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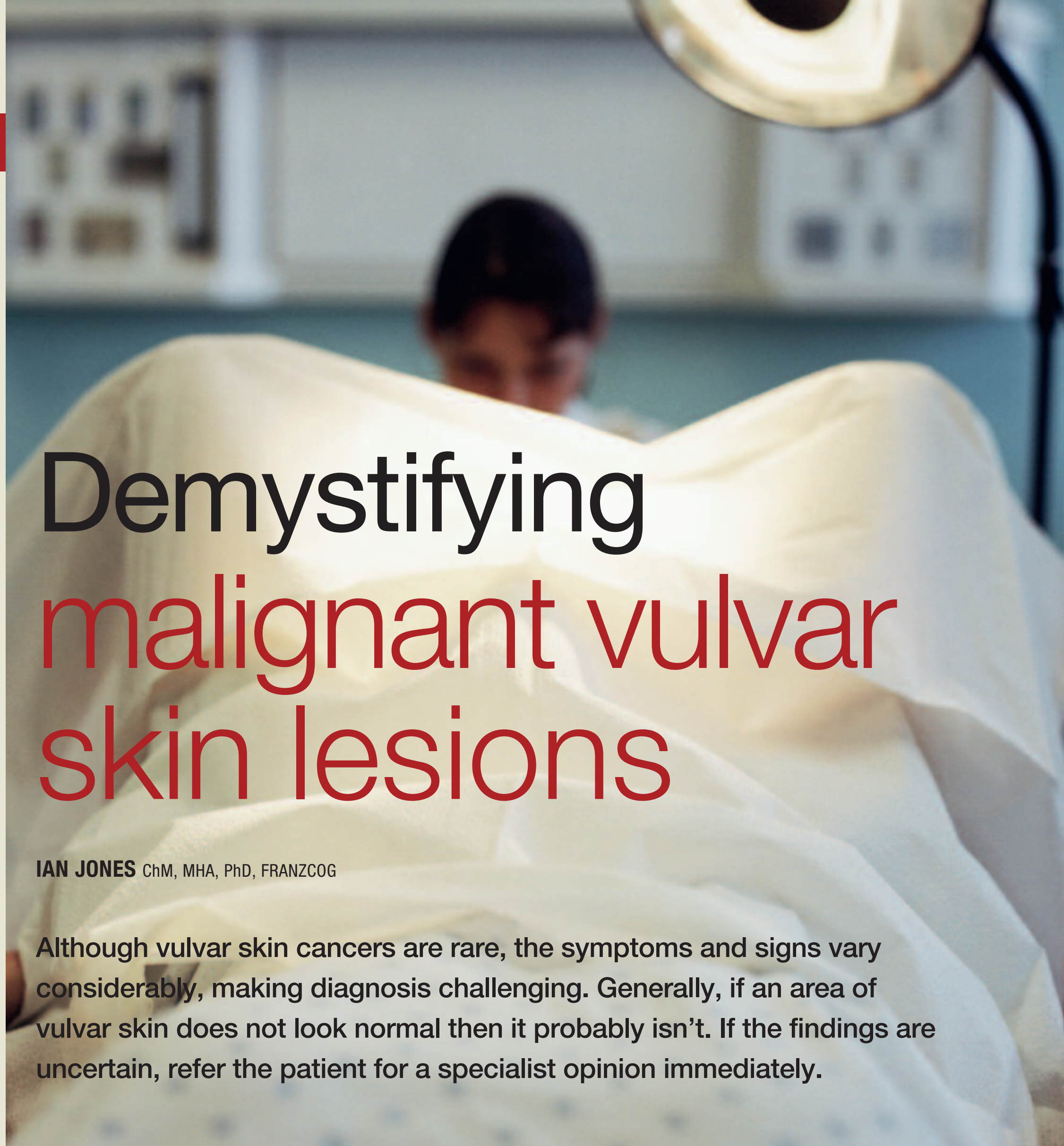

Demystifying malignant vulvar skin lesions

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Although vulvar skin cancers are rare, the symptoms and signs vary considerably, making diagnosis challenging. Generally, if an area of vulvar skin does not look normal then it probably isn't. If the findings are uncertain, refer the patient for a specialist opinion immediately.

Key points

- More conditions are missed by not looking than by not knowing.
- Vulvar cancer symptoms vary considerably. If an area of vulvar skin does not look normal, it probably isn't.
- Most vulvar lesions are benign, particularly when bilateral.
- Consider the possibility of a premalignant or malignant condition being present, especially if lesions are solitary or unilateral.
- The clinical appearance of a lesion does not always suggest the diagnosis.
- If a lesion is suspicious, referral of the patient to a gynaecologist is recommended.
- If a malignancy is diagnosed, refer the patient to a gynaecological oncologist for treatment and follow up.

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Vulvar cancer symptoms and signs can vary considerably, ranging from the entirely asymptomatic to symptomatic, with symptoms of pruritus, discomfort, pain and bleeding, and signs of fleshy, nodular or warty lumps, colour change, or any combination of these. Patient age at presentation, symptom pattern, anatomical location on the vulva and even the clinical appearance of the lesion does not always guide diagnosis. Vulvar lesions do not always have the same appearance when compared with the same condition situated in other locations on the body, or even between patients presenting with the same type of vulvar lesion. Although these varying symptoms and signs can make diagnosis challenging, most vulvar skin lesions are missed by not looking rather than by not knowing.

Vulvar skin conditions, including vulvar cancers, may be detected by a routine examination under good lighting (e.g. during PAP smear procedures) or when the patient presents with vulvar skin irritation, lumps, ulcers, split skin, plaques and skin colour changes. If an area of vulvar skin does not look normal, it probably isn't, and the main concern should be the possibility of a premalignant or malignant condition being present.

INCIDENCE AND RISK FACTORS

Although relatively rare, vulvar cancer is the fourth most common gynaecological cancer, after uterine, ovarian and cervical cancers. Vulvar cancer contributes to between 4% and 5% of all malignancies of the female genital

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CLINICAL APPEARANCES AND LIKELY DIAGNOSES OF VULVAR SKIN LESIONS

Reddened area

- Vulvar intraepithelial neoplasia (Figure 1); vulvar extramammary Paget's disease (Figure 7)

Reddened area with lesion

- Flat lesion – vulvar intraepithelial neoplasia (Figure 1)
- Raised pinkish lesion – squamous cell carcinoma (Figure 2)

Nodule

- Fleshy lump – vulvar squamous cell carcinoma (simplex type) with nodular appearance (Figure 2)
- Ulcerated fleshy lump – vulvar squamous cell carcinoma (simplex type) with ulceration (Figure 3)
- Raised nodule – basal cell carcinoma of nodular type (Figure 5)
- Flat nodule – basal cell carcinoma of superficial type (Figure 6)

Pigmentation

- Flat patch – melanosis (Figure 4)
- Dark patch – melanoma in situ (Figure 4)
- Raised irregular patch – melanoma (Figure 4)

tract and has an overall global incidence of 2 to 3.6 per 100,000 women, rising to 13 per 100,000 in women over the age of 65 years. The risk of vulvar cancer in Aboriginal women is 10 times the overall rate compared with the general population in Australia, and in particular there is a disproportionately increased risk in younger Aboriginal women.

Risk factors for vulvar cancer include cigarette smoking, vulvar lichen sclerosus, the premalignant conditions vulvar intraepithelial neoplasia (VIN) or cervical intraepithelial neoplasia (CIN), human papillomavirus (HPV) infection, immunodeficiency syndromes (including

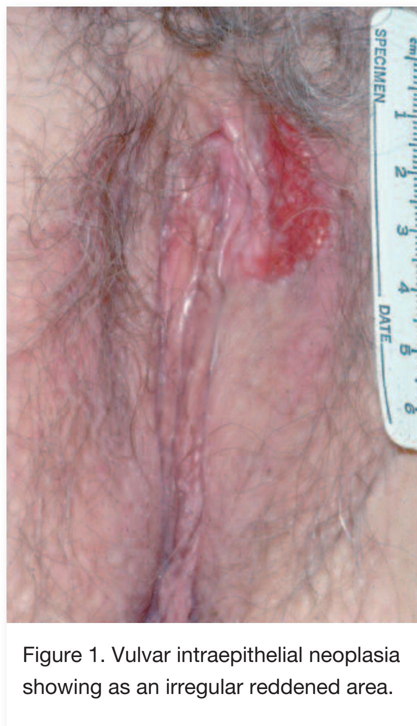

Figure 1. Vulvar intraepithelial neoplasia showing as an irregular reddened area.

immunosuppression in patients with organ transplants), a prior history of cervical cancer and northern European ancestry.

DIAGNOSIS

Vulvar malignancy, while relatively rare, is a condition affecting particularly vulnerable women. Patients are predominantly older (60 years and older) and may have modesty considerations that often result in delayed presentation. Similarly, there can be equal reluctance by the general practitioner to examine them. The reasons for this reluctance on the part of the general practitioner are multifactorial, and may include short consultation times that do not allow time for disrobing, natural disinclination to 'embarrass' the woman and uncertainty about vulval examination findings.

Upon examination, lesions may appear to be localised, multifocal or extensive. Histology provides a definitive diagnosis, but the interpretation of the vulvar biopsy specimen may not always be straightforward, with differentiation between squamous cell carcinoma (SCC), melanoma and extramammary Paget's disease (EMP) on occasions requiring special techniques.[1] Histochemistry is routinely performed on EMP as a way of determining whether the patient is more likely to have primary or secondary disease. The variations seen between the clinical appearances of vulvar cancers and the difficulties in separating different pathologies on clinical grounds are demonstrated in the box on this page and in the clinical figures (Figures 1 to 8).

Differential diagnoses for primary malignant conditions include VIN, SCC, melanoma (including amelanotic melanoma), basal cell carcinoma (BCC), EMP, Bartholin's gland adenocarcinoma and sarcoma.

Premalignant conditions

Vulvar intraepithelial neoplasia

The typical appearance of VIN is of a white or pigmented plaque, lump, fissure, ulcer or erosion (Figure 1).

VIN is divided into two types based on the histological findings. The more common type is the warty or basaloid type associated with HPV and younger women. The other type is the rarer differentiated type seen in older women. The risk factors for each include previous HPV infection.[2]

Early detection and treatment of VIN may prevent the development of cancer, as may the use of a HPV vaccine before VIN occurs. However, further studies are required before the use of the HPV vaccine in this setting is confirmed.

The main differential diagnoses of VIN include warts, seborrhoeic keratosis, lichen simplex chronicus, psoriasis, lichen sclerosus and traumatic ulcer.

Malignant conditions

Squamous cell carcinoma

SCC is the most common type of vulvar carcinoma, with an incidence of about 90% of all vulvar cancer (Figures 2 and 3). There are two subtypes of vulvar SCC,

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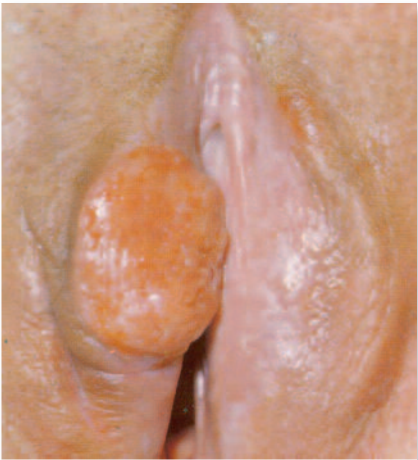
Figure 2. Vulvar squamous cell carcinoma (simplex type) with nodular appearance.

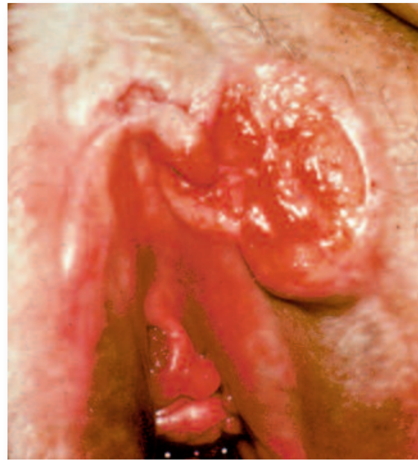
Figure 3. Vulvar squamous cell carcinoma (simplex type) with ulceration.

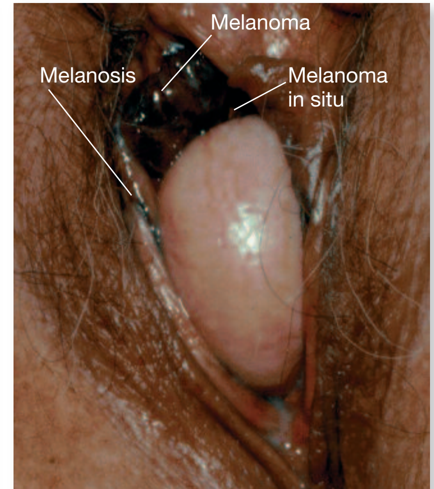

Figure 4. Vulva showing vulval melanosis, melanoma in situ and malignant melanoma. Note the large enterocoele present.

the keratinising, differentiated (or simplex) type not associated with HPV infection, and the warty (or Bowenoid) type associated with HPV subtypes 16, 18 and 33. The simplex type occurs in older women and is associated with vulvar dystrophies, whereas the Bowenoid type is found in younger women who have risk factors for HPV and/or human immunodeficiency virus (HIV) infections.

The differential diagnoses of vulvar SCC include VIN, ulcerative conditions of the vulva such as syphilis, donovanosis, venereal lymphogranuloma and chancroid, HPV warts and traumatic ulcerations associated with scratching.

Vulvar melanoma

Vulvar melanoma is the second most common vulvar malignancy, with the incidence variously reported as being between 1 and 10% of vulvar cancers (Figure 4). The cell origin for vulvar melanoma is the melanocyte, with about 10% of lesions arising in pre-existing vulvar naevi.[3] The amelanotic variant occurs in 1 to 2% of cases of vulvar melanoma. Queensland has the world's highest incidence rates of invasive cutaneous melanoma (50 per 100,000 for women

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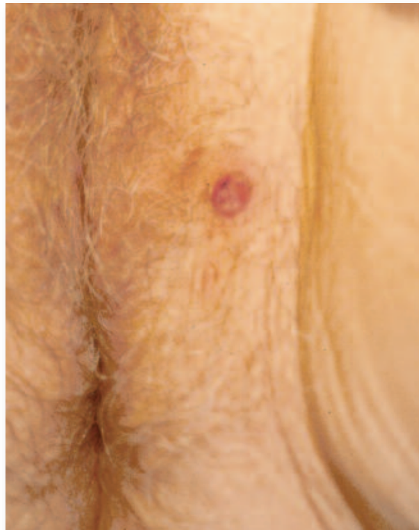


Figure 5. Basal cell carcinoma of nodular type.

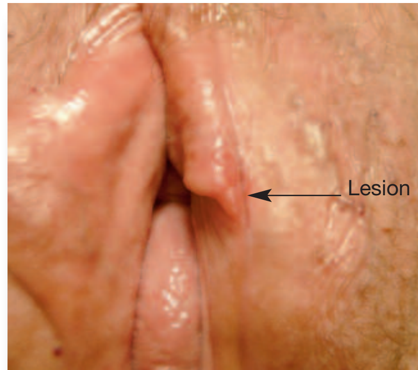


Figure 6. Basal cell carcinoma of superficial type.

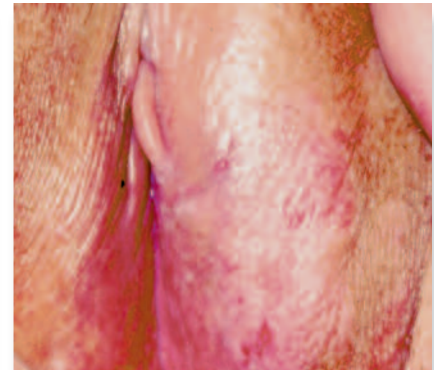


Figure 7. Vulvar extramammary Paget's disease (extensive areas of disease).

and 75 per 100,000 for men), but overall the vulva is an uncommon site of melanoma (incidence less than 1%).[4,5]

The differential diagnoses include any lesion containing melanocytic pigmentation, such as benign melanosis (also known as melanosis vulvae or lentigo), benign melanocytic naevi, seborrhoeic keratoses, vulvar angiokeratomas, premalignant melanoma in situ and melanoma. Several conditions causing pigmentation, including malignancy, may coexist (Figure 4).

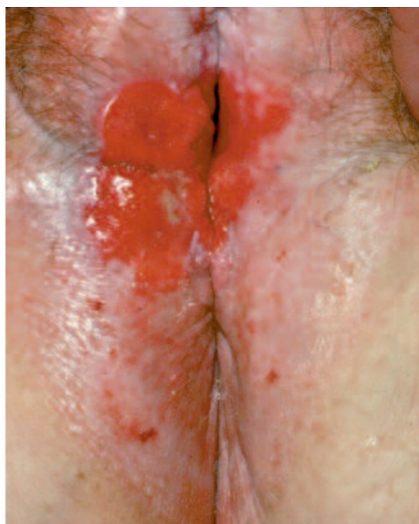
Vulvar BCC

Vulvar BCC is an uncommon disease, with incidence reports varying between 2% and 5% of vulvar malignancies (Figures 5 and 6). In contrast, BCC in nonvulvar sites is the most common human malignancy, accounting for 75% of all nonmelanoma skin cancers.[6] BCCs are categorised histologically as nodular, multifocal, superficial, cystic and infiltrative. In addition, vulvar BCCs can have squamous differentiation and be associated with VIN.

The differential diagnoses of vulvar BCC include VIN and SCC. As with other vulvar cancers, the diagnosis can be confusing if the infiltrative lesion has caused massive ulceration due to neglect.

Extramammary Paget's disease

EMP of the vulva is an uncommon disease, with incidence reports varying from less than 1 to 2% of vulvar malignancies (Figure 7). The appearance of EMP ranges from a nondescript red patch through to an eroded red plaque with 'icing-sugar' scales. The vulva is the most common site of EMP, with other sites being the groin, thigh, buttock, perianal region, axilla, eyelids and external ear canal. Common to all these sites is the presence of apocrine glands.[7] Vulvar EMP may be considered as having two separate types, an intraepithelial adenocarcinoma that arises in the vulva and perineum, and a pagetoid intraepithelial spread of primary carcinoma originating from an adjacent area including the anorectum, urethra, urinary bladder, Bartholin's gland and uterine cervix.[8] The cell origin of primary EMP is uncertain.



Figures 8a and b. Coexisting squamous cell carcinoma and vulvar intraepithelial neoplasia. a (left). Clinical appearance. b (right). vulvoscopic appearance.

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The differential diagnoses of EMP include psoriasis, dermatitis, vulvar BCC and lichen simplex chronicus.

Rare conditions

Bartholin's gland adenocarcinoma and sarcoma of the vulva are extremely rare and are only mentioned for completeness.

TREATMENT AND FOLLOW UP

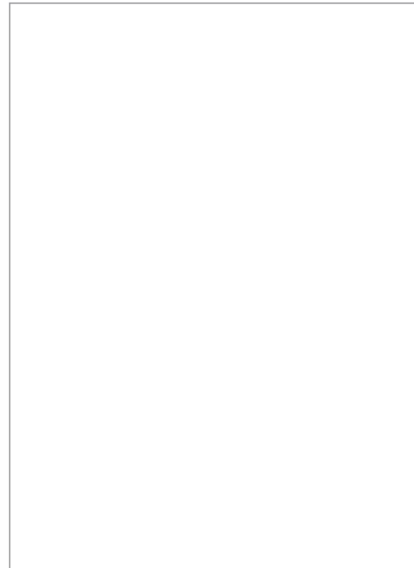
Rarely, in some situations, the use of colposcopy to assess the vulva (vulvoscopy) can assist in determining the extent of different pathologies to allow targeted multiple biopsies (Figure 8). Biopsies should include both normal and abnormal tissue. Surgical treatment is individualised to both the patient and her type of cancer. Definitive surgical options may include local excision, wide local excision, hemivulvectomy, radical hemivulvectomy, with or without groin dissection, and radical vulvectomy that includes sentinel node biopsy or lymph node groin dissection. In some advanced cases, radiation and/or chemotherapy may be used in conjunction with surgery.

Referral to a gynaecologist is recommended if a lesion appears suspicious. If a malignancy is confirmed, referral to a gynaecological oncologist for further treatment is appropriate. Long-term follow up in specialised gynaecological oncology units is standard management as late recurrences are not uncommon with many of these conditions.

SUMMARY

Vulvar skin conditions, including vulvar cancers, may be detected at routine examination (e.g. during PAP smear procedures) or when a patient presents with vulvar skin irritation, lumps, ulcers, split skin, plaques or skin colour changes. These conditions do not always have the same appearance when compared with the same condition situated in other locations on the body, or even between patients when the same lesion is located on the vulva.

All women who summon the courage to consult a doctor about vulvar symptoms deserve careful attention with a thorough history and inspection of the vulva and groin under good lighting. The only sure way to confirm the diagnosis



is to obtain a histological diagnosis, and this can be challenging for even the pathologist. If the findings are in any way uncertain, referral of the patient for a specialist opinion should follow at once. MT

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COMPETING INTERESTS: None.

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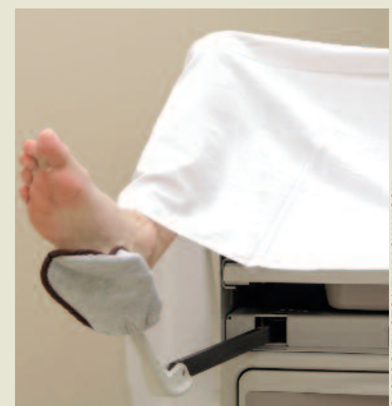

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