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CASE REPORT | PATHOLOGY

Acute Appendicitis as the First and the Only Presentation of Systemic Mastocytosis

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ABSTRACT

Systemic mastocytosis is a rare myeloproliferative disorder characterized by abnormal accumulation of mast cells in a variety of organs. When affecting the gastrointestinal tracts, it may manifest with steatorrhea, malabsorption, hepatomegaly, splenomegaly, portal hypertension, and ascites, among others. To our knowledge, only one case of systemic mastocytosis has been reported affecting the appendix. We present another case of a 47-year-old woman who was admitted for right-sided acute abdominal pain and found to have systemic mastocytosis in her appendectomy specimen as the first and only manifestation of her disease.

KEYWORDS: appendicitis; mast cell; systemic mastocytosis; CD117; tryptase; KIT D816V

INTRODUCTION

Mastocytosis is a rare myeloproliferative disorder characterized by abnormal clonal proliferation of mast cells.[1] Systemic mastocytosis involves extracutaneous infiltration of mast cells, and the most commonly affected organs are bone, liver, spleen, lymph nodes, and mucosal surfaces of the gastrointestinal tract.[2] The spectrum of mastocytosis in the gastrointestinal tract can range from indolent systemic mastocytosis to aggressive systemic mastocytosis and the rare entities of mast cell sarcoma and mast cell leukemia. Gastrointestinal symptoms are present in 60%–80% of patients with systemic mastocytosis, and abdominal pain is the most common symptom.[3]

Many case reports and review articles have described the gastrointestinal involvement in systemic mastocytosis. However, a thorough review of the literature revealed only one case report to date, which describes appendiceal involvement by systemic mastocytosis.[4] We present a case of systemic mastocytosis limited to the appendix as the first and only manifestation.

CASE REPORT

A 47-year-old African American woman presented with gradually increasing right lower quadrant abdominal pain of 3 days of duration. The pain was sharp, 7/10 in intensity, and was associated with nausea, vomiting, diarrhea, anorexia, and malaise. There were no aggravating or alleviating factors for the pain. The patient did not have fever, hematochezia, melena, hematuria, vaginal discharge, eczema, itching, rash, or flushing. Physical examination revealed tenderness in the right lower quadrant and hypoactive bowel sounds. The medical history was insignificant except for the presence of cervical incompetence.

Laboratory investigations showed a white cell count of $14.47 \times 10^3/\mu L$ with 72% neutrophils, 18.5% lymphocytes, 8.5% monocytes, 0.9% eosinophils, and 0.1% basophils. She had a hemoglobin level of 12.3 g/dL and a platelet count of 297k/μL. A complete metabolic panel was performed and showed no abnormality. Abdominal and pelvic computed tomography in the emergency department revealed acute uncomplicated appendicitis with fluid distention of the appendix and fat stranding of the adjacent mesentery. No abscess or free air/fluid was seen.

A laparoscopic appendectomy was performed. The appendix appeared slightly edematous. There were no adhesions between the appendix and adjacent tissues. On gross pathologic examination, the serosal surface appeared dull and tan-white in color, with no

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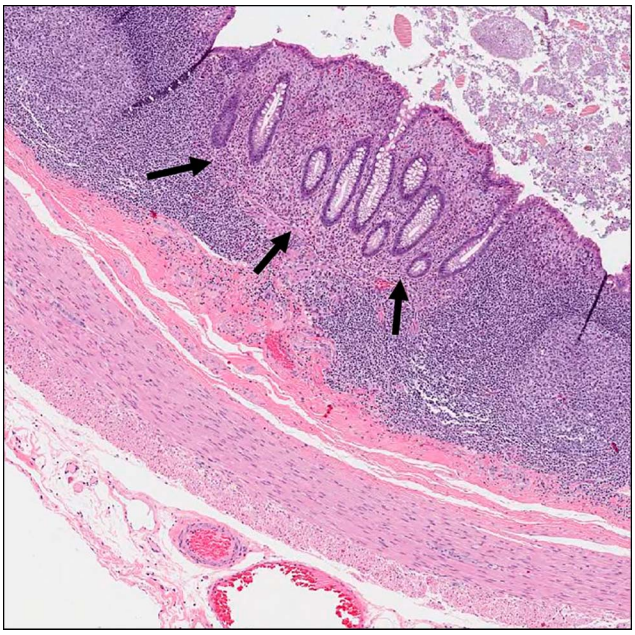

Figure 1. Low-power image depicting an appendiceal mucosa where the lamina propria is expanding by mast cell infiltrates (black arrows) (hematoxylin and eosin).

areas of exudate or perforation sites. The wall thickness was 0.2 cm, and the lumen diameter was 0.6 cm. No discreet masses were identified in the appendix grossly. The entire appendix was submitted for histologic evaluation.

The formalin-fixed, paraffin-embedded, and hematoxylin and eosin–stained tissue sections demonstrated appendiceal mucosa with involvement by sheet-like infiltrates and multifocal aggregates of neoplastic mast cells (numbering >100 mast cells in a single high-magnification field) with an associated prominent infiltration of eosinophils (Figures 1 and 2). The sections were also stained with antibodies to CD117, CD25, and CD2. The mast cells demonstrated diffuse immunoreactivity for c-kit (CD117) with strong aberrant coexpression of CD25 and focal/weak coexpression of CD2 (Figure 3). Based on the prominent eosinophilic infiltrate, a meticulous histologic evaluation was performed to exclude various parasitic infections and subtle clues to autoimmune diseases such as vasculitis. Furthermore, immunohistochemical stains for S-100 and CD1a were performed to evaluate the possibility of Langerhans cell histiocytosis, which were negative. Subsequent histologic and immunohistochemical findings are consistent with systemic mastocytosis involving the appendix based on the World Health Organization (WHO) 2016 diagnostic criteria.

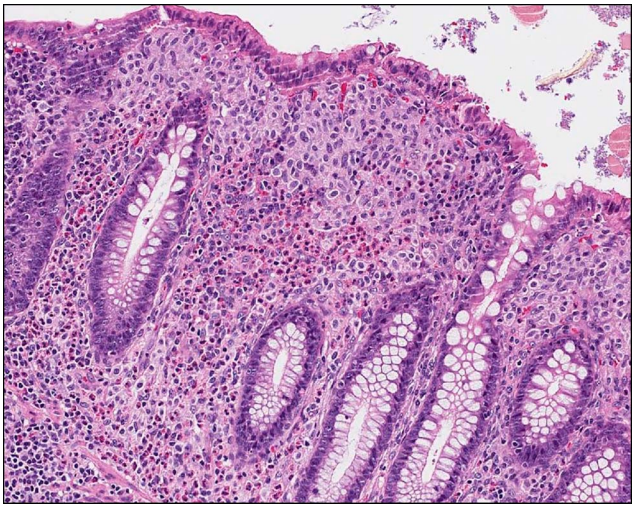

Figure 2. High-power view of mast cell infiltrates with associated eosinophils. The cells appear bland, with ovoid nuclei and abundant amphiphilic cytoplasm (hematoxylin and eosin).

The patient was followed up for 4 years. She did not develop any symptoms related to systemic mastocytosis. She had normal serum tryptase levels. Bone marrow biopsy was normal, including negativity of KIT D816V by polymerase chain reaction, and no additional lesions were discovered on computed tomography scans and skeletal surveys.

DISCUSSION

Mast cells are produced in the bone marrow and later migrate to reside in various tissues of the body. In a normal gastrointestinal tract, 2%–5% of the mononuclear cells in the lamina propria are mast cells, which is an average of 13 mast cells per high-power field.[5] They are preferentially located near the nerve terminals.

Based on the recent 2016 WHO classification updates, mastocytosis has been divided into cutaneous mastocytosis, systemic mastocytosis, and localized mast cell tumor.[6] The cutaneous form is common in children, whereas systemic mastocytosis is more common in adults and is characterized by extracutaneous infiltration of mast cells in one or more organs. The 2016 update subdivides systemic mastocytosis into indolent systemic mastocytosis, smoldering systemic mastocytosis, systemic mastocytosis with associated hematologic neoplasm, aggressive systemic mastocytosis, and mast cell leukemia.[6]

Clinical symptoms due to mast cell disorders are caused either by tissue infiltration of mast cells or by release of mediators such as prostaglandin D2 and histamine.[5] Abdominal pain is a very common symptom in systemic mastocytosis and is generally chronic.[4] However, the patient in the case we describe had acute abdominal pain localized to the right lower quadrant, nausea, vomiting, diarrhea, and an elevated white blood cell count, indicative of acute appendicitis with radiologic evidence supporting the diagnosis.

The presence of multifocal clusters containing at least 15 mast cells per cluster in the bone marrow and/or other extracutaneous organs is the major criterion for the diagnosis of systemic mastocytosis. The minor criteria include mast cells with abnormal morphology such as spindling or immature forms, CD2 and/or CD25 positivity in mast cells, activating mutation at the

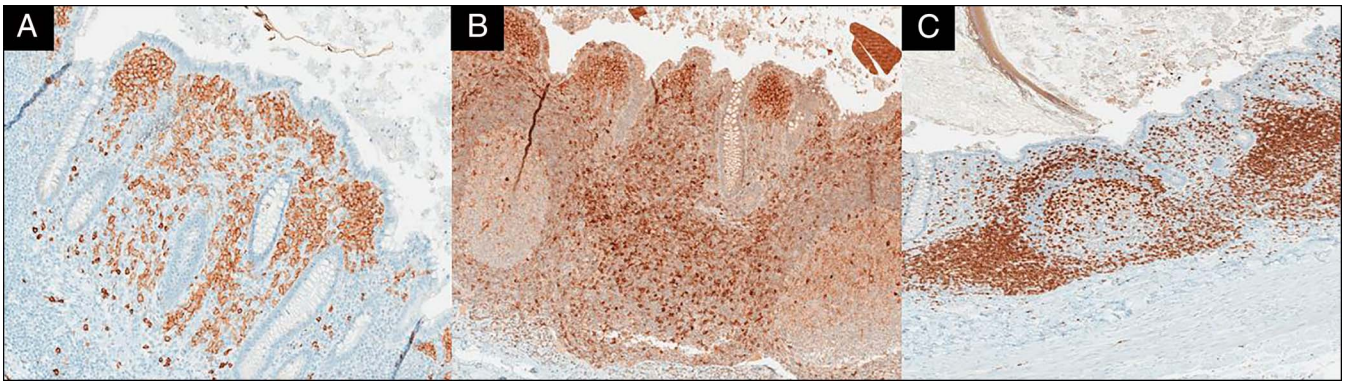

Figure 3. Mast cells showing diffuse positivity with CD117 antibody (A) along with aberrant expression of CD25 antibody (B) and CD2 (C).

KIT D816V region, and persistent elevation of serum tryptase levels above 20 ng/mL.[6] The presence of 1 major and 1 minor criteria or 3 minor criteria is sufficient for the diagnosis of systemic mastocytosis. Our case had the presence of 1 major criterion (multifocal clusters with more than 15 mast cells/cluster) and 1 minor criterion (positivity for CD25 and focally positivity for CD2); hence, a diagnosis of systemic mastocytosis was made. The latter finding of CD25 immunoreactivity of gastrointestinal mucosal mast cells has been shown to be specific for the diagnosis of systemic mastocytosis.[6] Although bone marrow involvement is frequently seen in many cases of systemic mastocytosis, our case showed a normal marrow, with no mast cell abnormality.[7] This observation was similar to the one reported by Johncilla et al, where all their patients with enterocolic mast cell aggregates who were evaluated for systemic mastocytosis were negative.[8] Thus, the authors conclude that the presence of mucosal mast cell aggregates is not a reliable indicator of systemic mastocytosis in patients without any established symptoms of the disease.[8]

In 2013, Akbar et al described the first case of systemic mastocytosis presenting with acute appendicitis.[4] The patient in their case report had a prior diagnosis of systemic mastocytosis and later presented with abdominal pain, acute appendicitis, and elevated serum tryptase levels. In our case report, acute appendicitis was the first presentation, leading to systemic mastocytosis diagnosis. In the 4 years of follow-up, the patient did not develop any other symptoms. To the best of our knowledge, this is the first case report of systemic mastocytosis limited to the appendix.

In conclusion, the appendix represents one of the common specimens received in a routine surgical pathology practice, which can be the first and sometimes the only site involved by a systemic disease. Hence, a careful gross and microscopic examination of the appendix is continued to be paramount.

DISCLOSURES

Author contributions: M. Sarwate prepared and wrote the introduction and case report section. A. Bakhshwin wrote the discussion and took the pictures.

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