

Langerhans Cell Histiocytosis Involving The Brain, Lungs, Salivary Glands And Vulva: Report Of A Rare Case And Review Of Literature

A Ehsani, P Hashemi, Z Naraghi, M Farivar, A Rashidi

Citation

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Abstract

Vulvar and salivary gland involvement are rare in Langerhans cell histiocytosis (LCH), for which less than 60 and 5 cases have been reported in the literature, respectively. We report a 22-year old woman with LCH and multisystem disease including involvement of the brain (diabetes insipidus), lungs (pneumothorax), salivary glands and vulva (skin lesion). Vulvar lesion included a 3×2 cm erythematous and ulcerated plaque on the fourchette and a 1×1 cm similar lesion on the right labia major. The lesions were slightly infiltrated and without any discharge. The diagnosis was confirmed by skin biopsies positive by immunohistochemistry for S100 and CD68. The skin lesion and the neck mass regressed completely with systemic chemotherapy. This case provides further support for using a combination of vinblastine and prednisolone in multisystem LCH.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a diverse group of clinical diseases in which a clonal population of cells with the phenotype of Langerhans cell accumulate in various tissues and cause damage [1]. The incidence of LCH is 4.0-5.4 per million of population, with a peak in children aged 1-3 years and male preponderance [2]. The estimated total mortality of LCH is approximately 3 % in adults and 15 % in children [3].

LCH can be local and asymptomatic or it can involve multiple organs (e.g. lungs, bones, pituitary gland, skin, reticuloendothelial system) with clinically significant symptoms and consequences. Multiple organ involvement increases mortality up to 66 % [4]. The range of clinical features of LCH in any organ is identical in children and adults, but the relative percentage of patients with multisystem disease versus single organ disease differs markedly. Localized disease appears more in children whereas in adults multisystem disease is most common [5]. The broad clinical spectrum of LCH introduces a wide range of differential diagnoses depending on the localization of the disease. Examples include osteomyelitis, metastases and Ewing sarcoma in the case of bone (the most commonly affected tissue in adults) involvement [6] and sarcoidosis, silicosis, hypersensitivity pneumonia, and

lymphangioleiomyomatosis when the lungs are involved [7].

Vulvar involvement in LCH is very rare, with less than 60 cases reported so far [8, 9]. Involvement of the salivary glands is also very rare in LCH, with only about 5 cases available in the literature [10, 11, 12]. Here, we report a case of multisystem LCH with involvement of the brain, lungs, salivary glands and vulva.

CASE REPORT

A 22-year-old woman was referred to our clinic with a 10-month constant itching in the vulva, starting one month after her first delivery. She did not complain of any abnormal discharge and had no associated temperature. Her past medical history was positive for a 5-year history of polyuria and polydipsia diagnosed as central diabetes insipidus with no further workup. She was on desmopressin spray two puffs per night since then. At the age of 19, she developed progressive dyspnea and a diagnosis of pneumothorax was made. The symptoms did not respond to chest tube insertion and supportive respiratory therapies. An open lung biopsy was performed which revealed diffuse interstitial lung disease with multiple pulmonary emphysematous blebs. Samples showed discrete patches or nodules of interstitial infiltrates separated either by cystic changes or normal lung tissue. The infiltrate formed a sheet like pattern and

consisted mainly of histiocytes with numerous lymphocytes and scattered eosinophils. Samples were positive in immunohistochemistry (IHC) for S100 and CD68 and a diagnosis of pulmonary eosinophilic granuloma was made. Since then she was a lung transplant candidate due to end-stage pulmonary disease.

On physical examination, a 2×2 cm asymptomatic firm non-tender mass was palpated in the right subauricular area. Examination of the vulvar region revealed a 3×2 cm erythematous and ulcerated plaque on the fourchette and a 1×1 cm similar lesion on the right labia major. The lesions were slightly infiltrated and without any discharge. No lymphadenopathy was detected. The rest of the physical examination brought no other disorders of interest to light. Routine laboratory tests including cell blood count, liver function tests and erythrocyte sedimentation rate were normal. No abnormality was detected in the abdominopelvic sonography, CT scans, bone scan or bone marrow aspiration biopsy. A CT scan of the neck revealed bilateral (especially on the right) enlargement of parotid and submandibular salivary glands with heterogeneous enhancement after contrast injection without any lymphadenopathy. .

A biopsy of the vulvar lesion was performed, which revealed extensive aggregates of histiocytic proliferation in the superficial dermis covered by an ulcerated epidermis. Histiocytes had broad cytoplasm and a nuclear groove which gave the nucleus a kidney-shaped appearance. Clusters of eosinophils and lymphocytes accompanied the infiltrate (Figure 1). Special staining for bacterial infection and herpes virus were negative. IHC staining including S100 and CD1a were strongly expressed by the large cells, confirming the diagnosis of LCH (Figure 2). The treatment protocol we used included oral prednisolone (started at 50 mg/d, continued for a month and then tapered to the current dosage of 12.5 mg/d) and intravenous vinblastine (2 mg every week for 2 months and then 2 mg every month). After three months, the genital lesion regressed completely and the neck mass disappeared.

Figure 1

Figure 1: Photomicrographs of the vulvar lesion Left (H&E $\times 40$) Epithelial hyperplasia with massive infiltration of histiocytes admixed with some lymphocytes and scattered eosinophils throughout the dermis. Right (H&E $\times 400$) Upward transmigration of the histiocytic cells within the overlying epidermis in form of large cells with eosinophilic cytoplasm and kidney-shaped vesiculated nuclei

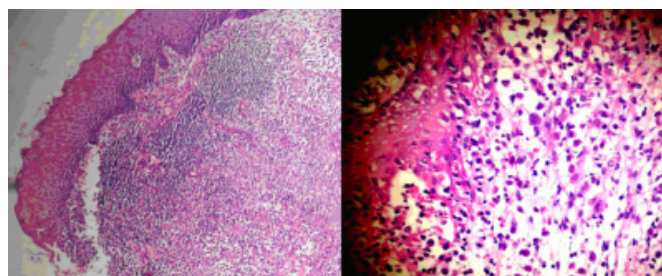
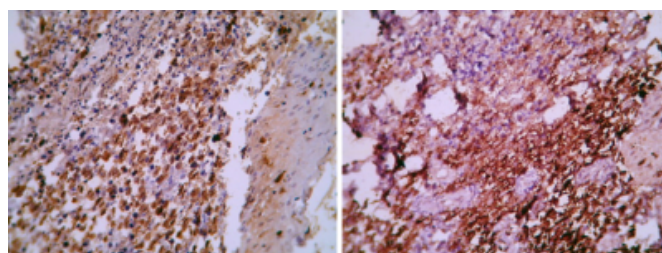


Figure 2

Figure 2: Immunohistochemistry (IHC) of the vulvar lesion Left ($\times 400$) Staining for S100 protein Right ($\times 400$) Staining for CD1a



DISCUSSION

We reported a rare case of LCH with central diabetes insipidus, severe diffuse lung involvement, salivary gland masses and vulvar lesion. LCH can involve several organs, including the brain, lungs and skin among others. Diabetes insipidus due to disruption of the hypothalamic-pituitary axis is observed in 10-50 % of patients [13, 14]. Such patients typically present with polyuria and polydipsia and are commonly treated with desmopressin to restore the normal levels of antidiuretic hormone (ADH). Pulmonary involvement is observed in 20-40 % of patients and may result in respiratory symptoms, such as cough, tachypnea, dyspnea, and pneumothorax. Diffuse cystic changes, nodular infiltrate and pleural effusion frequently occur in the course of disease. Pulmonary function test results may be abnormal, revealing restrictive lung disease [15, 16, 17, 18]. Cutaneous LCH is observed in as many as 50 % of patients with LCH and skin infiltrates can be maculoerythematous, petechial xanthomatous, nodular papular, or nodular in appearance [19].

Although the involvement of the brain and lungs is not unusual in LCH, our patient had a rare constellation of additional symptoms, i.e. vulvar lesion and salivary gland mass. The vulva is rarely affected by LCH, with less than 60 cases reported so far [8, 9]. Genital LCH can present as pruritic erythematous lesions, resembling eczema, or as erythematous papules. Single indurated ulcer and multiple painful vesicular lesions can be seen in syphilitic chancres and herpes genitalis, respectively [20, 21]. Given the broad range of differential diagnoses for genital LCH, a biopsy of the lesion is often mandatory. We are aware of only about 5 cases of LCH salivary gland involvement in the literature [10, 11, 12]. We did not confirm salivary gland LCH by biopsy in our patient. However, because the mass regressed completely with treatment, the presence of the same pathology in the salivary glands as in other involved organs seems very likely in our case.

LCH is diagnosed on the basis of demonstrating the presence of a histiocytic infiltrate and characteristic findings at IHC. Langerhans cells have a moderately abundant cytoplasm and a medium-sized folded, indented or lobulated nucleus with an elongated central groove producing a coffee-bean appearance. Characteristically, these cells express CD1a antigen and S-100 [22, 23]. Optimal treatment of LCH has not been established. 10-20 % of patients achieve spontaneous regression [24, 25, 26]. Combination therapy with vinblastine and prednisolone is a standard treatment approach in multisystem LCH with an overall response rate of about 60 % [27, 28]. The skin lesion and the neck mass both regressed significantly with vinblastine and prednisolone in our case, thus providing further support for using systemic chemotherapy with this protocol in multisystem LCH.

CORRESPONDENCE TO

Armin Rashidi, No 12, Aramesh Alley, Mellat Park, Tehran, Iran, Tel: +98-21-22042595, Email: rasidiarmin@yahoo.com

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Author Information

Amir Houshang Ehsani, MD

Assistant Professor of Dermatology, Tehran University of Medical Sciences

Pantea Hashemi, MD

Resident of Dermatology, Tehran University of Medical Sciences

Zahra Safai Naraghi, MD

Tehran University of Medical Sciences

Mohammad Sadri Farivar, Ph.D.

Assistant Professor of Mycology, Tehran University of Medical Sciences

Armin Rashidi, MD

Tehran University of Medical Sciences