ORIGINAL ARTICLE

Pathological findings in patients with acute appendicitis treated at the Cuban hospital in Qatar

Hallazgos patológicos en pacientes con apendicitis aguda atendidos en el hospital cubano en Catar

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ABSTRACT

Background: the histological study of the appendix is the gold standard for diagnosing pathologies that simulate acute appendicitis.
Objective: to characterize the pathologies associated or that simulate acute appendicitis, in a sample of patients treated at the Cuban hospital in Qatar, from January 2018 to December 2019.
Methods: a descriptive, observational, cross-sectional and retrospective study was carried out with patients admitted to the emergency room of the aforementioned hospital, diagnosed with acute appendicitis, who underwent computed tomography (CT) of the abdomen, appendectomy and biopsy of the appendix, in the period of time declared in the objective.
Results: in general, young patients were the most affected ones (the 21 to 30 age group with 40,54 % and the 31 to 40 age group with 35,13 %); the average age was 32,05 years with a standard deviation of 9,37. The main diagnosis was lymphoid hyperplasia; the largest group was that of Qatari nationality, followed by the Bangladeshi. Men were mostly affected by benign diseases and women by malignant tumors. There was some statistical significance among the tomographic variable of wall thickness, sex of the patient and histological findings.
Conclusions: the diagnosis of tumors and premalignant diseases was not so low, based on this, it is advisable not to delay or abolish the histological assessment of the appendix.

Keywords: APPENDICITIS; TOMOGRAPHY; BIOPSY; PATHOLOGIES.

Descriptors: APPENDICITIS; TOMOGRAPHY, X-RAY COMPUTED; BIOPSY; APPENDIX; HISTOLOGICAL TECHNIQUES.

RESUMEN

Fundamento: el estudio histológico del apéndice es la prueba de oro para diagnosticar patologías que simulan apendicitis aguda. Objetivo: caracterizar las patologías asociadas o que simulan apendicitis aguda, en una muestra de pacientes atendidos en el hospital cubano de Catar, desde enero de 2018 hasta diciembre de 2019.
Métodos: se realizó un estudio descriptivo, observacional transversal y retrospectivo, en pacientes admitidos en el departamento de emergencia del referido hospital, con diagnóstico de apendicitis aguda, a los que se les realizó tomografía axial computarizada (TAC) de abdomen, apendicetomía y biopsia de apéndice, en el periodo de tiempo declarado en el objetivo.
Resultados: en general los pacientes jóvenes fueron los más afectados (grupo de 21-30 años con el 40,54 % y con 31-40 años el 35,13 %), el promedio de edad fue de 32,05 años con una desviación estándar de 9,37. El principal diagnóstico fue la hiperplasia linfoidea, el grupo más numeroso fueron los de nacionalidad catarí, seguidos de los bangladesís. Los hombres resultaron ser los más afectados por enfermedades benignas y las mujeres por tumores malignos. Existió alguna significación estadística entre la variable tomográfica grosor de la pared, sexo del paciente y los hallazgos histológicos.
Conclusiones: el diagnóstico de tumores y enfermedades premalignas no resultó ser tan bajo, basado en ello, se sugiere no retrasar ni abolir la evaluación histológica del apéndice.

Palabras clave: APENDICITIS; TOMOGRAFÍA; BIOPSIA; PATOLOGÍAS.

Descriptores: APENDICITIS; TOMOGRAFÍA COMPUTARIZADA POR RAYOS X; BIPOSIA; APÉNDICE; TÉCNICAS HISTOLÓGICAS.

INTRODUCTION

Acute appendicitis is the leading cause of acute abdomen and emergency surgery in the world; however, mortality from this disease is quite low. It is characterized by pain in the right iliac fossa, preceded by pain in the epigastrium and vomiting, pain on palpation in the right iliac fossa with peritoneal reaction. (1)

For its diagnosis, clinical findings, laboratory tests and, if necessary, a series of contrasted computerized axial tomography (CT) images or, failing that, abdominal ultrasound is complemented, generally showing a dilated appendix, with a thickened wall, with edema of the surrounding fat and variable degree of contrast uptake without gas or oral contrast in the appendicular lumen, sometimes appendicolith is observed inside; in pediatric age, ultrasound is preferred to avoid ionizing radiation. (2,3)

Some pathologies can simulate, associate with it, or sometimes cause acute appendicitis (AA); within them, neuroendocrine tumors, some cecum and ascending colon tumors, appendicular mucinous tumors, polyps, diverticula, etc... These pathologies can change the behavior and treatment of these patients. (3) Diverticula of the appendix are true diverticula, they are rare, and can be congenital or acquired, mostly observed in the fourth decade of life, often associated with a high risk of neoplasm and mucinous tumor. (4)

On the other hand, neuroendocrine tumors are a rare entity, located in any part of the abdominal cavity, they can be functional or non-functional and, depending on the hormone they secrete, they can be classified into insulinomas, gastrinomas, VIpomas, etc., they have high mortality; the appearance of increasingly advanced diagnostic tools has favored its early diagnosis, also improving its prognosis. (5-7)

Due to its lymphoid embryogenesis, the observation of lymphoid hyperplasia of the appendix is frequent, especially in childhood, which can mimic or be associated with appendicitis; Sometimes lymphoid hyperplasia can be suspected on ultrasound due to thickening of the middle lamina, or represent a strong enhancement and thickening of the wall on the tomography, the appendicular lumen is usually permeable if it has not yet been complicated by appendicitis. (8)

Recent studies describe cases of chronic and recurrent appendicitis in some patients, which after surgery have detected fibrosis, follicular hyperplasia, xanthomatous inflammation, and other elements of chronicity. Studies carried out have related pain in the iliac fossa in women with chronic appendicitis, which has disappeared after the appendectomy and histologically showing signs of chronicity. (9,10)

Regarding the treatment, there is certain controversy regarding it, one group favors the use of antibiotics in uncomplicated appendicitis and another group favors the use of surgery, which can be open or laparoscopic. (1,3)

At this time, we do not have any study in our hospital on the behavior of pathologies associated with acute appendicitis and that can change the course of the disease or give an explanation to some phenomena associated with it; Based on this problem, we undertook the task of carrying out the present work to characterize the pathologies associated with or that simulate acute appendicitis, at the Cuban Hospital in Qatar.

MATERIALS AND METHODS

A descriptive, cross-sectional and retrospective observational study was carried out in the Cuban Hospital of Qatar to patients admitted to the emergency department with a clinical diagnosis of acute appendicitis, from January 2018 to December 2019, who underwent surgical recession and biopsy of the vermiform appendix, to characterize the different pathological findings or those associated with acute appendicitis; as a secondary objective to relate the histopathological findings with the tomographic variables, the age, and gender of the patients.

The universe consisted of 248 patients, who underwent computed tomography of the abdomen, from the diaphragmatic domes to the symphysis pubis, acquiring series of simple images, with oral and intravenous contrast with a 90-second delay, using CT equipment DEFINITION AS 64-slice multidetector and coupled double head pump from Siemens The sample consisted of 37 patients, who underwent appendectomy, biopsy and with a different pathological diagnosis or associated with acute appendicitis. Patients under 18 years of age, inmates, pregnant women, and staff working in the hospital were excluded.

The data were extracted from the patient's medical history, in the same way, the tomographic reports and images were reviewed in a radiological computer system (RIS), saved and analyzed in tables. The images were anonymized, the medical record numbers encoded and safeguarded on a password-locked computer, only accessible by the principal investigator. Besides, the permission of the corporation (Hamad Medical Corporation) was requested and the Helsinki principles were followed to avoid ethical-moral conflicts.

The dependent variable used was the histological diagnosis and the independent variables were the following: age (divided into age groups), nationality (according to origin), gender (male and female), tomographic findings: edema (presence of edema of

the peri-appendicular fat), diameter (transverse diameter of the appendix), appendicolith (presence or absence of appendicolith), gas (presence or absence of gas in the lumen of the appendix), thickness (thickness of the appendix wall), enhancement (if there was or no ring enhancement of the appendix wall) and contrast (presence or absence of oral contrast in the lumen of the appendix); in addition to the state of the appendix during the surgical procedure.

For the analysis of the qualitative factors, the percentages were calculated. In the frequency analysis of the variable "age group" the arithmetic mean, and standard deviation were calculated for each gender. The Chi-square test (X2) was used to determine independence between qualitative variables, obtaining the corresponding statistics, according to the degrees of freedom and level of statistical significance $\alpha = 0,05$.

RESULTS

The sample was made up of 37 patients, most of the patients were male, and the age group 21-30, followed by 31-40 years (**table 1**). The mean age was 32,05 years, with a standard deviation of 9,37 years.

TABLE 1. Distribution of patients according to age groups and gender

Age group	Female		Male		Total	
	Nº	%	Nº	%	Nº	%
< 20	0	0	1	2,70	1	2,70
21 - 30	5	13,51	11	29,72	16	40,54
31 - 40	1	2,70	12	32,43	13	35,13
41 - 50	0	0	6	16,21	6	16,21
50 >	0	0	1	2,70	1	2,70
Total	6	16,21	31	83,78	37	100

The probable relationship between the histological diagnoses and the nationality of the patients was evaluated (**table 2**) and it was shown that there is no significant statistical evidence ($p = 0,90$), the largest number of patients were Qatari (11,29 %), affected mainly by lymphoid hyperplasia and chronic appendicitis; followed by Bangladeshis, the vast majority also affected by lymphoid hyperplasia and fibrosis of the tip.

TABLE 2. Distribution of histological diagnoses and nationality of the patients, p = 0,90

Nationality	Histologic diagnosis									Total
	A. epiploic	Chronic	Diverticula	Fibrosis of the tip	Lymphoid hypertrophy	Omentum infarction	Polyp	Tumor mucinous	Tumor neuroendocrine	
Bangladeshi	0	1	0	3	3	1	0	0	0	8
Egyptian	0	0	0	1	1	0	0	0	0	2
Eritrean	0	1	0	0	0	0	0	0	0	1
Filipino	0	0	0	0	0	0	0	0	1	1
Indian	0	0	0	0	2	0	0	0	0	2
Mauritanian	0	0	0	0	1	0	0	0	0	1
Nepalese	0	0	0	1	1	0	0	0	0	2
Pakistani	0	1	0	1	3	0	0	0	0	5
Qatari	1	3	1	0	3	0	1	1	1	11
Somalia	0	0	1	0	0	0	0	0	0	1
Sudanese	0	0	1	0	1	0	0	1	0	3
Total	1	6	3	6	15	1	1	2	2	37

The most frequent histological finding was lymphoid hyperplasia, followed by chronic appendicitis and fibrosis of the tip, mostly in males; It is noteworthy that of the sample studied, five patients had some type of tumor lesion, constituting 13,5 % of the total sample, within them a polyp, two mucinous tumors, and two neuroendocrine tumors; malignant tumors represented 10,8 % and were more diagnosed in female patients, who were referred to their respective multidisciplinary oncology group; besides, three male diverticula, one omental infarction and one epiploic appendicitis of the male sex were diagnosed. The statistical evidence is not enough to affirm that there is a relationship between sex and the histological findings, but we cannot discard it completely either, p = 0,051 (**table 3**).

TABLE 3. Relationship between sex and pathological findings

Histopathologic diagnosis p=0,051	Female		Male		Total	
	Nº	%	Nº	%	Nº	%
Epiploic appendicitis	0	0	1	2,70	1	2,70
Chronic appendicitis	1	2,70	5	13,51	6	16,21
Diverticula	0	0	3	8,10	3	8,10
Fibrosis of the tip	0	0	6	16,21	6	16,21
Lymphoid hyperplasia	2	5,40	13	35,13	15	40,54
Omentum infarction	0	0	1	2,70	1	2,70
Polyp	0	0	1	2,70	1	2,70
Mucinous tumor	1	2,70	1	2,70	2	5,40
Neuroendocrine tumor	2	5,40	0	0	2	5,40
Total	6	16,21	31	83,78	37	100

Regarding the relationship between the variables tomographic findings and histological diagnosis, the relationship between each of them was analyzed and it was only statistically significant for the variable wall thickness, the results being shown in **table 4**, where it can be seen that most of the patients had the wall thickened to some degree.

TABLE 4. Relationship between wall thickness and histological diagnosis (p = 0,01)

Histopathologic diagnosis (n=37) p=0,03	Normal (1mm)	Thick wall (1-3mm)	Thick wall (1-3mm)	Total
Epiploic appendicitis	1	0	0	1
Chronic appendicitis	1	4	1	6
Diverticula	0	3	0	3
Fibrosis of the tip	1	0	5	6
Lymphoid hyperplasia	5	5	5	15
Omentum infarction	1	0	0	1
Polyp	1	0	0	1
Mucinous tumor	1	0	1	2
Neuroendocrine tumor	0	2	0	2
Total	11	14	12	37

No statistical significance was observed for variable appendix status and diagnosis histological p = 0,186. There was no type of suspicion reported by surgeons during the act surgical procedure for any pathology other than acute appendicitis, the most laparoscopic diagnosis edematous appendicitis was frequent (**table 5**).

TABLE 5. Distribution of findings during the surgical act

Histopathologic diagnosis (n=37) p=0,186	Normal	Edematous	Suppurative	Flemonous	Gangrenous	Total
Epiploic appendicitis	0	1	0	0	0	1
Chronic appendicitis	1	4	0	0	1	6
Diverticula	0	1	1	0	1	3
Fibrosis of the tip	0	2	1	0	3	6
Lymphoid hyperplasia	0	12	2	1	0	15
Omentum infarction	1	0	0	0	0	1
Polyp	0	1	0	0	0	1
Mucinous tumor	0	1	1	0	0	2
Neuroendocrine tumor	0	1	1	0	0	2
Total	2	23	6	1	5	37

DISCUSION

In our study, during the histological examination of the appendix, pathologies of both benign characteristics, mostly, and malignant, were detected, the latter requiring follow-up and treatment different from that of acute appendicitis; they were neither detected nor suspected during the imaging study or the surgical act. Benign pathologies were more frequent in males and malignant in females. In general, it was shown that young patients were the most affected (group of 21-30 years), similar behavior to acute appendicitis. The mean age was 32 years with a standard deviation of 9 years, it should be noted that, although there was no statistical significance between age and pathological findings, lymphoid hyperplasia (n = 15) was observed more in the third and fourth decade of life, one infarction of the omentum in the sixth decade of life, two mucinous tumors in the fifth decade of life, and two neuroendocrine tumors in the fourth decade of life. Other authors point out the most frequent lymphoid hyperplasia in children and young people, differing from our findings; [8,11-13,15-18] we will have to reevaluate this approach with larger cohorts and inferential statistics.

Most of our patients belonged to the male (31,83 %), compared to just six female patients, this is because population adjacent to the hospital is made up of mostly by repatriated workers. The use of imaging study was essential to define doubtful diagnoses, especially in patients female sex, who tend to suffer from processes gynecological, which they mistake for acute appendicitis; the same happens with men and stones right ureter. In the works of other authors reviewed there was a discrete higher representation male. [8,11-13,15-18]

Of the histological diagnoses made in our investigation, lymphoid hyperplasia was the most common finding, 42,1 % of the total sample, followed by chronic appendicitis (15,79 %) and fibrosis of the tip of the appendix, 13,51 %. The diagnosis of two mucinous tumors and two neuroendocrine tumors, in addition to a polyp, which represents a pre-malignant lesion, is striking, all of which constitute 16 % of the sample studied, a relatively high figure. These patients diagnosed with tumors were referred to the respective multidisciplinary oncology groups for their evaluation and follow-up; the incidence of these entities was higher than those of the reviewed literature. [8,11-13,15-18]

Lymphoid hyperplasia has been referred by most authors as a precursor of the acute appendicitis due obstruction, [11,12,14,16] however, for other authors it is only a histopathological finding, [8,15] Xu et al., in 2016, describe lymphoid hyperplasia as a finding that the organ responds to inflammatory processes, without causality in the development of this disease. [8] Due to the size of our sample, we can only describe its behavior. In future research, with larger samples, we will be able to infer more accurate results. It was determined that it is more frequent in males, with a thickened wall of the appendix, more frequent between the third and fourth decades of life and more frequently observed in edematous appendages during surgery, more diagnosed in patients of Qatari, Pakistani and Bangladeshi.

The pathologies diagnosed and described by other authors were very diverse in terms of frequency and type. Abd Al-Fatah et al., In 2017, diagnosed 19 Enterobius vermicularis, 12 granulomatous inflammations, 1 endocrine tumor, 3 mucinous, and 1 endometriosis. [12] Unver N et al., In 2019, 4 Enterobius vermicularis, 12 granulomatous inflammations, 1 neuroendocrine tumor, 1 mucinous tumor, and 1 endometrioma. [13] Duduyeni et al., 2016, 10 lymphoid hyperplasias, 15 fibrosis, 1 mucocele, 1 eosinophilia, 1 parasitosis, etc. [15] We all find benign and malignant findings in common that require treatment and follow-up different from that of acute appendicitis, which confirms the importance

of the histopathological study of the removed appendix, to avoid loss of other diagnoses such as these.

Appendicular diverticula can be congenital or acquired. In our work, three congenital patients were diagnosed in a Qatari patient, another Pakistani, and a Sudanese male, they presented with thickening of the appendix wall, mean age 40 years, standard deviation 6, 9 years and it was not necessary to take a different behavior after diagnosis. In all the reviewed works, Deng Dun-Wu, [19] Al-Brahim, [20] Marcaruzo A, [18] Basavaraj C, [21] Hwala S, [22] agree that it is a rare entity, more frequent in male and located in the fourth decade of life.

We also detected two mucinous neoplastic tumors in male patients, a Qatari and a Sudanese, both 42 years old, who required referral to a multidisciplinary oncology group. Hissong E et al., In a study carried out in 2019, in a sample of 97 patients, determined that lymphoid hyperplasia is more frequent than mucinous tumors; In this, we agree, some in their studies were able to suspect them during the CT examination, [23] which we did not achieve in our research.

Neuroendocrine tumors diagnosed incidentally in our study occurred, one in the third and the other in the fourth decade of life, both female with an average age of 33,5 years, Qatari and Filipino, respectively. In 2019, Zambrano et al. Reviewed 21 intra-abdominal neuroendocrine tumors, the main location of which was the appendix (38 %), of which 29 % were detected in therapeutic appendectomies and the other 9 % in prophylactic appendectomies. [24] Our studies seem to indicate that the diagnosis of a neuroendocrine tumor of the appendix is more frequently detected as an incidental finding. Canbak et al., 2019, also determined a higher frequency in females in a cohort of 402 appendectomies, where they found six incidental neuroendocrine tumors, average age 30 years. [25] Abdelaal and collaborators in their study carried out in Qatar, in the same corporation to which our hospital belongs, determined in their sample of 32 patients that 78 % were more frequent in men, and the average age was 25 years; agrees that the diagnosis was made in histological evaluations of specimens from an appendectomy, most of her patients were non-Arab. [26,27] The three studies collected are from small samples, hence the difference in the results, but we all agree that neuroendocrine tumors of the abdomen are mainly diagnosed incidentally.

Five chronic appendicitis were determined, mainly in male patients, with an average age of 29 years, standard deviation 9.8 years, the majority presented edema of the peri-appendicular fat, increased diameter, and thickening of the wall more than 1 mm. A case reported by Kothadia J (9) shows a 30-year-old patient with recurrent abdominal pain, who underwent an appendectomy and was diagnosed with chronic appendicitis, far from our results, because our diagnosis was made in a patient with appendicitis. There are no works reported in the bibliography, so ours should be continued and results that can be generalized should be obtained.

In the Chi-square analysis, among all the tomographic variables, it is only observed that the wall thickness has slight statistical significance, $p = 0.03$, concerning the diagnoses, so that lymphoid hyperplasia is characterized by having thickened wall, the two mucinous tumors have a very thickened wall, the two neuroendocrine tumors thickened, the normal polyp, and the fibrosis of the tip of the thickened appendix. A larger sample could give it a more significant value, we must take that into account for future research. These findings are not referenced in studies by other authors.

The edematous appendix was the most frequent finding and there was not a enough statistical relationship between what was described, and the histopathological diagnoses studied, nor was there any suspicion of an entity other than acute appendicitis in any of them.

The pathologies diagnosed vary depending on the population studied. There is insufficient statistical evidence to relate age, surgeon's findings, and tomographic variables with histological findings. There is a slight statistical significance between the tomographic variables, wall thickness, sex of the patient, and the pathological findings that should be studied later, using larger samples. The prevalence of tumors and premalignant diseases turned out not to be as low in our study as described by other authors, based on this, it is suggested not to delay or abolish the histological evaluation of the appendix.

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