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Unifocal Gastric Langerhans Cell Histiocytosis in a Child—A Unique Case to Remember

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Abstract: Langerhans cell histiocytosis (LCH) is the most common of the histiocytic disorders and occurs when the body accumulates too many CD1a/CD 207 positive Langerhans cells, a subset of the histiocytes in certain parts of the body where they can form tumors or damage organs. LCH is not a very common diagnosis in the pediatric age group. More than two-thirds of cases have the single-system disease with bones or skin as the commonly involved sites. Here, we present a 4-year-old child who had acute abdominal pain as chief complaint and etiological workup eventually led to a diagnosis of gastric LCH without affection of any other organ system. To the best of our knowledge, this is the first report of a unifocal gastric LCH in a child.

Key Words: Langerhans cells, histiocytosis, gastric, child, unifocal

INTRODUCTION

Histiocytic disorders comprise of a wide variety of conditions that can affect both children and adults. Langerhans cell histiocytosis (LCH) is the most common of the histiocytic disorders and occurs when the body accumulates too many CD1a/CD207 positive dentritic cells, a subset of the histiocytes in certain parts of the body where they can form tumors or damage organs. LCH is a rare disease of the pediatric population, with an estimated annual incidence in children <15 years of age being around 5 to $9/10^6$ and $1/10^6$ in patients older than 15 years of age. More than two-thirds of cases have single-system disease with bones or skin as the most commonly involved sites.[1] However, LCH is believed to be underdiagnosed, since some patients may have no symptoms, while others might have symptoms that are mistaken for other diseases. Here, we describe a 4-year-old child presenting with abdominal pain and etiological workup eventually led to a diagnosis of gastric infiltration of LCH. Surprisingly, he did not have any other manifestation or lesion involving any other organ at the presentation. This is the first report of a pediatric unifocal gastric LCH.

CASE REPORT

A 4-year-old boy presented with insidious onset abdominal pain lasting for a month. The pain was described as an excruciating ache localized in the mid and upper abdomen and was difficult to control with the usual pain-relieving medication. The pain did neither have a diurnal variation nor any relation to food intake or bowel movement. He never complained of any nausea, vomiting, or aphthous stomatitis, and his bowel movements were normal. His appetite was reduced, and he lost about 1 kg body weight in the last 1 month. Examination revealed a normal-looking boy, with weight under the third centile and height at the 25th centile line. He did not have pallor, icterus, clubbing, edema, or lymphadenopathy. Apart from a soft, 1 cm palpable liver, there was nothing remarkable in the abdominal examination. Complete blood count revealed hemoglobin of 10.5 g/dL with normocytic film. The liver function test was normal, and serum lactate dehydrogenase (LDH) was slightly higher than normal (517 mg/dL [upper limit 450 mg/dL]). Abdominal ultrasonography and CT scan showed essentially normal appearance without any significant lymphadenopathy. Due to persistent pain, an endoscopic evaluation of the gut was undertaken. An esophagogastroduodenoscopy revealed 2 punched-out ulcers on nodular lesions in the gastric body (Fig. 1) and antrum with mild scalloping of duodenal folds. Colonoscopy showed a sessile polyp in the left colon and lymphoid nodular hyperplasia in the ileum. Biopsy was taken from all the lesions in the stomach, as well as from the duodenum, colon, and ileum. The histopathology from the gastric ulcers disclosed abnormal clumps of histiocytes having reniform or cleaved nuclei and pale cytoplasm admixed with eosinophils (Fig. 2), which were S100 (Fig. 3), and CD68 positive on immunostaining (Fig. 3). The colonic sessile polyp was inflammatory and was S100 and CD68 negative. Therefore, a diagnosis of gastric LCH was suspected. He was referred to a tertiary F2,F3

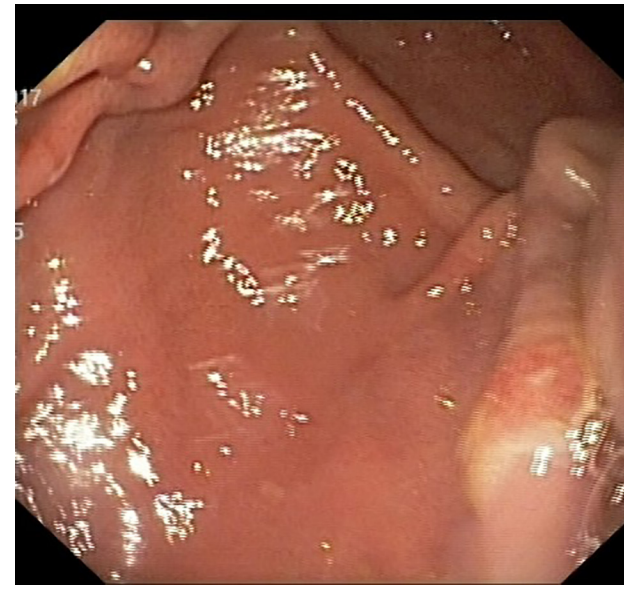

FIGURE 1. Gastric nodular ulcer on endoscopy.

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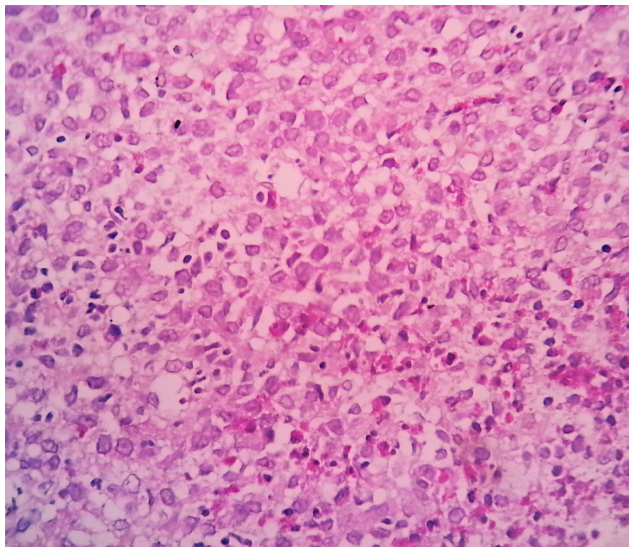

FIGURE 2. Histopathology (H&E staining) showing sheets of neoplastic histiocytes.

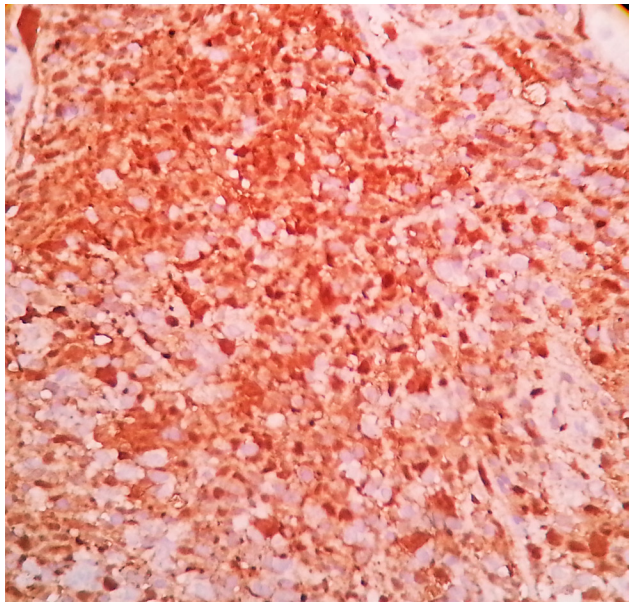

FIGURE 3. Histopathology (S100 immunostaining) showing nuclear and cytoplasmic staining of Langerhans cells.

pediatric hematooncology center of the city for further workup and treatment. There the CD1a-immunostaining of the cell-block from gastric biopsies was found to be positive and that confirmed the diagnosis of gastric LCH. The additional conventional spreading assessment undertaken did not reveal any affection beyond the stomach. There was no evidence of V600E *BRAF* mutation using conventional next generation sequencing. He was started on chemotherapy (details were not available to us) and showed improvement in pain and appetite. Unfortunately, histopathological photographs of CD1a staining and a repeat endoscopy of the lesions were not available to us, as treatment had been undertaken in a different center and the child was lost to follow up.

DISCUSSION

LCH is a rare clonal disease of the monocyte-macrophage system characterized by uncontrolled proliferation and accumulation of CD1a+/CD207+ dendritic cells.[1] Its clinical presentations are highly variable and may range from isolated, self-healing skin, and bone lesions to life-threatening multisystem disease.[2] Here, we described a unifocal gastric LCH in a toddler, presenting with isolated abdominal pain never described earlier.

LCH is classified into three distinct forms: single-system single site (SS-s), single-system multisite (SS-m), and multisystem type (MS). Approximately, 65% of patients have SS disease.[2] Gastrointestinal (GI) involvement in children with LCH was reported but uncommon and had been associated with systemic illness and poor prognosis. The peak incidence occurs in children <2 years old and shows a 2-fold female predominance.[3] The reported symptoms include vomiting, abdominal pain, intractable diarrhea, failure to thrive, and bloody diarrhea.[3] A long-drawn disease process before a diagnosis can lead to the development of full-blown malabsorption or protein-losing enteropathy and in extreme cases complications such as intestinal perforation.[2] Isolated abdominal pain as a presenting feature is extremely uncommon as experienced in the current case. Bansal et al reported a case series of 69 children from India but none of them had isolated abdominal pain as clinical presentation.[4] Catalan et al described two cases who presented with GI involvement, first child had colorectal involvement (colonoscopy done for hematochezia) and second child had duodenal infiltration, which was fortuitously detected during ruling out celiac disease.[5] Godoy et al described a 5-month-old with rectal bleeding who did not respond to amino acid formula and was detected to have erythematous rectosigmoid nodular lesions which were +ve for CD1a and CD68.[6] Singhi et al depicted multifocal involvement in colon and duodenum in 2 children but none in the stomach.[3] Small bowel involvement was described in 3 children.[7] To our understanding, in children GI manifestation being a few, endoscopy is not undertaken frequently until they present with the GI symptoms, described earlier.

Unifocal gastric involvement was depicted in adult literature (mostly case reports). In contrast to children, adult cases were mostly unifocal and had a more benign course.[8] All patients were in the fourth to sixth decade of life, five patients presented with abdominal pain like the current case and the rest were asymptomatic. In the adult series, endoscopic gastric lesions were described as a large, flat raised area, a single polyp, an ulcerating mass, or as multiple polyposes.[7,8] In the present case, macroscopically the gastric lesions were 2 flat-topped nodules with ulceration (Fig. 1). So far our case had a favorable outcome most likely due to early detection before systemic spread. A *BRAF* (V600E) mutation had been described in a recurrent and severe form of LCH,[1,9] but in the present case, the *BRAF* mutation was absent.

To conclude, gastrointestinal LCH may be a rare differential in a child where gastrointestinal symptoms are not explainable by usual clinical or investigational findings, where a timely endoscopy with an expert histopathological analysis could clinch the diagnosis.

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