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Adult Langerhans cell histiocytosis presenting as metachronous colonic polyps

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease characterized by proliferation of Langerhans-type cells that express CD1a, Langerin (CD207) and S100 protein. Birbeck granules are a hallmark by ultrastructural examination. LCH presents with a wide clinical spectrum, ranging from solitary lesions of a single site (usually bone or skin) to multiple or disseminated multisystemic lesions, which can lead to severe organ dysfunction. Most cases occur in children. Gastrointestinal tract involvement is rare and has been associated with systemic illness and poor prognosis especially in children under the age of 2 years. Adult gastrointestinal LCH is very rare. We report a case of a previously healthy, nonsmoking 48-year-old male who was referred for routine screening colonoscopy. Two sessile, smooth, firm and yellowish LCH polyps measuring 0.2 cm and 0.3 cm were detected in the sigmoid colon. Fifteen months later a second colonoscopy found two histologically confirmed hyperplastic polyps at the sigmoid colon. No other LCH lesions were seen. A third colonoscopy after 28 months of follow-up found a submucosal 0.5 cm infiltrated and ulcerated LCH polyp in the cecum, close to the ostium of the appendix. The patient had been asymptomatic for all this period. Imaging investigation for systemic or multiorgan disease did not find any sign of extracolonic involvement. On histology all lesions showed typical LCH features and immunohistochemical analysis showed strong and diffuse staining for CD1a and CD207. This case illustrates two distinct clinicopathologic features not previously reported in this particular clinical setting: metachronous colonic involvement and positivity for CD207.

Keywords: Histiocytosis; Langerhans Cells; Intestine, Large; Colonoscopy; Polyps; Immunohistochemistry.

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is a proliferation of Langerhans-type cells that express CD1a, Langerin (CD207) and S100 protein, and shows Birbeck granules by ultrastructural examination.[1] Discouraged historical synonyms include Histiocytosis X, eosinophilic granuloma, Hand-Schüller-Christian and Letterer-Siwe diseases.

Although classically postulated to originate from mature skin Langerhans cells, recent gene expression profiles studies have shown that LCH is derived from a myeloid dendritic cell, which expresses the same antigens (CD1a, CD207) as the skin Langerhans cell.[2]

LCH presents with a wide clinical spectrum, ranging from solitary lesions of a single site (usually bone or skin) to multiple or disseminated lesions within a single system or even a multisystem, sometimes leading to severe organ dysfunction.[3] The incidence of LCH in adults is about 1-2 per million per year.[4] Most cases occur in children (1 per 200,000).[5] Gastrointestinal tract involvement is rare and has been associated with systemic illness and poor prognosis especially in children under the age of 2 years.[6,7] Gastrointestinal LCH in adults is very rare and has been described only in case reports and small series.[8-16]

CASE REPORT

A previously healthy, nonsmoking 48-year-old male was referred for routine screening colonoscopy, which revealed two sessile, smooth, firm and yellowish LCH polyps in the sigmoid colon, measuring 0.2 and 0.3 cm (Figure 1A). Fifteen months later a second colonoscopy found two histologically confirmed hyperplastic polyps at the sigmoid colon. No other LCH lesions were seen. A third colonoscopy after 28 months of follow-up found a submucosal 0.5 cm infiltrated and ulcerated LHC polyp in the cecum, close to the ostium of the appendix (Figure 1B). The sigmoid was normal. The patient had been asymptomatic for all this period. Imaging investigation for systemic or multiorgan disease did not find any sign of extracolonic involvement. No specific treatment has been recommended so far.

On histology all lesions showed typical LCH features: sheets of large cells with indistinct cell borders and abundant lightly eosinophilic cytoplasm, reniform-to-oval-shaped nuclei with fine, vesicular chromatin, nuclear grooves and single, inconspicuous nucleoli. The three lesions were predominantly submucosal and showed areas of central necrosis (Figure 1C). The cecal polyp showed mucosal infiltration (Figure 1D) and ulceration. Enlarged nucleoli, mitosis and giant cells were absent.

Immunohistochemical analysis of the lesions showed strong and diffuse staining for CD1a (Figure 1E) and CD207 (Figure 1F). Staining for S100 and CD68 was weakly positive and multifocal in both lesions.

DISCUSSION

Adult colonic LCH is extremely rare. Fourteen cases have been reported to date.[11-16] Most patients presented with a solitary, non-ulcerative, incidental colonic polyp at colonoscopy and had a benign course.

The largest series of adult colonic LCH published to date included a total of eight cases. In this series, two out of eight adult patients with colonic involvement by LCH presented with multiple lesions, one of whom developed cutaneous disease 2 years after the initial diagnosis.[14] One patient died of disseminated disease after approximately 5 years of the first symptom (right hip pain related to involvement of the femoral head).[11]

Most reported cases suggest a more likely benign course of the disease for patients with a solitary, non-ulcerative, incidental colonic LCH polyp identified at colonoscopy (Table 1). We think the present case illustrates two distinct, although not surprising, clinicopathologic features not previously reported in this particular clinical setting: metachronous colonic involvement and positivity for CD207. This might be useful information for future studies in this field.

CD207 (Langerin) is a C-type lectin that binds sugar using carbohydrate recognition domains and acts as a pathogen recognition receptor in Langerhans cells. It is an intrinsic molecular component of the Birbeck granules and plays a significant role in their formation.[17]

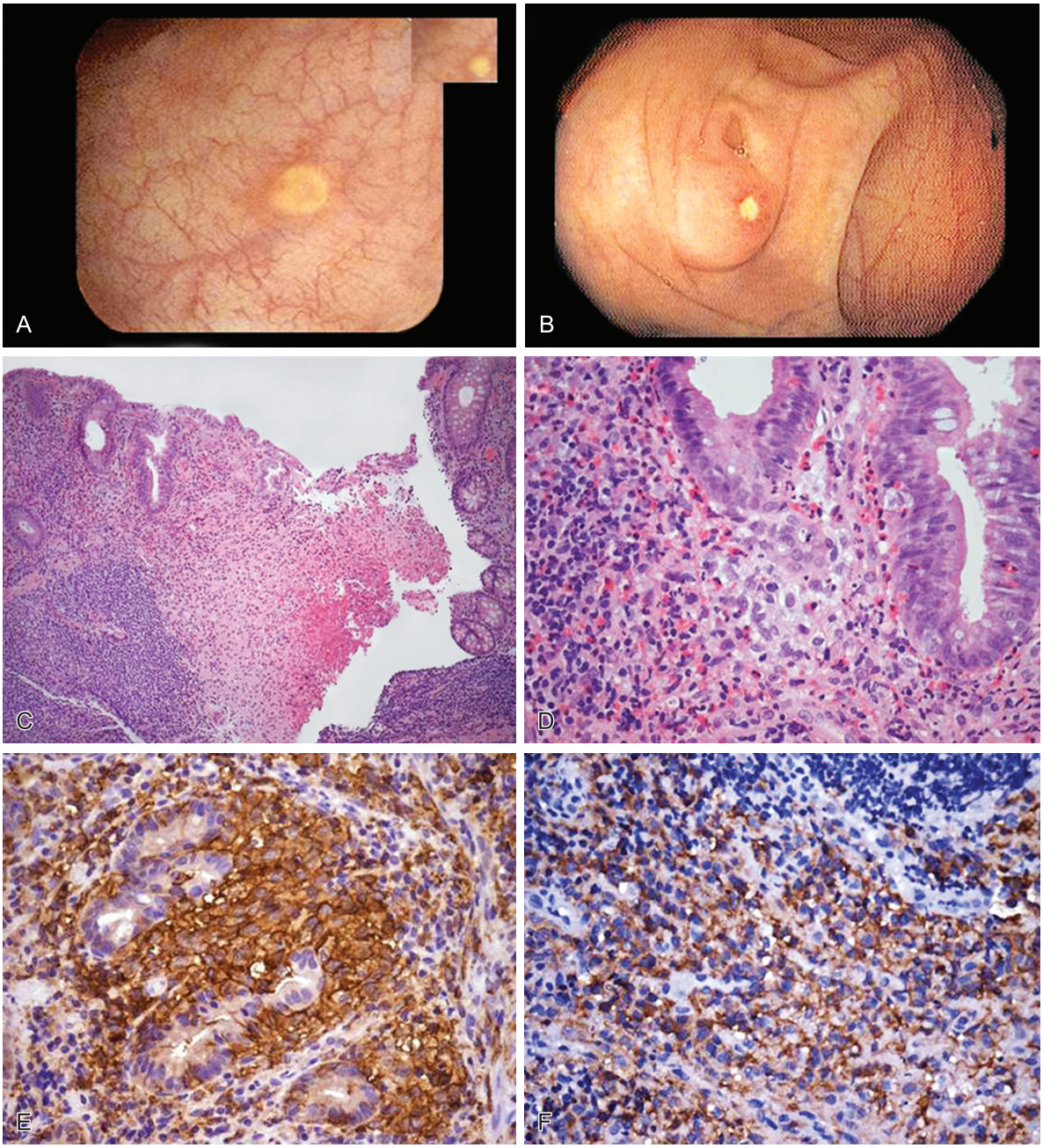

Figure 1 – A - Endoscopic view of a sessile 0.3 cm LCH polyp in the sigmoid colon; **B -** Endoscopic view of an ulcerated and infiltrated 0.5 cm LCH polyp in the cecum; **C -** Photomicrography of a submucosal LCH nodule with central necrosis and ulceration (H&E, 100x); **D -** Photomicrography of LCH destructive infiltration of colonic crypt (H&E, 400x); **E -** CD1a immunostaining of infiltrative lesion showed in (D) (400x); **F -** CD207 immunostaining of the same lesion in (D) (400x).

S100 positivity brings the differential diagnosis with malignant melanoma, which may present as a primary or metastatic lesion at the gastrointestinal tract.[12] However, malignant melanoma may have different endoscopic and pathological features such as melanin pigmentation, more pleomorphic and atypical cells and immunostaining for other melanocytic markers like HMB45 and Melan A. Melanoma cells are negative for CD1a and CD207.

In addition to differential diagnoses with other proliferative histiocytic lesions and malignant melanoma, it is important to rule out infection, especially parasitic, as a cause of "histiocytic" aggregates with eosinophils in the colon. Of course this is particularly relevant in tropical countries like Brazil. Parasites were not detected in the present case.

Another curious differential diagnosis is Crohn's disease. LCH presenting with colonic skip lesions may simulate Crohn's disease especially when accompanied by perianal fistulae or ulcers.[16,18] Biopsies with careful pathological examination

Table 1 – Clinical and endoscopic findings of reported adult colonic LCH cases

Patient	Ref.	Age(y)	Sex	Clinical presentation	Endoscopy	Location	No.	Size (mm)	Specimen	Other findings	Follow up (mo)
1	[11]	50	M	Abdominal pain, hypopituitarism	Polyps	TC	2	NA	Biopsy	Perianal disease; bone marrow clear	Probably ANED (18)
2	[11]	71	F	Right hip and abdominal pain, bloody diarrhea	Ulcerative	Sigmoid, rectum	Multiple	NA	Biopsy	Vulvar and multifocal bone disease	Died of disease†
3	[12]	49	M	Routine	Polyp	AC	1	2	Biopsy	Hypertension	NA
4	[13]	65	M	Routine	Polyp	DC	1	6	Biopsy	Ex-smoker	ANED (12)
5	[14]	40	F	Anemia	Polyp	AC	1	*	Biopsy	Adenoma	ANED (21)
6	[14]	60	M	Routine	Polyp	Cecum	1	*	Biopsy	None	ANED (7)
7	[14]	55	F	Routine	Polyp	Sigmoid	1	*	Biopsy	None	ANED (26)
8	[14]	60	F	Routine	Polyp	Cecum	1	*	Biopsy	None	ANED (12)
9	[14]	51	F	Routine	Polyp	TC	1	*	Biopsy	None	ANED (5)
10	[14]	77	F	Constipation	Polyp	Sigmoid	1	*	Biopsy	None	ANED (2)
11	[14]	56	F	Routine	Ulcerative	AC, TC, DC	Multiple	*	Biopsy	Hyperplastic polyp	Cutaneous Disease (24)
12	[14]	63	F	Cecal volvulus	NA	Cecum, AC	Multiple	*	Right colectomy	None	ANED (24)
13	[15]	53	F	Routine	Polyp	Rectum	1	4	Biopsy	Hyperlipidemia; hyperplastic polyps	ANED (12)
14	[16]	69	M	Abdominal pain, diminished appetite, anemia	Ulcerative	Colon (random)	Multiple	NA	Biopsy	Perianal and gastric disease, metabolic syndrome	NA; improved with prednisolone
15	Present case	48	M	Routine	Polyps, focal ulceration	Sigmoid, cecum	3	2 – 5	Biopsy	Metachronous; hyperplastic polyps	ANED (40)

AC = ascending colon; ANED = alive with no evidence of disease; DC = descending colon; F = female; M = male; mo = months; NA = not available; No. = number of lesions; Ref. = reference; TC = transverse colon; y = years. * Size was not specified for each patient; however, range was 1 – 8mm (mean = 4mm and median = 3mm). † Approximately 60 months after the first symptoms.

and immunohistochemistry make the correct diagnosis. Multiple and repeated biopsies might be necessary.[19] Lee-Elliott et al. described a rare case of LCH complicating small bowel Crohn's disease.[20]

Some less aggressive forms of LCH may remit spontaneously. For instance, adult pulmonary LCH is a disease of smokers in over 90% of the cases and is thought to represent a reactive process.[21] About 20% of the patients are asymptomatic and cigarette-smoking cessation is the first step in the treatment strategy, followed by steroid treatment. As a result, clinical and radiographic improvements are reported.[22] Considering the general benign behavior of isolated adult colonic LCH reported to date, we hypothesize that this may be a reactive process similar to adult pulmonary LCH. However, instead of cigarette-smoking, the noxious stimulus is unknown and further clonality studies with large case series are necessary.

In summary, adult colonic LCH is a very rare presentation of LCH. To the best of our knowledge this is the first Brazilian case report. The usual clinical picture is that of multiple or solitary asymptomatic benign colonic polyps. Colonic or cutaneous recurrence might occur. Immunohistochemistry is necessary for confirmation and differential diagnosis. Clinical follow up is recommended.

REFERENCES

1. Jaffe R, Weiss LM, Facchetti F. Tumours derived from Langerhans cells. In: Swerdlow SH, Campo E, Harris NL, et al., editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: International Agency of Research in Cancer; 2008. v. 2, p. 358-60.

2. Allen CE, Li L, Peters TL, et al. Cell-specific gene expression in Langerhans cell histiocytosis lesions reveals a distinct profile compared with epidermal Langerhans cells. J Immunol. 2010;184(8):4557-67. PMid:20220088 PMCid:3142675. http://dx.doi.org/10.4049/jimmunol.0902336

3. Chang KL, Snyder DS. Langerhans cell histiocytosis. Cancer Treat Res. 2008;142:383-98. PMid:18283796.

4. Baumgartner I, Von Hochstetter A, Baumert B, Luetolf U, Follath F. Langerhans'-cell histiocytosis in adults. Med Pediatr Oncol. 1997;28(1):9-14. http://dx.doi.org/10.1002/(SICI)1096-911X(199701)28:1<9::AID-MPO3>3.0.CO;2-P

5. Bhatia S, Nesbit ME, Egeler RM, Buckley JD, Mertens A, Robison LL. Epidemiologic study of Langerhans cell histiocytosis in children. J Pediatr. 1997;130(5):774-84. http://dx.doi.org/10.1016/S0022-3476(97)80021-2

6. Hait E, Liang M, Degar B, Glickman J, Fox VL. Gastrointestinal tract involvement in Langerhans cell histiocytosis: case report and literature review. Pediatrics. 2006;118(5):e1593-9.

7. Yadav SP, Kharya G, Mohan N, et al. Langerhans cell histiocytosis with digestive tract involvement. Pediatr Blood Cancer. 2010;55(4):748-53. PMid:20535829. http://dx.doi.org/10.1002/pbc.22663

8. Vazquez JJ, Ayestaran JR. Eosinophilic granuloma of the stomach similar to that of bone: light and electron microscopic study. Virchows Arch A Pathol Anat Histol. 1975;366(2):107-11. http://dx.doi.org/10.1007/BF00433584

9. Nihei K, Terashima K, Aoyama K, Imai Y, Sato H. Benign histiocytosis X of stomach. Previously undescribed lesion. Acta Pathol Jpn. 1983;33(3):577-88. PMid:6605021.

10. Iwafuchi M, Watanabe H, Shiratsuka M. Primary benign histiocytosis X of the stomach. A report of a case showing spontaneous remission after 5 1/2 years. Am J Surg Pathol. 1990;14(5):489-96. PMid:2183638. http://dx.doi.org/10.1097/00000478-199005000-00010

11. Hofman V, Hourseau M, Musso S, Martin A, Hofman P. [Langerhans cell histiocytosis of the large bowel]. Ann Pathol. 2002;22(6):461-4. PMid:12594388.

12. Sharma S, Gupta M. A colonic polyp due to Langerhans cell histiocytosis: a lesion not to be confused with metastatic malignant melanoma. Histopathology. 2006;49:438-439. PMid:16978213. http://dx.doi.org/10.1111/j.1365-2559.2006.02463.x

13. Kibria R, Gibbs PM, Novick DM. Adult Langerhans cell histiocytosis: a rare cause of colon polyp. Endoscopy. 2009;41(suppl2):E160-E161. PMid:19544280. http://dx.doi.org/10.1055/s-0029-1214689

14. Singhi AD, Montgomery EA. Gastrointestinal tract langerhans cell histiocytosis: A clinicopathologic study of 12 patients. Am J Surg Pathol. 2011;35:305-10. PMid:21263252. http://dx.doi.org/10.1097/PAS.0b013e31820654e4

15. Shankar U, Prasad M, Chaurasia OP. A rare case of langerhans cell histiocytosis of the gastrointestinal tract. World J Gastroenterol. 2012;18(12):1410-3. PMid:22493557 PMCid:3319970. http://dx.doi.org/10.3748/wjg.v18.i12.1410

16. Roeb E, Etschmann B, Gattenlöhner S. Is it always Crohn's disease in a patient with perianal fistulae and skip lesions in the colon? Gastroenterology. 2012;143(1):e7-8. PMid:22640732. http://dx.doi.org/10.1053/j.gastro.2011.12.013

17. Valladeau J, Ravel O, Dezutter-Dambuyant C, et al. Langerin, a novel C-type lectin specific to Langerhans cells, is an endocytic receptor that induces the formation of Birbeck granules. Immunity. 2000;12(1):71-81. http://dx.doi.org/10.1016/S1074-7613(00)80160-0

18. Mittal T, Davis MD, Lundell RB. Perianal Langerhans cell histiocytosis relieved by surgical excision. Br J Dermatol. 2009;160(1):213-5. PMid:19067696. http://dx.doi.org/10.1111/j.1365-2133.2008.08934.x

19. Magno JCC, D'Almeida DG, Magalhães JP, et al. Histiocitose de células de Langerhans em margem anal: relato de caso e revisão da literatura. Rev Bras Coloproct. 2007;27(1):83-8. Portuguese. http://dx.doi.org/10.1590/S0101-98802007000100012

20. Lee-Elliott C, Alexander J, Gould A, Talbot R, Snook JA. Langerhan's cell histiocytosis complicating small bowel Crohn's disease. Gut. 1996;38(2):296-8. PMid:8801215 PMCid:1383041. http://dx.doi.org/10.1136/gut.38.2.296

21. Yousem SA, Colby TV, Chen YY, Chen WG, Weiss LM. Pulmonary Langerhans' cell histiocytosis: molecular analysis of clonality. Am J Surg Pathol. 2001;25(5):630-6. PMid:11342775. http://dx.doi.org/10.1097/00000478-200105000-00010

22. Ng-Cheng-Hin B, O'Hanlon-Brown C, Alifrangis C, Waxman J. Langerhans cell histiocytosis: old disease new treatment. QJM. 2011;104(2):89-96. PMid:21084318. http://dx.doi.org/10.1093/qjmed/hcq206

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