Çoklu Organ Tutulumu Olan Langerhans Hücreli Histiositozis; Olgu Sunumu

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Langerhans Cell Histiocytosis with Multiple Organ Involvement; Case Report

ÖZET

Langerhans Hücreli Histiositozis (LHH) sebebi tam olarak bilinmeyen nadir görülen bir hastalıktır. Epitel yüzeylerde bulunan, dendritik hücrelerin alt tipi olan monoklonal langerhans hücrelerinin anormal çoğalması ile karakterizedir. Sıklıkla çocuk yaş grubunda gözlenir ancak nadiren erişkin yaş grubunda da gözlenebilmektedir. LHH sıklıkla tek organ tutulumu ile seyreder fakat akciğer, kemik, hipofiz bezi, deri, karaciğer gibi çok sayıda organ tutulumu da gözlenebilir. Organ tutulumlarına göre klinik seyirde farklılıklar ortaya çıkmaktadır. LHH nadir görülen bir hastalık olması ve hastamızda akciğer, karaciğer ve yaygın cilt tutulumu olması nedeniyle sunulmuştur.

Anahtar Kelimeler: Langerhans Hücreli Histiositozis, deri, çoklu organ tutulumu, sklerozankolanjit

ABSTRACT

Langerhans Cell Histiocytosis (LCH) is a rare disease of exactly unknown cause. It is characterized by the abnormal proliferation of monoclonal langerhans cells, a subtype of dendritic cells located on epithelial surfaces. It is often observed in children but rarely can be observed in the adult age group. LCH often progresses with single organ involvement, but many organ involvement such as lung, bone, pituitary gland, skin, and liver can be observed. The clinical course of LCH differs according to system involvement. It is presented because LCH is a rare disease and our patient has multiple organ involvement such as lung, liver and skin.

Keywords: *Langerhans Cell Histiocytosis, multiple organ involvement, sclerosing cholangitis, dermis*

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Introduction

LCH is a systemic disorders characterized by the abnormal proliferation of monoclonal langerhans cells which subtype of dendritic cells, located on epithelial surfaces (1). LCH is an extremely rare disease in the population. The annual incidence in children in the first three years is 3-5 per million, while the annual incidence in the adult age group is 1-2 per million. The cause of this disease is not known exactly. The abnormal proliferation and accumulation of Langerhans cells are determine the clinical course of the disease. In cases with more than one organ involvement, diagnosis is often delayed and is confused with other diseases with a multisystemic clinical course (2,3).

Here, we report a patient with LCH, who could not be diagnosed for a long time due to its multisystemic organ involvement.

Case Report

A 24 year-old male patient presented to the emergency department with complaints of productive cough, shortness of breath, hemoptysis and fever for a week. There were twice spontaneous pneumothorax, primary sclerosing cholangitis diagnosis with by performing liver biopsy in the gastroentereology clinic, and diabetes insiputus diagnosis in his medical history. Additionally, he had a history of follow-up and treatment with a preliminary diagnosis of psoriasis, seborrheic dermatitis due to scaly lesions on her scalp. smoking eight packs a year, and working in a plastic pipe factory.

In the physical examination; heart rate was 126 / min, respiratory rate was 30 /min, blood pressure (systolic/diastolic) was 130/90 mmhg. There was intercostal withdrawal and paradoxical breathing on inspection, and bilateral breathing sounds

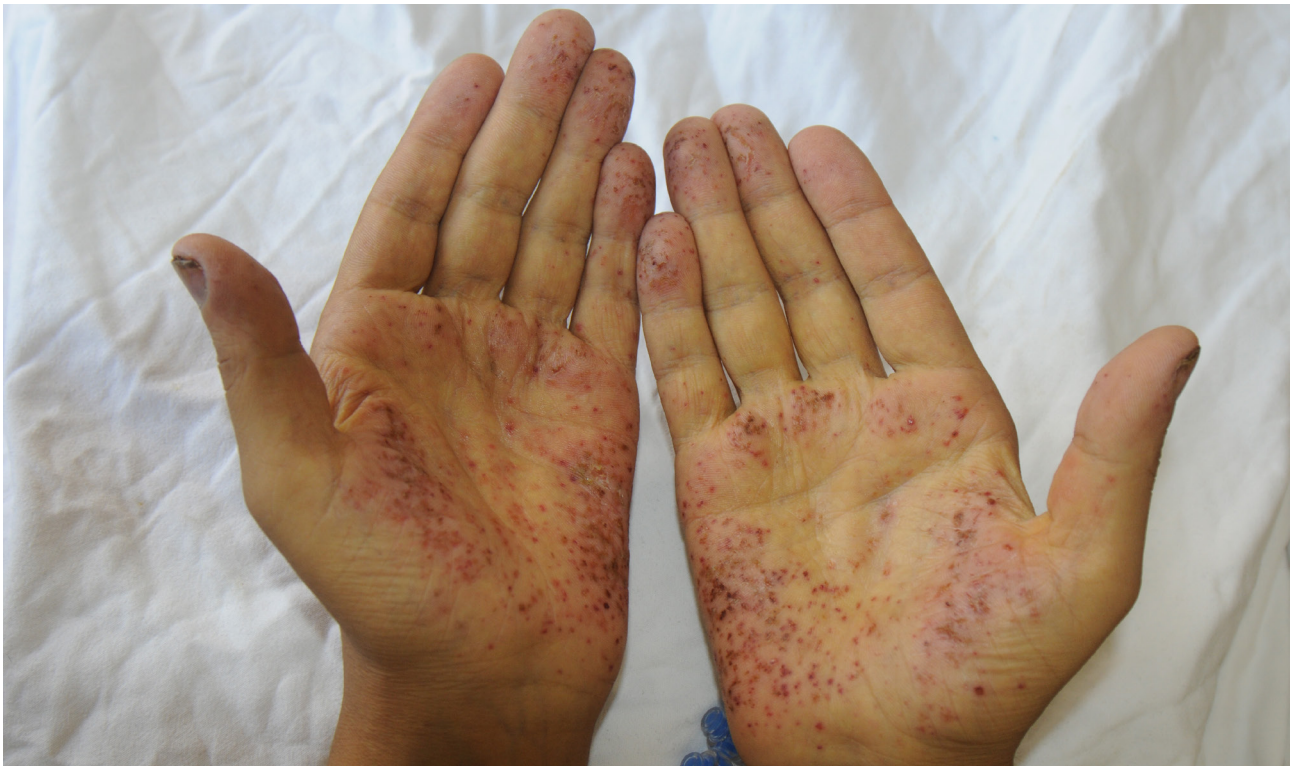

Figure 01

decreased on auscultation. On skin examination, there were erythematous and swollen lesions on the hands and feet, yellowish crusted lesions in front and behind the chest wall, widespread erythematous yellow squamous appearance on the scalp and erythematous plaque rashes in the perianal area (Figures 1-3). The skin and sclera are icteric appearance. Peripheral lymphadenopathy and hepatosplenomegaly are not detected. Other system examinations are normal.

In the laboratory findings; gamma glutamyl transferase 87 U/L, total bilirubin 16 mg/dL, direct bilirubin 13 mg/dL, aspartate aminotransferase 253 U/L, alanine aminotransferase 11 U/L, erythrocyte sedimentation rate 80 mm/hour, procalcitonin 0.317 ng/mL, C-reactive protein was 38.5 mg/L. Alpha-1 antitrypsin level is found to be normal. In arterial blood gas, pH is 7.35, pCO2 46.4 mmHg, pO2 42.6 mmHg, HCO3 31 mmol/L and SaO2 76%.

The patient was admitted to the intensive care unit due to hypoxemic and hypercapnic respiratory failure. Widespread cystic emphysematous changes were observed in the middle and lower areas of both lungs in thoracic tomography. There was consolidation in the left lung posterobasal (Figures 4-5). In cystic fibrosis genetic examination, V470M was found to be homozygous positive and it was accepted as polymorphism. Histopathological examination of the palmoplantar skin punch biopsy material taken from the patient revealed that Langerhans cells filling the papillary dermis and stained positively with CD1a and histiocytes stained positively with CD68 were detected. Histochemical study with Toluidine blue and immunohistochemical findings with CD117

were found to be compatible with LCH (Figures 6-8). Oxygen, bronchodilator and antibiotics (piperacillin-tazobactam + linezolid) were initiated

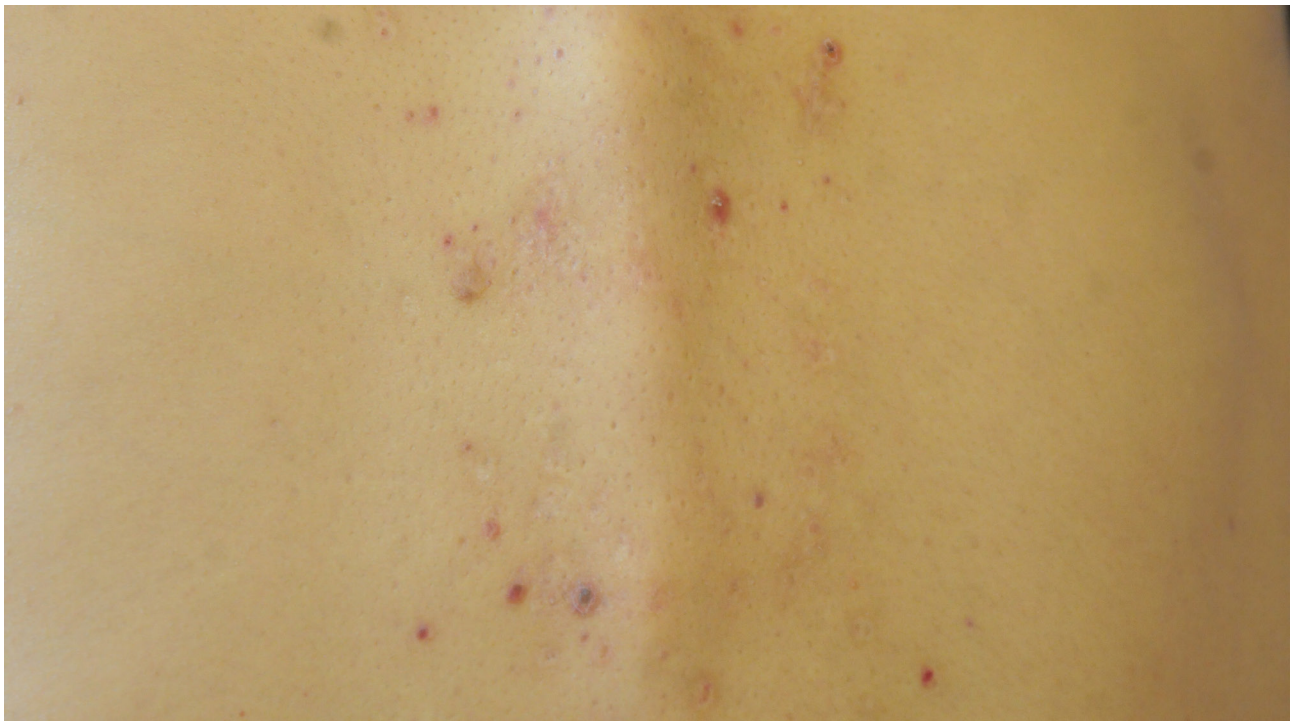

Figure 02

as medical treatment. Bone radiographs and peripheral smear examinations were evaluated as normal. There was mild right ventricular dilatation on echocardiographic examination. Pulmonary artery pressure was 45 mmHg.

Chemotherapy was planned for the patient whose fever, sputum purulence, leukocytosis and acute phase reactants regressed as a result of follow-up and treatments. However, chemotherapy treatment could not be given due to impaired general condition, hypoxemic respiratory failure and severe hyperbiluribinemia. He was transferred to a tertiary center for continuation of treatment.

Discussion

LCH is a rare neoplasm of Langerhans type cells. Although it is mostly seen in infants and children, it can rarely be seen in the adult age group. The incidence of LCH in adults is approximately 1-2/ million (2-3). In the adult age group, the mean age of onset is 33-35 years (4). These cases are often diagnosed in early childhood however, as in our case, the diagnosis is delayed due to different organ involvements and they are frequently followed up with different disease diagnoses.

According to the distribution of the lesions in the body, LCH is divided into two types as disseminated and localized. The localized type is divided as follows; [1] simplex rash, without affecting organs. [2] simplex bone damage, with or without DI, adjacent lymph nodes involvement or rash. [3] multiple bone damages, including more than one bones or one bone with more than two damages, with or without DI, adjacent lymph nodes involvement or rash. The disseminated type is divided as follows; [1] the internal organs were involved, with or without DI, adjacent lymph nodes involvement or rash, without dysfunction of lung, liver or hemopoietic system. [2] apart from the above symptoms, the internal organs are involved as well, with dysfunction of lung, liver or hemopoietic system (5) LCH seen in adults is often seen as disseminated types and its mortality is higher than those with localizated types. In the study of Aricò M et al. in which 274 adult patients who were diagnosed with LHH by biopsy from 13 different countries were examined, a single organ overall was detected in 86 cases (31.4%), while multi-organ involvement was found in 188 cases (68.6%). In 44 of the patients with single organ involvement, a single lung involvement was found (4).

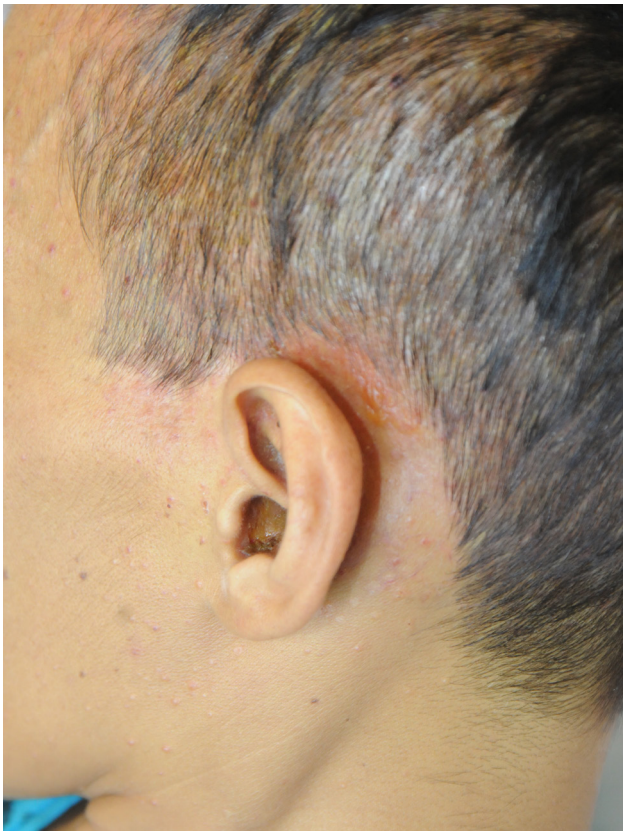

Figure 03

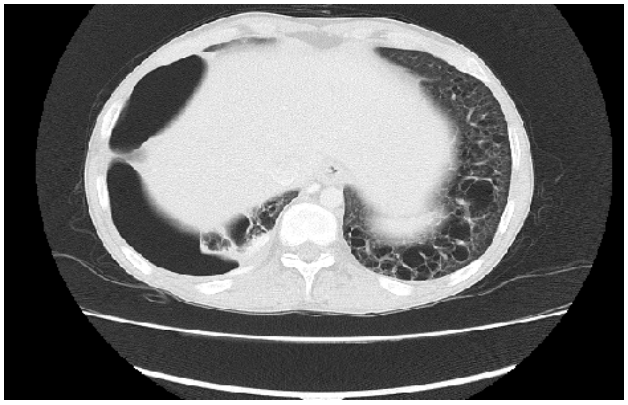

Figure 04

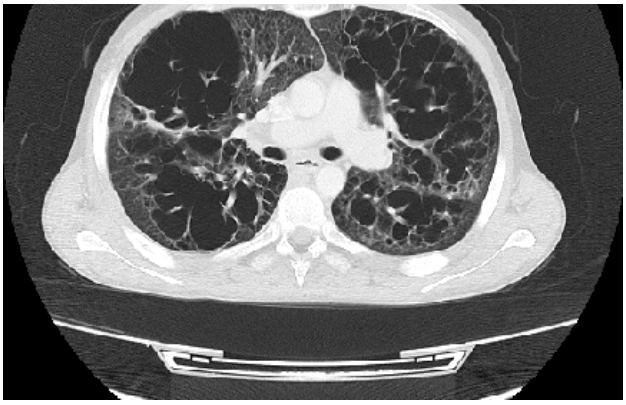

Figure 05

The clinical course of the disease varies depending on organ involvement (6, 7). The most frequently involved organs in LCH are skleton (80%) and the skin (33%), and the pituitary (25%) (8). It may progress only with lung or bone involvement, but it may also present with symptoms of multiple organ involvement such as the pituitary gland, mucosa, lymph nodes, and liver. The most common findings of LCH are local pain (34%), weight loss (11%), and fever (10%) (3). The most common complaints in pulmonary involvement are cough and shortness of breath. Pneumothorax is seen with a frequency of 15% and may be the first presentation finding. (7). Our case has complaints of dyspnea, sputum production, hemoptysis, skin rash and jaundice due to organ involvement. Our patient has a history of pneumothorax twice in the last year. More than 95% of LCH patients have a smoking history. Our patient also had a history of eight pack/year nicotine exposure.

Sclerocolangitis is seen in 10-18% of patients with multi-organ involvement and can progress to liver failure (9). The most common (26.9%) and permanent endocrinological finding in LCH seen in adults is DI, which is frequently seen in patients with multisystem involvement (3, 10). In our case, he was diagnosed DI and sclerocolangitis by liver biopsy approximately before two years the diagnosis,

In LCH disease, single skin involvement is rare in adults. Solitary papule, nodule or tumor, widespread reddish-brown papules, ulcerative lesions in the skin folds or in the anogenital region are the skin findings seen in the course of the disease. The prognosis of patients with single skin involvement was found to be significantly lower than that of patients with multiple organ involvement (11). Stephen J Simko et al. (12) evaluated 71 patients with single skin or multiple organ involvement accompanied by skin involvement. They stated that skin involvement in patients older than 18 months is associated with multiple organ involvement. Edelbroek J.R. et al. (11) examined the pathological samples and records of 18 LCH patients who were skin involvement, followed up in different centers their study. They concluded that patients presenting with skin involvement also have an increased risk of secondary hematological malignancy. Our patient has red papules on the hands and feet, scaly rashes on the scalp and erythematous plaque lesions in the perianal region and there was no clinical suspicion of hematological malignancy.

Definitive diagnosis in LCH is made by biopsy specimen showing multinucleated Langerhans cells, histiocytes, and eosinophils. Birbeck granules or CD1a glycoprotein structures should be shown in electron microscopy for diagnosis. In the

skin biopsy of our patient, we detected langerhans cells that stained positively with CD1a. (5)

The treatment of LCH depends on the extent of the disease, the age of the patient, and dysfunction of the mainly affected organs. The treatments of LCH include surgery, radiotherapy, systemic chemotherapy and combination therapy (5). Chemotherapy treatment for LCH include combined treatment with vinblastine, etoposide, mercaptopurine, corticosteroids, azathioprine, cyclophosphamide, chlorodeoxyadenosine, and cytosine arabinoside (3) Chemotherapy treatment could not be planned because of our patient's general condition disorder and hypoxemic respiratory failure. The patient was transferred to a tertiary center for continuation of treatment.

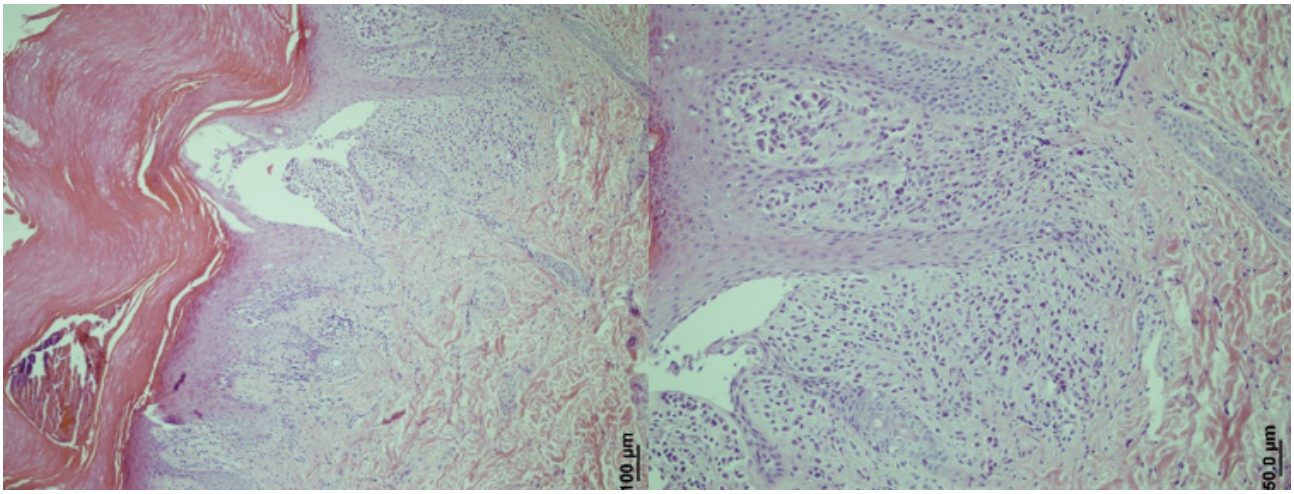

Figure 06 A-B: In skin tissue covered with keratinized stratified squamous epithelium, langerhans cells filling the papillary dermis and a small number of histiocytic cells (Hemotoxylin eosin, X400)

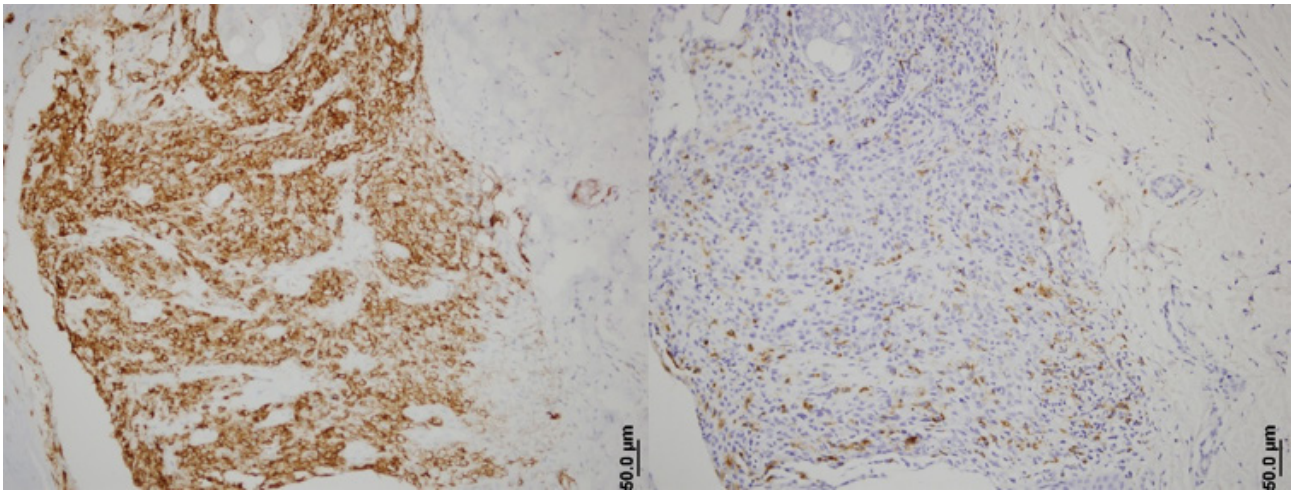

Figure 07A: Diffuse strongly positive langerhans cells (DAB, X400) with CD 1a by immunohistochemistry

Figure 07B: Immunohistochemically, focal positive histiocytic cells with CD 68 (DAB, X400)

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