS AND METHODS

This retrospective study enrolled the patients who were diagnosed with CT of the appendix as a result of an examination of the appendix specimen after the patients underwent an appendectomy. All the patients, who underwent appendectomy

in the pediatric surgery clinic of our hospital between November 2015 and November 2018, were included in the study. Patients' demographic characteristics, clinical findings, pre-operative laboratory and imaging results (Fig. 1), location, diameter and size of the tumor, mesoappendix invasion status, mitotic index and Ki-67 elevation (Fig. 2), cromogranin marker (Fig. 3), hospital stay duration, surgical types and complications, and results of laboratory and imaging tests were evaluated retrospectively. For this retrospective study, the ethics committee decision no. 3021156 dated August 17, 2018 was obtained from the Ethical Committee Board of Derince Training and Research Hospital.

RESULTS

Of the 621 patients, who underwent an appendectomy in the pediatric surgery clinic during the study period, eight were diagnosed with carcinoid tumor of the appendix. The median age of the patients was 13 years (range, 11–16 years). Of the eight

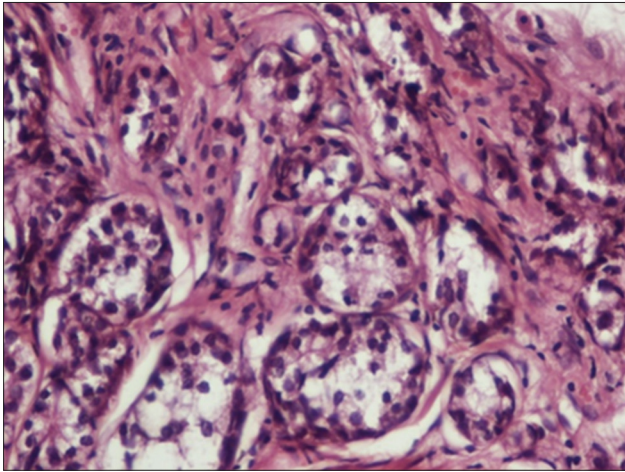


Figure 1: Appendix carcinoid tumor histopathological appearance

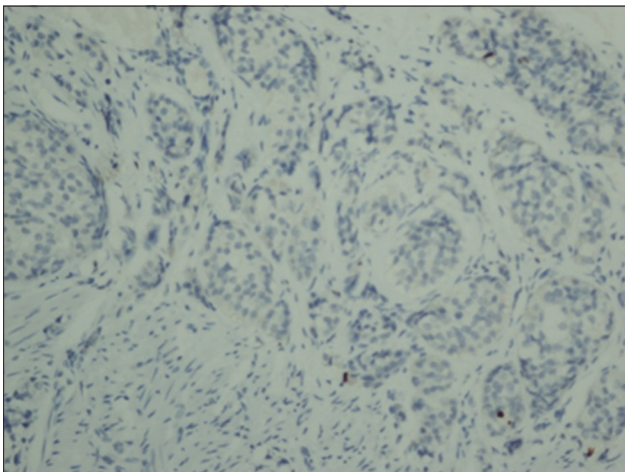


Figure 2: Carcinoid tumor Ki-67

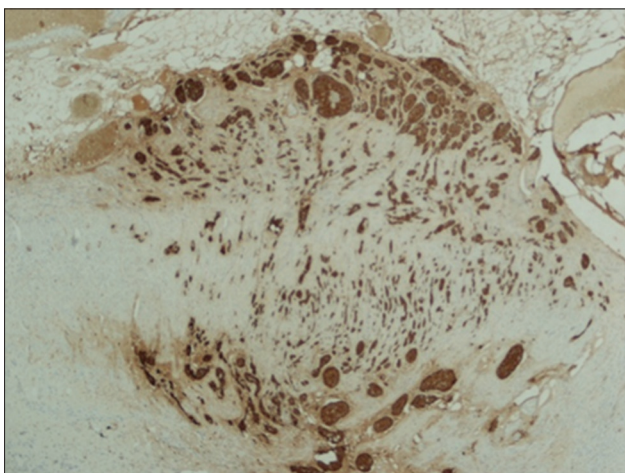


Figure 3: Carcinoid tumor chromogranin marker

patients, five (62.5%) were female and three (37.5%) were male. All patients presented to our clinic with abdominal pain. Four patients (50%) underwent appendectomy by the laparoscopic method and four (50%) underwent appendectomy with the open surgical method.

As a result of the examinations performed at the time of admission to the hospital emergency department, it was determined

that five patients (62.5%) had a leukocyte count of $>10,000/\text{mm}^3$ and seven patients (87.5%) had an acute phase reactant (C-reactive protein) $>5 \text{ mg/dl}$. A total of six patients underwent whole abdominal ultrasound sonography (USG). On the other hand, two patients underwent computed tomography of the abdomen. In one patient undergoing USG, the appendix was not visible. Only in one of the patients, there was the evidence of palpable mass during pre-operative anesthesia.

No surgical complications were observed during the operation and in the early post-operative period. The mean hospital stay was 2.7 days (2–5 days). Histopathological diagnosis of the patients was reported after 15 days. In all the patients, the tumor size was $<2 \text{ cm}$, the surgical margins were clean, the mitotic index was $<2\%$, the Ki-67 index was $<1\%$, and the tumor had not spread to the mesoappendix. Only in one of the patients, the carcinoid tumor was located in the appendix radix; in the other seven patients, the tumor was in the middle and end of the appendix. All patients underwent an appendectomy. No recurrence or metastasis has been detected to date in the follow-up of the patients (Table 1).

DISCUSSION

Although one of the rare cancer types, CT is more common in children and adolescents and is seen in the gastrointestinal tract [5]. CTs, generally, have a good prognosis; however, the diameter and depth of the mass are essential for metastasis [6]. In several studies, the incidence of CTs of the appendix in surgical specimens ranged from 0.08% to 0.7% [5-8]. In 1964, Willox argued that 0.2–0.5% of the surgically removed specimens in children contained CT [9]. Doede *et al.* and D'Aloe *et al.* reported the incidence of CT in the pathological specimens of children between 0.001% and 0.17%. These results indicate the rarity of the incidence of CTs in the pediatric age group [10,11]. CT is more common in White girls in the 12–13 age range [12,13]. Some authors reported CT at 3 years of age.

Clinical manifestations of CT of the appendix are similar to acute appendicitis. However, in some cases, they can be detected by coincidence in other surgeries due to other diagnoses. In most cases, recurrent abdominal pain attacks have been reported to indicate partial obstruction of the appendix lumen by a tumor. Redness, diarrhea, and heart disease are rare symptoms of carcinoid. In general, the first symptoms are associated with liver or retroperitoneal metastasis [8-17].

At present, the depth and size of CTs are examined more frequently in terms of tumor behavior [4]. In 75% of cases, the tumor is located at the top of the appendix; in 20% and 5%, it is located in the middle and at the base of the appendix, respectively [13]. The mean diameter of CTs is 6 mm. In general, CTs have a measurement of $<10 \text{ mm}$, which is similar to acute appendicitis. CTs larger than 20 mm at the base of the appendix indicate peritonitis table [12,18,19]. If the tumor is smaller than 2 cm and penetrates the serosa, the preferred treatment is appendectomy, regardless of location. Tumors $<2 \text{ cm}$ are extremely unlikely to recur after an appendectomy. Tumors with a diameter of 2 cm or more may have widespread metastasis when

Table 1: Findings of patients included in the study

Gender	Age	Tumor size (mm)	Tumor location	Mitotic rate (%)	Ki 67- index (%)	Chromogranin marker
M	11	12	Distal	>2	>1	+
F	11	11	Distal	>2	>1	+
F	12	13	Distal	>2	>1	+
M	13	14	Middle	>2	>1	+
F	14	14	Distal	>2	>1	+
F	14	12	Middle	>2	>1	+
M	15	16	Proksimal	>2	>1	+
F	16	14	Distal	>2	>1	+

detected. The invasive properties of these tumors are well known, but lymph node metastasis has been reported in only 4–5% of the cases [12]. CTs of the appendix are smaller and less aggressive in the pediatric age group.

Treatment depends on the size and region of the tumor. An appendectomy is sufficient for tumors smaller than 2 cm. However, if the tumor is larger than 2 cm, and especially when mesoappendix involvement is present, or in patients with residual tumor at the resection border, right hemicolectomy is recommended [10]. Deode *et al.* [8] reported the indications of right hemicolectomy in controversial cases as mesoappendix involvement, a tumor located at the base of the appendix after positive surgery, cecum involvement, mitotic index, and Ki-67 elevation. Some researchers, on the other hand, have considered perineural, lymphatic, and mesoappendix invasion as the indications of right hemicolectomy [14-16]. Ki-67 is used to predict both prognosis and local and distant metastasis. <2% Ki-67 is a good criterion. Mitotic index is usually <1%; however, the prognosis is poor if it is 2% or 3%. This information should be included in the pathology report.

CONCLUSION

CTs are the most common tumors of the appendix. They are more common in white girls with a mean age of 13 years. CTs are clinically similar to acute appendicitis but may be found incidentally during other surgical procedures other than an appendectomy. Diagnosis is made after the pathological specimen diagnosed with CT is histopathologically evaluated. The size, diameter, and depth of the tumor are used in the evaluation of the tumor. The localized disease has an excellent prognosis while the prognosis is worse in patients with metastasis.

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