

Case Report

A rare case report of Langerhans cell histiocytosis exclusive to the colon in adults

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease characterized by abnormal proliferation of atypical Langerhans cells, predominantly affecting children. Adult-onset LCH is even rarer and typically involves the lungs, bones, and skin. There is a shortage of knowledge regarding various aspects related to its origin, evolution, and treatment. We present a case of a 63-year-old female with an exceptional manifestation of single-organ LCH in the colon, discovered incidentally during routine colorectal cancer screening. The patient's past medical history included a right colectomy for an ileal neuroendocrine tumor with hepatic metastasis. A comprehensive diagnostic workup revealed a BRAF V600E mutation in LCH tumor cells. The patient did not receive any systemic therapy and remains asymptomatic at the 9-month mark post-diagnosis. This case underscores the complexity of LCH diagnosis and the need for multidisciplinary management.

Keywords: LCH, Colonic presentation, Case report

INTRODUCTION

Langerhans cell histiocytosis (LCH) is an idiopathic disease marked by the excessive growth of atypical Langerhans cells-antigen-presenting immune cells-within granulomatosis lesions. The abnormal cells in LCH have abnormal proliferation and lower antigen-presenting capability.¹

This condition exhibits features of both an aberrant reactive mechanism and a neoplastic process. LCH is a rare condition that usually affects children, being even rarer in adults-1 to 2 cases per million per year. LCH demonstrates a higher prevalence in males among children, with a male-to-female ratio of 2:1. Conversely, in adults, there is a predominance of females affected by this disease.¹⁻³

LCH has two variants, multisystem or single-organ. The multisystem variant may involve skin, bone, liver, lung, bone marrow, and lymph nodes and usually affects children younger than two years of age. The multisystem variant of LCH can manifest as a triad encompassing exophthalmos, diabetes insipidus, and osteolytic bone lesions. This particular presentation tends to impact children between the ages of two and six years old. The single-organ variant usually manifests as localized lesion either on bone or skin. LCH involvement of the gastrointestinal (GI) tract, however, is extremely rare.^{2,4}

The symptoms and physical examination findings will vary based on the affected organs at the time of presentation. Nevertheless, in some cases, the condition might be discovered incidentally without any overt symptoms. Adult patients with GI involvement are often asymptomatic, in which cases LCH lesions are

discovered on routine colorectal cancer screening. If symptoms are present, constipation, dysphagia, anemia, and cecal volvulus have been reported.²

This case report presents a rare manifestation of LCH in an adult.

CASE REPORT

Presented here is a case involving a 63-year-old female with a rare manifestation of LCH. Her medical history included an ileal neuroendocrine tumor (NET) with hepatic metastasis, categorized as stage IV-pT3G1N1M1b according to the 8th edition of the American joint committee on cancer staging manual tumor node metastasis classification.⁵ Diagnosis was made in 2020, and she subsequently underwent laparoscopic right colectomy with left lateral sectionectomy and cholecystectomy.

During the first year of follow-up, the patient underwent surveillance with a full-body 68-Gadolinium Edotreotide (68Ga-DOTATOC) positron emission tomography (PET)/computed tomography (CT), which revealed a lytic lesion on the L1 body, suspected to be a bone metastasis. The patient underwent radiotherapy, leading to total remission of the lesion.

In 2023, three years after the NET diagnosis and surgical intervention, the patient experienced constipation, prompting a lower endoscopy. The examination identified a millimetric polyp on the transverse colon, which was completely removed endoscopically. The anatomopathological examination disclosed a nodular lesion centered in the submucosa, consisting of sheets of epithelioid cells, with regular nuclei with slits and large cytoplasm with an infiltrate rich in eosinophils, and no foci of necrosis were identified (Figure 1).

Immunohistochemistry showed diffuse staining for S100 protein and CD1a, with no staining for CAM5.2, MELAN A, Synaptophysin, and CD56. Subsequent genetic testing also revealed the V600E variant of the BRAF gene, considered pathogenic. Based on these findings, a diagnosis of colonic LCH was confirmed (Figure 2). No further procedures deemed to be necessary following the endoscopic polypectomy.

Skin, bone, and lung involvement were ruled out after a comprehensive investigation, including cutaneous examination, skeletal survey with double markers FDG (fluorodeoxyglucose) and 68Ga-DOTATOC PET/CT-scan, and spine magnetic resonance imaging. Based on these findings, the diagnostic hypothesis was intestinal single-organ LCH. The patient remains asymptomatic at 9 months of follow-up after the diagnosis.

This case has been reported in line with the SCARE criteria.

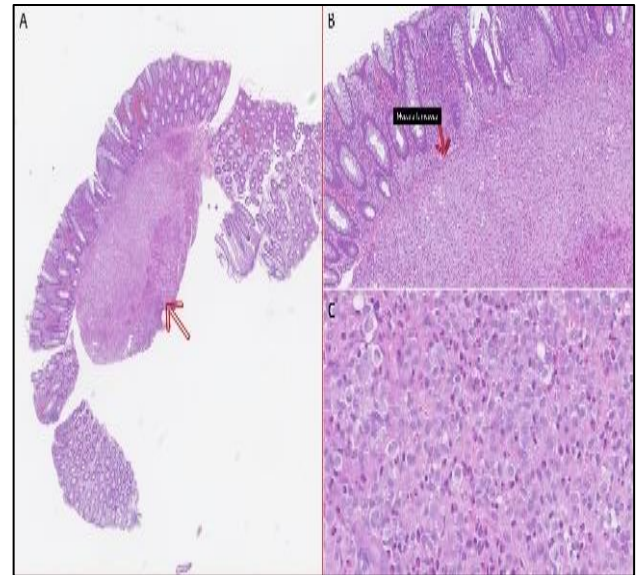


Figure 1 (A and B): Histopathological findings (Hematoxylin and eosin staining).

Polypoid lesion in the colonic mucosa (arrow)-magnification of $\times 5$. A detailed view emphasizes the lesion's location within the submucosa, occasionally extending beyond the muscularis mucosae-magnification of $\times 10$ and the tumor area consists of numerous large cells exhibiting abundant cytoplasm, each with irregular chromatin nuclei. Accompanying these cells are multiple eosinophils-magnification $\times 20$.

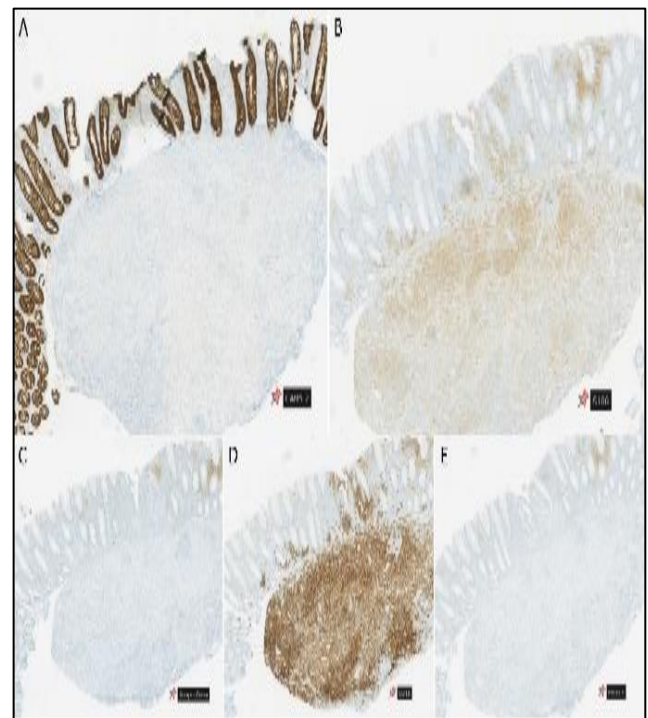


Figure 2 (A-E): Histopathological findings.

Immunohistochemical staining of the normal mucosal epithelium for cytokeratin CAM5.2 and absence of labeling of the tumor cell population; S100 protein staining, absence of staining for synaptophysin, staining for CD1a, and absence of staining for Melan-A.

DISCUSSION

LCH is a rare condition predominantly affecting young children and usually involves lungs, bones, and skin. Exclusive infiltration of the colon by LCH in adults is extremely rare.^{1,3}

The pathophysiology of LCH remains poorly understood. Langerhans cells, acting as dendritic antigen-presenting cells, exhibit abnormal proliferation and diminished antigen-presenting capability in LCH. The LCH lesion also involves inflammatory cells and cytokines, including T lymphocytes, eosinophils, neutrophils, and macrophages. The continued proliferation of abnormal Langerhans cells is thought to arise from the combined or interactive actions of these cells.¹

Genetic molecular testing revealed the presence of a BRAF V600E mutation in the patient's LCH tumor cells. Oncogenic BRAF mutations, usually V600E, have been detected in approximately 45% to 57% of patients with LCH. The BRAF protein is a crucial component of the mitogen-activated protein kinase (MAPK) pathway, which plays a pivotal role in phosphorylating proteins that regulate the cell cycle, proliferation, and differentiation. The variant c.1799T>A (p.V600E) in exon 15 of the BRAF gene is a missense alteration associated with probable gain of function.^{3,6}

In this case report, the previously identified NET bone metastasis was reconsidered as a potential manifestation of LCH, which may have been overlooked by the team due to the absence of an LCH diagnosis at that time. However, the medical team was inclined to consider it was less likely to be an LCH lesion, primarily because the 68Ga-DOTATOC PET/CT-scan is specifically conducted for NET metastasis. The 68Ga-DOTATOC is a somatostatin receptor-targeted ligand, that has been used clinically over the past decade for imaging NETs. On the other hand, for assessment and monitoring LCH during treatment, FDG is the indicated marker for PET scan, which makes it less likely or even impossible to identify these lesions with the use of another marker.^{1,7}

In adults, the treatment approach for LCH remains uncertain due to the rarity of the disease. The course of treatment is generally determined by factors such as age, the extent of the disease, and associated risk factors. In many cases no treatment is necessary, and the evolution is excellent, while other forms with multisystem disease have a serious and progressive course that can be fatal. Therefore, treatment approaches span from observation to systemic chemotherapy or stem cell transplantation. Notably, targeted therapies utilizing BRAF inhibitors have broadened the therapeutic arsenal for severe manifestations. In the current case, the patient did not undergo chemotherapy or systemic therapy, given the isolated presentation with a single transverse colon polyp which was totally removed without evidence of other organ involvement. Currently, systemic chemotherapy is

primarily advised for multisystem disease cases and when single-system disease shows insufficient response to alternative treatments.^{2,8,9}

CONCLUSION

In summary, we have presented a case of single-organ LCH affecting the colon, an exceedingly uncommon occurrence. Due to the rarity of the diagnosis and the lack of established guidelines, adopting a multidisciplinary approach is imperative for effective management. Future initiatives should focus on developing screening guidelines following the complete removal of colonic polyps with pathological evidence of LCH to enhance the quality and cost-effectiveness of care.

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