

Indolent systemic mastocytosis mimicking Crohn's disease

Alexandros Hadjivasilis^a, Kalliopi J. Ioakim^a, Anastasia Neocleous^a, Karolos Demetriou^a, Soni Panjiyar^a, Froso Iacovou^b, Demos Michaelides^c, George Potamitis^{a,d}

School of Medicine, European University Cyprus; ECC Labs-IHCS; Alpha Evresis Diagnostic Center; Nutrition Centre, Cyprus

Abstract

Mastocytosis is a rare and heterogeneous group of diseases whose common element is the presence of dense mast-cell infiltrates in various tissues. The gastrointestinal (GI) tract is frequently affected with vague and subtle manifestations, making the diagnosis of GI mastocytosis rather formidable and challenging. The diagnosis of the disease requires a high level of clinical suspicion and an index of familiarity. To our knowledge, this is the first case of indolent systemic mastocytosis with colonic ulcerations. Because of the unusual presentation of mastocytosis, it was initially misdiagnosed as Crohn's disease; the diagnosis of mastocytosis was established after further evaluation of the patient's history and further investigation. Systemic mastocytosis should therefore be considered in the differential diagnosis in patients presenting with abdominal manifestations that cannot be otherwise explained or attributed to common GI pathologies and in cases where the patient's trajectory does not follow the expected course. More research is needed into the epidemiology and the non-classical presentation of systemic mastocytosis in order to increase awareness of the disease in the medical community.

Keywords Systemic mastocytosis, colonic ulceration, Crohn's disease, mast cells, *urticaria pigmentosa*, c-kit

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Introduction

The term systemic mastocytosis (SM) is used to define a rare cluster of heterogeneous diseases characterized by the presence of dense mast-cell infiltrates at various body sites [1]. The precise incidence of mastocytosis in the general population remains unknown, because of the lack of epidemiologic studies [2].

As for the manifestations of mastocytosis, the skin is commonly affected in most patients, who may present with pruritus or urtication, and it may be the only organ affected (*urticaria pigmentosa*). The vast majority of patients presenting with *urticaria pigmentosa* are children—in contrast to SM, primarily detected in adult patients [1]. Additionally, SM

almost always involves the bone marrow and can also appear in the skin, gastrointestinal (GI) tract, liver, spleen, and lymph nodes [3]. Among the extracutaneous depositions, the GI system is frequently involved, but the subtle manifestation of the disease makes the diagnosis of GI mastocytosis rather formidable and challenging [1,2]. Patients usually complain of diarrhea and bloating, but they may have other symptoms such as abdominal pain and nausea [4]. Although these non-specific symptoms neither point to a definitive diagnosis nor impose an increased mortality risk on the patients, they ensure increased morbidity. We report a case of indolent SM presenting with an unusual clinicopathology.

Case report

A 33-year-old male presented to his physician complaining of blood per rectum and non-specific abdominal pain. His past medical history revealed a dermatological diagnosis of *urticaria pigmentosa* made when he was 7 years old. His physical examination was otherwise unremarkable. The laboratory examinations were all within normal limits, except for a fecal calprotectin of 334 µg/g.

A colonoscopy was performed, during which ulcerations were detected in the distal descending (Fig. 1) and sigmoid colon. Serial biopsies were taken and the histology report was

^aSchool of Medicine, European University Cyprus (Alexandros Hatjivasilis, Kalliopi J. Ioakim, Anastasia Neocleous, Karolos Demetriou, Soni Panjiyar, George Potamitis); ^bECC Labs – IHCS (Froso Iacovou); ^cAlpha Evresis Diagnostic Center (Demos Michaelides); ^dNutrition Centre (George Potamitis), Cyprus

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Correspondence to: George Potamitis, 11, Kyriacos Matsis Av., Nikis Center, 1082 Nicosia, Cyprus, Cyprus, e-mail: g.potamitis@logos.cy.net

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indicative of Crohn's disease with inflammatory infiltrates. According to the histology report, inflammatory infiltrates were lymphoplasmacytic, multifocal in pattern, with increasing intensity towards the rectosigmoid, with mild active mucosal damage, with rare crypt abscesses and focal cryptitis. The infiltrates were confined to the mucosa, although in some places they extended to the submucosa but without epithelioid cell granulomas. The goblet cells were largely preserved, although focally depleted (mainly left colon) and no Paneth cells. Immunophenotypes CD45, CD10, BCL2, CD2 and CD20 were also used, with colonic infiltrate cells being positive for CD20 and CD45 and background cells also being positive for CD2 and CD5. Hence, these findings are fully consistent with an inflammatory bowel disease (Crohn's disease) involving the sigmoid colon without evidence of mastocytosis. Therefore, in view of the histological report the initial diagnosis of Crohn's disease was made. The patient was treated for Crohn's disease with mesalazine and prednisolone. Additionally, a second histopathologist confirmed these findings.

The patient appeared to be responding well to the treatment until 3 years later, when he began complaining of abdominal distention, intense nausea, diarrhea and gas, without fever. A second colonoscopy with serial biopsies was performed, without any remarkable gross findings. However, this time the histology report was more suggestive of a possible SM with more than 25 tryptase-positive mast cells per high-power field (Fig. 2). In addition, mildly edematous mucosa and a moderate increase in the chronic inflammatory infiltrate, with prominent eosinophils and an increased density of mast cells were observed. Furthermore, a CD117 (c-kit) immunohistochemistry stain exposed isolated mast cells distributed evenly throughout the *lamina propria* of the terminal ileal and colonic mucosal biopsy. Subsequently, serum tryptase levels were checked, giving values between 25 and 30 ng/mL.

Further investigations, including computed tomography (CT) imaging of the thoracic bony cage, demonstrated multiple foci of bony sclerosis (Fig. 3). On provisional histological examination of the bone marrow, multifocal infiltrates of atypical mast cells were observed, confirming the diagnosis of SM. Considering all aforementioned findings, the consultant hemato-oncologist confirmed the diagnosis of an indolent form of SM. As a result, there are currently no indications for this patient to start any type of treatment. The hemato-oncologist recommended that the patient be followed up with blood tests at regular intervals of 3 months. After a few months the patient complained of abdominal distention; a gastroscopy was performed but revealed no pathological findings.

Discussion

GI manifestations of SM, such as abdominal pain, diarrhea, nausea and vomiting, are reported in up to 80% of all cases [5,6]. Rarely though, GI bleeding has also been reported in patients with SM [6]. The exact cause of these symptoms is still debatable and unclear. It is believed that the manifestations

are attributable to the uncontrolled proliferation of mast cells, affecting various tissues and organs; as a secondary effect due to the release of mediators such as histamine, heparin, leukotrienes and proteases by the mast cells; or even impaired mediator metabolism [5-7].

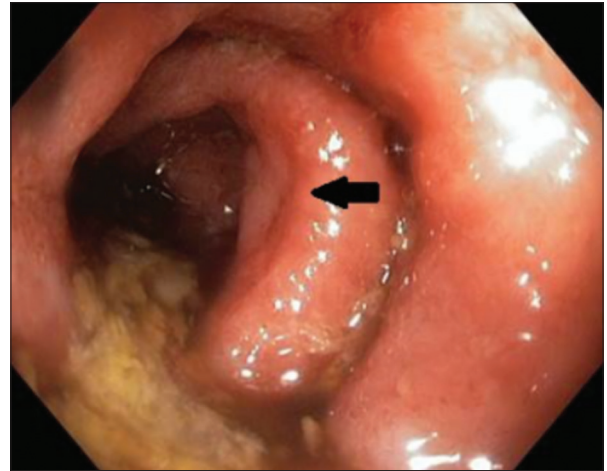


Figure 1 Well defined shallow colonic ulcer in the descending colon

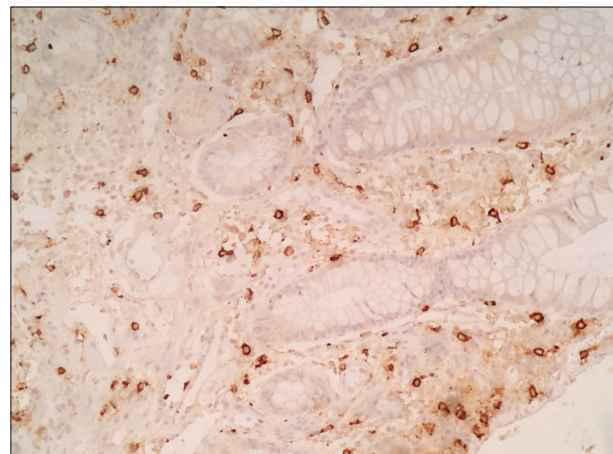


Figure 2 Increased mast cells visualized by immunohistochemical staining for mast cell tryptase

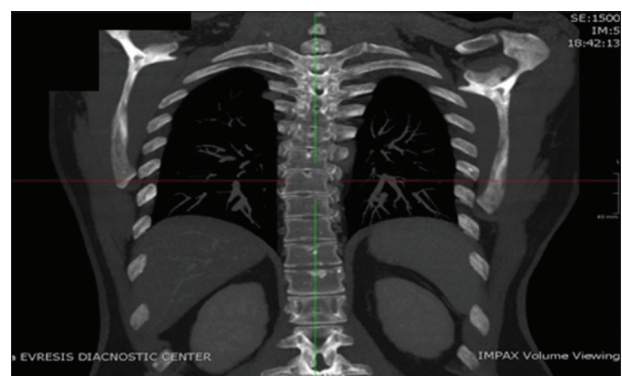


Figure 3 Computed tomography scan. Imaging of the thoracic bony cage demonstrates multiple foci of bony sclerosis

To our knowledge, this is the first case report where SM presented with colonic ulcerations. Interestingly, patients with mastocytosis have an increased chance of developing an ulcer, with gastroduodenal ulcers being the most common [4]. It is believed that histamine plays a role in the formation of ulcers [4].

Several studies in the literature report that mast cells have a significant role in the pathogenesis of various inflammatory diseases of the GI tract. Previous studies report that mast cells are also increased in Crohn's disease, ulcerative colitis, celiac disease, *Helicobacter pylori* gastritis, mastocytic enterocolitis, and parasitic infection [5].

Establishing the diagnosis of SM requires specific criteria [8]. To distinguish SM from Crohn's disease, a trustworthy immunohistochemical marker is CD25, present on mast cells in GI mucosa. Additionally, increased expression of CD2, CD25 or both is pathognomonic for mast-cell disorders [4]. Our patient expressed CD2 in the GI mucosal biopsies, tryptase levels of more than 20 ng/mL, as well as multifocal infiltrates of atypical mast cells in the bone marrow. All these are specific for SM, thus excluding other similarly manifesting diseases [5,6].

Last but not least, the patient's CT scan revealed multiple bony sclerosis in the thorax. Although not specific, along with the rest of the findings, this increases suspicion of the diagnosis. Those findings could be attributed to mastocytosis, either because of new bone formation or by the presence of protease, a mast cell mediator, which can lead to bony lesions [7].

This case report demonstrates a rare case of indolent SM with colonic ulceration mimicking Crohn's disease. Because of the tendency for misdiagnosis, especially of SM affecting the GI tract, gastroenterologists could possibly consider taking

multiple serial colonic biopsies in a patient with persisting GI symptoms, in addition to requesting CD117 staining for tryptase from the pathologist, even though the gross appearance of the colonic mucosa may be normal. Finally, more research is needed into the epidemiology and the pathophysiological classical and non-classical presentation of SM to increase awareness of the disease in the medical community.

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