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Original Article

Surgery Section

Carcinoid Tumors of the Appendix – Last Decade Experience

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ABSTRACT

Introduction: Carcinoid of the appendix is a rare clinical entity in childhood and usually has a good clinical outcome. The impact of the operative preparations appendix ranges between 0.1-0.9%. The aim of our study is to report the experiences of our department in the management of appendiceal carcinoid tumors in children.

Materials and Methods: Data of all patients aged 15 y or less who underwent appendectomy at the 2nd Department of Pediatric Surgery of Aristotle University of Thessaloniki between January 2004 and February 2014 were evaluated for the existence of appendiceal carcinoid tumors in pathological specimens. The collected data included: gender, patient's age, clinical indications and surgical intervention, tumor localization in the appendix and the diameter of lesion, histological type of the tumor and postoperative care (follow up) of patients.

Results: Four cases (3 girls, 1 boy) with carcinoid treated at our department during a 10 y period. Median patient age was 10.75 y (9- 12 y). In all cases the diagnosis was after appendectomy on ground of acute appendicitis. A single incident brought findings of gangrenous appendicitis. In three cases the tumor's diameter was smaller than 1cm, while the incident with the gangrenous appendicitis was larger than 1cm in diameter. In four cases the tumor was localized at the apex of the appendix without extending to the surrounding tissues. In all patients with carcinoid tumor followed a further testing based on specific monitoring protocol. In no case was residual or metastatic disease identified and no further treatment was required. No relapse was observed during follow-up.

Conclusion: Our study confirms the good prognosis of appendiceal carcinoid.

Keywords: Appendiceal carcinoid, Children, Tumor

INTRODUCTION

Langhans first described a gut carcinoid tumor in 1867. The term carcinoid (karzinoide tumoren) was introduced by Oberndorfer in 1907. In 1928 Masson indentified the subepithelial "Kultschitzky" cells as the origin of appendiceal carcinoids tumors and demonstrated their endocrine and neural characteristics. Carcinoid tumors are the most common neuroendocrine tumors, but at the same time they represent only 0,49% of all malignacies. Carcinoid tumors have been classified as foregut, mid-gut and hindgut carcinoid tumors [1].

The incidence of carcinoid tumors in the general population ranges from 0.1 to 0.9%. In pediatric patients, the rate is 0,08-0.5% [2,3-7]. The overall incidence of carcinoid tumors in surgical specimens has been estimated to 1 to 2 cases per 1000 appendectomies. The most common tumor localization is gastrointestinal system (74%) with the small intestine being (29%), the appendix (20%) and anus (13%) [8,9].

In the 75% of cases the tumor is localized at the apex of the appendix, in 20% and 5% affects the mid portion and the base respectively and discovered accidentally during appendectomy [10]. In children the tumor is usually smaller than 2 cm in diameter [11].

The clinical presentation of appendiceal carcinoids is similar to that of acute appendicitis, with intermittent abdominal pain or pain localized in the right lower adominal quadrant, without simultaneously excluded and symptoms of carcinoid syndrome (flushing , bronchospasm , diarrhea , weight loss) [10-12].

The prognosis for patients with complete tumor resection is good with the five-year survival rate in tumors smaller than 1cm, range from 90-100% [11].

The purpose of our study is to report the experiences of our department in the management of appendiceal carcinoid tumors in children and make a review of the literature regarding postoperative monitoring.

MATERIALS AND METHODS

Medical records of all patients aged 15 yrs or less who underwent appendectomy at the 2nd Department of Paedriatic Surgery of Aristotle University of Thessaloniki between January 2004 and February 2014, were evaluated for the existence of appendiceal carcinoid tumors in pathological specimens. The collected data included: gender, patient's age; clinical indications and surgical intervention, tumor localization in the appendix and the diameter of lesion, histological type of the tumor and postoperative care (follow up) of patients.

RESULTS

Eight hundred and twenty children underwent appendectomy during the study period and four of them (0.49%) were found to have histological evidence of carcinoid tumor of appendix. All cases of carcinoid tumors were incidental finding during open appendectomy. Among these children with confirmed carcinoid tumor three were girls and one was a boy with a mean age of 10.75 yrs (9-12yrs). In our study, all patients with histologically proven carcinoid of the appendix had symptoms of acute appendicitis preoperatively. In one case the operative findings were gangrenous appendicitis. In three cases the tumor diameter was smaller than 1cm, while in the incident with the gangrenous appendicitis the diameter was larger than 1cm. In all four cases the tumor localized at the tip of the appendix with no diffusion of the surrounding tissues and the exemption of the tumor was made on healthy boundaries without residual tissue.

In all patients followed further testing based on specific protocol [Table/Fig-1]. In no case was residual or metastatic disease identified and no further treatment was required. No relapses or other neoplasms occurred during a median follow-up period of 48 months (3-120 months).

DISCUSSION

The carcinoid tumors represent the majority of neuroendocrine tumors and constitute a significant diagnostic and therapeutic challenge for clinicians. Carcinoid tumors are quite rare, but the incidence is propably high because many people who have carcinoid tumor are often asymptomatic. Frequently this tumor occurs in girls aged 12 to 13 yrs. Similar to other studies, we detected a

Monitoring Protocol for carcinoid tumor of the appendix
Testing after confirmed histological diagnosis :
1) Serotonin serum (110- 330g / l)
2) chromogranin A (chromogranin A) serum (<18u / l)
3) 5-HIAA (serotonin metabolite 5 - hydroxyindoleacetic acid measured in urine 24 hours
4) Ultra Sound of abdomen for presence of liver metastases
5) Check for clinical manifestations of carcinoid syndrome (flushing , diarrhea , endocardial fibrosis murmurs , colicoid aches , weight loss)
If the above test is normal :
1) Serotonin Serum
2) serum chromogranin A
every 3 months during the 1st year
every 6 months for 5 years
every 12 months after 6 years
If the above test is abnormal :
1) MRI of abdomen
2) Chest radiograph
3) Scintigrafy of somatostatin receptors . The majority of carcinoid tumors , bear on their cell surface specific receptors which bind the somatostatin analogue labeled with ^{111}In okreotid

[Table/Fig-1]: Monitoring protocol

slight female preponderance [6,7]. Furthermore, the median age at diagnosis in the present study was 10.75 y, which is lower than the reported by most authors [8,11]. Most appendiceal carcinoid tumors in childhood are clinically silent and behave benignly. The uncommon occurrence of metastasis is related to the primary tumor size and depth. Tumors with a diameter smaller than 1cm constitute 70-90% of the cases with zero risk of metastases [12,13], while tumors measuring 2 cm or more in diameter may have widespread metastases upon detection, with a percent ranges from 20-45% [13,14].

These tumors can be adequately treated by a simple appendectomy. Our results are in accordance with this theory, as indicated by far monitoring of the patients. Cases where the tumor is localized at the base of the appendix or there are residual tumors at the margin of resection or there is an infiltration of mesoappendix larger than 3mm in diameter, require additional treatment.

In tumors with a diameter larger than 2cm, a right hemicolectomy is recommended. Tumors with a diameter of 1- 2cm treated with a simple appendectomy. The results of our study also confirmed the efficacy of this procedure. Only cases with tumor localization at the base of the appendix, transmural infiltration or infiltration of mesoappendix require additional therapy with right hemicolectomy or ileocecal resection [15,16] . Absolute indication for re-operation, is the existence of local lymph nodes and the existence of tumor's rupture.

The National Comprehensive Cancer Network's 2013 guidelines do not define precise criteria for monitoring tumors smaller than 2cm. Only for tumors larger than 2cm proposed monitoring protocol which includes history, physical examination and imaging every three months in the first year and every 6-12 months in the next 10 years and indicators measuring 5-HIAA and chromogranin A. The European Neuroendocrine Tumor Society 2012 guidelines do not suggest monitoring in tumors smaller than 1cm after appendectomy on healthy margins.

In tumors with a diameter of 1-2cm there is a divergence. However, most studies support that a further monitoring is not necessary [17,18]. The North American Neuroendocrine Tumor Society guidelines 2009 converge in, that low-grade tumors well differentiated with diameter smaller than 1cm have a low recurrence rate and do not require further monitoring. Also, tumors larger than 1cm treated with right hemicolectomy, without lymph node infiltrations does not require any monitoring at all. Tumors with a diameter of 1 - 2cm and a presence of aggravating factors (tumor's localization at the base, infiltration of the mesoappendix > 3mm , vessels infiltration, NET -G2), in which a simple appendectomy was performed, a stable monitoring is recommended.

CONCLUSION

Carcinoid tumors are the most common tumors of the appendix. In children, they occur more commonly in females. The median age at diagnosis in our study was 10.75 yrs. The clinical presentation of carcinoid tumors of the appendix is similar to acute appendicitis, but they can be an incidental finding during surgical procedures other than appendectomy. The site and the size of the tumors are used for the assessment of these tumors. Localized disease has an excellent prognosis. Single appendectomy is considered the appropriate treatment, while right hemicolectomy is indicated in tumor larger than 2 cm. A stable monitoring based on specific protocol for tumors larger than 2 cm is required.

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