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Langerhans Cell Histiocytosis Mimicking Crohn's Disease: a Case Report and Review of the Literature

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Abstract

The aim of this study was to report an unusual case of Langerhans Cell Histiocytosis (LCH) with terminal ileum and lung involvement which mimics Crohn's disease.

A 42-year-old male patient presented to our clinic with the complaints of intermittent diarrhea and abdominal pain in which he stated such complaints have continued almost along a year frequently. Colonoscopic examination revealed geographically shaped large ulcers with a deep-bottomed located the terminal ileum which initially suggests the diagnosis of Crohn's disease. Following treatment with azathioprine and budesonide, diarrhea regressed but abdominal pain persisted. In the third month of treatment, the patient re-presented with the complaints of cough, sputum and chest pain. Thorax CT followed by PET CT examination revealed multiple lung nodules suggesting malignancy. Histopathological examination of the nodules collected by segmentectomy further revealed that they were rich in histiocytic cells and positive for S-100 protein and CD1a antigen. When the terminal ileum biopsies of the patient with lung LCH were examined for a second time, histiocytic cells confirm the diagnosis of LCH through positive immune histochemical staining with CD-1a. The patient was administrated with prednisolone 1 mg/kg and then combined with vinblastine.

LCH may present with the ulcers mimicking Crohn's disease. Therefore, the possibility of LCH should be always kept in mind in the cases of non-response to the treatment for Crohn's disease or when non-gastrointestinal atypical symptoms develop.

Keywords: Crohn's disease; Langerhans cell histiocytosis; Gastrointestinal system

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Introduction

Langerhans cells are the distinct member of histiocytes placed in many tissues in our body. Langerhans Cell Histiocytosis (LCH) disease is characterized through uncontrolled proliferation and accumulation of Langerhans cells in various tissues. The etiology and pathogenesis have not been fully identified yet; however, it is generally thought that it is associated with immune system damage or a malignant process. While its incidence is very rare among the adults, it is most commonly seen in pediatric age especially between 1 and 3 years old [1]. The incidence is reported to be 0.5 to 4 per million. Although lung, bone, and skin are the most commonly involved organs in this disease, Gastrointestinal System (GIS) involvement is generally very rare [2]. Crohn's disease is a chronic inflammatory disease of GIS with granulomas. The aim of this study was to present the clinical, radiological and histopathological findings of LCH with terminal ileum and lung involvement along with discussing in the light of most recent findings in the literature.

Case Presentation

A 42-year-old male patient presented to our hospital with the complaints of intermittent diarrhea and abdominal pain which continued almost along a year frequently. He had also associated nausea, vomiting and weight loss. The white blood cell count in the laboratory examination of the patient was found to be 13 × 10^3/mL, hemoglobin was 11 g/dL, hematocrit was 30, platelet was 490 × 10^3/mL, sedimentation was 48 mm/h, CRP was 69 mg/L. Other biochemical values were found to be within the normal range. Colonoscopic examination revealed geographically shaped large ulcers with a deep-bottomed at the first 10 cm of the terminal ileum which initially suggests the diagnosis of Crohn's disease (Figure 1). The pathological examination of the ulcer biopsies was reported as chronic active colitis that may be compatible with Crohn's disease. The patients were then administrated immediately with azathioprine and budesonide. While patient's diarrhea regressed with the treatment, the abdominal pain still persisted. In the third month of treatment, the

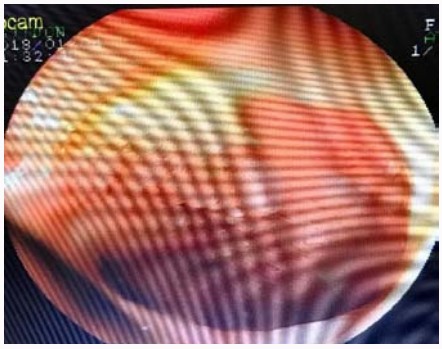

Figure 1: Endoscopic view of the deep ulcers in the terminal ileum.

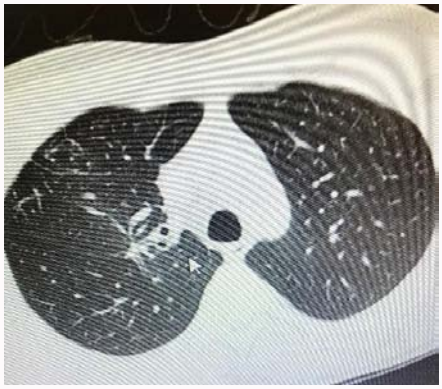

Figure 2: Multiple lung nodules in thorax BT.

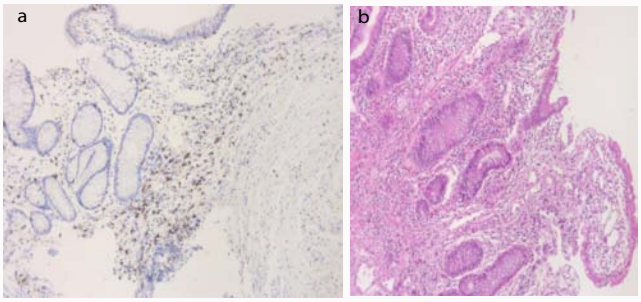

Figure 3: Histological examination of the terminal ileum, 3a) Immunohistochemical study showing the atypical cells are positive for CD1a 10x, 3b) HE staining-10x.

patient re-visited to the hospital with the symptoms of cough, sputum and chest pain. The patient has had a history of smoking for almost 10 years and stated that these complaints have been present for the past six months. He also stated that he associated these complaints with smoking since they were very mild and intermittent. Based on his statement, his complaints increased in the last three months. We observed the multiple lung nodules suggesting malignancy through Thorax CT (Figure 2) and PET CT examinations. Segmentectomy was performed for the scattered and deeply located nodules in the lung. Histopathological examination revealed that the nodules were rich in histiocytic cells and were positive for S-100 protein and CD1a antigen. When the terminal ileum biopsies of the patients diagnosed with the pulmonary LCH were examined for the second time because of abdominal pain, immune histochemical staining revealed histiocytic cells, which were positive for CD-1a, and confirmed the diagnosis of LCH (Figure 3a,3b). Our patient was administered with1mg/kg dosage of prednisolone and then combined with vinblastine. The treatment and follow-up of the patient has been still continuing, and both his GIS symptoms and lung-related symptoms regressed.

Discussion and Conclusion

LCH is among the very rare diseases, and is characterized by the proliferation of langerhans type of cells expressing CD1a, and S100 protein. In the active phase of the disease, granulomatous nodular lesions consisting of langerhans cells are existed. This disease is definitively diagnosed through the existence of positively stained Langerhans cells with CD1a antigen and S-100 protein in the biopsy taken from the lesion [1,2]. The disease can be clinically encountered as a single-focus or multi systemic disease. The systemic involvement has been associated with poor prognosis. GIS involvement with LCH in adults is very rare, and the cases often present as a solitary, polypoid lesion without a systemic involvement [3].

In our literature research (based on PubMed and Google Scholar), we identified 35 published studies reporting the cases with LCH and GIS involvement in which the first case was reported in 1968 and the last was in 2019 [4-37]. Among these 35 reported cases, its distribution based on the involved organs as follows: 1 esophagus, 8 stomachs, 4 small intestines, 20 colons (14 polyps), and 2 anal canals (Table 1). These patients also included the small case series of 12 patients reported by Singhi et al. [3]. In this series, GIS involvement was identified in 10 adults LCH patients in which nine of ten patients had colon involvement while one patient had stomach involvement and two had skin involvement. In this series, the mostly reported cases were single, non-ulcerated LCH polyps incidentally detected by colonoscopy [3].

There are limited numbers of cases on LCH involving the small intestine with only 4 reported cases in the literature [4,8,10,31] in which two of these mimicked Crohn's disease [8,10].

The first case with ileum and lung involvement was firstly described in 1968. In that case report, a 64-year-old male patient who previously diagnosed with LCH presented with bleeding and was diagnosed with LCH in the small intestine. The difference of this case from the case herein was that there was no diagnosis of Crohn's disease and diffuse involvement of the ileum and multiple ulcers were observed [4].

Sakanoue et al. [8] reported that a patient, who had been diagnosed with Crohn's disease involving the small intestine for five years and improved dramatically with steroid treatment during this period, experienced an attack leading to segmental ileal resection during the follow-up period. In the pathology findings of the resected specimen, diffuse histiocyte aggregates and langerhans cells were observed and then the case was confirmed as LCH at the end of five years [8].

In the recent case of LCH mimicking Crohn's disease, the disease had colon involvement, unlike our case. Therein they presented a case of ulcers, perianal lesion and Primary Sclerosing Cholangitis (PSC) involvement in the colon. Biopsy of deep ulcers in the colon suggested Crohn's disease. During the follow-up of the patient who did not respond to infliximab treatment, skin lesions developed and the examination of skin lesion biopsy revealed as LCH. Subsequently, biopsy specimens of ulcers in the colon were re-examined and LCH was confirmed in the colon [33].

In another case report consisting the LCH mimicking Crohn's disease, Roeb et al. [17] described a 69-year-old male patient who

Table 1: Studies description of cases with LCH and GIS involvement in adults.

Patientno	Ref.no	Age	gender	Location	Endoscopic view
1	4	64	E	smallintestine	ulcer
2	5	59	K	stomach	ulcer
3	6	47	K	stomach	polyp
4	7	49	K	stomach	polyp
5	8	30	E	smallintestine	ulcer
6	9	53	K	stomach	polyp
7	10	76	K	smallintestine	ulcer
8	11	52	E	stomach	ulcer
9	12	50/71	E/K	colon/colon	polyp/ulcer
10	13	49	E	colon	polyp
11	14	65	E	colon	polyp
12	15	55	E	colon	polyp
13	16	51	E	stomach	polyp
14	17	69	E	colon	ulcer
15	18	53	K	colon	polyp
16	19	56	E	colon	polyp
17	20	48	E	colon	polyp
18	21	51	E	colon	polyp
19	22	68	K	colon	ulcer
20	23	49	K	colon	polyp
21	24	59	E	esophagus	ulcer
22	25	27	E	anorectal	ulcer
23	26	64	E	stomach	polyp
24	27	46	K	colon	ulcer
25	28	58	K	colon	polyp
26	29	20	K	colon	polyp
27	30	33	K	analcanal	polyp
28	31	55	K	smalintestine	ulcer
29	32	60	E	colon	polyp
30	33	39	E	colon	ulcer
31	34	37	E	stomach	erosion
32	35	28	K	colon	ulcer
33	36	60	K	colon	polyp
34	37	37	E	colon	polyp

had been diagnosed with Crohn's disease with perianal fistula and deep colon ulcers for 4 years. This patient was diagnosed with LCH by the second examination of colon Bx samples at the end of 4 years [17]. Similar to our case reported herein, another case mimicking Crohn's disease along with lung involvement was also reported. In this case, a 46-year-old female patient had diffuse ulcers extending from the anal canal to the terminal ileum in her colonoscopy because of her complaint of chronic diarrhea. The pathological examination and clinical findings of the patient were consistent with Crohn's disease. The patient was then initially administered with prednisone, 6-mercaptopurine, and infliximab and had been using this treatment for the 23 months. The patient was limitedly benefited from this treatment and re-presented to another hospital due to severe diarrhea, dehydration, and renal failure. His anamnesis was then deepened and they realized that the patient was also diagnosed with LCH lung involvement in a different hospital. Thereafter, when the colon Bx samples were examined the second time, histiocytic infiltration of the colon and terminal ileum with granulomas was shown. Biopsies were positive for CD1a and S-100 [27].

In another case report where both lungs were involved and mimicking Crohn's disease, a 70-year-old woman who had chronic diarrhea presented to the hospital with the chronic diarrhea. Her colonoscopy examination revealed deep ulcers in the entire colon, indicating Crohn's disease while the terminal ileum was normal. She had recently diagnosed with cirrhosis of the liver and pulmonary fibrosis in the lung. Cirrhosis was thought to be associated with PSK secondary to the underlying inflammatory bowel disease. Therefore, intravenous prednisolone treatment was initiated and diarrhea was treated. Before the treatment, patchy rashes developed on the back of the patient. The colon bx samples were then re-examined since the findings in biopsy was consistent with LCH. Colonic ulcers were also compatible with LCH. Bx samples were collected from both lung and liver. While histiocyte infiltration suggests the diagnosis of LCH in lung samples, liver Bx samples were not compatible with LCH [22]. More recently, another case report of a 55-year-old woman who underwent laparotomy for acute onset abdominal pain and subacute intestinal obstruction have reported. In this case report, granulation tissue was observed in the periumbilical region and pathological diagnosis was reported as LCH in the small intestine [31]. The largest series in the literature has been reported by Goyal et al. [38]. In the study, 186 adult LCH patients were investigated retrospectively and no GIS involvement was reported. Lung involvement was the most common in the series.

To the best of our knowledge, the case presented herein is the first case of LCH involving the isolated terminal ileum and lung. Since GIS involvement with LCH is very rare and it is a disease with granulomas, the possibility of misdiagnosing the disease is very high. As in the four aforementioned cases [17,22,27,33], our case was diagnosed as LCH even following the second examination of colon biopsy samples along with the use of special marker staining. Since immune histochemical staining for S100 and CD1a is not a routine practice in the clinic, the diagnosis of LCH can easily be overlooked. Therefore, pathologist awareness is critical in such a case. If pathologists report an increase in eosinophilia or histiocytic cells in microscopic examination of biopsy specimens, the clinician should frequently think of the possibility of LCH.

There is no standard treatment of LCH available for adults because the pathogenesis of LCH has not been clear yet. However, the current recommended first-line therapy in multisystem LCH patients is the combination of prednisone and vinblastine drug therapy. In addition, local excision is considered as the preferred treatment modality especially for unifocal involvement, but a long-term follow-up is required in this case [39].

Mansour et al. [37] recently reported the case of multiple polyps from the rectum to the cecum and LCH with lung involvement. In the case report, the recurrence of colon lesions was observed after vinblastine treatment. Following the recurrence, the patient was administered a combination of gemcitabine and cisplatin, a chemotherapy regimen that was previously not tried and not reported for adult LCH treatment. They obtained a positive response with this combined treatment. The authors highlighted that this combination may be an alternative treatment regimen in LHD cases with symptomatic diffuse GIS involvement [37]. In our patient, 1 mg/

kg prednisolone treatment was initiated and then combined with vinblastine. The treatment and follow-up of the patient have been still continuing.

Taking all into consideration, the possibility of LCH should be always kept in mind in the case of non-response to the treatment for the patients with a diagnosis of Crohn's disease, when atypical skin rashes develop or when lung nodules are detected. The definitive diagnosis of Crohn's disease should be questioned in such cases.

References

1. Detlefsen S, Fagerberg CR, Ousager LB, Lindebjerg J, Marcussen N, Nathan T, et al. Histiocytic disorders of the gastrointestinal tract. Hum Pathol. 2013;44(5):683-96.
2. Abla O, Egeler RM, Weitzman S. Langerhans cell histiocytosis: Current concepts and treatments. Cancer Treat Rev. 2010;36(4):354-9.
3. Singhi AD, Montgomery EA. Gastrointestinal tract langerhans cell histiocytosis: A clinicopathologic study of 12 patients. Am J Surg Pathol. 2011;35(2):305-10.
4. Pops MA, Campbell T. Gastrointestinal bleeding from ileal ulcerations in histiocytosis X. Arch Intern Med. 1968;122(3):271-2.
5. 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;366:107-11.
6. 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.
7. 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.
8. Sakanoue Y, Kusunoki M, Shoji Y, Yanagi H, Nishigami T, YamamuraT, et al. Malignant histiocytosis of the intestine simulating Crohn's disease. Report of a case. Dis Colon Rectum. 1992;35(3):266-9.
9. Wada R, Yagihashi S, Konta R, Ueda T, Izumiyama T. Gastric polyposis caused by multifocal histiocytosis X. Gut. 1992;33(7):994-6.
10. 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.
11. Terracciano L, Kocher T, Cathomas G, Bubendorf L, Lehmann FS. Langerhans cell histiocytosis of the stomach with atypical morphological features. Pathol Int. 1999;49(6):553-6.
12. Hofman V, Hourseau M, Musso S, Martin A, Hofman P. [Langerhans cell histiocytosis of the large bowel]. Ann Pathol. 2002;22(6):461-4.
13. 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(4):438-39.
14. Kibria R, Gibbs PM, Novick DM. Adult Langerhans cell histiocytosis: A rare cause of colon polyp. Endoscopy. 2009;41(2):160-1.
15. Lee SJ, Kim KJ, Yoon SM, Ye BD, Byeon JS, Myung SJ, et al. A case of Langerhans cell histiocytosis that involved the colon. Korean J Gastrointest Endosc. 2009;38(3):166-70.
16. Lee CK, Lee SH, Cho HD. Localized Langerhans cell histiocytosis of the stomach treated by endoscopic submucosal dissection. Endoscopy. Endoscopy. 2011;43(Suppl 2) UCTN:E268-9.
17. 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.
18. 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.
19. Seo HW, Han KH, Kim S, Hong MY, Yun JH, Eom DW, et al. Colonic langerhans cell histiocytosis presenting as an isolated polyp. Korean J Med. 2013;84(5):704-7.
20. Felipe-Silva A, Assef MS, Rodriguesa RA, Pagliari C. Adult Langerhans cell histiocytosis presenting as metachronous colonic polyps. Autops Case Rep. 2013;3(1):39-44.
21. Gu MJ, Bae YK, Jang BI. Isolated Langerhans cell histiocytosis in rectum: case report and literature review. Pathology. 2013:45(5):516-7.
22. Podjasek JO, Loftus CG, Smyrk TC, Wieland CN. Adult-onset systemic Langerhans cell histiocytosis mimicking inflammatory bowel disease: The value of skin biopsy and review of cases of Langerhans cell histiocytosis with cutaneous involvement seen at the Mayo Clinic. Int J Dermatol. 2014;53(3):305-11.
23. Hameed A, Taggart MW, Shafi MA. Adult Langerhans Cell Histiocytosis in a Solitary Colon Polyp. JSM Clin Case Rep. 2014;2(2):1023.
24. Behdad A, Owens SR. Langerhans cell histiocytosis involving the gastrointestinal tract. Arch Pathol Lab Med. 2014;138(10):1350-2.
25. Waters J, Fajardo A, Holcomb B, George V, Robb B, Ziegler M. Langerhans cell histiocytosis with anorectal involvement: A rare manifestation of adult disease. Int J Colorectal Dis. 2015;30(5):707-8.
26. Lee SJ, Hwang CS, Huh GY, Lee CH, Park DY. Gastric Langerhans Cell Histiocytosis: Case Report and Review of the Literature. J Pathol Transl Med. 2015;49(5):421-3.
27. Coronel E, Micic D, Rubin DT. Patchy colitis and interstitial lung disease. Gastroenterology. 2015;148(1):26-7.
28. Androulaki A, Klimis A. Adult Langerhans cell histiocytosis with caecal and regional lymph node involvement. Hellenic Journal of Surgery. 2016;88:201-4.
29. Karimzada MM, Matthews MN, French SW, DeUgarte D, Kim DY. Langerhans cell histiocytosis masquerading as acute appendicitis: Case report and review. World J Gastrointest Endosc. 2017;9(3):139-44.
30. Abdou AG, Taie DM. Perianal Langerhans cell histiocytosis: A rare presentation in an adult male. Autops Case Rep. 2017;7(3):38-43.
31. Gupta P, Dhull AK, Kaushal V. Langerhans cell histiocytosis of small intestine. J Evid Based Med. Healthc. 2018;5(53):3682-3683.
32. Bhinder J, Mori A, Kurtz L, Madhavi Reddy. Langerhans cell histiocytosis of the gastrointestinal tract - a rare entity. Cureus. 2018;10(2):2227.
33. Therrien A, El-Haffaf Z, Wartelle-Bladou C, Cote-Daigneault J, Nguyen BN. Langerhans cell histiocytosis presenting as Crohn's disease: A case report. Int J Colorectal Dis. 2018;33(10):1501-4.
34. Yan F, Zhou Q, Gao Y, Chang H, Li X, LiY, et al. Isolated Langerhans cell histiocytosis of the stomach: A case report and literature review. Int J Clin Exp Pathol. 2018;11(12):5962-68.
35. Carthy AJM, Soofi ME, Mujeeb I, Chetty R. Langerhans cell histiocytosis of the gastrointestinal tract. Diagnostic Histopathology. 2018;24(4):154-9.
36. Zaiem F, Beydoun R. Adult Langerhans cell histiocytosis arising in colonic polyp: A case report and literature review. Human Pathology: Case Reports. 2019;17:200311.
37. Mansour MJ, Mokbel F, Fares E, Maddah J, Nasr F. Adult Langerhans cell histiocytosis with pulmonary and colorectoanal involvement: A case report. J Med Case Rep. 2017;11:272.
38. Goyal G, Hu M, Young JR, Vassallo R, Ryu JH, Bennani NN, et al. Adult Langerhans cell histiocytosis: A contemporary single-institution series of 186 patients. J Clin Oncol. 2019;37(15 Suppl)7018.
39. Leung AKC, Lam JM, Leong KF. Childhood Langerhans cell histiocytosis: A disease with many faces. World J Pediatr. 2019;15(6):536-45.