



should be paid to unexpected side-effects, including polyarthralgia, during the treatment with dupilumab.

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Vulvar endometriosis. A clinical, histological and dermoscopic riddle

Editor

Endometriosis is characterized by the presence of functional endometrial tissue in ectopic sites such as ovaries, fallopian tubes and pelvic peritoneum. Rare extra-pelvic localizations are possible, including skin involvement. Cutaneous endometriosis is divided into primary and secondary endometriosis. The latter occurs on scar tissue, mostly following caesarean section. Endometriosis may present cyclical pain, bleeding and swelling depending on the menstrual cycle even though most cases are asymptomatic.

A 69-year-old woman presented with a 2.5 cm diameter, brownish plaque on the left labia minora of her vulva. This formation has been present for about 20 years but has gradually increased over the last few months with mucous and blood

secretions. The patient denied symptoms. The plaque presented a medial blackish macule and a small central ulcer (Fig. 1a).

Dermoscopic examination showed a brownish background, with globules arranged both irregularly and featuring parallel and ring-like patterns. A fusiform, blue-greyish structureless area was sited on the medial side (Fig. 1b,c). No atypical vessels were found. A melanotic or melanocytic lesion was suspected.

A biopsy was performed. Histopathology showed proliferation of spindle stromal cells and presence of macrophages (CD68+) filled with pigments, undergoing a ciliate epithelium (Fig. 1b). Search for melanocytic markers, namely S100 and MLA, was negative, while a positive Perls reaction for iron revealed the nature of the intracellular pigment. Considering the presence of the ciliate epithelium, search for estrogenic receptor (ER) and CD10, a marker of endometrial stroma, was performed and resulted positive (Fig. 2b,c). A diagnosis of endometriosis was made.

Vulvar endometriosis is a rare condition, and its diagnosis can be difficult. Main differential diagnoses include mucous cysts, Bartholin's cysts or abscesses, epidermal inclusion cysts, Skene's duct cysts, lipomas, fibromas, fibromyomas, vascular tumours and squamous cell carcinomas. So far, no dermoscopic description of vulvar endometriosis has been reported. Only a few cases of primary skin endometriosis have been described, without well-defined and univocal dermoscopic features. Skin endometriosis may show the presence of homogeneous reddish

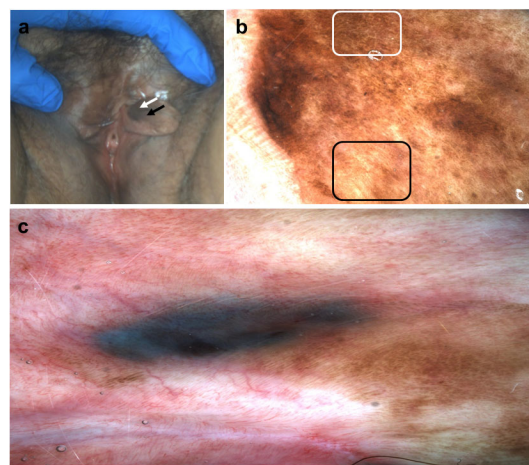


Figure 1 (a) Clinical presentation of the brownish plaque located on the patient's left labia minora; black arrow indicates the brown part on the outside, white arrow indicates the medial blackish macule; (b) dermoscopy of a brown area of the lesion [corresponding to the black arrow in (a)] showing a brownish background with globules arranged in an irregular distribution as well as in parallel [black rectangle] and ring-like [white rectangle] patterns; (c) dermoscopic image of the blue-greyish, structureless, medial area [corresponding to the white arrow in (a)].

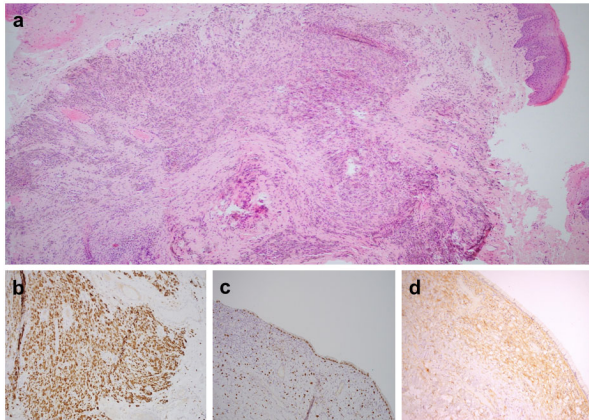




Figure 2 (a) Histological features of the reported case of vulvar endometriosis (haematoxylin and eosin, magnification $\times 20$); (b) positive staining with CD68 (magnification $\times 10$); (c) positivity of search for estrogenic receptor on the ciliate epithelium (magnification $\times 20$); (d) CD10 staining (magnification $\times 20$).

pigmentation with¹ or without² small, defined structures characterized by a deeper red hue, called “red atolls”. In one case, amorphous brown areas interspersed by normal skin network, mimicking melanocytic lesions, have been described.² Some authors found dotted vessels homogeneously distributed over milky-red areas with undefined structures.³ Several factors, including fluctuation of serum hormonal levels, topography and histological subtype, further concur to this pleomorphic presentation. For example, in a case of umbilical endometriosis the dermoscopic features changed in the transition from follicular to luteal phase.⁴ In a scar endometriosis, dermoscopy showed a tree-like appearance with parallel distribution of pigments over the scar area (branches-like) and in circles in the criptae of the papillomatous surface (fruits-like).⁵

Histopathology is also widely changeable depending on the endometrial phase in which the biopsy is performed. Cytomorphology of the glandular structures as well as intraluminal content varies cyclically. Dermal fibroblast proliferation presents as spindle-shaped cells. Haemosiderinic macrophages may be present in the dermis, representing the late stage of prior bleeding. Staining with CD10, which is diffusely expressed in the cytoplasm of endometrial stroma, can be helpful in the case of lack of glands and/or uncertainty about the origin of the stroma, like in skin endometriosis. ER and progesterone receptor (PR) immunostains show strong nuclear positivity in the glands and stroma.⁶

In conclusion, clinical diagnosis of skin endometriosis may be challenging. Dermoscopic assessment can be of little help, due to the extreme variety of its dermoscopic features. The vulvar case described confirms the remarkable variability and unspecificity

of dermoscopic patterns of endometriosis. Biopsy with staining for ER, PR and CD10 is therefore mandatory for diagnosing and ruling out malignant conditions.

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Pemetrexed-induced oedema of the eyelids and scalp in a patient with metastatic lung cancer

Editor

Pemetrexed is an anti-metabolite that targets multiple enzymes in the folate pathway, and it is indicated in the treatment of locally advanced or metastatic non-small-cell lung carcinoma and malignant pleural mesothelioma. On September 2008, the U.S. Food and Drug Administration approved its use in combination with cisplatin for the initial treatment of patients with stage IIB/IV non-squamous non-small-cell lung carcinoma.¹ The main toxicities associated with pemetrexed are myelosuppression and skin reactions. However, cutaneous adverse events are inaccurately reported in the literature as a rash or skin eruption. We report the clinical description of severe oedema confined to the eyelid and the scalp in a patient receiving treatment with pemetrexed.