Case Report

Received: October 26, 1992

Accepted: November 9, 1992

Gynecol Obstet Invest 1993;36:189-190

Primary Langerhans Cell Histiocytosis of the Vulva

K.		Voelklein ^a
H.-P.		Horny ^b
K.		Marzusch ^a
J.		Dietl ^a

Departments of ^aObstetrics and Gynecology and ^bPathology, University of Tübingen, FRG

Key Words

Langerhans cell histiocytosis

Vulva

Immunohistochemistry

Abstract

Primary Langerhans cell histiocytosis (LCH) of the female genital tract is very uncommon. Since the natural history of this tumor is unpredictable, with spontaneous remissions and exacerbations, establishment of the diagnosis is often difficult. In the few reported cases of LCH involving the vulva there were systemic manifestations of the disease. We report the clinical and **histopathological** findings in the case of a **36-year-old** woman who presented with a 9-year history of vulvar lesions. The diagnosis of LCH was established by immunohistochemical techniques, which demonstrated sheets of S-100 **protein-positive** histiocytes in the dermal tumor. The patient received radiotherapy to the vulva and responded with complete remission.

Johannes Dietl, Department of Obstetrics and Gynecology, University of Tübingen, Schleichstrasse 4 D-72076 Tübingen (FRG)

Introduction

The concept that eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer Siwe disease represent a single histomorphological entity with divergent clinical presentation was proposed by Lichtenstein [1]. These three syndromes are characterized by tumorous proliferation of histiocytes with granuloma formation. The term histiocytosis X was chosen by Lichtenstein [1] to signify the presumed, but still unproven, common etiology, that of a distinct inflammatory process involving histiocytes.

Langerhans cell histiocytosis (LCH) primarily involving the vulva appears to be extremely rare. Some cases have been reported in which patients with systemic disease exhibited vulvar involvement [2, 3]. Only one case of 'pure' cutaneous LCH of the vulva has been reported in the literature [4]. We described a second case of primary LCH of the vulva.

Case Report

The patient, a 36-year-old Kurdish woman (para 5, gravida 5), presented to the Department of Obstetrics and Gynecology of the University of Tübingen in 1988 with a 5-year history of vulvar pruritus and intermittent vulvar ulceration. Gynecological examination of the vulva revealed two extremely edematous tender, white nodules measuring 1 cm in maximum diameter in the right and left labia minora. The histologic features noted in a small biopsy specimen were interpreted as representing a nonspecific inflammatory process. Treatment with ointment and bathing initially produced some improvement. Four months later the tumor was found to have enlarged.

The diagnosis of LCH was established on the basis of investigation of a second and larger biopsy specimen.

Clinical evaluation, including bone scan, abdominal computed tomography (CT), abdominal sonography, and chest X-ray failed to reveal involvement of other organs. The patient refused further treatment. In 1991 the vulvar tumor was found to have enlarged further. A deep sharply demarcated, ulcerating lesion measuring 5 cm across and extending into the distal third of the vagina close to the external urethral orifice was seen. The clitoris had disappeared. The patient again refused specific treatment and was discharged from hospital.

Three months later the patient complained of severe dysuria due to urethral infiltration and underwent external radiotherapy to the vulva consisting of 10 Gy (in five 2-Gy fractions). Three weeks later the patient was symptom-free and the vulvar ulcer had decreased in size by half. At the time of this report the patient continues to be free of symptoms.

Pathologic Findings

Histologic examination revealed hyperplasia of the epidermis with signs of pronounced leukodiapedesis. The dermis contained dense heterogeneous lymphoreticular infiltrates consisting of eosinophils, neutrophils, tissue mast cells, plasma cells, macrophages, and lymphocytes. The histologic picture was dominated by sheets of histiocytic cells with pale cytoplasm and irregular, often indented nuclei (fig. 1). The nucleoli were inconspicuous. Immunohistochemical investigation revealed these cells to exhibit intense diffuse reactivity with antibodies against S-100 protein (fig. 2), but none with the macrophage-associated antibodies KP1 (CD68), Ki-MIP, and MAC 387, or the lymphocyte markers UCHL1 (CD45RO), DF-T1 (CD43), and L26 (CD20). Thus, the definitive diagnosis of Langerhans cell histiocytosis was established.

Discussion

Although the skin is one of the tissues frequently involved in systemic LCH, the female genital tract only rarely shows LCH infiltration. Rose et al. [4] described the first and up to now only case of 'pure' cutaneous LCH of the vulva. The macroscopic differential diagnosis includes specific and nonspecific ulcerating conditions such as syphilis, herpes virus infection, granuloma inguinale, tuberculosis and sarcoidosis, certain dermatologic disorders, such as eczema, seborrheic dermatitis, fungal dermatitis, and neoplastic processes, such as squamous cell carcinoma and sarcoma [5, 6]. Establishment of the correct diagnosis in LCH is not difficult when appropriate immunohistochemical stains are employed. Granulomatous lesions and malignant tumors, in particular amelanotic malignant melanoma, have to be excluded. The LCH infiltrates contain pleomorphic Langerhans-type histiocytes characterized mainly by their indented nuclei. In typical cases the histiocytes are intermingled with eosinophils, lymphocytes, and plasma cells. Immunohistochemical investigation reveals intense reactivity in the cytoplasm and nucleus of the tumor cells for S-100 protein [7]. Electron-microscopic examination reveals the characteristic Birbeck granules [8]. The reports of 'pure' cutaneous LCH in the literature describe a wide variety of approaches to management, including radiation, surgical resection, systemic administration of vinblastine or corticosteroids, or no therapy [4, 9]. The patient we describe received external radiotherapy of 10 Gy in five fractions of 2 Gy, which produced an excellent response. The patient described by Rose et al. [4], received a second course of 20 Gy after relapse, which resulted in complete remission with relief of local pain.

In summary, LCH involving the vulva and without systemic manifestations is extremely rare, and to the best of our knowledge the case reported is the second in the world literature. The diagnosis of histiocytosis X is established by identifying the Langerhans histiocyte, which shows characteristic cytologic features and immunoreactivity for S-100 protein. The treatment of choice in LCH exclusively involving the vulva, seems to be radiotherapy.

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