A case of Langerhans Cell Histiocytosis with Multisystemic Involvement in an Adult Patient

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare group of idiopathic diseases characterized by abnormal proliferation of bone marrow-derived dendritic cells called histiocytes. It is more common in childhood, but in the literature, some adult cases have been reported. For several reasons, the disease is more familiar to pediatricians than it is to physicians handling adult cases; therefore, the diagnosis of adult cases is often delayed or missed. The clinical course of LCH is variable, ranging from a self-healing solitary bone lesion to a widely disseminated life-threatening disease. The diagnosis of LCH should be based on histologic and immunophenotypic examination of perilesional skin. In this report, we present a case of LCH in a 66-year-old woman with bone, skin, and pituitary gland involvement; this case emphasizes that a patient with LCH should undergo careful multidisciplinary evaluation.

Keywords: Langerhans cell histiocytosis, adult, multisystemic, dendritic cells, multidisciplinary

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare group of diseases with unknown etiology. It is characterized by abnormal proliferation of atypical histiocytic cells derived from bone marrow and presents with different clinical findings (1). Diagnosis is confirmed by immunohistochemical demonstration of CD1a and S-100 markers and by the presence of Birbeck granules on electron microscopy. Pathologic Langerhans cells may be observed in the skin, bone, hypothalamus, liver, lung, and lymph nodes (1-3). Although familial cases are reported, there is no definitive evidence for genetic transmission of disease. There is no marked difference between sexes in terms of incidence. Although the incidence is 1–2/1,000,000 in children, it is even rarer in adults (4, 5). LCH may have different clinical presentations depending on involved areas. It may have local or systemic presentations (1). In this report, we present a case referred to our clinic with atrophic xanthomatous plaque in the scalp and diagnosed with LCH upon histochemical investigation, bone involvement, and diabetes insipidus with further investigations.

CASE REPORT

A 66-year-old female patient was referred to our clinic with a lesion in her scalp, which she noticed 6 months ago. On physical examination, a yellow plaque with an atrophic base and a diameter of 3 cm was detected on the scalp in the left parietal region; it was surrounded by a slightly erythematous halo (Figure 1). There was no palpable lymph node. She had fatigue and bone pain. Ten years ago, she went to an outpatient clinic for polyuria and polydipsia. At this time, some laboratory and radiographic evaluations were performed and she was diagnosed with diabetes insipidus. She received desmopressin treatment (0.6 mg once a day). However, she had not visited the doctor for 3 years and she was not taking the medication.

Skin biopsy was obtained with the provisional diagnoses of LCH, necrobiotic xanthoma granuloma, and necrobiosis lipoidica.

On histopathological investigation, hyperkeratotic layer partly infiltrated with neutrophils and an ulcerated area were observed (Figure 2a). In addition, foamy histiocytes banded in the upper dermis and chronic-type inflammatory cell reactions clustered in focal areas were observed (Figure 2b). On immunohistochemical investigation, reactions with CD68, CD1a, and S-100 were observed (Figure 3).

On laboratory investigations, erythrocyte sedimentation rate was found to be 53 mm/h (normal: 0–20 mm/h); C-reactive protein, 93.6 mg/L (normal: 0–8 mg/L); and hemoglobin, 10.5 g/dL (normal: 12–18 g/dL). Hematology department was consulted, and bone marrow biopsy was carried out; no pathological finding was seen. The patient was reported to have anemia of chronic disease.
No pathological findings were observed in abdominal computed tomography (CT) and cranial magnetic resonance imaging. She consulted with endocrinology department, and they suggested drug-free followup. Bone scintigraphy revealed an increase in osteoblastic activity on right femoral and tibial area. It was more marked at the end of bones. In addition, linear scattered increased activity was observed in sternoclavicular joint and T10 levels, which was more marked in the proximal areas of both forearms. With PET-CT, lithic and sclerotic involvement areas suggesting malignancy were observed in the same localizations. Based on these findings, the patient was diagnosed with LCH with skin, hypophysis, and bone involvement.

The patient consulted with the hematology and radiation oncology departments. Lung radiography and CT were performed to check for pulmonary involvement. In addition, pelvic and abdominal ultrasonography and abdominal CT investigation were carried out for other organ involvement and thyroid function tests for thyroid pathology, all of which yielded normal results.

For lesions on tibia, radiotherapy was initiated; and for other areas, vinblastine, etoposide, and prednisolone chemotherapy protocol was administered. When progress in lesions was observed with follow-up PET-CT carried out on the sixth week of treatment, the chemotherapy protocol was replaced with imatinib. During treatment process, deep vein thrombosis developed and low molecular weight heparin was commenced. Imatinib treatment continues since 6 months. Topical mometasone furoate was applied to skin lesion which regressed within 1 month. Treatment still continues for other organ system involvements. Patient provided consent for publication.

DISCUSSION

Langerhans cell histiocytosis is rare disease group characterized by abnormal proliferation of Langerhans cells. Variable clinical presentation and multiorgan involvement often require a multidisciplinary approach for successful diagnosis. Its etiology remains unknown, and it occurs usually in children. The Histiocyte Society proposed a revised classification schema in 2008 including division into (i) dendritic cell disorders: Langerhans cell histiocytosis (LCH), secondary dendritic cell processes, juvenile xanthogranuloma, solitary dendritic cell disorders (LCH is also in this group), and histiocytomas with a dendritic phenotype; (ii) macrophage-related disorders: primary and secondary hemophagocytic syndromes, Rosai–Dorfman disease, and solitary histiocytoma with a macrophage phenotype; and (iii) malignant histiocytic disorders: monocytelated leukemias, extramedullary monocytic tumor, and dendritic cell or macrophage-related histiocytic sarcoma (6).

Failure to recognize the disease at an early childhood can lead to progression into adulthood. Patients are usually asymptomatic or may have mild symptoms. The most common symptoms are dyspnea, cough, bone pain, an abnormal growth of soft tissue over the involved bone, rash, itch, thirst, polyuria, polydipsia, and lymphadenopathy (7). Our patient had joint pain all over the body. In addition, she had referred with polydipsia and thirst complaints before being diagnosed with DI.

Depending on the localization or extension of disease at the time of diagnosis, if there is only a single organ system involvement, it is termed single-system LCH, and if there are two or more organ/system involvement multisystem LCH (4). Multisystemic disease accounts for less than 30% of LCH cases (8). Liver, spleen, bone marrow, and lung involvement is considered especially risky (2). In the present case diagnosed with multisystemic LCH, no risky organ involvement was observed.

In adults, bones (52%), lungs (40%), and skin (7%) are most commonly involved (8). Cases with only skin involvement usually have favorable prognosis, and 50% may spontaneously resolve within a few months. Lung involvement which usually occurs in adult patient groups leads to tachypnea, chest retraction, and cough. Pulmonary LCH is usually associated with smoking (1). Diagnosis is usually made with high-resolution CT. Our patient did not smoke and in investigations, lung involvement was not detected.

Langerhans cell histiocytosis may mimic many dermatoses in appearance. Its differential diagnosis includes eczema, psoriasis,
seborrheic dermatitis, intertrigo, and candidal infections (7). In suspected cases, biopsy is imperative in order not to overlook systemic involvement. Treatment options are surgical excision in isolated lesions, as well as topical nitrogen mustard, psoralen+UVA (PUVA), tacrolimus, and thalidomide and interferon combination (9-11). In our patient, the isolated lesion localized in the scalp regressed with topical steroid treatment.

Bone involvement is the most common single organ involvement in children (4). In adults, skeletal involvement usually presents with bone pain and spontaneous fractures in skull, ribs, and long bones. For treatment, excision, curettage, and intralesional steroid injection may be used in local lesions and radiotherapy and chemotherapy for systemic disease (11, 12). Our case had multiple bone metastases without any symptoms detected by screening bone scintigraphy and PET-CT. Radiotherapy and chemotherapy were instituted for bone lesions.

The most common endocrine disease occurring in LCH cases is diabetes insipidus, which occurs in about 30% of the cases. It usually presents with polydipsia and polyuria. More rarely, growth hormone, gonadotropin, and thyroid hormone deficiency may be detected (1). In our case, no endocrine abnormality was seen except for diabetes insipidus.

There are no data in the literature regarding the time period between the onset of symptoms and diagnosis. In our case, skin symptoms emerged approximately 20 years after the diagnosis of diabetes insipidus. LCH has many different clinical presentations, and the patients are evaluated by different departments and branches, which may have led the diagnosis to be missed. The practitioners must be aware that LCH may involve almost any organ system, but the frequency of involvement, as well as the extent of the disease, is often age dependent. LCH may have systemic involvement both in children and adults. Therefore, multi-disciplinary approaches to the disease should be developed.

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authors’ Contributions: Conceived and designed the experiments or case: NST, BGD, FB, MA. Performed the experiments or case: BGD. Analyzed the data: BGD. Wrote the paper: BGD, NST, RK. All authors have read and approved the final manuscript.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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