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# RETROSPECTIVE CLINICO-PATHOLOGICAL AND MORPHOLOGICAL ANALYSIS OF APPENDICULAR TUMORS ON APPENDECTOMY SPECIMENS FOR ACUTE APPENDICITIS

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**ABSTRACT:** ***Background and Study Aims:*** *Appendiceal Tumors are rare. Difficult to diagnose, these tumors are often accidentally discovered following acute appendicitis. The aim of this study is to describe the clinical, pathological and morphologic characteristics of these tumors in order to define an appropriate management.* ***Patients and Methods:*** *From a pathological database, all appendiceal tumors found on appendectomy specimens performed between January 2017 and July 2019 were retrospectively analysed.* ***Results:*** *Among the 1480 appendectomies performed, 15 cases of appendiceal tumors were collected (1.01%). The mean age was estimated at 44.7 ± 21.5 years (17-80). Pain in the right iliac fossa was present in all patients. Abdominal ultrasonography coupled with computed tomography (CT) scan led to the diagnosis of appendiceal tumors in 40% of cases (6/15). All patients underwent emergency surgery. An appendectomy was performed in 13 patients (86%). A mucinous tumor was found in 9 patients (60%). In 40% of the cases (6/15), it was a neuroendocrine tumor.* ***Conclusion:*** *Appendiceal tumors are often discovered incidentally on appendectomy specimens for acute appendicitis. They can be seen at any age and their diagnosis is not easy, even with the support of imaging. Ideally, the diagnosis of these tumors should be made preoperatively; this can change the surgical approach and avoid the need for additional surgery. All appendectomy specimens should be examined in histopathology.*

**KEYWORDS:** Acute appendicitis, appendicular tumors, appendiceal neuroendocrine tumors, mucinous neoplasm, treatment.



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## INTRODUCTION

Appendiceal tumors are rare. They are most often found incidentally on appendectomy specimens for acute appendicitis (1), and their diagnosis remains difficult preoperatively. Occasionally, the discovery is made during abdominal imaging, colonoscopy or a surgical procedure (1). The aim of this study is to describe the clinicopathological and morphological characteristics of these tumors in order to define an appropriate management.

### Patients and Methods

We conducted a retrospective analysis of all adult patients over 16 years old, who underwent appendectomy for acute appendicitis from January 2017 to July 2019 at our tertiary health care center. From our pathological database, all patients who had an appendiceal tumor were collected. Their epidemiological, clinical and morphological characteristics as well as the modalities of their therapeutic management were analyzed. Continuous and categorical variables were expressed as mean ± standard deviation and percentages, respectively.

## RESULTS

The review identified 1480 patients who had appendectomy, 15 of whom had appendiceal tumor (1,01%), including eight women (sex ratio = 1.1). The average age was estimated at 44.7 ± 21.5 years (17-80). An appendicular syndrome was the mode of presentation in more than half of the cases, and right iliac fossa pain was present in all patients. The duration of the symptoms was 5.2 ± 7.2 days (1-30). All patients underwent imaging preoperatively; abdominal ultrasound coupled with CT scan allowed the diagnosis of appendiceal tumor in 6 of 15 cases (40%). All patients underwent emergency surgery; appendectomy was performed in 13 patients (86%). Two patients had an immediate right colectomy (14%) and one patient was taken back for additional treatment. A mucinous tumor was found in 9 patients (60%). The remaining 6 patients had a neuroendocrine tumor.

All cases are summarized in Table 1.

**Table 1: Demographic, Clinicopathological and Morphological Characteristics of Patients**

| Pts | Age/Sex | Symptoms | Duration | WBC | Imaging/Perop Diag | Procedure | Histology (Day) |
|---|---|---|---|---|---|---|---|
| 1 | 26/F | RIFP + fever | 6 | 21,900 | CT: pancolitis/peritonitis | appendectomy | NET G1 <1cm pT1N0 R0 |
| 2 | 22/M | RIFP + vomit | 1 | 15,400 | Us: AA /AT | appendectomy<br>Add Treat: Rt Colec | NET G2 >2cm<br>pT3N1 R1V1 |
| 3 | 76/M | RIFP + vomit | 7 | 13,500 | Us: ACT/mucocele | appendectomy | LAMN R0 |
| 4 | 17/F | RIFP + fever | 1 | 25,800 | Us + CT: AA/AA | appendectomy | LAMN R0 |
| 5 | 70/F | RIFP | 3 | 3,700 | US + CT: ACT/mucocele | Rt Colec* | LAMN R0 |


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|---|---|---|---|---|---|---|---|
| 6 | 49/M | RIFP + vomit | 3 | 8,800 | US + CT: peritonitis/AT | appendectomy | LAMN R0 |
| 7 | 57/F | RIFP + vomit | 7 | 6,800 | CT: ACT/mucocele | appendectomy | LAMN R0 |
| 8 | 58/M | RIFP | 1 | 7,700 | Us: AA /AT | Rt Colec | NET G2 >2cm pT2N0M0 R0 |
| 9 | 62/F | RIFP | 30 | 7,300 | Us + CT: ACT/mucocele | appendectomy | LAMN R0 |
| 10 | 36/F | RIFP + vomit | 2 | 11,900 | Us: ACT/mucocele | appendectomy | LAMN R0 |
| 11 | 19/M | RIFP + fever | 1 | 12,000 | Us + CT: AA /AA | appendectomy | NET G1 pT1N0 R0 |
| 12 | 35/M | RIFP + fever | 3 | 14,500 | Us + CT: AA /AA | appendectomy | NET G1pT2N0 R0 |
| 13 | 22/M | RIFP + fever | 7 | 13,800 | Us + CT: abcess/abcess | appendectomy | NET G1pT2N0 R0 |
| 14 | 80/F | RIFP + vomit | 3 | 10,000 | Us + CT: ACT/mucocele | appendectomy | LAMN R0 |
| 15 | 42/F | RIFP + fever | 3 | 10,300 | Us + CT: abcess/mucocele | appendectomy | LAMN R0 |

*Pts: patients, WBC: white blood cells, Perop Diag: peroperatory diagnostics, F: female, M: male, RIFP: right iliac fossa pain, CT: computed tomography, Us: ultrasonography, NET: neuroendocrine tumor, R0: clear resection margin, Vomit: vomiting, AA: acute appendicitis, AT: appendiceal tumor, Add Treat: additional treatment, Rt Colec: right colectomy, V1: lymphovascular invasion, ACT: appendiceal cystic tumor, LAMN: low grade appendiceal mucinous neoplasm, G: tumor grade. (*): In this patient, right colectomy was an overtreatment for LAMN.*


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## DISCUSSION

Appendectomy for acute appendicitis is a very common surgery since surgical treatment became the standard of care in the late 19th century (2). In the US, approximately 300,000 procedures are performed annually (3).

Appendiceal tumors are found in 0.9 to 1.4% of appendectomies for acute appendicitis (4).

In the present series, this prevalence was estimated at 1.01%, about 1.5 times higher than the one reported by Collins et al. (4). As for colon cancer, recent series have shown an increasing incidence of malignant tumors of the appendix, between 5.9 and 12% (5). Forty percent (40%) of our population was over 50 years old, and 53% were women (8/15). Indeed, advanced age and female gender are considered independent risk factors for appendiceal tumors (6,7).

In more than half of the cases (10/15), a typical appendicular syndrome was the mode of revelation, a fact widely found in the literature (8). In a retrospective study, Sadot et al. (7) clearly identified complicated forms, in particular, perforation, as an independent risk factor. The duration of symptoms was 5.2 ± 7.2 days (1-30). This seems to be a determining factor for the performance of a CT scan when it exceeds 24 hours, as well as an atypical symptomatology or an age higher than 40 years (9). In our series, a CT scan was performed in 11 patients, allowing to establish the diagnosis in only 45% of cases (5/11). This demonstrates the difficulty of preoperative diagnosis despite the use of the CT scan.

The primary tumors of the appendix are multiple; they can be epithelial tumors, neuroendocrine tumors, lymphoma or even mesenchymal tumors (10). In this series, 60% of the tumors found were mucinous ones, i.e., 0.6% of the appendectomy specimens, almost twice the rate reported by Smeenk et al. (11). The incidence of these tumors is increasing, while the age at diagnosis seems to be decreasing (12). Other findings may include a palpable mass, intestinal obstruction by intussusception, or abdominal distension related to a peritoneal pseudomyxome (13). Appendiceal mucinous tumors (AMTs) result in a "mucocele" (Figure 1), which remains a purely macroscopic description whose preoperative diagnosis is essential (13).


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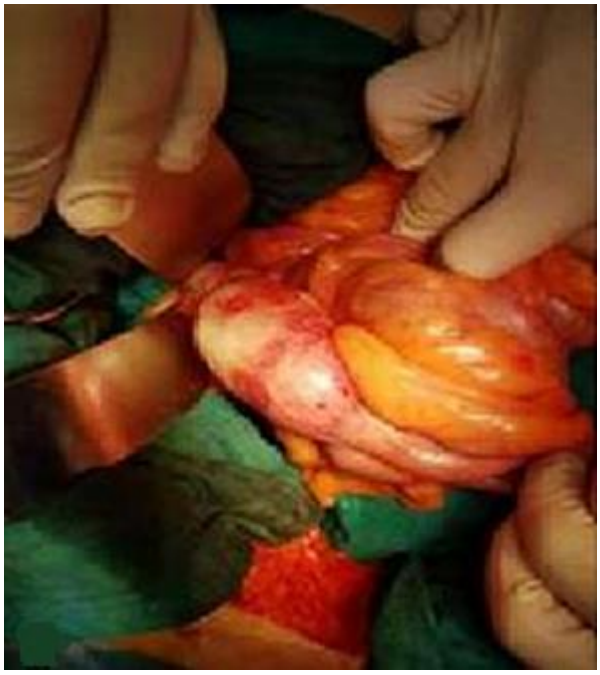

**Figure 1: Operative View of an Appendicular Mucocele**

On ultrasound, it has the appearance of a target image (onion skin sign) which is pathognomonic (14). CT remains the key test; the typical image is a well encapsulated, rounded cystic mass that may contain calcifications (Figure 2).

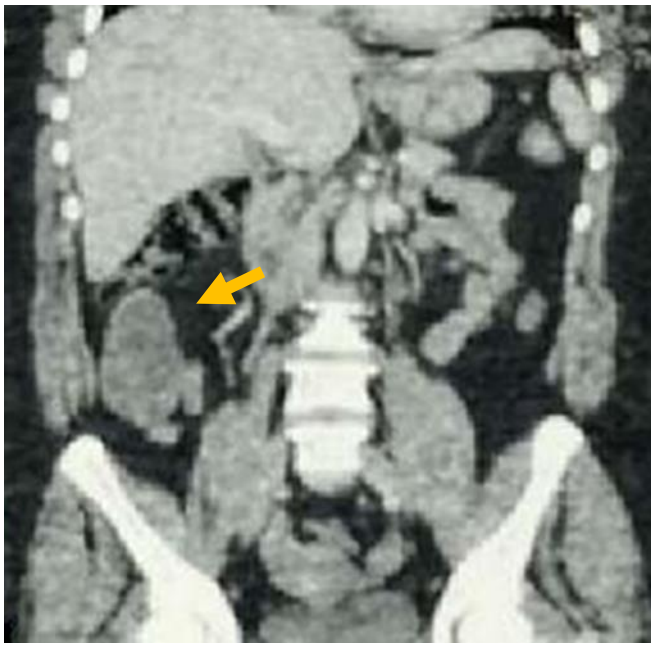

**Figure 2: Scanographic Aspect of an Appendicular Mucocele (Yellow Arrow)**


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Imaging (ultrasound and/or CT) allowed us to diagnose mucocele in two-thirds of the cases (6/9), and in 2 patients the diagnosis was rectified intraoperatively. The PSOGI (Peritoneal Surface Oncology Group International) classifies AMTs according to their grade (15). Based on this classification, all the AMTs collected were Low-grade Appendiceal Mucinous Neoplasms (LAMN). Surgery is the curative treatment for AMTs. Appendectomy with clear margins was performed in 8 patients (88%), which is more than sufficient for non-invasive tumors, such as LAMN (12). In case of doubt, a frozen section when available seems to be useful for decision making, knowing that additional surgery may be necessary after the final histological examination (8). A carcinological right colectomy was performed for a tumor larger than 2cm. This option is appropriate in case of insufficient margin after appendectomy, in case of high grade tumor, more than 2cm or lymph node metastases (12). Any manipulation must remain cautious. Also, for more safety, some authors recommend a laparotomy approach (16).

In case of spontaneous or iatrogenic perforation, it is recommended to perform a cytology of the peritoneal fluid followed by an appendectomy with abundant washing of the peritoneal cavity. Accordingly, Gonzalez-Moreno et al. (17) have not shown any survival benefit after right colectomy in case of peritoneal dissemination. Adjuvant chemotherapy is indicated in high grade tumors, or in case of lymph node metastases or lymphovascular invasion (12). Because of their slow progression, an annual CT follow-up with tumor markers (CEA, CA19.9) is proposed for at least five years, in order to detect an eventual peritoneal pseudomyxome (11). Other tumors observed in this series are neuroendocrine tumors, found in 40% (6/15) of patients. In the literature, appendiceal neuroendocrine tumors (ANETs) remain the most common subgroup which accounts for about 30 to 80% of all appendiceal tumors (18). According to data from the American SEER registry, their incidence is about 0.4 per 100,000/year (19). Unlike Western series (20), where the mean age at diagnosis is around 40 years, with a slight female predominance, the mean age of our patients was 30.3 ± 14.7 years (19-58) with a clear male predominance. Rarely symptomatic, ANETs are often incidentally discovered. A typical appendicular syndrome was the mode of presentation in 5 of 6 patients. In 70% of cases, ANETs are located at the appendicular tip and measure less than 1 cm, making their detection on preoperative imaging difficult (21). Indeed, imaging (ultrasound and/or CT) could not detect the tumor in any of our patients. Despite the almost constant infiltration of the muscularis, ANETs are in the vast majority of cases benign. Exceptionally, they may experience a carcinoid syndrome in relationship with a metastatic disease (21).

The latest version of the WHO classification of tumors of the digestive system should be adopted (22). It classifies ANETs according to their molecular characteristics, their histological differentiation and their tumor grade. Following the 2007 European Neuroendocrine Tumors Society (ENETS) classification (23), the tumor was in the majority of cases (5/6), less than 2cm, of low grade (G1), limited to the muscularis (T2). The therapeutic options for ANET on appendectomy specimens are determined by the size of the tumor, its location, its grade, the degree of meso invasion, the quality of the resection margins, and finally the existence or not of lymphovascular and perineural involvement. In our series, an appendectomy was sufficient in 4 patients (66%). In fact, this attitude is indicated for infra centimetric tumors of low grade G1. No further exploration or treatment is recommended if the resection was complete R0. Moreover, no benefit of performing an additional colectomy for G2 tumors of 1cm has been demonstrated (24). However, a carcinological right colectomy is recommended for tumors larger than 2cm, which was performed in one of our patients with a G2 grade ANET, more


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than 2cm. Another patient was taken back for a complementary right colectomy after an appendectomy revealing a tumor classified as pT3N1M0 R1V1. Tumors measuring between 1 and 2 cm justify a right colectomy in case of G2 tumor grade, lymph node metastasis, extension to the mesoappendix beyond 3 mm, lymphovascular invasion or incomplete resection R1 (24). No adjuvant treatment is recommended (20).

The prognosis of ANETs remains favorable, with a 5-year survival rate close to 100% for low-grade tumors. However, it varies between 12 and 28% for advanced stages (20). Follow-up should be considered for high-risk tumors larger than 2 cm. No rhythm or modalities of surveillance have yet been validated (20). In our practice, we perform a CT scan every 6 to 12 months for at least 5 years. A colonoscopy is carried out to look for synchronous tumors. In this study, the median follow-up was 13 ± 9.1 months (1-28). All patients were alive, without local or distant recurrences.

## CONCLUSION

Appendiceal tumors are a rare entity, often discovered incidentally on appendectomy specimens for acute appendicitis, and can be found at any age. Ideally, the diagnosis of these tumors should be made preoperatively; this can modify the surgical approach and avoid the need for additional surgery. Mostly benign, the treatment of these tumors consists of appendectomy. All appendectomy specimens must be submitted to a histopathological examination, which should allow a correct classification.

**Conflict of interest statement:** The authors declare no conflict of interest.

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