A Retrospective Evaluation of Cases with Adult-Onset Langerhans Cell Histiocytosis: A Single-Center Experience of 14 Cases

Erişkin Başlangıçlı Langerhans Hücreli Histiositozis Tanılı Olguların Retrospektif Değerlendirilmesi: 14 Olguluk Tek Merkez Deneyimi

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ABSTRACT

Objective: Langerhans cell histiocytosis (LHH) is a disease group of unknown etiology that causes tissue injury as a result of the local or systemic accumulation of atypical histiocytes in various tissues such as skin, bone, lungs, liver, lymph nodes, mucocutaneous tissues, and endocrine organs. We aimed to report the demographic and clinical properties of 14 LLH cases diagnosed and followed at our center.

Material and Methods: This study retrospectively enrolled 14 patients (7 females, 7 males) having a diagnosis of LLH who were followed up at the Health Sciences University Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Hematology between 01-March-2011 and 30-September-2019.

Results: Five patients had bone involvement; 5 had lymph node, 3 had skin, 2 had brain, 1 had liver, 1 had lung, 1 had uterine, 1 had parotid, 1 had colon, and 1 had thyroid involvement. At the end of a total follow-up period of 103 months, all patients are alive. All patients with single organ involvement were treated surgically while 3 patients with multisystemic involvement received chemotherapy containing cladribine.

Conclusion: There were only 14 adults diagnosed with LHH at our center over a period of 8 years. Treatment is tailored to patient's symptoms and compressive signs of a mass. While patients may be managed conservatively, without treatment, they may have a rapid and grave prognosis that requires commencing urgent therapy. Is a variable clinical course a characteristic feature of the disease or do inadequate and ineffective treatments unfavorably affect prognosis? Are solely local treatments effective? There is a need for studies with larger patient series.

Key Words: Langerhans Cell Histiocytosis, Adult-onset, Single-Center Experience

ÖZ

Amaç: Langerhans hücreli histiyositoz (LHH), nedeni bilinmeyen, atipik histiyositlerin lokal veya yaygın olarak deri, kemik, akciğer, karaciğer, lenf nodları, mukokutanoz dokular ve endokrin organlar gibi çeşitli dokularda birikmesi sonucunda hasara sebep olan bir hastalık grubudur. Biz bu çalışmada merkezimizde tanısı konulan ve takip edilen 14 LHH olgusunun demografik ve klinik özelliklerini sunmak istedik.

Gereç ve Yöntemler: Çalışmada 01-Mart-2011/30-Eylül-2019 tarihleri arasında Sağlık Bilimleri Üniversitesi Ankara Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi Hematoloji Bölümünde LHH tanısı ile izlenen 14 hasta (7 kadın, 7 erkek) retrospektif olarak değerlendirildi.

Bulgular: Olguların 5'inde kemik tutulumu, 5'inde lenf nodu, 3'ünde cilt, 2 hastada beyin, 1 hastada karaciğer, 1 hastada akciğer, 1 hastada uterus, 1 hastada parotis, 1 hastada kolon, 1 hastada tiroid, tutulumu mevcuttu. Toplam takip süresi 103 ay sonunda tüm hastalar hayattadır. Tek lezyonu olan hastaların tamamı cerrahi olarak tedavi edilirken, multisistemik tutulumu olan 3 hasta cladribine içeren kemoterapi aldı.

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Sonuç: Merkezimizde 8 yıllık süre içerisinde erişkin yaş grubunda LHH tanısı alan sadece 14 hasta vardı. Tedavi planı hastanın klinik şikayetlerine ve kitlenin bası bulgularına göre belirlenir. Hastalar tedavisiz izlemle takip edilebildiği gibi, acil tedavi başlanacak kadar hızlı ve kötü seyirli prognoza sahip olabilirler. Değişken klinik seyir, hastalığın doğası gereği midir yoksa, az ve etkin olmayan ve zamanında verilmeyen tedaviler prognozu olumsuz mu etkilemektedir? Sadece lokal uygulanan tedaviler başarılı mıdır? gibi sorulara cevap bulmak amacıyla daha büyük hasta serileri ile yapılacak çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Langerhans hücreli histiositoz, Erişkin başlangıçlı, Tek merkez deneyimi

INTRODUCTION

Langerhans cell histiocytosis (LHH) is a disease group of unknown etiology that causes tissue injury as a result of the local or systemic accumulation of atypical histiocytes in various tissues such as skin, bone, lungs, liver, lymph nodes, mucocutaneous tissues, and endocrine organs (1). Although its exact incidence is unknown due to its various features such as having systemic manifestations involving non-hematological disciplines and inadequate LLH awareness, it is reported that the incidence of LLH of bone origin has an incidence of 2/1,000,000 in the childhood era, making it classified in the rare diseases category (3). Whereas all organs may be involved, it most commonly involves bones, the skin, pituitary gland, and lungs. As it is a rare disorder reported only in a limited number of cases, many treatment modalities are of uncertain benefit and controversial (2). Treatment modalities depend on disease extent. Herein, we aimed to report the demographic and clinical properties of 14 LLH cases diagnosed and followed at our center.

MATERIAL and METHOD

This study retrospectively enrolled 14 patients (7 females, 7 males) having a diagnosis of LLH who were followed up at the Health Sciences University Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Hematology between 01-March-2011 and 30-September-2019. The patients' pathological diagnoses and sites, involved sites, laboratory results, disease extents, and treatment responses were recorded from their medical reports. Bone involvement was assessed by total bone scan with X-Ray or scintigraphy. All patients underwent abdominal ultrasonography, chest computerized tomography, cranial magnetic resonance imaging (MRI), and pituitary MRI. Bone marrow aspiration and biopsy was performed in all patients with multisystemic involvement. Pathology reports were retrospectively analyzed, and all patients were found to have positive immunohistochemical staining for CD1a and S100.

Ethical approval and informed consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. As a standard of care/action of Ankara Diskapi Yildirim Beyazit Research and Training Hospital, the patient records confirmed that all the study patients gave informed consent at the time of hospitalization and before the administration of chemotherapy and other relevant diagnostic/therapeutic standards of care. This study was approved by the Ethics Committee and the approval number is 62/15.

RESULTS

Of a total of 14 patients, 7 (50%) were female and 7 (50%) were male. The median age was 47.85±16.84 years. Five patients had bone involvement; 5 had lymph node involvement; 3 had skin involvement; 2 had brain involvement; 1 had liver involvement; 1 had lung involvement; 1 had uterine involvement; 1 had parotid involvement; 1 had colonic involvement; and 1 had thyroid involvement. Four (28.6%) patients had multisystemic involvement; 10 (71.4%) had single organ involvement. All patients with single organ involvement were treated surgically while 3 patients with multisystemic involvement received chemotherapy containing cladribine. Patients with skin involvement were treated by the dermatology department with topical steroids. The overall characteristics of the patients are presented in Table I. At the end of a total follow-up period of 103 months, all patients are alive. One patient was referred to a tertiary hospital due to multisystemic involvement and 3 recurrences required an allogenic stem cell transplant.

DISCUSSION

LHH is a clonal, pleomorphic, neoplastic disease group of unknown cause that occurs as a result of abnormal proliferation of histiocytes with dendritic cell properties of bone marrow origin. Its incidence ranges between 0.5 and 5.4 per million population. It is twice as more common in men than in women (4). Although it is seen in every age group, it is particularly observed at the 1-3-year age group. However, it is encountered as rare, ill-defined cases in adults (5). There were only 14 adults diagnosed with LHH at our center at a period of 8 years. The largest series reported from Turkey so far was the series reported by Yağcı et al. and involved 217 patients (6). Our patients had a median age of 47 years and an equal sex distribution.

In a retrospective analysis of adult-onset Langerhans cell histiocytosis cases performed by Şahin F. et al. from Turkey,

the mean age was 27.5 (18-40) and there were 7 patients (4 males, 3 females) (7). In this study, no bone marrow or extrapulmonary organ involvement was observed in any of the patients. However, multiple organ involvement was seen in our 3 patients and all received systemic chemotherapy. 1 patient underwent allogeneic stem cell transplantation because of no response to 3 lines of systemic chemotherapy.

LHH may manifest a variable presentation ranging from a self-healing lesion to life-threatening diffuse disease in both children and adults. Considering organ involvement, the rate of bone involvement is 80%, skin involvement 33%, pituitary involvement 25%, liver, spleen, hematopoietic system or lung involvement 15%, lymph node involvement 5-10%, and non-pituitary CNS involvement 2-4% (8). Unlike literature data, our patients showed the most common involvement in bone and lymph node (about 30%) and skin (about 20%). At the same time, interestingly, two patients showed endocrine system (thyroid and parathyroid) and one patient had uterine involvement. As one may see from these findings, LHH may involve almost any organ, albeit some to a rarer degree.

Treatment is tailored to patient's symptoms and compressive signs of a mass. While patients may be managed conservatively, without treatment, they may have a rapid and grave prognosis that requires commencing urgent therapy. Treatment options recommended for LHH include surgery, methylprednisolone injection, or radiotherapy for bone lesions, smoking cessation for lung lesions, and topical corticosteroids for skin lesions while systemic treatments include vinblastine, prednisone, or 2-chlorodeoxadenosine and ARA-C treatment when recurrences occur. Twenty-eight percent of our patients had multisystemic involvement and 71% had single organ involvement. Four patients were being managed without treatment. All patients with a single lesion were treated surgically while three patients with multisystemic involvement received systemic therapy including cladribine. Patients with skin involvement received topical steroids. Hematopoietic stem cell transplant is another treatment option, and new treatment targets include BRAF V 600 and KIR 2DL4 (CD158d) (Killer cell immunoglobulin like receptor) mutations (9,10).

There is a need for studies with larger patient series in order to answer questions such as whether effective and systemic treatment is necessary for diffuse involvement and CNS involvement, whether CNS involvement, although rare, is associated with a poor prognosis, whether a variable clinical course is a characteristic feature of the disease, whether inadequate and ineffective treatments unfavorably affect the prognosis, and whether solely local treatments are effective.

Table I: General characteristics of patients followed with Langerhans Cell Histiocytosis.

Case No.	Diag. Age	Diag. Region	Involved Fields	Treatment
1	35	Hip Bone	Bone, Mediastinum LAP, Ribs, Liver, Sphenoid Bone, Brain	3 Cycles of Cladribin, 1 Cycle of Ara-C, Cladribin
2	68	Right Periauricular Soft Tissue	LAP	None
3	16	Frontal Region Bone	Bone	None
4	68	Skin	Skin	None
5	41	Thyroid	Thyroid	Surgery
6	54	Skin	Skin	Surgery
7	33	Frontal Region Bone+Dura Invaded	Bone+Brain	2 Cycles of Cladribin+Ara-C
8	64	Skin	Skin	None
9	53	Lung	Lung	Surgery
10	65	LAP	LAP	Surgery
11	32	LAP	Inguinal LAP, Uterus, Ribs, Femur, Mediastinum LAP	2 Cycles of Cladribin+Ara-C, 12 Cycles of Prednol, Vinblastin, 6 Mercaptopurine, Cladribin, Ara-C
12	29	LAP	LAP	Surgery
13	62	Parotid	Bone, Parotid	Surgery
14	50	Colon	Colon	Surgery

REFERENCES

1. Jaffe R. The diagnostic histopathology of Langerhans cell histiocytosis. In: Weitzman S, Egeler RM, eds. Histiocytic Disorders of Children and Adults. Basic Science, Clinical Features, and Therapy, Cambridge: Cambridge University Press, 2005; p14.
2. Gadner H, Grois N, Pötschger U, Minkov M, Aricò M, Braier J, Broadbent V, Donadieu J, Henter JI, McCarter R, Ladisch S. Improved outcome in multisystem Langerhans cell histiocytosis is associated with therapy intensification. Blood 2007; 111:2556-62.
3. Guyot-Goubin A, Donadieu J, Barkaoui M, Bellec S, Thomas C, Clavel J. Descriptive epidemiology of childhood Langerhans cell histiocytosis in France, 2000-2004. Pediatr Blood Cancer 2008; 51:71-5.
4. Lipton JM. Histiocytic disorders. In:Hoofman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE, McGlave P, eds. Basic Principals and Practice. 3rd ed. New York: Churchill Livingstone, 2000:783-93.
5. Arico M, Girschikofsky M, Genereau T, Klersy C, McClain K, Grois N, Emile JF, Lukina E, De Juli E, Danesino C. Langerhans cell histiocytosis in adults. Report from the international registry of the Histiocyte Society. Eur J Cancer 2003; 39:2341-8.
6. Yağci B, Varan A, Cağlar M, Söylemezoğlu F, Sungur A, Orhan D, Yalçin B, Akyüz C, Kutluk T, Büyükpamukçu M. Langerhans cell histiocytosis: Retrospective analysis of 217 cases in a single center. Pediatr Hematol Oncol 2008; 25:399-408.
7. Şahin F, Özen KP, Vural F, Kamer S, Argın M, Anacak Y, Hekimgil M, Saydam G. Retrospective analysis of seven patients with adult-onset langerhans cell histiocytosis syndromes: A single center experience. Turk J Haematol 2007; 24(2):75-9.
8. Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, Requena-Caballero L, Jordan MB, Abdel-Wahab O, Allen CE, Charlotte F, Diamond EL, Egeler RM, Fischer A, Herrera JG, Henter JI, Janku F, Merad M, Picarsic J, Rodriguez-Galindo C, Rollins BJ, Tazi A, Vassallo R, Weiss LM. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016; 127(22):2672-81.
9. Hegemann MV, Schreml S. Multisystemic Langerhans cell histiocytosis in an adult. JAAD Case Rep 2017; 3(2):162-4.
10. Takei Y, Ueshima C, Kataoka TR, Hirata M, Sugimoto A, Rokutan-Kurata M, Moriyoshi K, Ono K, Murakami I, Iwamoto S, Haga H. Killer cell immunoglobulin-like receptor 2DL4 is expressed in and suppresses the cell growth of Langerhans cell histiocytosis. Oncotarget 2017; 8(23):36964-72.