



An Inflammatory Myofibroblastic Tumor of the Appendix Mimicking an Appendicular Malignant Lesion

Mauricio Gonzalez-Urquijo^{1,2} , Andrea Romero-Davila¹, Samuel Eugene Kettenhofen^{1,2}, Rogelio Gonzalez-Ramirez² and Gerardo Gil-Galindo^{1,2}

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¹Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Monterrey, Mexico.

²Department of Surgery, Hospital Metropolitano “Dr. Bernardo Sepúlveda,” San Nicolás de los Garza, Mexico.

ABSTRACT: Inflammatory myofibroblastic tumor (IMT) is a very rare lesion of unknown etiology. Cases of IMT involving the appendix are exceptional, and they can mimic malignant appendicular tumors. We present a case of a 65-year-old man who presented to our emergency room on septic shock and acute abdomen secondary to visceral perforation. The patient underwent exploratory laparotomy; massive bowel dilatation was encountered, along with 3L of purulent intraperitoneal fluid and a perforated appendicular mass of 6 cm. An appendectomy was performed. Histopathologic examination established the diagnosis of inflammatory pseudotumor with appendiceal perforation. This study constitutes the 14th confirmed case report of an appendicular IMT. It is important to include IMT in differential diagnoses of appendicular masses to avoid excessive resections.

KEYWORDS: Inflammatory myofibroblastic tumor, inflammatory pseudotumor, appendicular tumor, appendectomy

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CORRESPONDING AUTHOR: Mauricio Gonzalez-Urquijo, Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Dr. Ignacio Morones Prieto O 3000, 64710 Monterrey, Mexico. Email: mauriciogzzu@gmail.com

Introduction

Inflammatory myofibroblastic tumor (IMT), also called inflammatory pseudotumor is a rare disease of mesenchymal origin, first described in 1937.^{1–3} Inflammatory myofibroblastic tumor has distinct clinicopathological entities characterized by a dense inflammatory cell component and amid myofibroblastic proliferation. Its histopathologic nature is benign, but it may not be differentiated from a malignant tumor because of its local invasiveness, aggressive behavior, and its tendency to recur and metastasize.^{1,4,5} In 2003 was classified as an intermediate neoplasm in the current World Health Organization histologic typing.⁶

It was initially described in the lung, which is also the site where it is most commonly presented.⁷ Subsequently, it was seen that it can also be presented in soft tissue, the mesentery, the omentum, and retroperitoneum⁸; thenceforth, it was recognized that any anatomic location can be involved, making IMTs of the gastrointestinal tract extremely rare, being only 13 confirmed cases of appendicular origin.^{9,10} Most of these reported cases of IMT of the appendix are adolescents or young adult men.¹ Herein, we present a case of a 65-year-old man who presented to our emergency department on septic shock with an acute abdomen secondary to visceral perforation. Surgery was performed finding a perforated appendix with a tumor-like lesion on it. On histological examination, the lesion was identified as an IMT. A review of the literature is also presented.

Presentation of Case

A 65-year-old male patient with family history of diabetes mellitus and medical history of prostatic hyperplasia and a simple

umbilical hernia repaired presented to the emergency department. He arrived complaining of a 5-day history of diffuse abdominal pain, nausea, vomiting, and abdominal distension. The patient referred inability to pass flatus or to evacuate for the past 24 hours. On physical examination he was tachycardic and hypotensive. He presented with diffuse abdominal tenderness, suggestive of peritoneal irritation and severe distension. Digital rectal examination revealed an empty rectum, without abnormalities.

Complete blood count confirmed the presence of leukocytosis of 17.9×10^3 with hemoglobin of 18.1 g/dL and platelet count of 207×10^3 . Blood chemistry revealed acute renal failure, with a serum creatinine of 3 mg/dL, blood urea nitrogen 60 mg/dL, and urea of 210 mg/dL.

Simple abdominal radiographs displayed dilated loops and no signs of gas in the rectum, suggesting bowel obstruction, and no free air was seen. A noncontrast computed tomography (CT) of the abdomen was ordered, revealing a thick and irregular fibrous capsule at the base of the appendix with central low-attenuation necrotic component. Surrounding inflammatory changes were present with periappendiceal reactive nodal enlargement, pneumoperitoneum, and dilated large bowel. The appendix was enlarged with a perforation at the tip (Figure 1).

A preoperative diagnosis of bowel perforation with peritonitis was obtained, on the basis of clinical and radiological findings. The patient's blood pressure could not be stabilized despite reanimation with crystalloids; therefore, the patient was transferred to the operating room where the attending surgeon and the surgical resident performed an emergency laparotomy. Massive bowel dilatation was encountered and



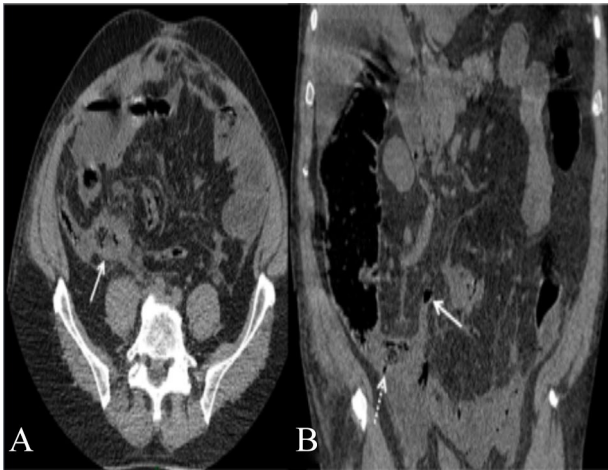


Figure 1. (A) Axial abdominal CT shows a thick and irregular fibrous capsule at the base of the appendix with necrotic component (arrow) and surrounding inflammatory changes. (B) Coronal reconstruction of the same patient reveals fibrous capsule and inflammatory changes at the base of the appendix (dotted arrow) and perforation at the tip of the appendix (solid arrow). Distention of the ascending colon is seen.

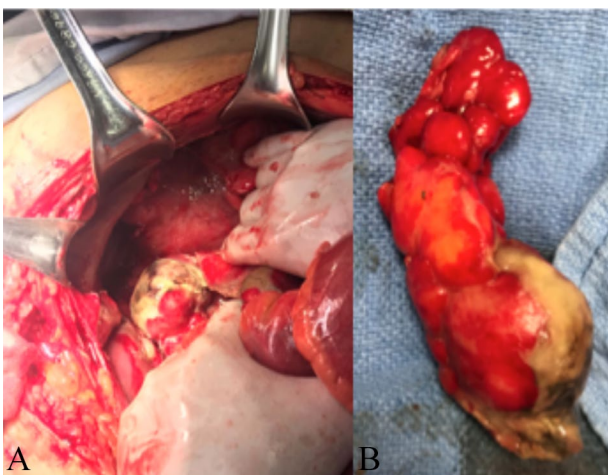


Figure 2. (A) Abdominal cavity with appendicular tumor measuring 6 cm × 6 cm. (B) Resected appendix with the tumor involving the middle and distal third.

approximately 3 L of purulent intraperitoneal fluid was aspirated. A mass measuring 6 cm × 6 cm was seen at the tip of the appendix with a perforated area of about 1 cm in diameter. The base of the cecum was healthy, and an appendectomy was successfully performed (Figure 2). The patient was transferred to the surgical intensive care unit for 48 hours and had an adequate postoperative outcome, referring only moderate pain during the initial days. Oral intake was reintroduced on the third day, without complications. On the postoperative day 7, the patient was discharged home, with good oral intake and with normal evacuations. The patient was seen in the ambulatory clinic at 1 and 6 months after surgery for a follow-up examination with a satisfactory evolution with normal renal function.

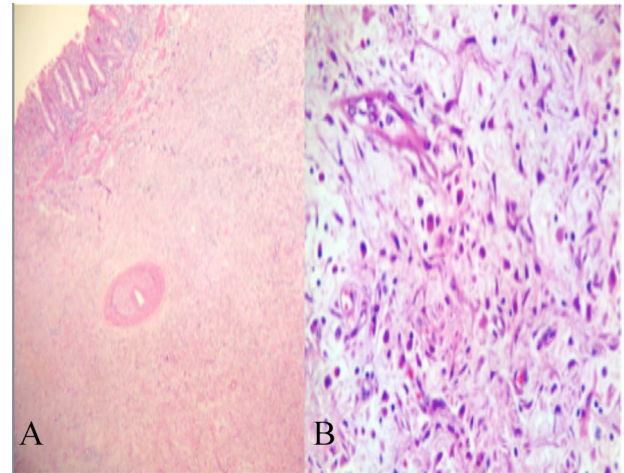


Figure 3. (A) Panoramic view of the appendix. Notice the clear thickening of the submucosa, with the dense inflammatory infiltrate in the mucosa. (B) High-power view of inflammatory myofibroblastic tumor. On a myxoid background with spindle cells, it shows alternating with polyclonal plasma cells and lymphocytes.

Histological examination of the specimen dyed with hematoxylin and eosin, revealed a mass showing fibroblastic proliferation accompanied by a dense inflammatory infiltrate in the mucosa and a clear thickening of the submucosa. A few areas showed myxoid changes with spindle cells, alternating with polyclonal plasma cells and lymphocytes (Figure 3). A perforation was identified in the section from the tip of the appendix lined by fibrinoid exudates. The immunohistochemistry of the paraffin section was positive for vimentin and smooth muscle actin and negative for anaplastic lymphoma kinase (ALK) (Figure 4). Final diagnosis was inflammatory pseudotumor with appendiceal perforation.

Discussion

Inflammatory myofibroblastic tumor is an atypical pseudosarcomatous, inflammatory, and histopathologic entity that most often affects children and young adults. When we performed a comprehensive search of English and Spanish literature, no more than 13 cases reported were found. Of note, most of the reported cases are in pediatric patients and young adult men.⁸ The first case report was published in 1984 and describes an 8-year-old boy who presented with symptoms of acute appendicitis,¹¹ and the most recent report, published in 2018 by Bashir et al,¹⁰ described a 14-year-old boy with the same preoperative diagnosis. Our patient constitutes the oldest patient who has presented with this appendicular tumor, making it the 14th case of this entity and also the first to present with septic shock secondary to perforation. It is most similar to a case reported by Kumar³ in which the patient was also a male adult who presented with peritonitis.

A variety of substitutes have been attributed to these lesions, such as plasma cell granuloma, mast cell granuloma, histiocytoma, xanthomatous pseudotumor, fibroxanthoma, fibromyxomatous

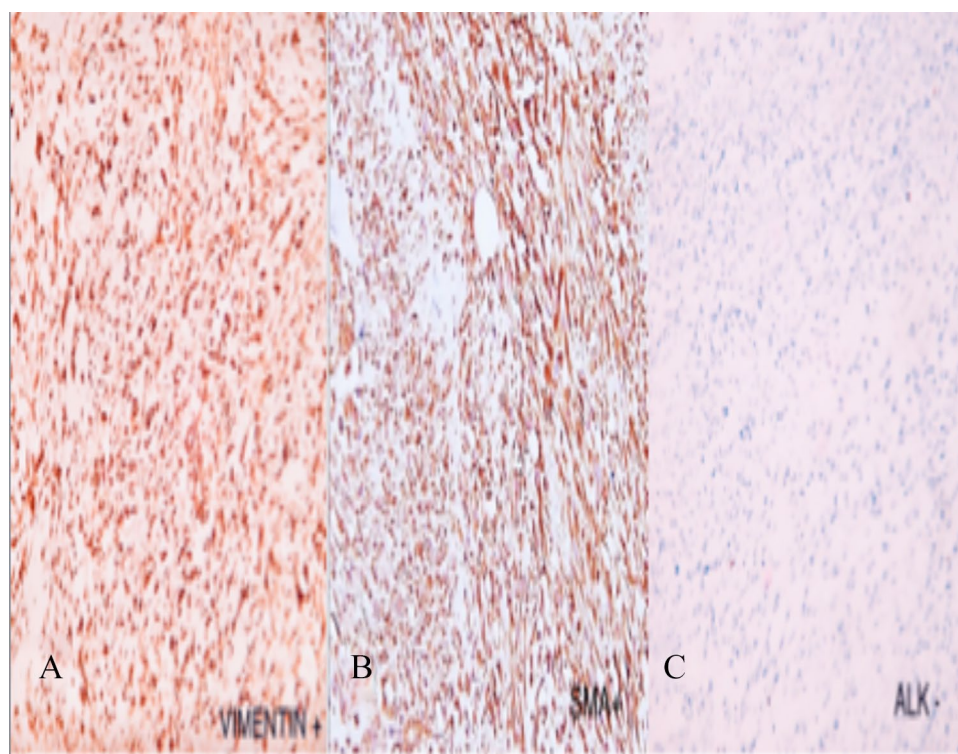


Figure 4. (A) Vimentin stain shows a strong positive stain to cytoplasm with mesenchymal differentiation. (B) Smooth muscle actin shows positive stain to myofibroblast. (C) Anaplastic lymphoma kinase stain results negative to cytoplasmatic and nuclear staining.

tumor, pseudosarcomatous myofibroblastic proliferation, inflammatory fibrosarcoma, pseudosarcomatous fibromyxomatous tumor, and reactive pseudosarcomatous response.^{3,7} The etiology of IMT remains unclear, and in most cases no causative agent is evident. Its development has been described after trauma, neoplasia, and surgery.⁹ There are reports of an association with Castleman disease, Hodgkin disease, peptic ulceration, Behçet disease, and chronic infections (*Campylobacter jejuni*, *Helicobacter pylori*, *Escherichia coli*, Epstein-Barr virus, *Coxiella burnetii*, *Klebsiella pneumoniae*).^{3,5,8} We do not know the exact origin of our patient's appendiceal pseudotumor; however, we do not consider acute appendicitis to be an etiological factor for developing this entity. Nonetheless, we believe that appendicitis occurred secondary to obliteration of the appendiceal lumen by the tumor, leading to perforation. Another rare presentation of this tumor was described by Majumdar et al⁸ describing a case with concomitant mucosal dysplasia, first impression of which was pseudomyxoma peritonei.

Surgery remains the most effective treatment for this pseudotumor^{1,3}; however, it must be noted that IMTs present with inconstant biological behavior that ranges from benign lesions (most frequent) to more aggressive variations. Whether complete surgical resection can be achieved depends on several factors such as the location of the tumor, multinodularity, and proximity to neighbor structures.^{3,4} For multiple and invasive lesions, chemotherapy with cisplatin, doxorubicin, and methotrexate may be considered, as well as radiotherapy for local recurrence or incomplete removal of the tumor.^{1,3}

The clinical presentation of IMT varies markedly, depending on the site at which the tumors originated. Most of the patients with appendiceal IMT presented with abdominal pain in the right lower quadrant, nausea, and vomiting, mimicking acute appendicitis.^{7,8,10,12} In some patients, imaging studies were ordered suspecting this last diagnosis, thus revealing an appendicular mass.^{1,5,9,13,14} Despite detection during preoperative screening methods, its radiological appearance is nonspecific and insufficient to make a specific diagnosis. Therefore, the final diagnosis is made by histopathologic examination.⁷

In our case, our patient had abdominal tenderness to palpation and presented with septic shock. We therefore ordered a CT of the abdomen preoperatively, which reported changes consistent with complicated appendicitis and bowel obstruction, leading to an emergent laparotomy.

The microscopic descriptions of IMT are relatively uniform. In general, these tumors are composed of a dominant spindle cell proliferation with inflammatory polyclonal mononuclear infiltrates, including plasma cells, lymphocytes, and histiocytes, arranged in a collagenous and slightly myxoid background. Our patient's tumor presented these histologic changes. Three histological patterns are described: fibromyxoid or vascular, proliferating, and sclerosing. Immunostains on spindle cells have often been found positive for vimentin, smooth muscle actin, muscle-specific actin, desmin, and focally for cytokeratins in most of the cases. Specific immunostaining techniques can help differentiate these tumors, with a favorable prognosis.^{5,7,10} The expression of ALK, may be a specific marker for IMT. Immunostaining for ALK produced fibrillary

Table 1. Reported appendiceal inflammatory myofibroblastic tumors.

REFERENCES	COUNTRY	AGE/ GENDER	PRESENTATION	IMAGING	PROCEDURE	MICRO	IHC
1 Narasimharao et al ¹¹	Japan	8/M	Intermittent fever	US: 7 cm × 5 cm mass in right hypochoondrium	Laparotomy, simple appendectomy	Destruction of the appendicular mucosa and replacement of the wall by diffuse inflammatory cells, predominantly plasma cells	NA
2 Yamagiwa et al ¹²	Japan	41/M	Abdominal pain	US: tumorous mass in the appendix	Laparotomy, simple appendectomy	Eosinophilic cell and fibroblastic infiltrations	NA
3 Jougon, 1991 ¹⁶	France	NA	NA	NA	NA	NA	NA
4 Bonnet et al ¹³	France	15/M	Fever, anorexia, weight loss	US: 4 cm retrovesical soft-tissue, noncalcified mass	Laparotomy, simple appendectomy	Cellular proliferation with plasma cells, lymphocytes, histiocytes, and mesenchymal cells in a poor collagenous stroma	Positive: vimentin Negative: desmin, leukocyte common antigen, and S-100
5 Khoddami et al ¹⁴	Iran	29/M	RLQ pain	CT and US: 10.5 cm × 2.5 cm paracecal mass in the right lower quadrant	Laparotomy, right hemicolectomy and ileo-transverse colon anastomosis	Extensive spindle cell proliferation with mixed inflammatory cells and lymphoid follicle formation	Positive: Vimentin, desmin, and muscle-specific actin
6 Vijayaraghavan et al ⁵	India	34/M	RLQ pain, fever, vomiting	US: appendicular mass	Laparoscopic appendectomy	Spindle-shaped myofibroblasts amid inflammatory cells consisting of eosinophils, lymphocytes, plasma cells, and neutrophils	Positive: vimentin, smooth muscle actin Negative: neuron-specific enolase, S-100, desmin, CD34, and CD117
7 Uludag et al ⁷	Belgium	20/M	RLQ pain, nausea, vomiting, fever, anorexia	NA	Conventional appendectomy	Fibroblasts with pleomorphic swollen nuclei and a mixed type inflammation formed by histiocytes and dispersed neutrophil leukocytes, plasma cells, and small lymphocytes	Positive: vimentin, smooth muscle actin, and CD68

(Continued)

Table 1. (Continued)

REFERENCES	COUNTRY	AGE/ GENDER	PRESENTATION	IMAGING	PROCEDURE	MICRO	IHC
8 Majumdar et al ⁸	India	41/M	RLQ pain, palpable growing mass, fever, anorexia, weight loss	US: 7 cm × 5 cm mass involving the appendix	Laparotomy. Right hemicolectomy and ileo-transverse colon anastomosis	Dysplasia of mucosal lining, stroma rich in collagen, intense myofibroblastic proliferation, and a polymorphic infiltrate comprising plasma cells, lymphocytes, histiocytes	Positive: smooth muscle actin and desmin Negative: S-100
9 Eunji et al, 2014 ¹⁷	Korea	85/M	History of gastric cancer	Incidental appendicular mass	Conventional appendectomy	Proliferation of spindle cells in a collagenous and slightly myxoid background with scattered blood vessels	Positive: vimentin and smooth muscle actin Negative: S-100, ALK, c-kit, desmin, CD21, CD23, and CD35
10 Schoonjans et al, 2016 ¹⁸	Belgium	42/F	RLQ pain, nausea, fever	CT: appendicular mass of 2.3 cm × 1.8 cm × 1.9 cm	Laparoscopic appendectomy	Spindle cells, accompanied by a prominent inflammatory infiltrate, composed of plasma cells and lymphocytes	Positive: Vimentin and cytokeratin AE1/AE3 Negative: CD68, desmin, CD117, and ALK
11 Kumar ³	India	50/M	RLQ pain, vomiting, anorexia	Chest X-Ray with free gas under the right dome of the diaphragm	Laparotomy, simple appendectomy	Fibroblastic proliferation accompanied by a prominent infiltrate of chronic inflammatory cells	Positive: vimentin, smooth muscle actin, and CD68 Negative: ALK
12 Henrique et al ¹	Brazil	33/F	RLQ pain, vomiting	CT: enlarged appendix with appendiceal mucocoele	Conventional appendectomy	Fusocellular pattern permeated by inflammatory cells rich in plasma cells and lymphoid aggregates	Positive: Vimentin, CD138, CD45, and myeloperoxidase Negative: ALK-1
13 Bashir et al ¹⁰	Saudi Arabia	14/M	RLQ pain, nausea, vomiting	US: 3.1 cm × 2.6 cm mucocoele of the appendix	Laparotomy, simple appendectomy	Spindle-shaped myofibroblastic cells in an edematous myxoid background with proliferating blood vessels and an infiltrate of plasma cells, lymphocytes, and eosinophils	Positive: desmin Negative: CD117, CD34, DOG-1, and ALK-2

Abbreviations: ALK, anaplastic lymphoma kinase; CT, computed tomography; IHC, immunohistochemistry; NA, not available; RLQ, right lower quadrant; US, ultrasonography.

or granular cytoplasmic staining in the neoplastic cells, sometimes with cell membrane accentuation. This marker is implicated selectively in younger patients and is generally associated with a favorable outcome.¹⁵

Because of the presence of spindle cells in bundles, soft-tissue sarcomas such as malignant fibrous histiocytoma, rhabdomyosarcoma, and fibrosarcoma should be kept in mind in the differential diagnosis of IMT; nonetheless, these tumors will express mitotic activity.³ Final diagnosis of our case was diagnosed as benign IMT because there was eosinophilic infiltration, with no mitotic activity, and because of the occurrence of dense inflammatory cells and fibroblasts with reactive swollen nuclei.

The incidence of local recurrence has been reported to be 15% to 37% in a large series of children presenting with IMT of mesentery and retroperitoneum; furthermore, infrequent distant metastases also have been suggested to occur.⁴ Predictors of a potentially malignant behavior include cellular atypia, ganglion-like cells, necrosis, nucleolar prominence, atypical or increased mitotic figures, expression of p53, and DNA aneuploidy. However, a unique and consistent chromosomal abnormality has not been identified.^{7,8} Nonetheless, none of the 13 appendicular IMT reported cases had an aggressive behavior. They are summarized and detailed in Table 1.

Conclusions

This study constitutes the 14th confirmed case report of an appendicular IMT. It is important to include IMT in differential diagnoses of appendicular masses to avoid excessive resections; however, appendectomy should be sufficient for this relatively indolent lesion. Although IMT is a benign tumor, which rarely presents malignant behavior, long-term clinical and radiological follow-up is recommended due to the lack of scientific data of this particular tumor at this specific anatomical site.

Author Contributions

MGU: Conceptualization, data curation, writing original draft
ARD: Data curation, formal analysis, investigation
SEK: Project administration, supervision
RGR: Supervision and editing
GG: Validation, Writing-review & editing.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of Tecnológico de Monterrey ethics committee and institutional

review board number 122 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

ORCID iD

Mauricio Gonzalez-Urquijo  <https://orcid.org/0000-0001-5101-1541>

REFERENCES

- Henrique P, Caf F, Hmm L, Ar P, Mg S. Inflammatory myofibroblastic tumor of appendix—case report. *J Hepatol Gastroenterol*. 2017;1:6-8.
- Zhao J, Ling J, Fang Y, et al. Intra-abdominal inflammatory myofibroblastic tumor: spontaneous regression. *World J Gastroenterol*. 2014;20:13625-13631.
- Kumar N. An interesting case of inflammatory pseudotumour appendix presenting as appendicular perforation with peritonitis. *Hell J Surg*. 2016;88:352-355.
- Karnak I, Senocak ME, Ciftci AO, et al. Inflammatory myofibroblastic tumor in children: diagnosis and treatment. *J Pediatr Surg*. 2001;36:908-912.
- Vijayaraghavan R, Chandrashekar R, Belagavi CS. Inflammatory myofibroblastic tumour of appendix. *J Clin Pathol*. 2006;59:999-1000.
- Fragoso AC, Eloy C, Esteveo-Costa J, Campos M, Farinha N, Lopes JM. Abdominal inflammatory myofibroblastic tumor: a clinicopathologic study with reappraisal of biologic behavior. *J Pediatr Surg*. 2011;46:2076-2082.
- Uludag M, Citgez B, Polat N. Inflammatory pseudo-tumour of the appendix and acute appendicitis: a case report. *Acta Chir Belg*. 2008;108:451-453.
- Majumdar K, Sakhuja P, Sukhpreet K, Archana R, Gondal R, Agarwal A. Inflammatory myofibroblastic tumor appendix with concomitant mucosal dysplasia, simulating pseudomyxoma on preoperative aspiration cytology. *J Cancer Res Ther*. 2012;8:317-319.
- Oh E, Ro JY, Gardner JM, Kim JW, Jung W, Yoon SO. Inflammatory myofibroblastic tumor of the appendix arising after treatment of gastric cancer: a case report and review of the literature. *APMIS*. 2014;122:657-659.
- Bashir MR, Al Sohaibani MO, Al-Rikabi AC. An unusual case of inflammatory myofibroblastic tumor of the appendix masquerading as acute appendicitis. *Oman Med J*. 2018;33:250-252.
- Narasimharao KL, Malik AK, Mitra SK, Pathak IC. Inflammatory pseudotumor of the appendix. *Am J Gastroenterol*. 1984;79:32-34.
- Yamagiwa YT, erada N, Hashimoto O, Itano S. An inflammatory pseudotumor of the appendix. *Japan J Cancer Clin*. 1990;36:1059-1062.
- Bonnet JP, Basset T, Dijoux D. Abdominal inflammatory myofibroblastic tumors in children: report of an appendiceal case and review of the literature. *J Pediatr Surg*. 1996;31:1311-1314.
- Khoddami M, Sanae S, Nikkhoo B. Rectal and appendiceal inflammatory myofibroblastic tumors. *Arch Iran Med*. 2006;9:277-281.
- Chan JKC, Cheuk W, Shimizu M. Anaplastic lymphoma kinase expression in inflammatory pseudotumors. *Am J Surg Pathol*. 2001;25:761-768.
- Jougon J, Amar A. Inflammatory pseudotumor of the appendix. Apropos of a case. Review of the literature. *Journal de chirurgie*. 1991;128(2):86-88.
- Oh E, Ro JY, Gardner JM, Kim JW, Jung WH, Yoon SO. Inflammatory myofibroblastic tumor of the appendix arising after treatment of gastric cancer: a case report and review of the literature. *Acta Pathologica, Microbiologica, et Immunologica Scandinavica*. 2014;122:657-59.
- Schoonjans C, Caluwé G, Bronckaers M. Appendiceal inflammatory myofibroblastic tumor: a rare postoperative finding. *Acta Chirurgica Belgica*. 2016; 116(4):243-46. doi:10.1080/00015458.2016.1139940.