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

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 $13 \times 10^3$/mL, hemoglobin was 11 g/dL, hematocrit was 30, platelet was $490 \times 10^3$/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 patient 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
The 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,b). Our patient was administered with 1mg/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...
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