Original Article

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Appendicular Neuroendocrine Tumours in Children: Unicentric Retrospective Study

Hayet Zitouni MD, Hamdi Louati MD*, Mohamed Zouari MD, Ahmed Khalil Ben Abdallah MD, Manel Belhajmansour MD, Mahdi Ben Dhaou MD, Mohamed Jallouli MD, Riadh Mhiri MD

Department of Pediatric Surgery.HediChaker Hospital. 30219 Sfax, Tunisia.
*Corresponding author: Hamdi Louati, MD, Department of Pediatric Surgery, HediChaker Hospital, 3029 Sfax, Tunisia.
E-mail: drhamdilouati85@yahoo.com.

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Abstract

Background: Neuroendocrine Neoplasms (NEN) represent 60% of all appendicular tumours. This type of cancer is predominantly benign. In this study, appendicular NEN tumours in children were investigated.

Materials and Methods: This retrospective study was conducted on 540 patients underwent emergency appendectomy for the treatment of clinically suspected appendicitis at the department of pediatric surgery in Hedi Chaker hospital in Sfax, Tunisia. This study was performed between January 2013 and December 2016. Data on appendicular NEN demographic, preoperative diagnoses, investigations, operative findings, pathological reports, and follow up were reviewed and analysed.

Results: Out of 540 patients, there were 309 males (57.3%) and 231 females (42.7%). The Mean age of the patients was 9.23 ± 2.78 years. One hundred and thirty seven patients (25.4%) had laparoscopic appendectomy and 74.6% were operated by the traditional open approach. The diagnosis of appendicular NEN tumours was histologically confirmed in 4 appendectomy specimens. Clinically, all patients presented with acute appendicitis with raised inflammatory markers and positive ultrasound for appendicitis. The mean of tumour size was 1 cm. Complete resection was successfully achieved in all patients. The mean of follow-up was 3 years.

Conclusion: Appendicular NEN tumours were diagnosed postoperatively with a histological examination. It seems that surgical management with simple appendectomy seems to be curative for the majority of cases especially with tumours less than 2 cm. according to this study, the prevalence of appendicular NEN tumours is low between all gastrointestinal tumors.

Keywords: Appendiceal neoplasm, Appendicitis, Child, Neuroendocrine Tumor

Introduction

Appendix cancer is rare (1). The appendix has been identified as the most common site of carcinoid tumors (2). Neuroendocrine tumours (NET) arise from endocrine and nervous. This type of cancer is predominantly benign. The major location of this cancer is the pancreas, lungs, and etc. Appendiceal Neuroendocrine Neoplasms (NEN) (carcinoid tumors of the appendix) represent 60% of all appendicular tumors (2). Based on epidemiologicasl data, 0.4% of all gastrointestinal tumors are appendix cancer. In different studies, results show carcinoid tumors with frequency of less than 1% in histopathological assay after appendectomy. The size of appendiceal NEN was evaluated between 1 and 2 cm. Therefore, this type of tumour has low risk for metastases. However, metastases are unlikely to occur in tumors larger than 2 cm. Appendicular carcinoids in children is most commonly presented with features of acute appendicitis (3). The clinical presentation of NEN may be similar to that of acute appendicitis, but majority of these tumors are either identified on histological examination of resected appendix or incidentally found during abdominal surgery performed for another pathology reason (4). In this study, we reviewed our own experience with NEN appendicular tumours in children.

Materials and Methods

This retrospective study was conducted on children underwent emergency appendectomy for the treatment of clinically suspected appendicitis. This study was performed between January 2013 and December 2016 at the department of pediatric surgery in Hedi Chaker hospital in Sfax, Tunisia. Data on appendicular NEN demographic, preoperative diagnoses, investigations, operative findings, pathological reports, and follow up were reviewed and analysed. Data were analysed by using SPSS (version 20) and running statistical analysis.

Results

Between January 2013 and December 2016, 540 patients who underwent emergency appendectomy for the treatment of clinically suspected appendicitis were studied. There were 309 males (57.3%) and 231 females (42.7%). The Mean age of the patients was 9.23 ± 2.78 years. One hundred and thirty seven patients (25.4%) had laparoscopic appendectomy and 74.6% were operated by the traditional open approach. The diagnosis of appendicular NEN tumors was histologically confirmed in 4 appendectomy specimens (0.74% of all appendectomy was done in this department). All of patients were females with a mean age of 11 years (range: 7 to 14 years). All patients presented with clinically suspected acute appendicitis. Laboratory investigations revealed raised white cell count and positive C-reactive protein levels in 4 patients. Ultrasound scan was positive for appendicitis (diameter of the appendix greater than 6mm) in all 4 patients without any associated radiological signs of appendicular NEN tumor or of any other pathology (Table I). Emergency laparoscopic appendectomy was successfully performed in 3 patients (75%) while one patient had her appendix surgically removed via the traditional open approach.

The mean of tumor size was 1 cm (range 0.5 to 2 cm); complete resection was successfully achieved in all patients. The tumour was located in the tip of the appendix for the 4 patients. Serosa invasion was not reported in the 4 patients and immunohistochemistry with chromogranin and synaptophysin were positive in tumor cells for our four patients (Table II).

The median of hospital stay was 3 days (range: 2 to4 days) and it was without complications or carcinoid syndrome for all the four patients. None of the patients developed evidence of metastases or recurrence during the follow-up (Table I). Follow-up imaging included normal Computed Tomography (CT) scan in two patients and normal Octreotide scan in one patient. In addition, each patient had at least one normal control ultrasound.

TableI: Demographic, clinical, and imaging characteristics of 4 patients with appendicular neuroendocrine tumors

P	Sex	Age (Years)	Clinical Parameters	Surgery	Follow-up (years)
1	F	7	Pain in RLQ+ fever WBC 13600 CRP 33 mg/L Ultrasound diameter of the appendix: 7mm	Appendectomy	4
2	F	11	Pain in RLQ+ fever + nausea WBC 11800 CRP 41 mg/L Ultrasound diameter of the appendix: 8mm	Appendectomy	3
3	F	12	Pain in RLQ+ fever + vomiting WBC 17800 CRP 59 mg/L Ultrasound diameter of the appendix: 8mm	Appendectomy	3
4	F	14	Pain in RLQ+ fever + vomiting WBC 10780 CRP 19 mg/L Ultrasound diameter of the appendix: 7mm	Appendectomy	2

F = Female; RLQ = Right Lower Quadrant; WBC = White blood cells; CRP = C-reactive protein.

Table II: Histological Characteristics of 4 patients with appendicular neuroendocrine tumors

Patient	Location of NEN tumor	Size (cm)	Immunohistochemistry with chromogranin and synaptophysin
1	Tip of the appendix	1	+
2	Tip of the appendix	0.5	+
3	Tip of the appendix	0.5	+
4	Tip of the appendix	2	+

Discussion

The most common tumor that involved appendix in children is carcinoid (5). Due to the lack of specific symptoms, appendix carcinoid tumors are diagnosed as an incidental finding in 19% to 71% (6). The incidence of appendicular NEN tumors in children (≤14years) was ranged from 0.08% to 0.7% of operated appendicitis (7). The incidence of NEN appendicular tumor in our series was 0.74%. Presentation of appendicular NEN tumors in children was variable; the most common presentation was like acute appendicitis (4). The preoperative diagnosis of appendicular NEN tumor is challenging unless patients present with symptoms and signs of carcinoid syndrome or features of metastatic disease (8). In our series, all patients were operated for suspected appendicitis and no one was suspected to have appendicular NEN tumor preoperatively or intraoperatively. Moreover, standard laboratory tests and radiography exploration done during pre-operation for detecting acute appendicitis could not predict the appendicular NEN tumor in this study, which was in contrast with previous studies (9). Tumor size was less than 1 cm in diameter in 64% of the cases that was consistent with previous studies (10). Most of the appendicular NEN tumors are localized at the tip of the appendix but they have also been reported in the mid portion (20%) and at the base of the appendix (5%) (11). In these four patients, the size of tumour was less than 2 cm (75% less than 1 cm) and all were localized at the tip of the appendix.

The National Comprehensive Cancer Network (NCCN) recommended simple appendectomy as a treatment method for tumors less than 2 cm confined to the appendix with follow-up as clinically indicated (12). The consensus guidelines of the European Endocrine Tumor Society (ENETS) published in 2012 also recommend simple appendectomy for tumors less than 2 cm, which appears to be curative independent of the tumor site and a right hemicolectomy is within 3 months following the initial appendectomy operation in patients with tumors more than 2 cm (13). Prognosis depends on the size of the tumour, so tumours which are less than 2 cm in size and found at the tip of the appendix are adequately treated with simple appendectomy (4). Metastasis and recurrence have been rarely reported, larger tumors at the base of the appendix most commonly metastasize to regional lymph nodes. However, metastases to liver causing carcinoid syndrome are rare in appendicular NEN tumors (14). For all our four patients, appendectomy was sufficient for the treatment of appendicular NEN tumor because their size was less than 2 cm.

There is no consensus regarding the guidelines of clinical follow-up and utility of imaging and neuroendocrine markers in pediatric patients with appendicular NEN tumours because few series have been published in pediatric literature. In some series, the children were followed up clinically and with ultrasound imaging (15). Small tumors diagnosed histologically do not require follow-up, while a 3-year follow-up is recommended in larger tumors (8). NEN tumour carries the best survival rates (>95%) compared to all other tumour types located in the appendix (16). These favourable outcomes may be attributed to the localization, prompt identification, diagnosis and excision, the biopathology of the tumor itself, or the usual size that characterize NEN tumours (17). The young age of the patients that are mostly affected by NEN tumors and an early stage of the disease at the time of diagnosis further justify the high 5-year survival rates (17, 18).

Conclusion

Appendicular NEN tumours are diagnosed postoperatively with a histological examination. Surgical management with simple appendectomy seems to be efficient for the majority of cases especially with tumors less than 2 cm.

Conflict of interest

Authors declared no conflict of interst.

References

1. Margaret E. Primary malignant neoplasms of appendix: a population-based study from the surveillance, epidemiology and end-results program, 1973-1998. Cancer 2002; 94: 3307-3312.
2. Murray Y, Sara E, Ricardo V, Rebecca S. Postoperative surveillance of small appendiceal carcinoid tumors. American J Surg 2014; 207(3); 342-345.
3. Pelizzo G. Carcinoid tumors of the appendix in children. Pediatr Surg Int 2001; 17(5): 399-402.
4. Mandhan P, Falah A , Mansour J A. Appendicular neuroendocrine tumors in children. Surgical Science 2014; 5(6): 246-255.
5. Khan RA, Ghani I, Chana RS. Routine histopathological examination of appendectomy specimens in children: is there any rationale? Pediatr Surg Int 2011; 27(12): 1313-1315.
6. Roggo A, Wood WC, Ottinger LW. Carcinoid tumors of the appendix. Ann Surg 1993; 217(4): 385-389.
7. Dall'Igna P, Ferrari A, Luzzatto C, Bisogno G, Casanova M, Alaggio R . Carcinoid tumor of the appendix in childhood: the experience of two Italian institutions. J Pediatr Gastroenterol Nutr 2005;40(2):216-219.

8. Coursey CA, Nelson RC, Moreno RD, Dodd LG, Patel MB, Vaslef S. Carcinoid tumors of the appendix: are these tumors identifiable prospectively on preoperative CT? Am Surg 2010 ;76(3):273-275.
9. Amr B, Froghi F, Edmond M, Haq K, Thengungal Kochupapy R.Management and Outcomes of Appendicular Neuroendocrine Tumours: A Retrospective Review with 5-year Follow-up. Eur J Surg Oncol 2015 ;41(9):1243-1246.
10. Shapiro R, Eldar S, Sadot E, Papa MZ, Zippel DB. Appendiceal carcinoid at a large tertiary center: pathologic findings and long-term follow-up evaluation. Am J Surg 2011;201(6):805-808.
11. San Vicente B, Bardají C, Rigol S, Obiols P, Melo M, Bella R. Retrospective evaluation of carcinoid tumors of the appendix in children. Cir Pediatr 2009;22(2):97-99.
12. NCCN clinical practice guidelines in Oncology 2014.
13. Pape UF, Perren A, Niederle B, Gross D, Gress T, Costa F, et al. ENETS Consensus Guidelines for the management of patients with neuroendocrine neoplasms from the jejuno-ileum and the appendix including goblet cell carcinomas. Neuroendocrinol 2012;95(2):135-156.
14. Fornaro R, Frascio M, Sticchi C, De Salvo L, Stabilini C, Mandolfino F.Appendectomy or right hemicolectomy in the treatment of appendiceal carcinoid tumors? Tumori 2007;93(6):587-90.
15. Kulkarni K, Sergi C. Appendix carcinoids in childhood: Long-term experience at a single institution in Western Canada and systematic review. Pediatr Int 2013; 55(2): 157-162.
16. McGory ML, Maggard MA, Kang H, O'Connell JB . Malignancies of the appendix: beyond case series reports. Dis Colon Rectum 2005; 48: 2264-2271.
17. Moris D, Tsilimigras DI, Vagios S, Ntanasis-Stathopoulos I, Karachaliou GS. Neuroendocrine Neoplasms of the Appendix: A Review of the Literature. Anti cancer Res 2018;38(2):601-611.
18. Wu H, Chintagumpala M, Hicks J, Nuchtern JG, Okcu MF.Neuroendocrine tumor of the appendix in children. J Pediatr Hematol Oncol 2017;39(2):97-102.