



Case report

Isolated vulvar Langerhans cell histiocytosis

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1. Introduction

Primary Langerhans cell histiocytosis (LCH) is very rare and is generally encountered more in the childhood and adolescent populations (Lichtenstein, 1953). Its etiology and pathophysiology as well as reliable modes of therapy remain elusive and variable amongst many institutions. It is characterized by proliferation of dendritic cells derived from myeloid precursors (Badalian-Very et al., 2013; Broadbent et al., 1994). These cells share immunophenotypic and morphologic characteristics with skin Langerhans cells and are therefore characterized amongst other histiocytic and dendritic cell neoplasms (Rosso et al., 2006). The disease carries variable presentation and is rarely encountered in the female reproductive tract (Broadbent et al., 1994). The first documented involvement of the female reproductive tract was in 1939 and since then, four patterns of involvement have been reported: i) pure genital LCH, ii) genital LCH with multi-organ involvement, iii) cutaneous or oral LCH with genital and multi-organ involvement, and iv) diabetes insipidus with organ involvement (Axiotis et al., 1991). The vulva is the most commonly encountered site of involvement, but disease can also involve the cervix, vagina, and endometrium (Axiotis et al., 1991). We report a case of a patient that presented with isolated LCH of the vulva and clitoris that underwent wide local resection and metastatic workup including robotic assisted laparoscopic pelvic lymph node dissection.

1.1. Case

A 31-year-old woman (gravida 0) with known history of Turner syndrome presented with complaints of a pruritic, painful vulvar and

peri-clitoral mass with a 2-month onset. Additional symptoms included increased discharge and dyspareunia. On physical examination, the patient had a 2.5 cm exophytic lesion on the inner edge of the clitoral hood that appeared worrisome for at least vulvar intraepithelial neoplasia (VIN). She had an additional exophytic and friable 3 cm lesion at the base of the vaginal mucosa ventral to the introitus. There were no other visible lesions noted on exam. The patient ultimately underwent a wide local excision of both lesions with pathology demonstrating Langerhans cell histiocytosis in both specimens extending to the margins of resection. The pathologic specimen demonstrated increased epidermal and dermal sheets of Langerhans cells with grooved (“coffee bean”) nuclei with finely dispersed chromatin and eosinophilic cytoplasm and admixed eosinophils (Fig. 1). Confirmatory immunohistochemical staining of the neoplastic LCH cells had strong membranous staining for CD1a (MTB1) (Fig. 2).

The patient had a metastatic workup that included a Positron Emission Tomography and Computed Tomography (PET/CT) that demonstrated hypermetabolic bilateral external iliac chain lymph nodes, hypermetabolic cutaneous thickening at the level of the right breast and at the intergluteal cleft, as well as a single focal area of uptake involving the left scapula. Consequently, additional vaginal biopsies were obtained and a robotic-assisted laparoscopic bilateral external iliac lymphadenectomy was performed that demonstrated no evidence of residual disease or metastasis. The hypermetabolism near the right breast and at the gluteal clefts demonstrated psoriasis upon biopsy. To complete the metastatic disease workup, she also underwent a bone marrow biopsy that was unremarkable. No adjuvant treatment was recommended, and the patient was entered into surveillance. She had repeat PET/CT at 3-month intervals after excision that were

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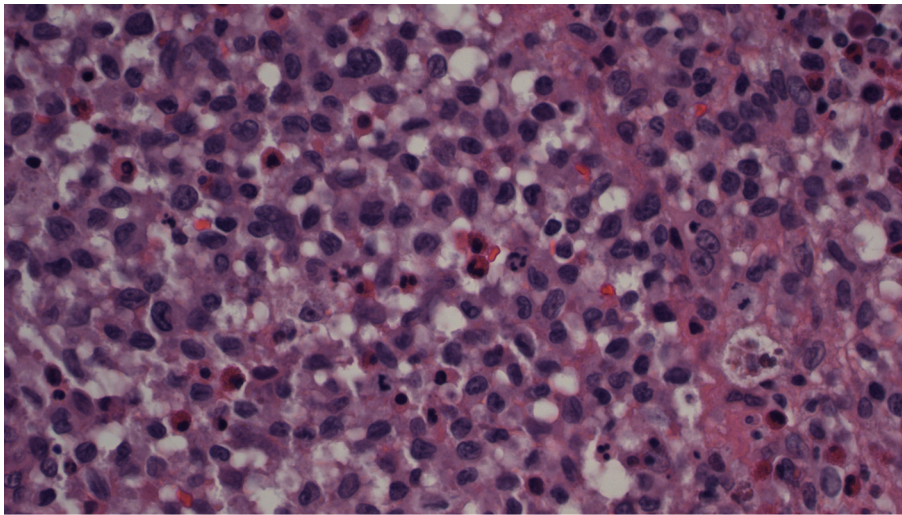


Fig. 1. Sheets of Langerhans cells with grooved (“coffee bean”) nuclei with dispersed chromatin and eosinophilic.

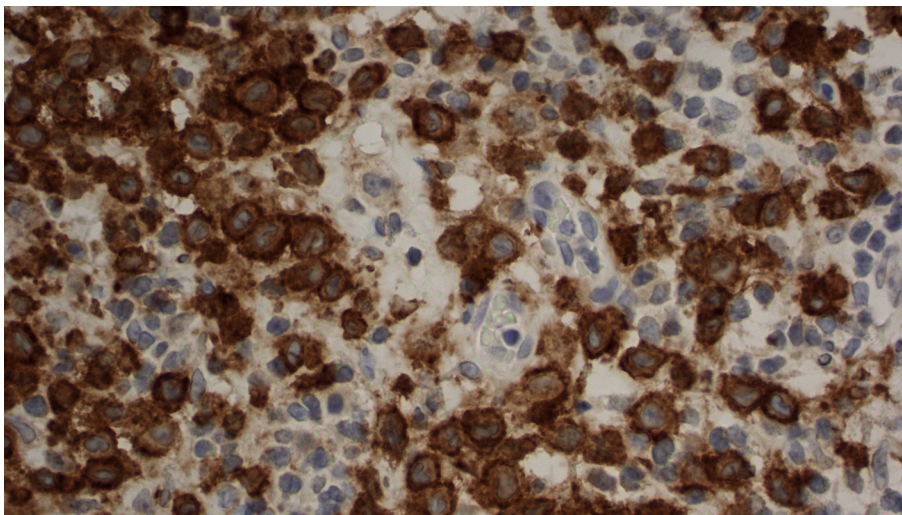


Fig. 2. Immunohistochemical staining of neoplastic LCH cells with strong membranous staining for CD1a (MTBI).

unremarkable. The patient remains disease free from her LCH.

2. Discussion

LCH was initially very difficult to differentiate from other hematologic and lymphoid tumors, and even little still is known about the true incidence and epidemiologic characteristics of the disease. LCH was initially termed as “Histiocytosis X” and has previously been described as Hand-Schuller-Christian disease (combination of diabetes insipidus, exophthalmos, and multifocal lytic bone lesions), Letterer-Siwe disease (acute dissemination with multisystem involvement), and eosinophilic granuloma (a benign lesion restricted to one organ), based on its presentation and clinical symptoms (Lichtenstein, 1953). These names, however, have collectively been replaced by LCH (Broadbent et al., 1994).

LCH of the female genital tract is very rare. The diagnosis is confirmed via biopsy with careful histopathologic and immunohistochemical studies. The biopsy classically consists of Langerhans cells associated with an eosinophilic-rich inflammatory infiltrate (Rosso et al., 2006). However, Langerhans cells are medium to large cells with an abundance of pale cytoplasm that may bear resemblance to melanocytes. An isolated S100 immunostain can be immunoreactive,

therefore, pathologic confirmation is established with positive staining for CD1a or CD207 markers to avoid an erroneous diagnosis of a melanocytic lesion. It is believed that the paucity of reported cases of LCH isolated to the female genital tract prior to the widespread availability of immunostains may partly reflect under-recognition and underdiagnosis of this condition.

Due to the rarity of LCH occurring at the vulva, treatment protocols vary widely and there is not an established standard of care for this population (Axiotis et al., 1991). Treatment options include complete surgical excision with or without adjuvant radiation or chemotherapy, topical or oral steroids, and immune modulators. A recent review reported a 62% rate of local recurrence even after prolonged periods of clinical remission (El-Safadi et al., 2012). Neither local excision, topical steroids, nor radiation as first line treatment demonstrated superiority in achieving remission (El-Safadi et al., 2012). Some authors suggest that thalidomide should be considered as first-line or as maintenance therapy due to reported long lasting remission and few adverse events (El-Safadi et al., 2012).

The association of LCH with solid and hematologic malignancies has been previously described, therefore, prompt metastatic workup is warranted to rule out multisystem involvement. Imaging modalities that evaluate the head, chest, abdomen and pelvis as well as a bone marrow

biopsy are indicated to rule out hematogenous and other organ involvement. Upon diagnosis of LCH, our patient underwent PET/CT that demonstrated suspicious pelvic lymph nodes, which were assessed surgically to rule out metastatic disease. To our knowledge, this represents the first reported case of pelvic lymph node dissection to assess the presence of metastatic disease. Additionally, re-excision due to positive margins did not demonstrate residual disease. Post-treatment surveillance with quarterly PET/CT and annual pelvic exams have not shown any disease recurrence. In summary, although uncommon, vulvar LCH should be considered in the differential diagnosis when a woman presents with pruritus and vulvar lesions. A biopsy is necessary for immunohistologic confirmation of the diagnosis. Once the diagnosis is made, the possibility of distant organ metastasis should be investigated radiologically, and treatment should be individualized.

3. Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

NG was primarily responsible for drafting the manuscript. Slide

pictures and pathology review of LCH were provided by DW. Reviews were equally performed by both DW and NM.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Lichtenstein, L., 1953. Histiocytosis X: integration of eosinophilic granuloma of bone, Letterer Siwe disease, and Schuller-Christian disease as related manifestations of a single nosologic entity. *Arch. Pathol.* 56, 84–102.
- Badalian-Very, G., Vergilio, J.A., Fleming, M., Rollins, B.J., 2013. Pathogenesis of Langerhans cell histiocytosis. *Annu. Rev. Pathol.* 24, 1–20.
- Broadbent, V., Egeler, R.M., Nesbit Jr, M.E., 1994. Langerhans cell histiocytosis-clinical and epidemiological aspects. *Br. J. Cancer Suppl.* 23, S11–S16.
- Rosso, D.A., Karis, J., Braier, J.L., Henter, J.I., Fadeel, B., 2006. Elevated serum levels of the decoy receptor osteoprotegerin in children with Langerhans cell histiocytosis. *Pediatr. Res.* 59, 281–286.
- Axiotis, C.A., Merino, M.J., Duray, P.H., 1991. Langerhans cell histiocytosis of the female genital tract. *Cancer* 67, 1650–1660.
- El-Safadi, S., Dreyer, T., Oehmke, F., Muenstedt, K., 2012. Management of adult primary vulvar Langerhans cell histiocytosis: review of the literature and a case history. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 163, 123–128.