Systemic Mastocytosis Presenting as Acute Appendicitis: A Case Report and Review of the Literature

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Key Words

Systemic mastocytosis · Appendicitis · c-KIT D816V (+) · Eosinophilia

Abstract

Systemic mastocytosis is characterized by abnormal growth and accumulation of mast cells in various organs. Gastrointestinal (GI) symptoms are common disease manifestations in this disease and can significantly impair the quality of life. Signs of GI systemic mastocytosis include steatorrhea, malabsorption, hepatomegaly, splenomegaly, portal hypertension, and ascites. Acute appendicitis as a presenting feature in systemic mastocytosis has not been reported in the literature previously. In this report, we discuss the case of a female patient with systemic mastocytosis (c-KIT D816V (+)) who was admitted for right-sided acute abdominal pain. Laboratory study revealed a normal white blood cell count with eosinophilia and an elevated serum tryptase level of 23 µg/l. CT of the abdomen and pelvis showed an enlarged appendix of 12 mm in diameter, with minimal wall enhancement. Laparoscopic appendectomy was performed. The appendix was found to be hyperemic and firm, and it was densely adherent to the posterior cecum, the surrounding peritoneal wall, and the overlying mesenteric fat. Pathology revealed acute appendicitis with greater than 30 mast cells per high-power field by immunoperoxidase studies with mast cell tryptase and CD117. The patient subsequently improved and was discharged home. This case is the first reported case with a histological diagnosis of acute appendicitis resulting from mast cell infiltration. Physicians should be aware of acute appendicitis as a manifestation of systemic mastocytosis. Prompt diagnosis and management may prevent potentially fatal complications of appendiceal perforation and peritonitis.

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Introduction

Systemic mastocytosis is a rare disease with abnormal proliferation and infiltration of mast cells in the skin, bone marrow, and viscera including the mucosal surfaces of the digestive tract, liver, spleen, and lymph nodes [1]. The clinical course of these patients is variable ranging from asymptomatic for years to highly aggressive and rapidly devastating or even mast cell leukemia [2]. Clinical manifestations of systemic mastocytosis reflect either mediator release from mast cells or infiltration of mast cells into tissues. They include constitutional signs, skin lesions, mediator-related findings (flushing, syncope, diarrhea, hypotension, headache, and/or abdominal pain), and musculoskeletal disease [3]. Due to the rarity of the disease, there are few prospective studies of gastrointestinal (GI) involvement, so the actual frequency of upper and lower GI lesions is unknown. Hepatomegaly, portal hypertension, splenomegaly, and ascites occur frequently in patients with systemic mastocytosis [3].

To the best of our knowledge, mast cell infiltration in the appendix due to systemic mastocytosis has not been described until to date. In this report, we describe a case of systemic mastocytosis presenting as acute appendicitis, which has successfully been treated with laparoscopic appendectomy. Histology revealed dense infiltrates of mast cell aggregates found in tryptase-stained biopsy sections with c-KIT D816V positivity.

Case Presentation

A 38-year-old Caucasian female with systemic mastocytosis c-KIT D816V (+) diagnosed in 2006, who had been on symptomatic therapy with anti-histamines (H1 and H2 blockers) for pruritus, was admitted to the hospital for acute right-sided abdominal pain which become progressively worse after a duration of 24 h. The pain was constant and sharp in intensity and was not relieved with narcotics. She complained of nausea but denied vomiting and diarrhea. Physical examinations revealed severe tenderness in the right and lower abdominal quadrant. Laboratory studies showed a normal white blood cell count of $8 \times 10^3/\mu\text{l}$ with eosinophilia of $1.6 \times 10^3/\mu\text{l}$, a hemoglobin level of 11.2 g/dl and a platelet count of $253 \times 10^3/\mu\text{l}$. A comprehensive metabolic panel, amylase, and lipase were all within normal limits. The serum tryptase level was elevated at 23 $\mu\text{g/l}$ (normal value: 0.4–10.9 $\mu\text{g/l}$). A CT of the abdomen and pelvis noted an enlarged appendix of 12 mm in diameter, with minimal wall enhancement. General surgery was consulted and finally the patient underwent a laparoscopic appendectomy. The appendix was found to be hyperemic and firm, and it was densely adherent to the posterior cecum, the surrounding peritoneal wall, and the overlying mesenteric fat. Histological exam of the appendix revealed acute appendicitis with mastocytosis (greater than 30 mast cells per high-power field) by immunoperoxidase studies with mast cell tryptase and CD117 (fig. 1, fig. 2, fig. 3, and fig. 4). She subsequently improved and was discharged home.

Discussion

Mastocytosis is a disorder involving neoplastic proliferation of mast cells and their CD34+ precursors. There are two major forms of mastocytosis: cutaneous mastocytosis, which is defined by the presence of one or more lesions limited to the skin (the face, palms, and soles are usually not affected) [4], and the systemic form of mastocytosis (systemic

mastocytosis), characterized by lesions affecting various internal organs, mainly the bone marrow and the GI tract, as well as the liver and spleen [4]. Notably, a point mutation in position 816 of the receptor (KIT D816V mutation) is found in up to 85% of all patients with systemic mastocytosis [5]. Clinical symptoms in patients with mastocytosis are caused either by release of biological mediators from the mast cells and/or their accumulation in various organs of the body, the skin and the bone marrow being more commonly associated [6]. In their review, Jensen et al. [3] have reported GI symptoms in 60–80% of patients with systemic mastocytosis, rendering GI symptoms as common as pruritus in these patients. The various GI manifestations reported in systemic mastocytosis are presented in table 1.

In this case report, we detected acute appendicitis with a histologic diagnosis of systemic mastocytosis. Abdominal pain is a very common GI manifestation in patients with systemic mastocytosis, and it has been reported in up to 80% of patients [11]. The abdominal pain is most frequently chronic and the major source of distress caused by the disease [12]. In our case report, the patient also suffered from chronic abdominal pain for the last 5 years, which was controlled with narcotics.

Acute appendicitis resulting from mast cell infiltration has not been reported before and should be considered as a potential cause in patients with systemic mastocytosis presenting with acute worsening abdominal pain. Appendicitis typically presents when an obstructed fecalith leads to an acute inflammatory response. Some studies suggest that mucosal inflammation may lead to mast cell infiltrates as part of an acute inflammatory response [13]. Other studies indicate that mast cell degranulation in the lamina propria may directly interact with motor neurons and silent nociceptors leading to smooth muscle contraction, diarrhea, and abdominal pain [14].

The initial clinical picture (like in our patient) may be confounded in this patient population since patients may experience chronic abdominal pain and may be on narcotics for pain control, which can mask the typical signs and symptoms of acute appendicitis. After appendectomy, our patient was discharged on antihistamines and is asymptomatic after 5 months of follow-up.

Conclusion

We have reported the first case of histologic evidence of acute appendicitis due to mast cell infiltration in a patient with systemic mastocytosis.

Since the majority of patients with abdominal complains have chronic abdominal pain and are on narcotics, it is important for the physician to identify patients with acute appendicitis. Failure to identify these patients may cause appendiceal perforation and peritonitis.

Disclosure Statement

The authors have no conflicts of interest to disclose.

References

- 1 Valent P: Systemic mastocytosis. *Cancer Treat Res* 2008;142:399–419.
- 2 Valent P, Akin C, Sperr WR, Escribano L, Arock M, Horny HP, Bennett JM, Metcalfe DD: Aggressive systemic mastocytosis and related mast cell disorders: current treatment options and proposed response criteria. *Leuk Res* 2003;27:635–641.
- 3 Jensen RT: Gastrointestinal abnormalities and involvement in systemic mastocytosis. *Hematol Oncol Clin North Am* 2000;14:579–623.
- 4 Arock M, Valent P: Pathogenesis, classification and treatment of mastocytosis: state of the art in 2010 and future perspective. *Expert Rev Hematol* 2010;3:497–516.
- 5 Orfao A, Garcia-Montero AC, Sanchez L, Escribano L: Recent advances in the understanding of mastocytosis: the role of KIT mutations. *Br J Haematol* 2007;138:12–30.
- 6 Horny HP, Sotlar K, Valent P: Mastocytosis: state of the art. *Pathobiology* 2007;74:121–132.
- 7 Wienbeck M, Rohner HG, Rodermund OE, Berges W, Strohmeyer G: Esophageal function in mastocytosis. *Verhandlungen der Deutschen Gesellschaft für Innere Medizin* 1978;84:977–979.
- 8 Grundfest S, Cooperman AM, Ferguson R, Bejamin S: Portal hypertension associated with systemic mastocytosis and splenomegaly. *Gastroenterology* 1980;78:370–373.
- 9 Mutter RD, Tannenbaum MA, Ultmann JE: Systemic mast cell disease. *Ann Intern Med* 1963;59:887–906.
- 10 Christensen AH, Matzen P: Duodenal ulcer in systemic mastocytosis. *Ugeskrift for Laeger (Copenhagen)* 1991;153:1945–1946.
- 11 Cherner JA, Jensen RT, Dubois A, O'Dorisio TM, Gardner JD, Metcalfe DD: Gastrointestinal dysfunction in systemic mastocytosis. A prospective study. *Gastroenterology* 1988;95:657.
- 12 Horan RF, Austen KF: Systemic mastocytosis: retrospective review of a decade's clinical experience at the Brigham and Women's hospital. *J Invest Dermatol* 1991;96:5S–14S.
- 13 Ogilvie-McDaniel C, Blaiss M, Osborn F, Carpenter J: Mastocytic enterocolitis: a newly described mast cell entity. *Ann Allergy Asthma Immunol* 2008;101:645–646.
- 14 Ramsay D, Stephen S, Borum M, et al: Mast cells in gastrointestinal disease. *Gastroenterol Hepatol* 2010;6:772–777.

Table 1. GI manifestations [3, 7–10]

Esophagus	Esophagitis, gastro-esophageal reflux disease, esophageal varices
Stomach	Peptic ulcer disease, prominent gastric folds
Small intestine	Malabsorption syndrome, celiac disease
Large intestine	Diverticulitis, polypoid lesions, diffuse intestinal telangiectasia
Other manifestations	Hepatomegaly, portal hypertension, ascites, splenomegaly, hypersplenism, splenic infarction, cholangitis, Budd-Chiari syndrome, abdominal lymphadenopathy

Fig. 1. Neutrophilic infiltration within the surface epithelium.

Fig. 2. Hypercellular lamina propria with mast cells infiltration.

Fig. 3. Mast cell tryptase highlighting the mast cells.

Fig. 4. Mast cells positive for c-kit (CD117).