Case Report
Mastocytosis involving rectum: a case report and literature review

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Abstract: Mastocytosis is a rare heterogeneous group of diseases with multi-organ involvement. Gastrointestinal (GI) tract infiltration by neoplastic mast cell is uncommon in systemic mastocytosis. In our literature review, there are only 11 published mastocytosis reports including 42 cases of biopsy confirmed direct colon involvement. We report here a rare case of focal mastocytosis in the rectum without evidence of systematic mastocytosis, incidentally identified in a 66-year-old asymptomatic male. Endoscopically it appeared as a polyp-like lesion and histologically it showed aggregates of neoplastic mast cells infiltrating the rectal mucosa and superficial submucosa. The lesional mast cells showed typical mast cell morphology including oval and spindle shape, abundant cytoplasm, large dark blue nuclei and fine basophilic granules. They were also positive for CD117 and tryptase, and negative for CD138 and CD25. No increase of eosinophils or lymphocytes was identified in the areas adjacent to the mast cells. CD25 is a systematic mastocytosis marker, and is usually positive for a systemic mastocytosis, and negative in the cases of local mastocytosis. The immunohistochemical and morphological findings are suggestive of a mastocytosis with primarily GI origin, which could be a diagnostic challenge. Pathologists and clinicians need to have increased awareness of this entity. However, it is still possible that our patient had an indolent form of systemic mastocytosis involving the bone marrow and rectum. Our summary of reported cases shows that the patients with mastocytosis involving the colon were 50-years-old on average, more likely female (female:male = 25:5), and mostly presented with a polypoid or elevated lesion. Diarrhea, abdominal pain and weight loss were the most common complaints of these patients, although our patient was asymptomatic. In short, we provide early evidence that local mastocytosis may present as solitary involvement of rectum in an asymptomatic patient, and immunohistochemistry and histology features could confirm the diagnosis.

Keywords: Mastocytosis, rectum, histology, immunohistochemistry

Introduction

Systemic mastocytosis is a rare disease characterized by clonal neoplastic mast cell proliferation in the bone marrow, skin, and other organs. The release of histamine and other inflammatory mediators could cause gastrointestinal (GI) symptoms in 70% to 80% cases, such as abdominal pain, diarrhea, nausea, and vomiting [1, 2]. However, neoplastic mast cells less frequently infiltrate the colon. The reported sites of GI involvement included the colon, duodenum, and terminal ileum [3]. Only 11 reports with 42 cases of mastocytosis involving colon confirmed by biopsies have been published in the English literature. Primary mastocytosis in the colon without evidence of systemic mastocytosis is rarely reported.

Case report

Here, we report a case of local mastocytosis involving the rectum. The 66-year-old asymptomatic male underwent a colonoscopy procedure for screening. Five 4-8 mm colorectal polyps were identified and submitted for pathology. The specimen submitted as a rectal polyp showed sheets of aggregates of mast cells in
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the rectal mucosa, with classical fried egg appearance: round to oval shaped cells, abundant light eosinophilic cytoplasm filled with small basophilic granules, and large centrally located dark blue nuclei with prominent light nucleoli. The cells had distinct cytoplasmic boundaries and infiltrated the lamina propria and lamina muscularis mucosae. No accompanying eosinophils or increased lymphocyte infiltrates were seen (Figure 1A-D). CD117 immunohistochemistry showed positive cell membrane staining and tryptase immunohistochemistry showed strong cytoplasmic positivity (Figure 2A-D). The mast cells were negative for CD138 and CD25 (Figure 3A-D). CD25 is a marker for systemic mastocytosis, and is negative in mast cells of GI tract origin [4]. The histological and immunohistological features are consistent with mastocytosis of GI tract.

Concurrent significant pathological findings from the remaining specimens collected during the same procedure included reflux esophagitis, intestinal metaplasia at the gastroesophageal junction, mild chronic gastritis with no H. Pylori identified, and multiple tubular adenomas in the descending colon and the sigmoid colon.

Interestingly, the patient had no complaints of GI symptoms, such as abdominal pain, nausea, vomiting, and diarrhea. He had a personal history of multiple adenomatous polyps during his previous colonoscopy five years ago, for which he was considered to have an increased risk of colon cancer and recommended to undergo surveillance once every three years. He also had a medical history of primary hypertension and uncomplicated type II diabetes.
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Discussion

Mastocytosis is a heterogeneous myeloproliferative neoplasm defined by the 2008 World Health Organization (WHO) Classification of Tumours of Haematopoietic and Lymphoid Tissues. It is characterized by the accumulation of clonal expansion and infiltration of neoplastic mast cells in one or more organs. The bone marrow is almost always involved, and the skin is involved in about 80% cases [5]. Cutaneous mastocytosis is defined as mastocytosis that only involves skin. On the other hand, systemic mastocytosis is characterized by the involvement of bone marrow and one or more extra-cutaneous organs, such as liver, spleen, lymph nodes, and the GI tract, and/or the skin. Systemic mastocytosis is more common in adults. The clinical presentation and the prognosis of mastocytosis are also various, ranging from asymptomatic to multiorgan dysfunction, and highly aggressive life-threatening diseases such as mast cell leukemia [5]. The release of histamine and other inflammatory regulators and/or infiltrating of mast cells could cause GI symptoms include nausea, vomiting, abdominal pain, and diarrhea.

Our literature search in November 2015 showed that 11 reports with 42 cases of systemic mastocytosis with aggregates of mast cells in the colon have been published (Table 1). The mean age at the diagnosis was 49.5 years, with a female dominant pattern (Female:Male = 5:1). Mastocytosis involving only the GI is a rare condition, and it has not been well characterized. During endoscopy, it may present as a polyp, nodule, mucosal fold, or a non-specific finding.

Figure 2. A-D. The rectum biopsy specimen with immunohistochemistry showing mast cell were positive for tryptase and CD 117. A, B. Tryptase showing strong cytoplasmic positivity, magnification 40 X and 200 X; C, D. CD117 showing membranous positivity, magnification 40 X and 200 X.
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The normal mast cell density in colonic mucosa is not well established [1]. Mast cells could be slightly increased in inflammatory conditions such as inflammatory bowel dis-

**Table 1. Summary: literature of mastocytosis involving colon**

<table>
<thead>
<tr>
<th>First author</th>
<th>Publish year</th>
<th>Case number</th>
<th>Age *mean</th>
<th>Gender</th>
<th>Symptoms</th>
<th>Endoscopic findings</th>
</tr>
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<tbody>
<tr>
<td>Kochi S</td>
<td>2014</td>
<td>1</td>
<td>64</td>
<td>F</td>
<td>abdominal pain</td>
<td>polyp</td>
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<tr>
<td>Doyle LA</td>
<td>2014</td>
<td>19</td>
<td>56.5*</td>
<td>F, 3 M</td>
<td>diarrhea, abdominal pain, nausea</td>
<td>N/A</td>
</tr>
<tr>
<td>Behdad A</td>
<td>2013</td>
<td>1</td>
<td>32</td>
<td>F</td>
<td>intermittent abdominal pain, diarrhea</td>
<td>nodular mucosal irregularities</td>
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<td>Elvevi A</td>
<td>2011</td>
<td>1</td>
<td>30</td>
<td>M</td>
<td>diarrhea, flushing, weight loss</td>
<td>N/A</td>
</tr>
<tr>
<td>Liu AY</td>
<td>2010</td>
<td>1</td>
<td>40</td>
<td>F</td>
<td>diarrhea, vomiting, weight loss</td>
<td>edema, mucosal nodularity</td>
</tr>
<tr>
<td>Lee LA</td>
<td>2008</td>
<td>1</td>
<td>75</td>
<td>M</td>
<td>chronic diarrhea</td>
<td>mucinous material, slightly raised mucosa</td>
</tr>
<tr>
<td>Kirsch R</td>
<td>2008</td>
<td>5</td>
<td>38**</td>
<td>F</td>
<td>diarrhea, abdominal pain, nausea, weight loss, vomiting</td>
<td>mucosal nodularity, thickening of mucosal folds</td>
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<tr>
<td>Hahn HP</td>
<td>2007</td>
<td>6</td>
<td>N/A</td>
<td>N/A</td>
<td>diarrhea, epigastric pain, vomiting</td>
<td>N/A</td>
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<tr>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Takasaki Y</td>
<td>1998</td>
<td>1</td>
<td>35</td>
<td>F</td>
<td>weight loss, facial flushing, et al</td>
<td>polypoid lesions</td>
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<tr>
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<td>1982</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
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</table>

**Summary Reports Cases Age (mean) Gender N/A N/A Total**

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<thead>
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<td>1982</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
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Note: *mean age, **median age.

[3, 6] (Table 1).
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ease and irritable bowel syndrome [7]; however, the aggregation of mast cells is usually seen only in mastocytosis, not in inflammatory conditions. It is considered to be a key feature to identify mastocytosis [4, 8]. Immunohistochemistry could facilitate the detection of neoplastic mast cells in mastocytosis. CD117 and mast cell tryptase are usually utilized to highlight mast cells. CD25 is also utilized to identify the neoplastic mast cells in systematic mastocytosis [5], but is negative in mast cells of GI origin—a very helpful feature of non-systematic mastocytosis [4]. In our case, the rectum biopsy showed sheets of mast cell aggregates in the mucosa, muscularis mucosae and superficial submucosa. The lesional cells are large, pleomorphic, having ample amount of cytoplasmic granules, dark nuclei with prominent nucleoli (Figure 1); these morphological features are consistent with neoplastic mast cells. Tryptase stain showed strong cytoplasmic stains and CD117 showed membranous stain, while CD 25 is negative. The findings therefore are most suggestive of a neoplastic mastocytosis from GI origin, not a systematic disease.

The major differential diagnoses for this case are inflammatory diseases with increased mast cells and systematic mastocytosis. As we mentioned above, the aggregation of sheets of mast cells is usually seen only in mastocytosis. This feature, together with the neoplastic morphology of the reported lesion, and the lack of a clinical history and histological findings of an inflammatory disease, supports the diagnosis of mastocytosis. However, systemic mastocytosis cannot be completely ruled out without a bone marrow biopsy to exclude systemic disease. It still is possible that our patient has an indolent form of systemic mastocytosis involving the rectum. In addition, CD25 is unusually positive in a systemic mastocytosis, but there are exceptions. In rare cases of well differentiated indolent systemic mastocytosis, expression of CD25 could be negative [9]. Solitary mastocytosis is an extremely rare entity. Previously, there were three case reports of pulmonary primary mastocytosis, presented as incidentally identified asymptomatic solitary nodules in the lung. The female to male ratio was 2:1, and the mean age at diagnosis was 59.3. There was no evidence of systematic disease nor local recurrence in these cases [10, 11].

The clinical course and prognosis of systemic mastocytosis vary greatly; from asymptomatic and indolent to highly aggressive mast cell leukemia. Our patient currently had no GI symptoms or any other complains. The mastocytosis was identified focally in the rectum, showing an indolent clinical course. Mastocytosis could be multifocal and without obvious endoscopic abnormalities, therefore multiple random biopsies throughout the rest of the colon and other portions of the GI tract are recommended for follow-up.

In conclusion, we present here a unique case of highly likely solitary mastocytosis involving the rectum of an asymptomatic 66-year-old man, a very rare entity. The immunohistochemical and histologic features are critical for diagnosing the case. This entity should be considered in cases with suspicious histologic features regardless of the location of the lesion and presenting symptoms (or the lack of them). It would be highly recommended to follow up with the patient for other GI lesions and possibly systemic disease for a potential disease progression.

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References


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