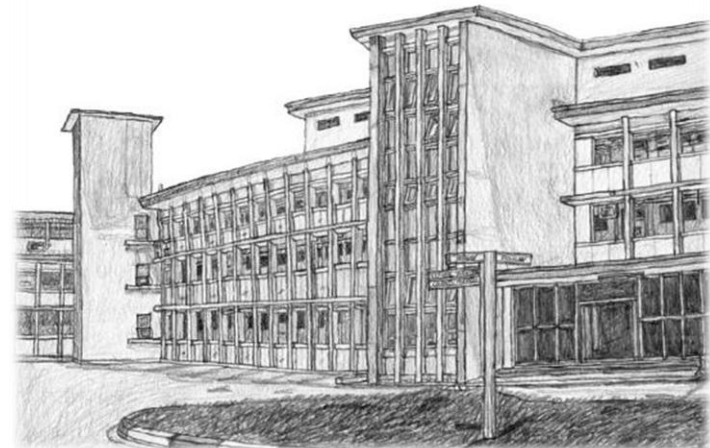


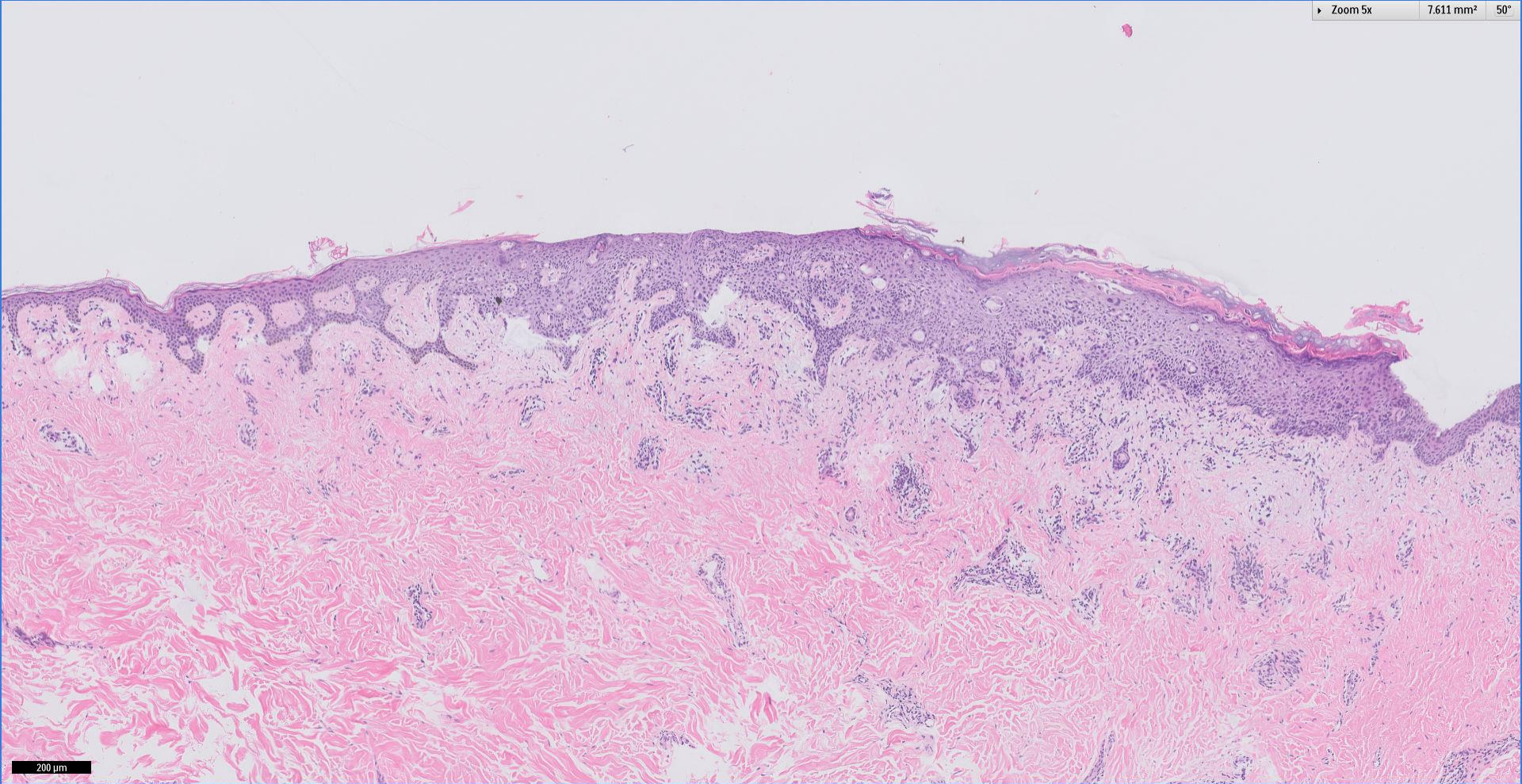
Case 1

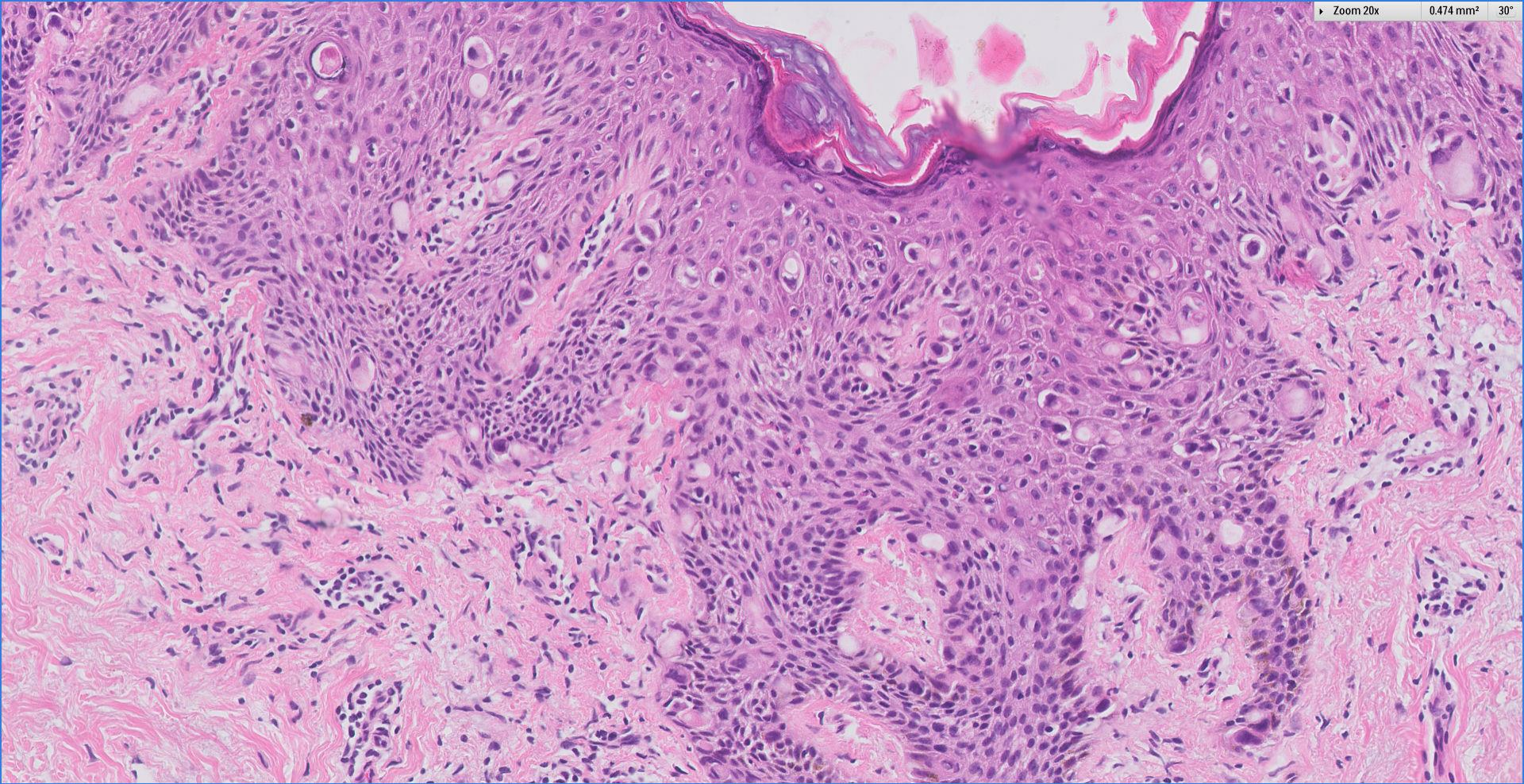
42 year old female.

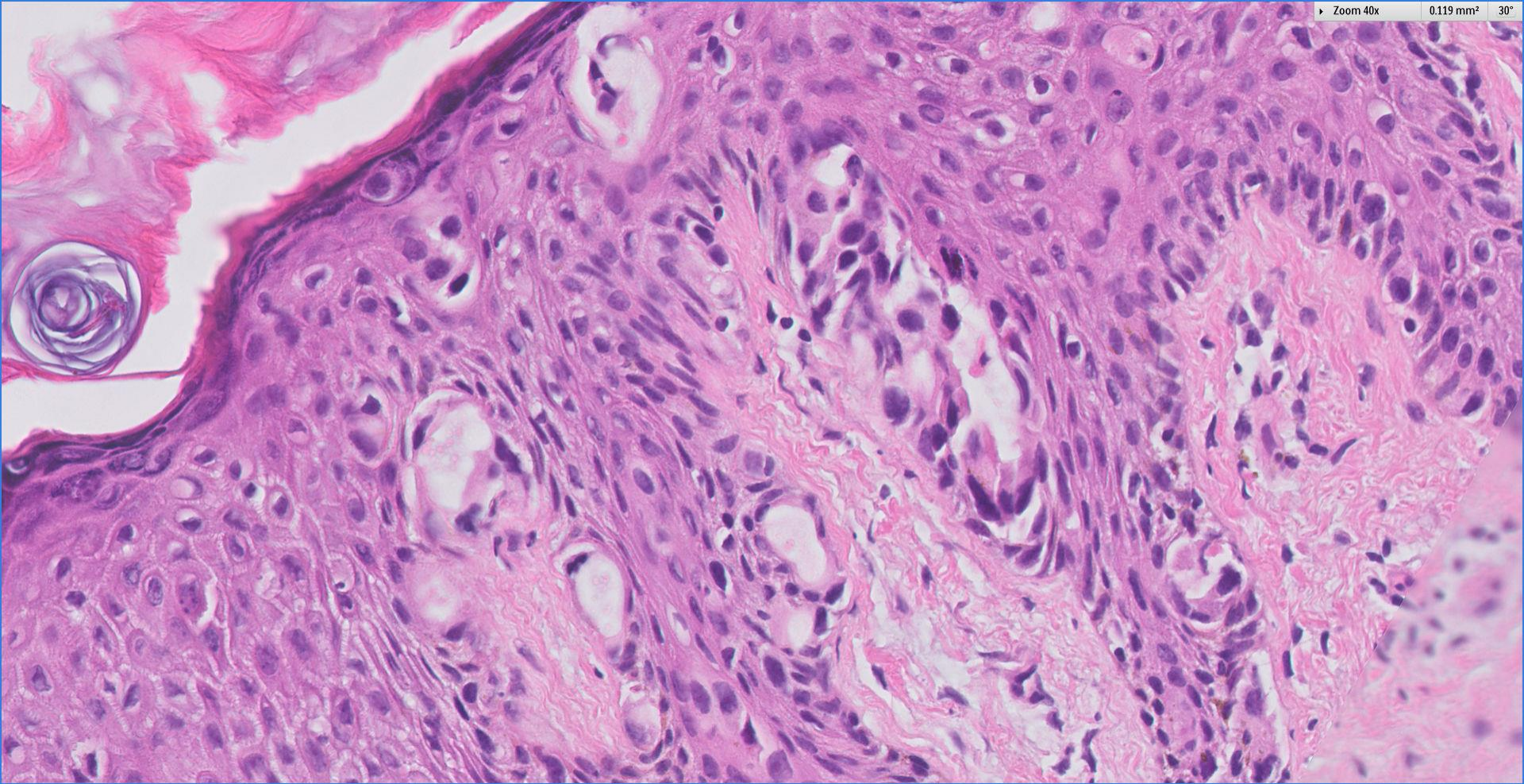
Right breast lower quadrant skin nodule.

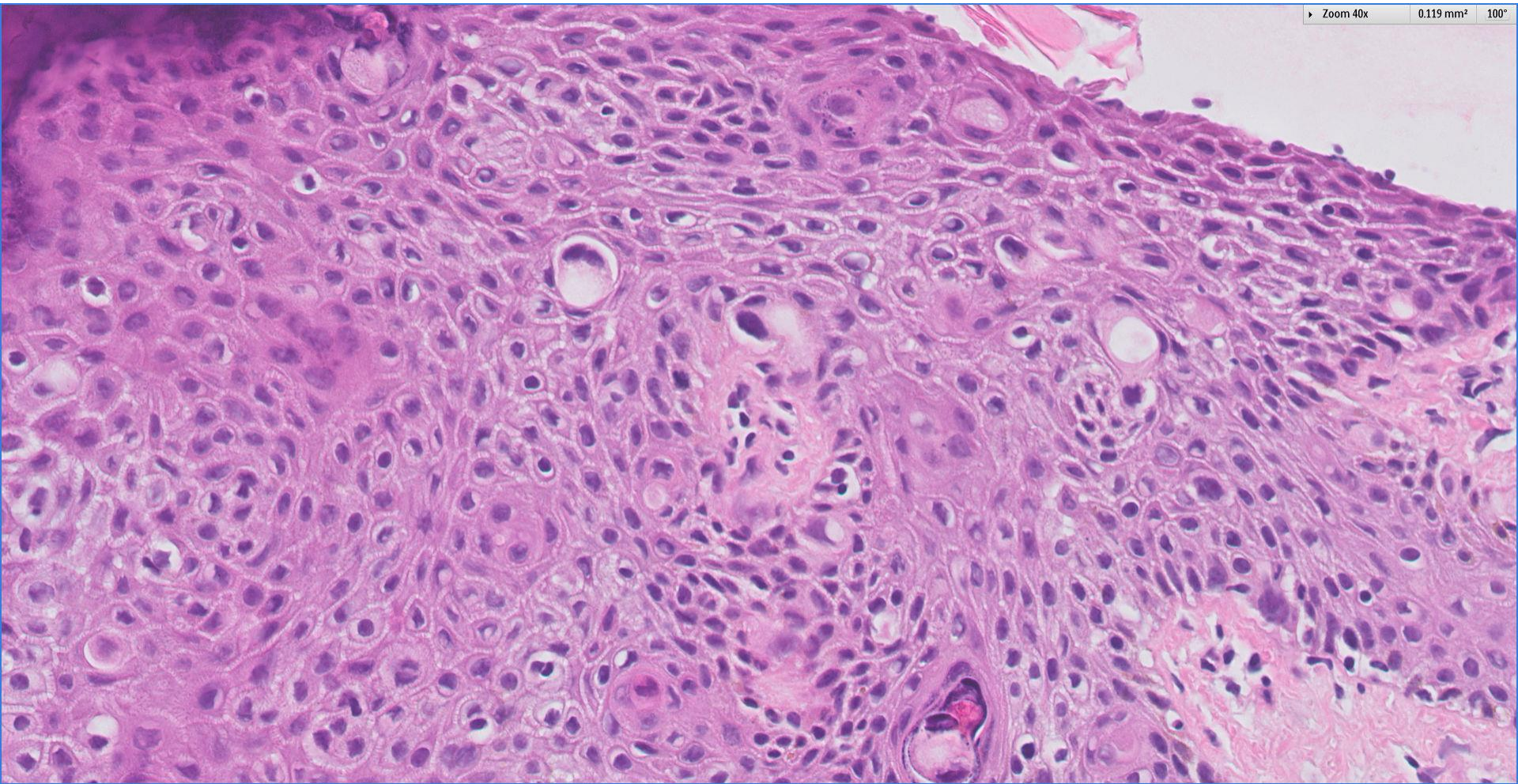
Past history of skin-sparing mastectomy performed for high grade ductal carcinoma in situ of the same breast.

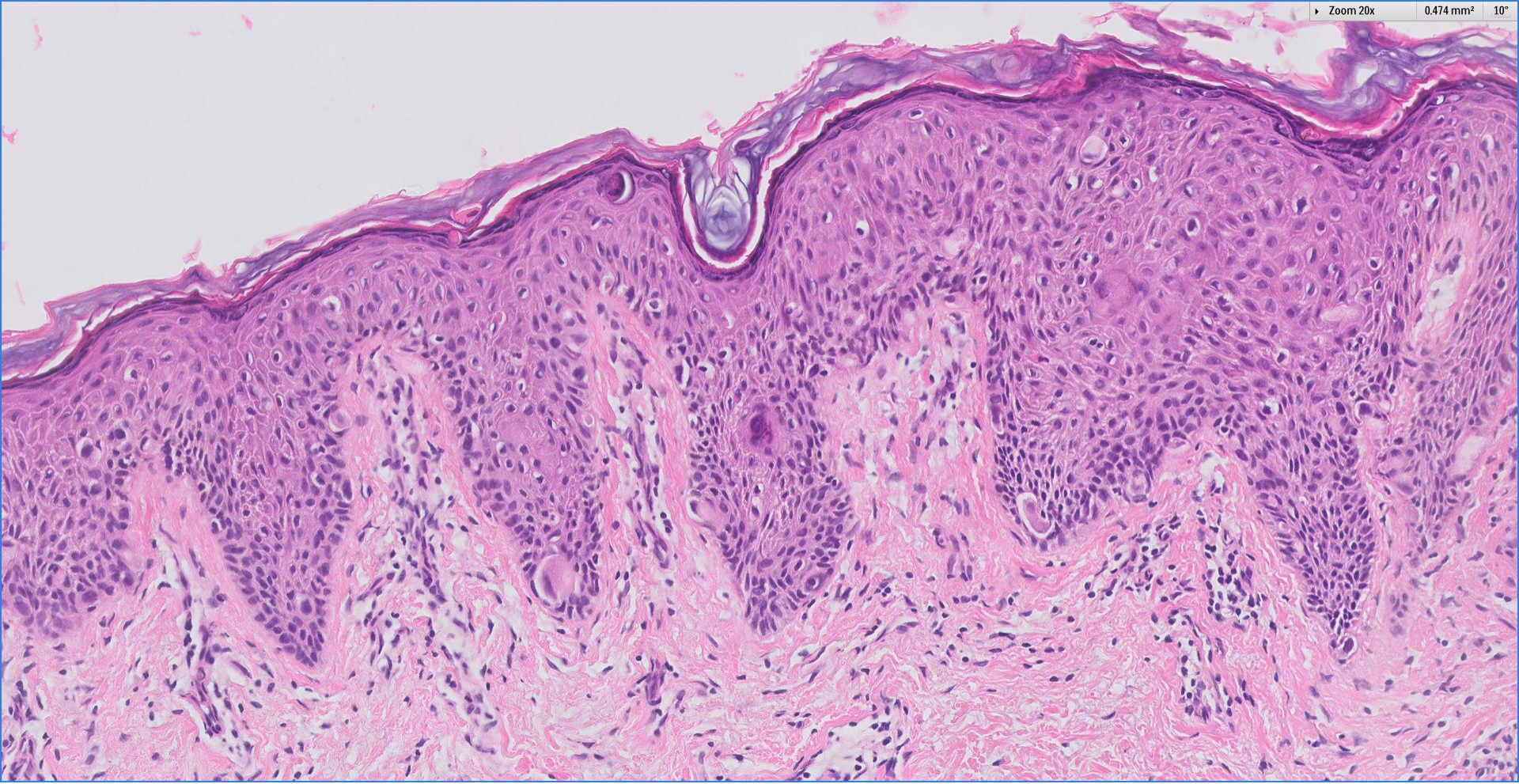




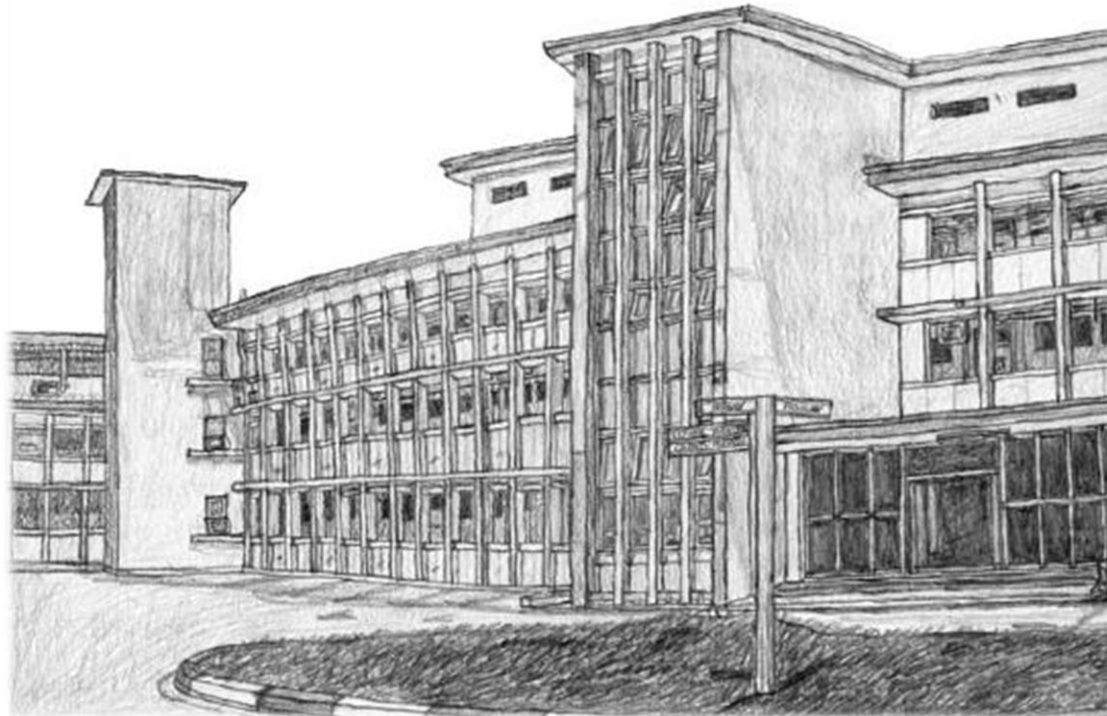








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Past history

- Right skin-sparing mastectomy 2 years prior to the current episode, for high grade DCIS diagnosed pre-operatively on core biopsy.
- At that time, she had presented with a 6-month history of an enlarging 5 cm lump in the upper outer quadrant of her right breast, measured on ultrasound as 5.7 cm and subsequently assessed as 5.5 cm of high nuclear grade DCIS on pathological examination of the resected specimen.
- No invasive disease was seen.
- DCIS was positive for HER2 and negative for hormone receptors (ER and PR).
- The nipple was free of malignancy and Paget disease.
- Four sentinel lymph nodes were negative for metastasis.
- The superficial margin, however, was focally involved by tumour.

4–5 mm erythematous lesion at the 8 o'clock position of the right breast noted 18 months post-mastectomy, resembling a hypertrophic scar that corresponded to the site of the original core biopsy scar, and hence no diagnostic skin biopsy was performed.



Case 1

- Upon review 6 months later, the appearance remained similar with no lesional enlargement.
- Two months later, the patient underwent a punch biopsy of the persistent skin lesion, followed by excision.
- Section provided is from the excision of the skin lesion.

Differential diagnosis

- Inflammatory skin lesion
- Paget disease
- Bowen disease
- Basal cell carcinoma
- Malignant melanoma

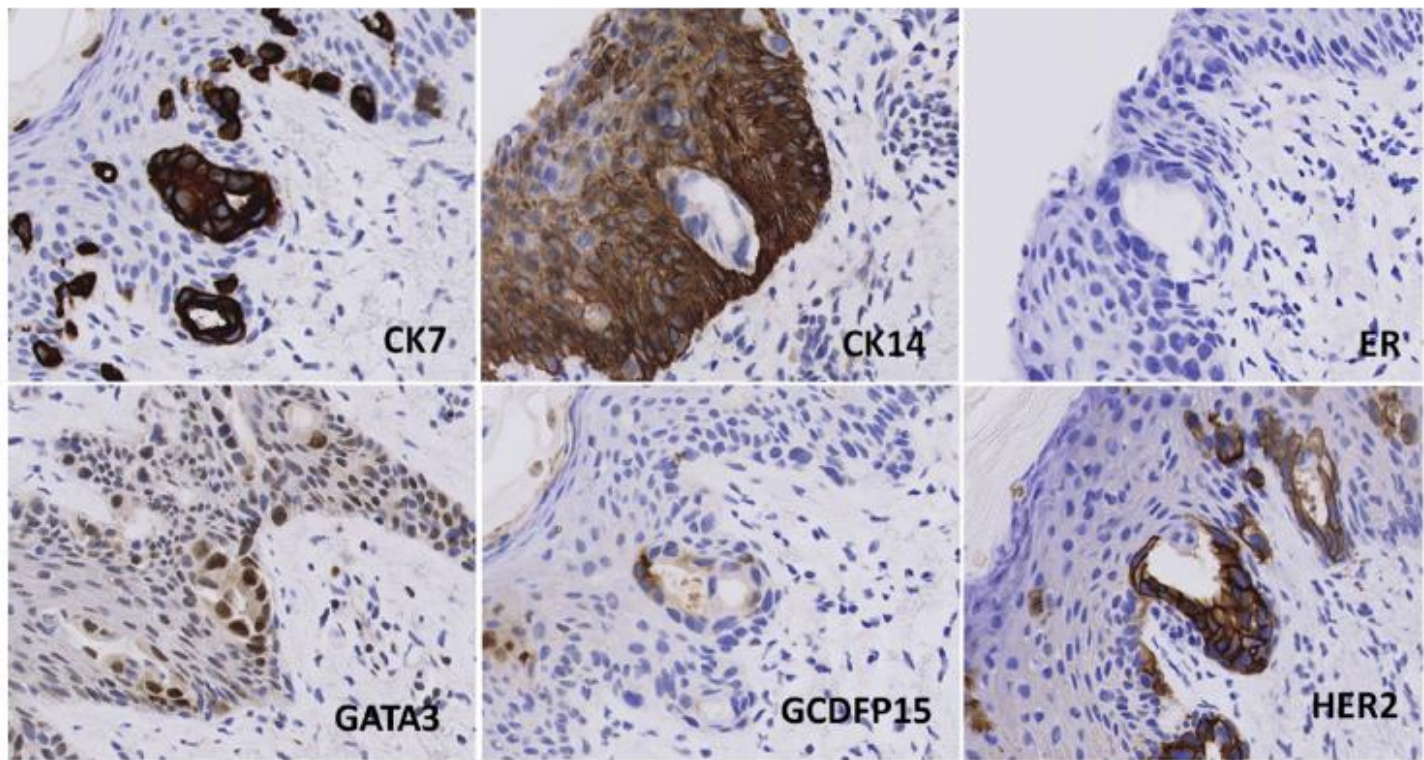
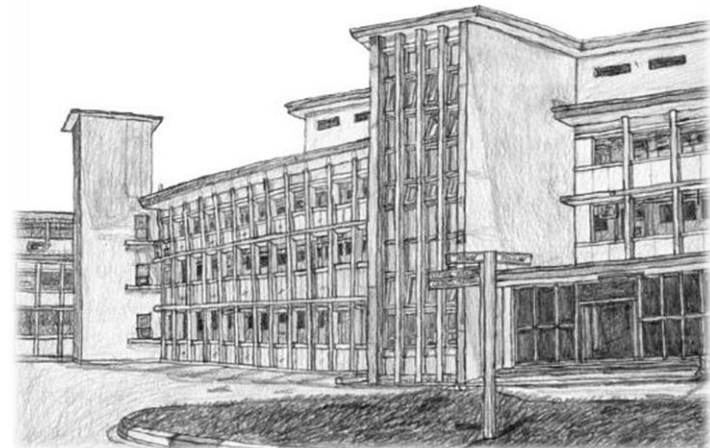


Fig. 3. Immunohistochemistry of the skin lesion from Case 1. The tumour cells are diffusely and strongly positive for CK7 and HER2, focally positive for GATA3 and GCDFP-15 and negative for ER and CK14.

Diagnosis

Paget disease



Paget disease

- Nipple-areolar location.
- Often associated with underlying carcinoma, especially high nuclear grade DCIS.
- Presentation of Paget disease at a non-nipple areolar location is extremely rare.
- Even rarer as a manifestation of recurrent breast carcinoma.

Our case 1

- Previous DCIS diagnosed at the right upper outer quadrant.
- Initial core biopsy was performed through an inferior-superior approach, leaving a biopsy scar at about 8 o'clock on the breast skin.
- High nuclear grade appearance of the intraepidermal cells together with similar immunoprofiles and location close to the initial core biopsy site favour the Paget disease being a recurrence of the underlying breast DCIS.

Paget disease at non-nipple areolar location

- 2 case reports of mammary Paget disease at a non-nipple areolar location presenting as a recurrence of breast carcinoma:
 - one occurred over the prior biopsy site, *K.Z. Calvillo, L. Guo, V. Brostrom, et al., Recurrence of breast carcinoma as Paget disease of the skin at a prior core needle biopsy site: case report and review of the literature, Int. J. Surg. Case Rep. 15 (2015) 152–156.*
 - other at the previous mastectomy scar, *M. Giovannini, C. D'Atri, Q. Piubello, et al., Mammary Paget's disease occurring after mastectomy, World J. Surg. Oncol. 4 (2006) 51.*

Paget disease at non-nipple areolar location ~ *prior biopsy site*

- 38-year-old woman with a history of right skin-sparing mastectomy for DCIS with microinvasion.
- No adjuvant therapy given.
- One and a half years later, she had an erythematous skin lesion over the previous core biopsy site which was diagnosed as Paget disease.

Paget disease at non-nipple areolar location ~ prior mastectomy scar

- 57-year-old woman who had a simple mastectomy and axillary clearance for invasive mucinous breast carcinoma and unifocal Paget disease of the nipple with clear surgical margins.
- No lymph node metastasis and she was given adjuvant tamoxifen therapy.
- Four years later, she presented with an eczematoid erythematous lesion at the mastectomy scar.
- Lesion remained stable for another 4 years with little disease progression.
- An excision was then performed which revealed Paget disease.

Our case 1

- Presence of focal dermal scarring in the skin specimen, indicating a prior procedural site, could be secondary to the recent punch biopsy, although the more temporally remote pre-mastectomy core biopsy or even the mastectomy scar are other possibilities.
- Documented focal involvement of the superficial margin in the previous resection, despite without record of its exact location, is another risk factor contributing to local recurrence.

Paget disease away from the nipple

- Arises from an ectopic nipple along the normal milk line.
- Extramammary Paget disease is thought to arise from apocrine glands in the genital, perianal, and axillary regions, or rarely from eccrine glands when occurring in skin without apocrine glands.
- In our Case 1, there was no breast tissue present in the specimen - presence of a few benign sweat glands unrelated to the lesion also excludes the likelihood of apocrine/eccrine gland origin.
- The similar location of newly developed Paget disease of the breast skin to the previous preoperative core biopsy position that found DCIS supported the consideration of tumour recurrence at the biopsy site.

Paget disease away from the nipple

- Possible that the Paget disease in our case 1 also occurred via displacement of tumour cells from the original in-situ carcinoma to the epidermis through tumour seeding during the initial core biopsy.
- Epithelial displacement into needle tracks immediately after the procedure is not uncommon.
- A systematic review involving over 5000 patients evaluated tumour cell seeding and/or epithelial cell displacement after a preoperative core needle biopsy in patients with breast cancer
 - Malignant tumour cell displacement in surgical excision specimens was found in 22% of patients (range 2% to 63%), but there was no significant difference in the local recurrence rate between patients who underwent a preoperative diagnostic needle biopsy (1.1% to 3.7%) and those who underwent an excisional biopsy (2.1% to 10.3%).
 - It was concluded that there was no increased morbidity associated with iatrogenic seeding after core needle biopsy, despite limited data.

(F. Liebens, B. Carly, P. Cusumano, et al., Breast cancer seeding associated with core needle biopsies: a systematic review, Maturitas 62 (2) (2009) 113–123.)

Needle track recurrence

- Rate is extremely low considering that tumour cell displacement is not uncommon.
- Diaz et al. observed that the likelihood of finding cells in the needle track diminished over time, suggesting that in many cases these cells do not persist possibly due to lack of a developed blood supply (*AJR Am. J. Roentgenol.* 173 (5) (1999) 1303–1313).
- Calvillo et al. stated that radiation therapy possibly played a role, as none of the 14 patients with needle track recurrences received this therapy; the impact of systemic therapy was less clear (*Int. J. Surg. Case Rep.* 15 (2015) 152–156).
- Currently there are no definite risk factors for needle track recurrence.
- Removal of the needle track with the aim of eliminating any residual tumour cells is still debatable.

Paget disease of breast skin

- Is Paget disease the appropriate diagnostic term to use, as the lesion occurred outside of the nipple-areolar region?
- According to the 2012 WHO classification of breast tumours, Paget disease of the nipple is defined as a breast cancer characterized by the presence of malignant glandular epithelial cells within the squamous epithelium of the nipple that may extend into the areola and adjacent skin.
- In our case 1, presence of malignant glandular epithelial cells within and confined to the squamous epithelium of the breast skin, especially when associated with a prior diagnosis of high grade DCIS, supports the use of the terminology of Paget disease, similarly applied by Calvillo et al.

Follow-up

- 5 months after the excision of Paget's disease, the patient was well, without further evidence of recurrence.
- She declined adjuvant radiotherapy in consideration of the risk to implant contracture.



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Intraepidermal malignancy in breast skin: A tale of two tumours

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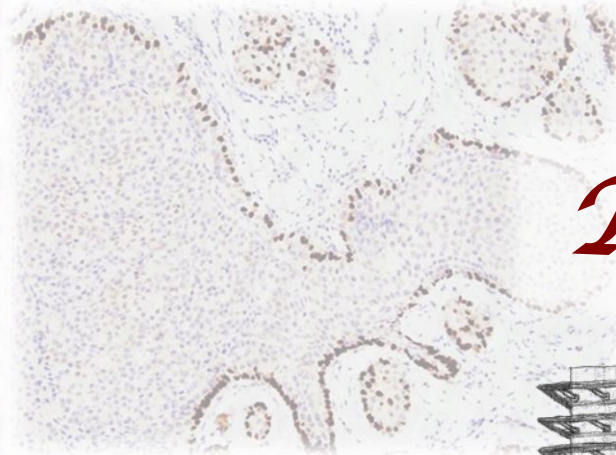
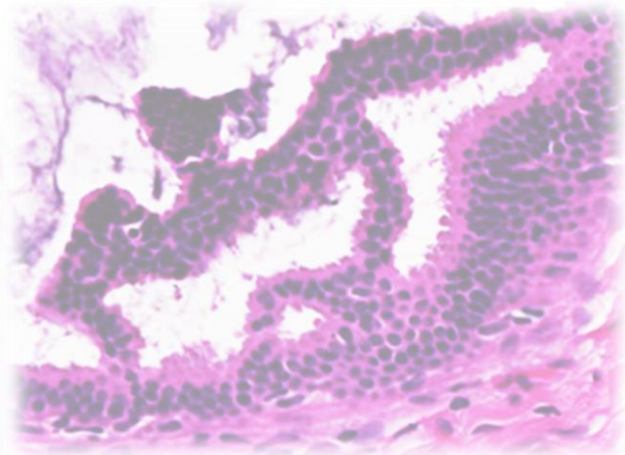
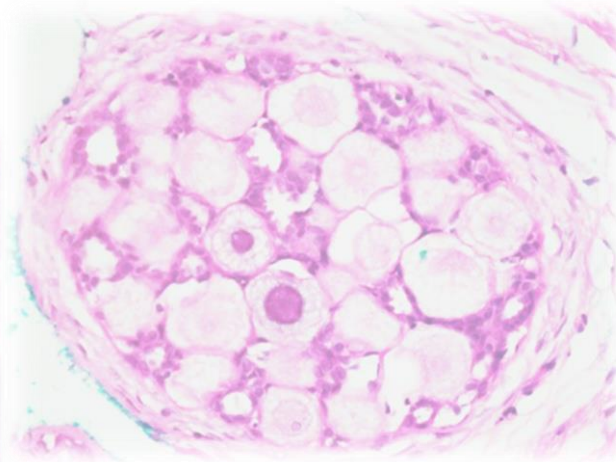
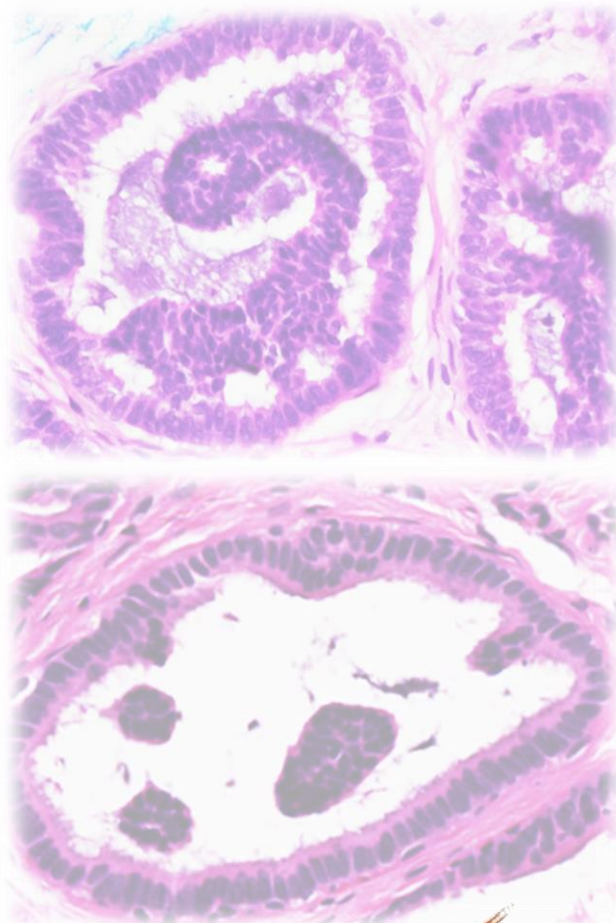
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Thank you!

