Case Report

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Gastrointestinal LCH: a rare manifestation of Langerhans cell histiocytosis

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Introduction: Langerhans cell histiocytosis (LCH) is a rare neoplasm marked by the proliferation of Langerhans cells, primarily affecting children under 2 years old. Gastrointestinal (GI) involvement in LCH is uncommon and often part of widespread disease.
Case Presentation: We report a 16-year-old female with a history of LCH, previously treated with 6-mercaptopurine and vinblastine, who presented with bloody diarrhoea, abdominal pain, and vomiting. Examination revealed hypopigmented skin lesions, lymphadenopathy, and hepatosplenomegaly. Laboratory tests indicated anaemia and eosinophilia, and colonoscopy was suggestive of GI LCH.
Discussion: Gastrointestinal LCH often presents with nonspecific symptoms. It is crucial to maintain a high degree of suspicion for GI LCH in atypical GI presentations, as treatment outcomes can be challenging if diagnosed late or misdiagnosed.
Conclusion: GI symptoms in LCH are rare but may occur in isolation. Early diagnosis and treatment are crucial to reduce morbidity and improve prognosis.

Keywords: colonoscopy, gastrointestinal involvement, Langerhans cell histiocytosis

Introduction

Langerhans cell histiocytosis (LCH) is a rare neoplasm involving the monoclonal proliferation of a type of antigen-presenting cells called Langerhans cells and marked by the presence of S100, CD1a and langerin protein[1]. LCH has an estimated incidence rate of 4.0–5.4 per 1 million individuals and primarily affects children under 2 years old, though it can occur at any age[1,2]. It shows a male preponderance and has a significantly lower adult incidence of 0.07 cases per million per year[3]. Although the exact aetiology for developing LCH is not well understood, popula tion-based studies indicate a higher incidence in Hispanic popula tions and a lower incidence in Black populations[3]. Moreover, the increased incidence in monozygotic twins of patients suggests a potential genetic predisposition for this condition[3]. This condi tion manifests a wide range of clinical features ranging from solitary bone or skin lesions to widespread disease affecting multiple organs and causing severe organ dysfunction[2]. Treatment strategies for this condition depend on the disease extent and site, such that solitary lesions require local therapy or observation while systemic therapy is required for more wide spread involvement[3].

HIGHLIGHTS

- Gastrointestinal involvement in LCH is rare and often part of multisystem disease.
- GI LCH frequently presents with nonspecific symptoms, complicating early diagnosis.
- High suspicion for GI LCH is essential in cases with atypical GI presentations.
- Treatment outcomes can be challenging if LCH is diagnosed late or misdiagnosed, emphasizing the need for early detection.

Gastrointestinal (GI) involvement in LCH is uncommon. GI involvement in LCH is generally a part of widespread disease, and only a few cases have been reported where the gastrointestinal tract is affected in isolation[4]. GI symptoms of this condition are completely nonspecific and present as bleeding, dysphagia, constipation, and diarrhoea[2]. Greater awareness of the varied pre sentations and symptoms of LCH could help in the earlier detec tion of this condition, even in the absence of typical bone or skin findings.

Following the CARE guidelines[5], we hereby report a rare case of a 16-year-old female with LCH presenting with GI manifestations.

Case presentation

A 16-year-old female with a history of Langerhans cell histiocytosis, diagnosed 4 years ago and previously treated with chemotherapy, presented to the emergency department with a

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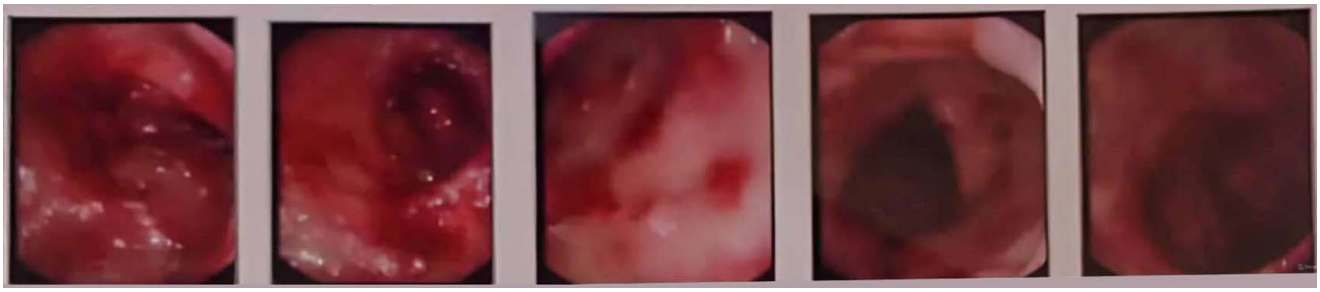

Figure 1. Colonoscopic findings suggestive of gastrointestinal Langerhans cell histocytosis (GI LCH).

complaint of blood-mixed stool for the past 3 months. The onset was sudden, and blood was initially scanty in amount, which gradually increased in quantity. Ten days prior to coming to the hospital, she started passing mucoid blood-mixed stool 5–6 times per day. The passing of stool was associated with non-radiating abdominal pain of unspecified character in the infraumbilical region, which was somewhat relieved by medication. Moreover, she experienced abdominal fullness and vomiting immediately after food intake, which was non-bilious, non-blood-stained, and contained undigested food particles. During this period, she had progressive pallor, generalized weakness, and intermittent jaundice. There was no history of fever, chills, night sweats, cough, haemoptysis, palpitations, or chest pain.

On her 15th day after birth, she developed seborrhoeic dermatitis-like lesions on her head and face, which later generalized across her body. She had multiple admissions for fever, rashes, jaundice, and pneumonia in the past and had also undergone repeated blood transfusions (10–12 times). Four years ago, immunohistochemistry from a skin biopsy was performed, which revealed positive S100 results and vimentin positivity in the vasculature, which is highly suggestive of Langerhans cell histiocytosis. A whole-body scan showed no significant scintigraph evidence of skeletal metastasis. She was treated with 6-mercaptopurine for 16 months and vinblastine for 16 weeks. The therapy was effective, and she completed her treatment 6 months prior to presenting to our hospital with multiple episodes of bloody diarrhoea.

On physical examination, her vital signs were stable, with a temperature of 98.6°F, a heart rate of 92 beats per minute, a respiratory rate of 18 breaths per minute, and a blood pressure of 110/70 mmHg. Capillary refill time was less than 2 s. Her weight was 30 kg (less than the 3rd percentile), and her height was 139 cm (less than 3rd percentile).

Multiple hypopigmented skin lesions were observed throughout the body, along with bilateral anterior cervical lymphadenopathy measuring 0.4×0.4 cm – soft, non-tender, and mobile. The liver was palpable 4 cm below the right costal margin, spanning 11 cm, and the spleen was palpable 4.5 cm below the left costal margin. The abdomen was soft and non-tender.

Laboratory tests revealed anaemia (haemoglobin 8.8 g%), reduced packed cell volume (26.9%), low RBC count (2.70 million/mm^3), thrombocytopenia (92 000/mm^3), neutropenia (32%), and eosinophilia (31%). Serum direct bilirubin was elevated at 8 mg/dl, and albumin was 34 g/l. Stool microscopy identified pus cells (12–14 cells/HPF), red blood cells (10–12/HPF), undigested food particles, and a positive occult blood test. Colonoscopy revealed erythema and erosions in the anal canal with diffuse erosive ulceration, loss of vascular arcades, nodular lesions, and a snakeskin pattern mucosa throughout the colon, indicative of GI LCH (Fig. 1). The patient received symptomatic treatment with IV cefixime, metronidazole, and prednisolone, leading to significant improvement in gastrointestinal symptoms. She remained asymptomatic at the time of discharge

Discussion

LCH is a rare idiopathic disease characterized by the proliferation of bone marrow-derived Langerhans cells and mature eosinophils[3]. Though the exact aetiology of the disease remains unclear, recent discussions favour a neoplastic mechanism involving mutations in the Ras/Raf/MEK/ERK pathway, as evidenced by biopsy samples from lesions[6]. The clonal proliferation of dendritic cells in LCH attracts other inflammatory cells such as T lymphocytes, neutrophils, macrophages, and eosinophils, leading to granuloma formation in various tissues[3]. It can affect any organ or system, with the most common sites being the ske leton (80%), skin (33%), and pituitary gland (25%). The patho physiology varies depending on the affected organ, resulting in erythematous scaly rashes on the skin, lytic lesions in bones, and gastrointestinal symptoms like diarrhoea, bloody stools, and protein-losing enteropathy[7].

LCH involvement in the gastrointestinal tract is rare ($<2\%$ cases)[8] and most often found in males with high-risk multisystem diseases[2]. Reported GI symptoms include vomiting, abdominal pain, constipation, intractable diarrhoea, malabsorption, bloody stools, protein-losing enteropathy, and even intestinal perforation[1,2,4]. Some patients also present with failure to thrive, anaemia, and hypoalbuminemia[2]. A similar presentation of abdominal pain, bloody diarrhoea and anaemia were observed in our case. Some studies have reported abnormal laboratory parameters associated with LCH, such as anaemia[4,9], hyperbilirubinemia[9], thrombocytopenia[9], decreased haematocrit[4,10], hypoalbuminemia[4], eosinophilia[8] associated with LCH, which were consistent with our patient's results.

While no gold standard investigation for Langerhans cell histiocytosis is established, diagnosis usually relies on histopathological examination of the affected tissue. In cases where classic pathological findings are absent or when tissue samples are inaccessible or insufficient, a presumptive diagnosis can be made based on characteristic clinical, radiographic, or molecular features[11]. On tissue biopsy, LCH is identified by clusters of intermediate-sized cells with kidney-shaped nuclei, prominent longitudinal nuclear grooves, dispersed chromatin, and abundant eosinophilic cytoplasm[12]. These lesions typically stain positive for CD1a[1,2,8], S-100[8,13], and langerin (CD207)[1,14], with

variable expression of CD68[2,14] and vimentin[13,14]. In this patient, histological examination was not performed, but immunohistochemistry showed positive results for S100 and vimentin proteins, leading to the diagnosis of LCH.

Various studies and reported cases of gastrointestinal Langerhans cell histiocytosis (GI LCH) had shown subepithelial haemorrhages, multiple superficial ulcerations, nodular mucosal hyperplasia, and polyps as endoscopic or colonoscopy findings[2,4]. Though the sensitivity and specificity of colonoscopy for the diagnosis of gastrointestinal LCH are not mentioned, its use in the visualization of morphology of lesions for screening purposes and obtaining biopsies cannot be overlooked. This also helps in making the diagnosis of certain diseases based on the morphological feature of the lesion after clinically correlating it with the symptoms in low-resource settings. In our case, a colonoscopy revealed diffuse erosive ulceration, loss of vascular arcades, nodular lesions, and a snakeskin pattern mucosa throughout the colon, suggestive of gastrointestinal LCH. Differential diagnoses for GI LCH include poorly differentiated carcinoma, lymphoma, malignant melanoma, and Langerhans cell sarcoma (LCS)[1].

Treatment and prognosis of LCH differs according to the severity of the disease and the sites involved. Patients with isolated disease confined to a single site usually require only local therapy or observation with vinblastine and prednisone proving effective and are often accompanied by curettage or excision of lesions. For more extensive disease, a clinical trial is recommended, typically starting with a 6-month induction phase of chemotherapy using cytarabine, vinblastine, and prednisone[15].

Several international protocols for treating multisystem Langerhans cell histiocytosis (MS-LCH) had recommended a standard treatment regimen for LCH involving steroids and vinblastine (VBL)[16]. The primary treatment typically includes administering vinblastine at 6 mg/m^2 intravenously as a weekly bolus for 6 weeks, combined with prednisone at 40 mg/m^2 per day orally in three divided doses for 4 weeks, followed by a tapering period over the next 2 weeks[16]. Our patient initially responded to vinblastine and 6-mercaptopurine but later relapsed with GI symptoms after the medication was stopped. The patient's condition was improved on symptomatic management.

Owing to the limited data available to inform LCH treatment, the disease progression and prognosis may differ on an individual basis. In general, patients with multifocal and multisystem involvement tend to have poorer outcomes[15]. In a study of 43 adults with LCH, including three with GI lesions, a 36-week regimen of vinblastine, prednisolone, methotrexate, and daily 6-mercaptopurine led to a complete response. Two patients remained disease-free for 4–5 years, while one experienced a relapse 1 year and 7 months later, requiring further chemotherapy[17].

Conclusion

In conclusion, the gastrointestinal system may be the only system involved in LCH, either as a primary manifestation or a recurrence. Therefore, LCH should always be considered in the differential diagnosis when a child presents with nonspecific gastrointestinal symptoms. For patients with confirmed LCH, a high index of suspicion for GI LCH should be maintained when common GI symptoms such as abdominal pain and haematochezia arise. Although gastrointestinal LCH may respond well to chemotherapy, the long-term prognosis is difficult to predict, particularly due to the potential for rapid recurrence after treatment cessation. Thus, early diagnosis and treatment are crucial, as they can significantly reduce morbidity. Any abnormalities found during GI screening should be suspected and thoroughly evaluated for GI LCH.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Consent

Written informed consent was obtained from the patient to publish this report as per the journal's patient consent policy.

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Author contribution

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