Indolent Systemic Mastocytosis mimicking Crohn's Disease

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Abstract:

Mastocytosis is a rare and heterogeneous group of diseases with the presence of dense mast cells infiltrates in various tissues being the common element. 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 index of familiarity. This report demonstrates a rare case of indolent systemic mastocytosis (SM) initially misdiagnosed as Crohn's disease (CD), but after proper and in-depth investigations the correct diagnosis was established. SM 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 the patient's trajectory does not follow the expected course. More research is needed regarding the epidemiology and the non-classical presentation of SM to increase the awareness about the disease in the medical community.

Keywords: Systemic mastocytosis (SM), Crohn's disease (CD), Gastrointestinal tract (GIt), Mast cells (MC), Urticaria Pigmentosa (UP), c-kit

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 in various body sites [1]. The precise incidence of mastocytosis in the general population remains unknown, due to the lack of epidemiologic studies [2].

According to the updated WHO report published in 2016 [3], Mastocytosis is no longer considered a subgroup of the Myeloproliferative Neoplasms (MPNs) owing to its unique clinical and pathologic features; and thus, is now a separate entity in the classification. Diagnostic criteria of Mastocytosis are also shown in the updated report [3,4].

As for the manifestations of Mastocytosis, the skin is commonly affected in most patients that may present with pruritus or urtication and it may be the only organ affected (urticarial pigmentosa). The vast majority of patients presenting with urticaria pigmentosa are children - contrary to SM - which is primarily detected in adult patients [1]. Additionally, SM almost always involves the bone marrow and can also appear in the skin, gastrointestinal tract, liver, spleen, and lymph nodes [5]. 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 diarrhoea and bloating but they may have other symptoms such as abdominal pain and nausea [6]. Although these non-specific symptoms neither point to a definitive diagnosis nor impose an increased mortality risk to the patients, they ensue 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 UP since seven years. His physical examination was otherwise unremarkable. The laboratory examinations were all within normal limits, except for a faecal calprotectin of 334 μg/g.

A colonoscopy was performed during which ulcerations at the distal descending and sigmoid colon were detected. Serial biopsies were taken, and the histology report was indicative for CD. In conclusion, the patient was initially diagnosed with CD for which he was treated with mesalazine and prednisolone.

He appeared to be responding well to the treatment until three years later, at which point the patient began complaining of abdominal distention, intense nausea, diarrhoea and gas, without fever. Further tests were done including blood tests and a second colonoscopy with serial biopsies. The patient's serum tryptase levels were between 25 and 30ng/ml and the second colonoscopy's gross findings were unremarkable. However, the histology report was suggestive of possible SM with more than 25 tryptase-positive mast cells per high power field, mildly edematous mucosa and a moderate increase of the chronic inflammatory infiltrate, with prominent eosinophils and increased density of mast cells. 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.

Further investigations were required to make a final diagnosis, including a CT scan and bone marrow (BM) biopsy. CT imaging of the thoracic bony cage demonstrated multiple foci of bony sclerosis. On provisional histological examination of the BM, multifocal infiltrates of atypical mast cells were observed, confirming the diagnosis of SM. Considering all aforementioned findings, the consultant haemato-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 is followed up with blood tests done at regular intervals of three months.

Discussion

The term mastocytosis involves a heterogenous group of diseases characterized by abnormal growth and accumulation of mast cells in various organs and tissues. Cutaneous mastocytosis (CM) is found in most cases, with urticaria pigmentosa (UP) being the most common form. When other systems or organs are affected such as the bone marrow, liver, spleen lymph nodes or gastrointestinal (GI) tract, the term systemic mastocytosis (SM) is used [7].

GI manifestations of SM such as abdominal pain, diarrhoea, nausea, and vomiting are reported in up to 80% of all cases [8,9]. Rarely though, GI bleeding has also been reported in patients with SM [9]. The exact cause of these symptoms is still debatable and unclear. It is believed that the manifestations are attributed to either the uncontrolled proliferation of mast cells affecting various tissues and organs; as a secondary effect due to mediators such as histamine, heparin, leukotrienes, and proteases being released by the mast cells; or even due to impaired mediators' metabolism [8,9,10].

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 CD, Ulcerative Colitis (UC) [8], Celiac disease [8], H. pylori gastritis [8], mastocytic enterocolitis [8] and parasitic infection [8]. However, when Hahn and Hornick [8] compared the mucosal mast cell numbers of patients with inflammatory GI disorders and control groups, they did not find a noteworthy increase. Nevertheless, worthy of mention is that a parasitic infection should always be included in the differential diagnosis in a patient presenting with increased mast cells in microscopy, as this could constitute a diagnostic pitfall [8].

Establishing the diagnosis of SM requires specific criteria [4]. 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 [6]. 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 BM. All these are specific for SM, thus excluding other similarly manifesting diseases [8,9].

Last but not least, the patient's CT scan revealed multiple bony sclerosis in the thorax. Although not specific, this along with the rest of the findings 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 [10].

Conclusion

This case report demonstrates a rare case of indolent SM mimicking CD initially, but the correct diagnosis was established after proper and in-depth investigations. Since SM is a rare disease with very few cases in the literature [6,8,9], it is neither well known nor studied so it is easily misdiagnosed with other diseases which share similar clinical manifestations. Great clinical suspicion and good collaboration between physicians is therefore required to achieve a faster and more accurate diagnosis. Because of the tendency for misdiagnosis especially of SM affecting the GIT, gastroenterologists could possibly consider taking multiple serial colonic biopsies in a patient with persisting GI symptoms, even though gross appearance of the colonic mucosa may be normal, in addition to requesting CD117 staining for tryptase from the pathologist. Finally, more research is needed regarding the epidemiology and the

pathophysiological classical and non-classical presentation of SM to increase the awareness about the disease in the medical community.

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