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Cancers of the appendix.
Case report and literatures review

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Cancers of the appendix. Case report and literatures review

Cancers of appendix are very uncommon. As reported in the case of 85 years old man, that underwent right emicolectomy with restoration of bowel continuity, the appendix was found to be gangrenous and perforated during the surgery. The hystology that comes out was adenocarcinoma of appendix that after 1 yars of follow up ramanins asymptomatic. At last the emicolectomy rappresent the best surgical treatment for all appendix neoplasm, that could be recognised from the surgeon when possible wiht intraoperavite histological examination.

KEY WORDS: Appendix, Cancer, Incidental diagnosis, Right emicolectomy

Introduction

Cancers of the appendix are rare. Most of them are found accidentally during surgery performed for appendicitis or other non appendiceal pathologies. When reviewed, majority of the tumors were carcinoid, adenoma, and lymphoma. Adenocarcinomas of appendix are only 0.08% of all cancers and less than 0.5% of all gastrointestinal neoplasms. Frequently is associated with synchronous and metachronous colorectal or extraintestinal cancers. The correct management is the right hemicolectomy for all histologic types (colonic, adenocarcinoid, mucinous), Dukes A tumors, and in presence of perforation.
We reported a case of primary adenocarcinoma of the appendix occurred in a 85 year-old man, diagnosed incidentally during surgery performed for suspected adenocarcinoma of right colon.

Case Report

We are reporting a 85-year-old Italian male presented to our department with right lower quadrant pain, and intestinal subocclusion .Physical examination revealed no palpable masses in the abdomen. Laboratory showed anemia (hemoglobin level 86 g/l), leukocytosis, and increased levels of ca125. Colonscopy revealed an ulcerative mass on ileo-caecal region. CT Scan showed no repetitive lesions and parzial dilatation of the last ileal loops (Fig. 1). Patient was taken to the operating room and underwent right emicolectomy with restoration of bowel continuity by mechanical ileus colonic anastomosis. During the surgery, the appendix was found to be gangrenous and perforated with an associated abscess. The surgical pathology showed adenocarcinoma of appendix, moderately differentiated with no lymphovascular invasion (Fig. 2). The tumor was found to be 2,6 cm, grade 2. Postoperative course was uneventful. Subsequently, he came to oncology clinic for further recommendations. He declined consideration of adjuvant chemotherapy. After 1 year of followup, he remained asymptomatic.

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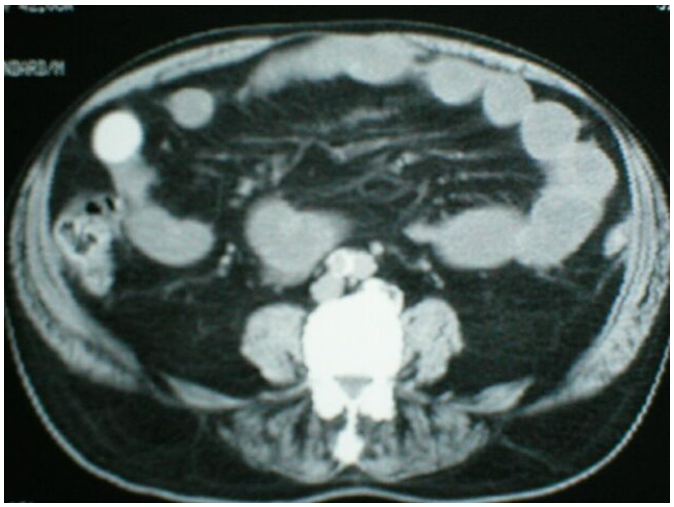

Fig. 1: Preoperatory CT Scan.

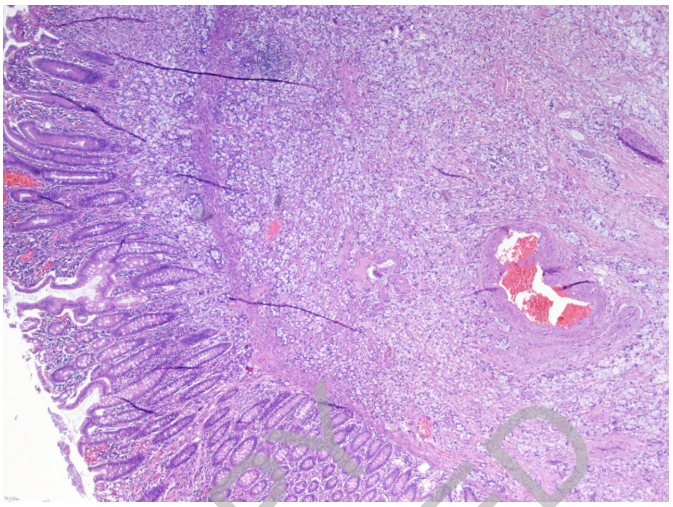

Fig. 2: Adenocarcinoma of appendix, moderately differentiated with no lymphovascular invasion (E/E 40X).

Literatures Review

Epidemiology and Classification

Cancer of the appendix is very rare and is typically found incidentally in approximately 1% of appendectomies [3] or surgery for other non appendiceal pathologies. According to a report published by the National Cancer Institute using the Surveillance, Epidemiology, and End Results (SEER) database, appendiceal neoplasms account for approximately 0.5% of gastrointestinal tumors [2]. It was described the first time from Beger in 1882 and in literature are presents only cases reports and few numerous case studies [1] (Table I).
There are several histologic types. Carcinoids are the most common, accounting for approximately 66%, with cyst-adenocarcinoma accounting for 20% and adenocarcinoma accounting for 10% [3]. Then there are the rare forms of cancers which include adenocarcinoid, signet ring, non-Hodgkin's lymphoma, ganglioneuroma, and pheochromocytoma. Benign primary processes are mainly mucinous epithelial neoplasms, also called adenomas, cystadenoma, and benign neoplastic mucocele.
The majority of primary cancers of the appendix occur in 55-65 years of age, except for malignant carcinoid, which has a mean age diagnosis of 38. Men and women seem to be at equal risk for all appendiceal neoplasms except for malignant carcinoid which may have woman to man ratio in excess of 3:1. [2]

Table I

Study	Appendicectomy N°	Cases of adenocarcinoma	%
D. C. Collins	71000	57	0,08
R.W. Gilhome	9380	10	0,1
H. Ito	7980	8	0,1

Adenocarcinoma

Of the appendix is very rare, accounting for 0.5% of all gastrointestinal cancers. Within the adenocarcinoma malignancies there are three subtypes: mucinous (55%), colonic type (34%), and adenocarcinoid (11%) which has a mixed morphology. The mean age of diagnosis is in the sixth decade of life, with an even male to female ratio for all but colonic type, which may have a higher incidence in men [1].

Mucinous Adenocarcinoma

It is the malignant counterpart to the mucinous adenoma. Both present with similar symptoms.
Adenocarcinoid, also called Goblet cell carcinoid, has features of both carcinoid tumor and mucinous adenocarcinoma. They account for 5% of cancers of the appendix, with an average age diagnosis of 58 years, and an even distribution between men and women [3] .
As is the case with most cancers of the appendix, the most common presentation is that of acute appendicitis. This may be from distention of the appendix causing pain or from a superinfection. Those with mucinous adenocarcinoma may present with a gradually distending abdomen which may be seen with pseudomyxoma peritonei.
The mucinous type, also called mucinous cyst-adenocarcinoma, causes a mucocele by the neoplasm occluding the narrow lumen which allows the mucin to build up

and distend the appendix. Perforation may occur allowing the spill of cancerous cells out into the peritoneum, which creates the condition of pseudomyxoma peritonei. These cells then seed the organs of the peritoneum and continue to produce the mucin. As the mucin accumulates, the abdomen becomes distended which is referred to as "jelly belly" [4]. Colonic type adenocarcinoma is less likely to present with a mucocele. Instead, they are more likely to present with a focal mass in the right lower quadrant.

Adenocarcinoma

Adenocarcinoma of the appendix is rarely diagnosed preoperatively. In a study by Nitecki et al., none of the 96 patients with adenocarcinoma of the appendix were diagnosed preoperatively, and it was only considered in the differential diagnosis in 10 patients.

CT imaging is helpful in identifying a mucocele caused by the neoplasm. Calcifications increase the likelihood that this process is malignant and not infective or inflammatory. If there is a superinfection associated with the malignancy, there may be air bubbles present on the CT. If the patient presents with a distended abdomen due to pseudomyxoma peritonei, a CT would show widespread heterogeneous locules in the peritoneal cavity [5, 6]. Since there are no imaging studies specific for diagnosing adenocarcinomas, the final diagnosis is most often made postoperatively on microscopic examination.

It has been generally accepted that a right hemicolectomy is the preferred surgical intervention for all subtypes of adenocarcinoma. While some surgeons suggest that a simple appendectomy is sufficient for tumors exhibiting only local disease, many studies have shown that there is a clear survival benefit to the addition of a hemicolectomy [7-9]. In a study by Nitecki, the 5-year survival rate for hemicolectomy was 73% versus 44% in the appendectomy group. These studies have found that the colonic and goblet cell subtypes are invasive, and approximately half the patients present with nodal metastasis [7]. However, there are some studies that disagree. Gonzalez-Moreno and Sugarbaker found that those patients with mucinous type cancer had no survival benefit from hemicolectomy versus appendectomy [10]. They further mention that hemicolectomy is recommended in those patients where (1) it is necessary to clear the tumor or perform complete cytoreduction; (2) lymph node involvement is demonstrated by histopathological examination of the appendiceal or ileocolic lymph nodes; or (3) a nonmucinous subtype is identified by histopathological examination.

In a study done by Pahlavan and Kanthanon adenocarcinoid tumors, he states that even though Goblet cell carcinoma is an aggressive tumor, a simple appendectomy is appropriate in most cases. However, he further states that a right hemicolectomy should be performed in the following scenarios: (1) cellular undifferentiation, (2) increased mitotic activity, (3) involvement of the base of the appendix, (4) lymph node metastasis, or (5) tumor size greater than 2 cm [11]. These guidelines allow the surgeon some direction in deciding whether or not to reoperate after a patient has had an appendectomy for an apparent appendicitis.

While there are small studies and anecdotal case reports that suggest a response to regimens containing 5-FU, the role of chemotherapy has yet to be clearly defined. Most oncologists agree that in the presence of nodal involvement, systemic and intraperitoneal chemotherapy regimens should be used [7,4,11]. Sugarland suggests postoperative intraperitoneal chemotherapy in the setting of pseudomyxoma peritonei, as long as cytoreduction and debulking have been accomplished, reducing recurrence rates [4].

Prognosis of adenocarcinoma depends on the subtype and extent of disease. Mucinous adenocarcinoma is considered to have a more favorable prognosis because it does exhibit hematogenous or lymphatic spread [4,8]. While it would be natural to assume that those patients with intraperitoneal seeding due to appendiceal perforation, would have a worse prognosis versus those who did not. However, in a study by Nitecki and others, there actually was no difference in 5-year survival rates between the two groups [7]. Perforation did in often times lead to earlier medical intervention and treatment.

Goblet cell subtype is considered to have a worse prognosis with one study listing a 55% 5-year survival rate while Pahlavan states a 60-80% 5-year survival rate [8,11]. The discrepancy may be due to differences in lymph node involvement for the two studies. The first had 43% lymph node involvement where Pahlavan only showed an 8.76% involvement.

Carcinoid Tumors

In 1907, German pathologist Dr. Oberndorfer described a collection of tumors he found on the small intestine as looking like carcinoma but also exhibiting features of benign adenomas, as carcinoid (carcinoma-like) [12]. In 1914, Dr Gosset and Dr Mason postulated that carcinoid tumors were made up of enterochromaffin cells, a type of neuroendocrine cells within the lamina propria and submucosa. These cells produce and contain approximately 90% of the serotonin in our bodies [13].

It has been widely accepted that the majority of carcinoids arise in the appendix,; however, recent data suggests that other locations, such as the rectum and small intestine may actually be more common [14]. In a study by Mggard et al., 11.427 cases were analyzed, and it was found that 44.7% of tumors were found in the small intestine, 19.6% in the rectum, 16.7% in the appendix, 10.6% in the colon, and 7.2% in the stomach [14]. Data from the SEER database also suggest that there is a

greater proportion of pulmonary and gastric carcinoids compared to appendiceal carcinoids, however, these changes may be due to variation in reporting as benign looking carcinoids were not added to the SEER database until 1986 [15].

Most carcinoid tumors of the appendix are asymptomatic. The average time for a carcinoid tumor to become symptomatic is 9 years [16]. When the tumor is located in the tip of the appendix, which it is in approximately 75% of the cases, it generally does not present with symptoms until it becomes metastatic. When the tumor is located at the base of the appendix, it can occlude the lumen and give the patient similar signs and symptoms of appendicitis [3]. In these patients, the diagnosis of carcinoid cancer is typically made by pathology after an appendectomy has been performed.

In rare cases, the patient can present with signs and symptoms related to a carcinoid syndrome. These include flushing, tachycardia, severe explosive diarrhea, and hypotension. These effects are mostly caused by the serotonin that the enterochromaffin cells are producing. The carcinoid tumor also produces vasoactive substances such as histamine, prostaglandins, kallikrein, bradykinins, substance P, gastrin, corticotrophin, and neuron-specific enolase. The lungs and the liver are able to clear many of these agents along with the serotonin, therefore, able to avoid carcinoid syndrome. It is not until these organs have carcinoid metastasis that the ability to clear these substances becomes impaired, and symptoms of carcinoid syndrome become apparent [16]. Carcinoid syndrome affects approximately 10% of those with carcinoid tumors.

As stated before, diagnosis of carcinoid tumor of the appendix is usually made after an appendectomy. When the patient presents with signs and symptoms of appendicitis, a CAT scan of the abdomen is typically performed. These imaging studies usually show a process of acute appendicitis or have associated calcifications [14,15].

The extent of surgery is based upon the size of the tumor, but since the majority of carcinoid tumors are found incidentally on simple appendectomies, a second surgery is sometimes needed. The National Comprehensive Cancer Network (NCCN) guidelines for treatment of carcinoid tumors state that tumors <2 cm confined to the appendix can be treated with simple appendectomy with no followup required. For tumors >2 cm, or those with extra-appendigeal invasion, an appendectomy with right hemicolectomy and cytoreductive surgery is necessary.

Generally, the prognosis for carcinoid tumors of the appendix is very good. If the tumor is confined to the appendix, the disease is said to have 95% 5-year survival rate. For patients with regional disease, there is an 85 % 5-year survival rate, and for distant metastasis, which occurs in approximately 4% of the time in appendiceal carcinoid-tumors, there is a 34 % 5 year survival rate [17].

Conclusions

The adenocarcinoma of the appendix is very uncommon. It was found accidentally during surgery performed for appendicitis or other non appendiceal pathologies, because the clinical-strumental techniques of study showed no clear signs of cancer. Reviewing the literature, what happened is most often an incidental finding of this neoplasm and the patient underwent right emicolectomy in the second time. For this reason the surgeon must know this possibility and prevent the second surgery when possible, proceeding for example intraoperative histological examination when the appendix is suspect.

At moment the emicolectomy represent right surgical treatment for all kinds of appendix neoplasms. We want to remember also that, given the high rate of concurrent cancer, during the operation, must carry out a thorough exploration of the abdominal organs.

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