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Case Report

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Non Langerhans Cell Histiocytosis of the Rectum: Case Report and Review of the Literature

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Keywords:

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Abbreviations:

NLH: non-Langerhans cell histiocytosis; GI: gastrointestinal; EUS: endoscopic ultrasound; LCH: Langerhans cell histiocytosis; ECD: Erdheim-Chester disease; RDD: Rosai-Dorfman disease

1. Abstract

Histiocytosis is a condition resulting from the abnormal proliferation of dentritic cells of the mononuclear phagocytic system. Previously classified as Langerhans cell histiocytosis and non-Langerhans cell histiocytosis, and recently into 5 categories (L, C, R, M and H), it can be localized to an organ or have a systemic manifestation, affecting most commonly the bone, skin and lymph nodes. Gastrointestinal involvement is extremely rare especially for the non-Langerhans group. We report a rare case of a non-Langerhans cell histiocytosis affecting the rectum, manifesting as a large, nodular, ulcerated, continuous lesion found during a colonoscopy, in an elderly man with initial presentation of rectorrhagia and abdominal pain. The importance of this case report is to highlight the manifestations of digestive involvement by a non-Langerhans histiocytosis, in addition to the characteristic features of histiocytosis on trans-rectal endoscopic ultrasound.

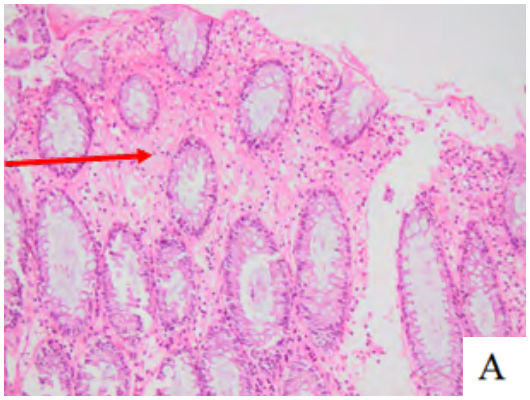
2. Introduction

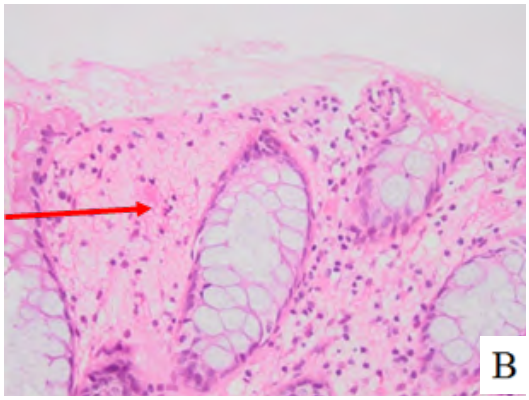
Histiocytosis is a condition resulting from the abnormal proliferation of dentritic cells of the mononuclear phagocytic system, mostly the CD34+ stem cell. This stem cell will differentiate, according to the cytokine milieu, into the CD14 negative cells that will turn into langherhans cell in the presence of TNFα and GM CSF, and the CD14 positive cell that will differentiate, based on the cytokines effect, into monocyte/macrophage lineage or dermal dendrocytes, the later considered to be the precursor cell of non-Langerhans cell histiocytoses (NLCH) [1]. Histiocytosis can be localized to an organ, or have a systemic manifestation, affecting most commonly the bone, skin and lymph nodes [2]. However, gastrointestinal (GI) involvement is extremely rare especially for the non-Langerhans group [3]. We report a rare case of a non-Langerhans cell histiocytosis (NLCH) affecting the rectum, manifesting as a large continuous, nodular, ulcerated lesion during colonoscopy, in an elderly man with initial presentation of rectorrhagia and abdominal pain.

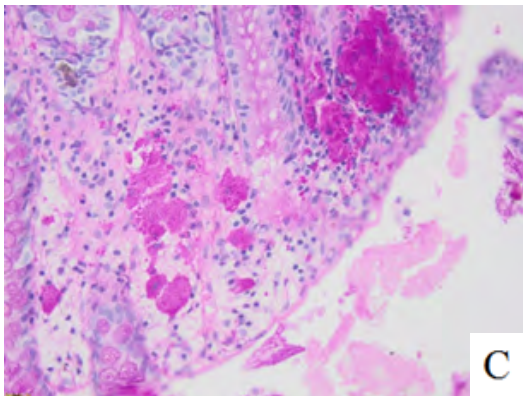
3. Case Report

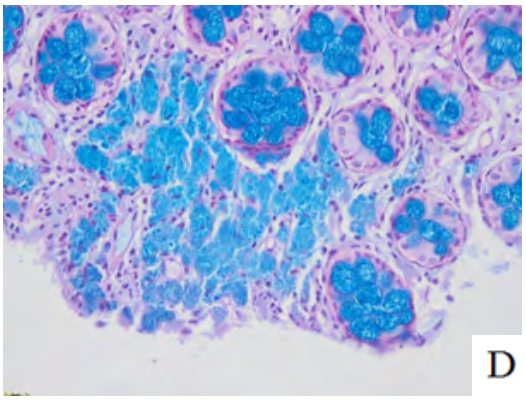
A 71 years old man, smoker of 30 pack-years, presented to our clinic complaining of more than one-year history of an intermittent mild abdominal pain, recently associated with occasional rectorrhagia of few weeks ago, with an altered bowel movement. He denied weight loss, decrease in appetite or a family history of GI malignancy. Physical examination revealed minimal diffuse abdominal tenderness mainly in the lower quadrants with palpable nodular lesions on digital rectal examination but with no signs of rectorrhagia. Blood test drawn, and showed normocytic anemia with an hemoglobin of 11,5. An ileum-colonoscopy was done and showed a reduced lumen at the level of the rectum with a severe inflammatory nodular aspect of the wall with some digging ulcerations. These lesions were extending continuously from the bottom of the rectum to the recto-sigmoid junction, with no other lesions noted elsewhere (Figure 1 and 2). Multiple biopsies using the forceps were applied and tissue was

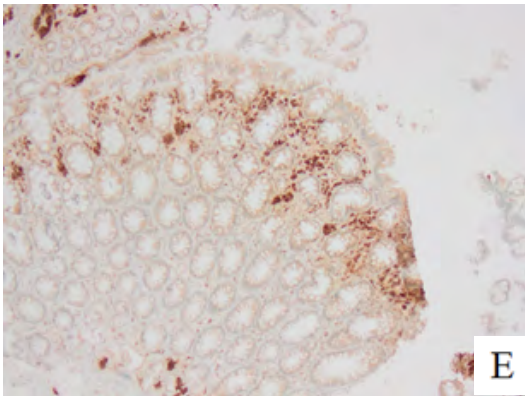
sent to the pathology unit. One week later, microscopic examination showed a colorectal type mucosa with a generally respected architecture. The lamina propria was enlarged by cells having an abundant cytoplasm, with a foamy or microvacuole-like appearance (Figure A and B). These cells stained positive for PAS, PAS-D (Figure C), and alcian blue (Figure D). These clusters of cells were found both at the level of the superficial and deep part of the lamina propria, and infiltrated the muscularis mucosa fibers. The submucosa was not represented. The adjacent glands showed focal erosions with regenerative changes. These clusters of cells showed positive staining for CD68 (Figure E). PS100, Pancytokeratin and CD117 were negative. Special stains were done and did not demonstrate any specific infection. The overall picture was that of a mucinous histiocytosis. After this result of the biopsy, a trans-rectal endoscopic ultrasound (EUS) was done for a better evaluation of the extension of the identified lesion, and to eliminate a sub-mucosal invasion with biopsies taken again. EUS showed a circumferential thickening of the rectal walls, the thickening was mainly seen in the sub-mucosa and the muscularis propria, an aspect strongly in favor of colorectal plastic linitis (Figure 3). However, the biospies turned again positive for a NLCH infiltration of the rectum, eliminating a rectal plastic linitis. The patient has been transferred to an hemato-oncologist and started a combination of steroid with chemotherapy.











H&E staining: Figure A(200X), B (400X): Lamina propria enlarged by cluster of cells with abundant foamy or microvacuole-like cytoplasm (arrow). These cells stained positive for PAS-D (Figure C), alcian blue (Figure D), and positive staining for CD68 (Figure E).

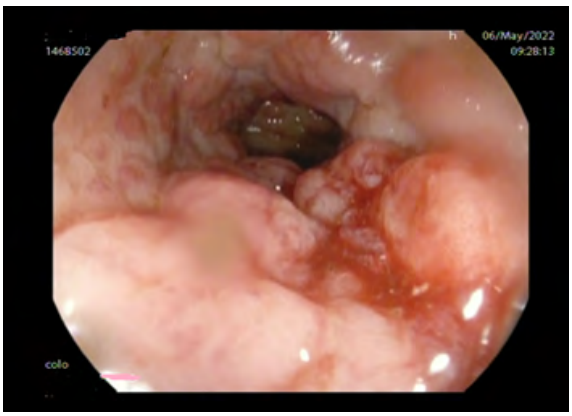


Figure 1: Endoscopic findings of colorectal mucosa (diffuse ulcerations and erosions with friable mucosa).

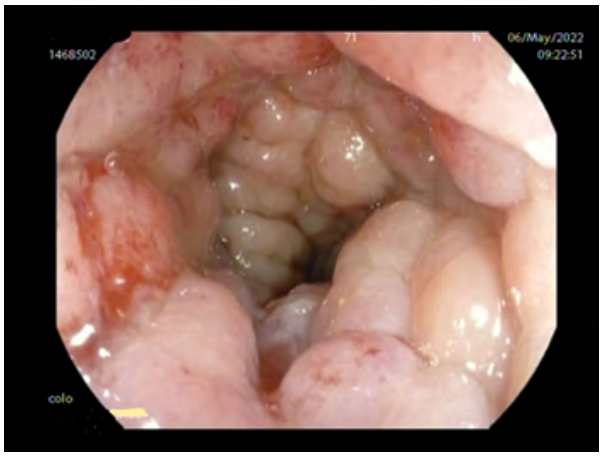


Figure 2: Endoscopic findings of colorectal mucosa (diffuse pseudo polypoid aspect with friable mucosa).

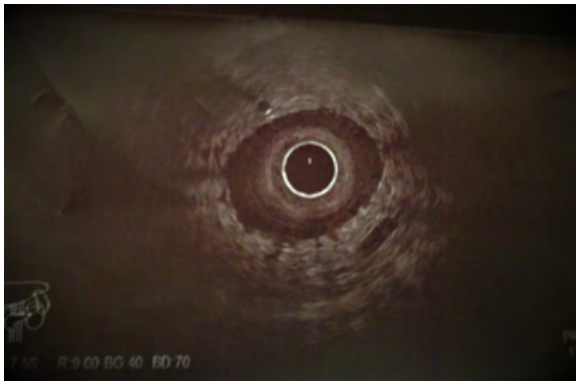


Figure 3: Findings on trans-rectal EUS, thickening of the rectal wall mainly the sub-mucosa and the muscularis.

4. Discussion

On the basis of the clinical, endoscopical and the histopathological findings, this patient had a definitive diagnosis of a NLCH of the rectum. The exact pathogenesis of histiocytosis is still unclear, with genomic alteration playing a growing role, especially the BRAF V600E mutation. Previously classified as Langerhans cell histiocytosis (LCH) and non-Langerhans cell histiocytosis (NLCH), the later including mainly the Erdheim-Chester disease (ECD) and Rosai-Dorfman disease (RDD) [1]. Recently, histiocytosis had been regrouped into 5 categories: the 'L' Langerhans group, including the bone, skin manifestations and the ECD – the C group including cutaneous and mucocutanuous histiocytosis – the R group including the xanthogranuloma family- the M group including the malignant histiocytosis – and the H group including the hemophagocyticlymphohistiocytosis and macrophage activation syndrome [4]. In general, the histiocytosis can be localized to an organ or have a systemic manifestation, the spread of the attack conditioning the prognosis [1]. The most common affected organs is the bone [2]. Knowing that GI involvement is rare, histiocytosis can affect any part of the GI tract. In the case of colorectal involvement, mucosal ulcerations, erosions, petechia and nodularities may exist. These lesions varies in size, and may be continuous or patchy, either marginated or have an infiltrative growth pattern. Solitary polyps are more common in the LCH group. Diagnosis is based on clinical data and skin biopsy with immunohistochemistry, mainly for the expression of the S100 protein, CD1a and CD68 antigens [5].

Non Langerhans cell histiocytosis is a neoplastic proliferation of histiocyte derived from dermal dendrocyte. It is characterized by positive immune-staining for factor XIIIa with different phenotypic criteria from the Langerhans ones. It can be classified, clinically, into three categories: those limited to the skin, those with cutaneous and systemic manifestations, and those mainly with extra-cutaneous presentation such as sinus histiocytosis with massive lymphadenopathy (RDD) and ECD. Usually affecting the children (in contrary to our case), the diagnosis is mainly based on histopathology, the immunohistochemistry allowing the differentiation between subtypes, and categorization into two group the juvenile xanthogranuloma and the non-juvenile xanthogranuloma [1].

Non-Langerhans histiocytosis are extremely rare causes of gastrointestinal inflammation, and only few case reports were found in the literature, mainly the ECD and the RDD subtypes. The hepato-biliary, the mesenteric, the pancreatic and colonic NLCH were barely involved. The first case reported was in 2017, in a Lady presenting with fever of a non-infectious origin, with hematochezia (similar to our case) and found to have segmental colitis due to NLCH, specifically the ECD sub-type, after histopathological and immunohistological examination of the colonic mucosa segment biopsied during colonoscopy, which revealed an area of ulcerations with friable granular mucosa at the splenic and hepatic flexure (contrary to our case, where the lesions were localized only in the rectum, with no other lesions noted elsewhere). Despite empiric treatment with steroids, the patient developed progressive distributive shock due to a cytokine storm [3].

A review on all published cases had shown that most digestive system manifestation of NLCH occurs in the tubular GI tract, mainly the left colon. Abdominal pain and rectal bleeding (as in our case report), diarrhea and weight loss are the main presenting features. Asymptomatic patient with an incidental finding, during screening colonoscopy, may occur. Hepatic and pancreatic lesions are rare, usually presenting with nodular lesions found upon abdominal imaging.

For better evaluation of the digestive manifestation of NLCH, especially the RDD subtype, Zainab I Alruwaii et al conducted a study on 12 specimens from 11 patients, with extranodal histiocytosis due to RDD affecting the digestive tract, and found that abdominal pain was the most common presenting symptom. The lesions were distributed endoscopically in different sites, mainly in the left colon, one in the appendix, and 2 in the right colon. Other lesions were found in the pancreas and the liver (6). Our case had a rectal presentation with extension to the recto-sigmoid junction.

On histopathology, histologic examination of non-Langerhans cell histiocytosis, show that histiocytes are positive for CD68 and CD163 and negative for CD1a and S100 protein (4). Our case showed that the histiocytes were positive for CD68 and negative for S100. These

findings are in favor of a Non-Langerhans Cell histiocytosis.

What make our case interesting, beside the rarity of GI involvement in histiocytosis, especially the NLCH, in addition to the presentation in an elderly (in contrary to the usual pediatric range population) men (where usually in adults, female are more commonly affected), is that a trans-rectal endoscopic ultrasound was done for better evaluation of the extension of rectal histiocytosis. After review of the literature, and to our knowledge, this is the first case report highlighting the characteristic finding of histiocytosis affecting the rectum on endoscopic ultrasound. Based on the results in our patient, we can assume that GI involvement of the histiocytosis share similar findings with plastic linitis, with transmural extension due to the circumferential thickening of the rectal wall, mainly in the sub-mucosa and muscularis propria. The importance of this reported finding reside in the necessity to include histiocytosis in the differential diagnosis of circumferential thickening of rectal wall, beside the plastic linitis, confirmed by the histological examination of the biopsied lesions, implicating a different therapeutic approach.

Concerning Langerhans cell histiocytosis (LCH), it is a rare inflammatory neoplastic proliferation of progenitor dentritic cells of the mononuclear phagocytic system. This abnormal proliferation occurs in the bone marrow, characterized by the infiltration of CD1a+ / CD207+ dendritic cells in many organs, mainly the bone and the skin. The incidence is estimated at 5 per million, typically affecting childrens with a male predilection [7]. Clinical presentation is variable, and the diagnosis is difficult because patchy presentation of LCH may occur in the GI tract [8]. Only few hundred cases of adult histiocytosis involving the GI tract have been reported in the literature. The presentation and severity of LCH involving the GI tract differ between the pediatric and adult group: in the pediatric group, GI involvement, presenting clinically with abdominal pain, protein-losing enteropathy, failure to thrive, bloody diarrhea or malabsorption symtoms, occurs mostly in the settings of a multisystemic disease. In contrary, in adults, it usually present as an isolated finding, mainly an incidental polyp discovered during routine colonoscopy in asymptomatic individuals [7].

A review of literature of GI LCH involvement found that LCH affect mainly the children. The location varies, with duodenal and colorectal area being the most commonly involved. A study reported a sex predilection toward the female, in the adult population, with a mean age of 58 years, mostly with a silent clinical presentation, where a solitary incidental polyp is discovered in the colon-rectum during a routine screening colonoscopy [8].

As noted before, genomic alterations may constitute an essential factor in the pathogenesis of histiocytosis. Recurrent activating mutations affecting the mitogen-activated protein kinase/extracellular signal regulated kinase (MAPK/ ERK) pathway were demonstrated in the majority of the patients, especially the Langerhans and EDD subtypes. These genomic alterations have led to the implementation of multiple therapeutic regimen, one of which the vemurafenib, has been approved by the Food and Drug Administration, for the first time in the treatment of histiocytosis, targeting the BRAF V600e-mutant [2].

5. Conclusion

Our case report is one of the rarest presentations of non-Langerhans cell histiocytosis affecting the gastrointestinal tract. The importance of this reported case resides in highlighting the different aspects of gastrointestinal manifestations in a histiocytic disorder. In addition, to our knowledge, this case report is the first to highlight the characteristic finding of rectal NLCH on endoscopic ultrasound, with the resulting necessity to include histiocytosis in the differential diagnosis in front of circumferential thickening of rectal wall, beside the rectal plastic linitis, implicating a different therapeutic approach.

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