

## Case 12

73 year old Malay female.

Left breast simple mastectomy and sentinel lymph node biopsy.



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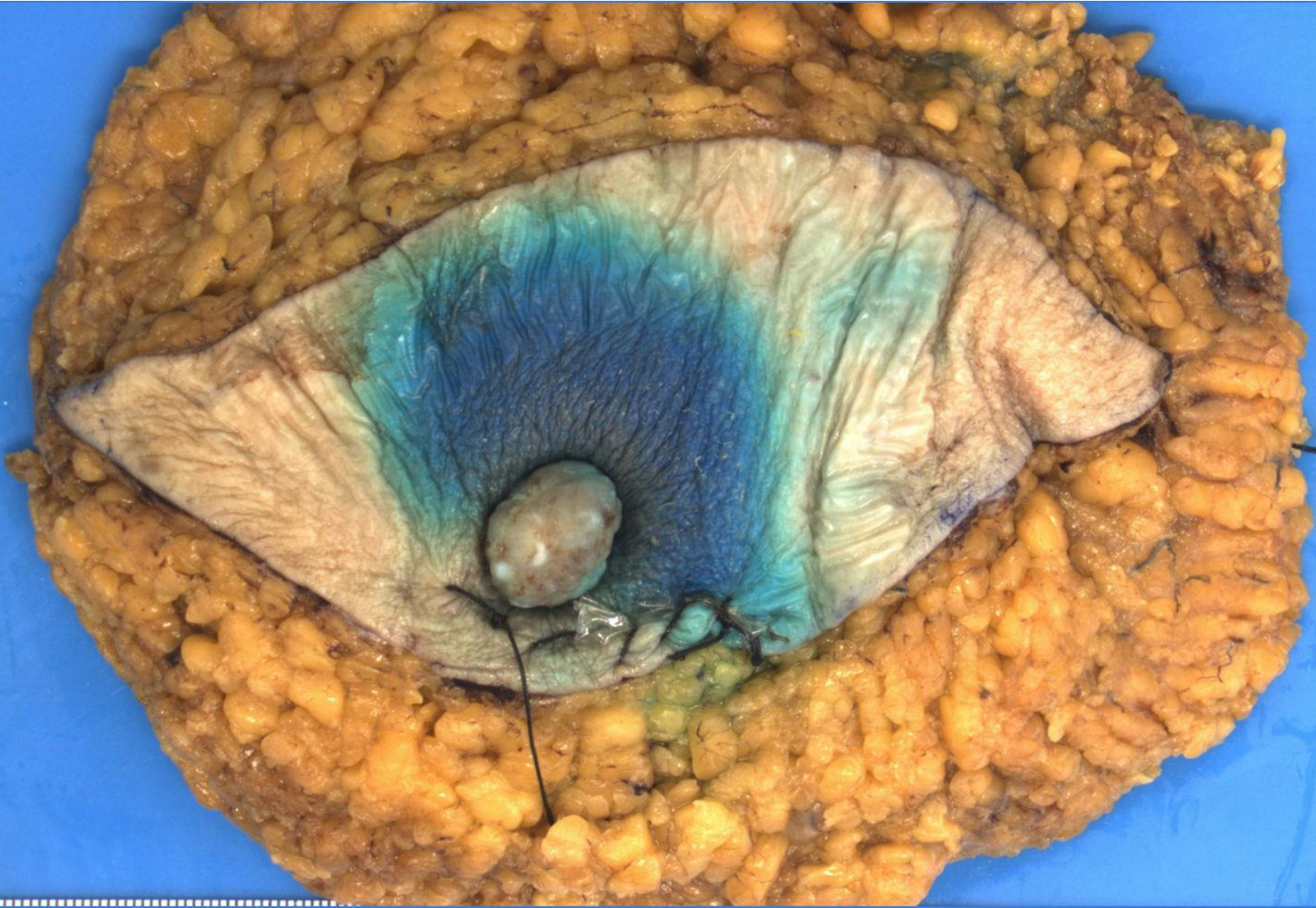


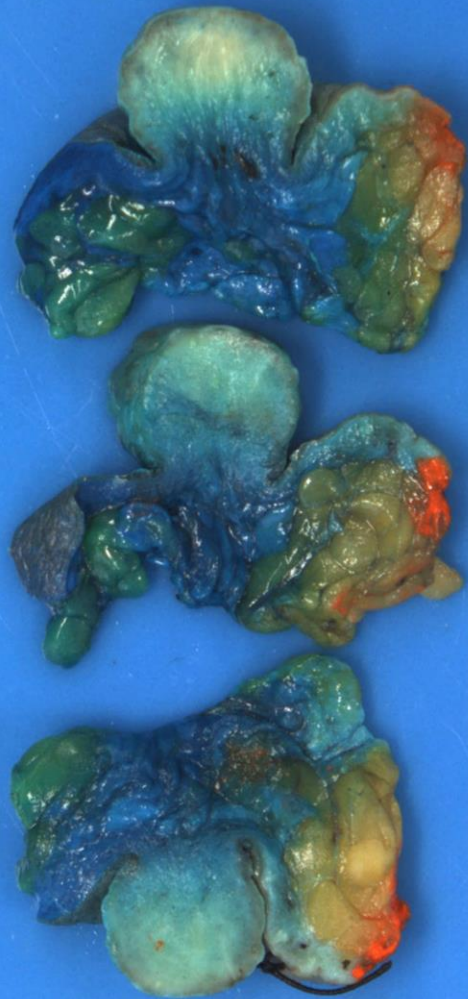
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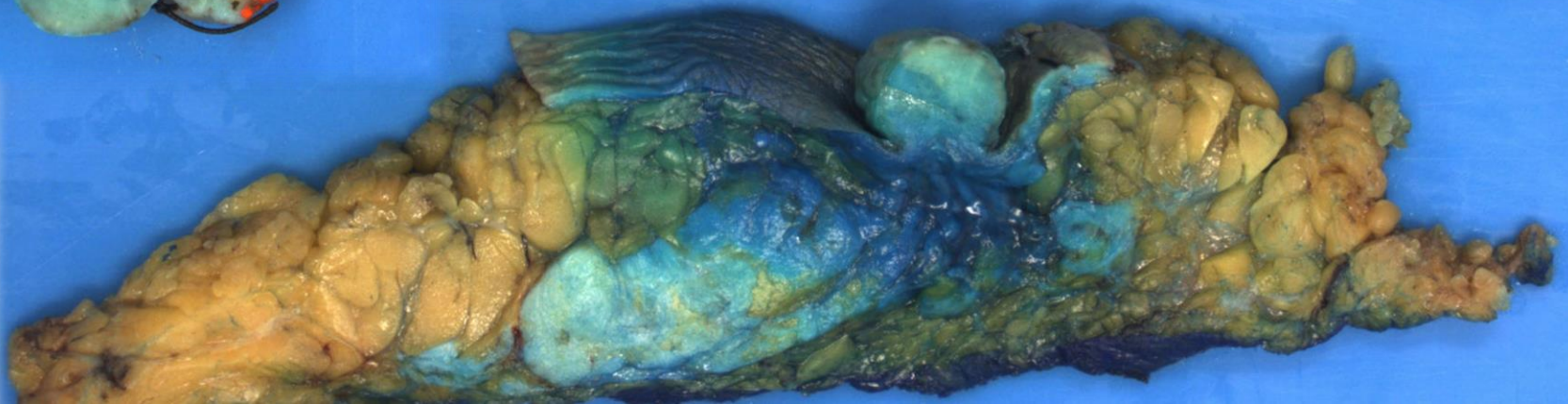
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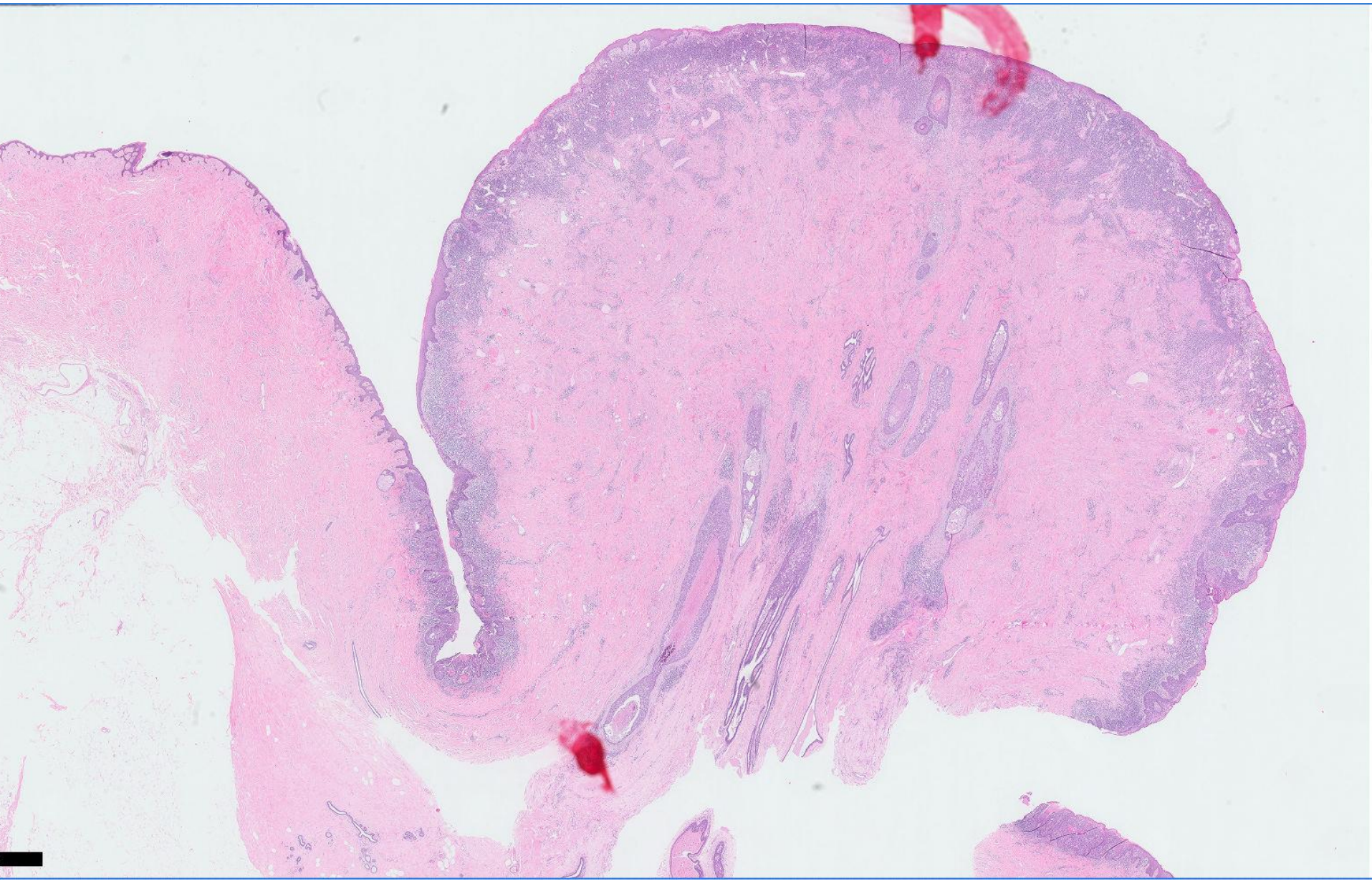


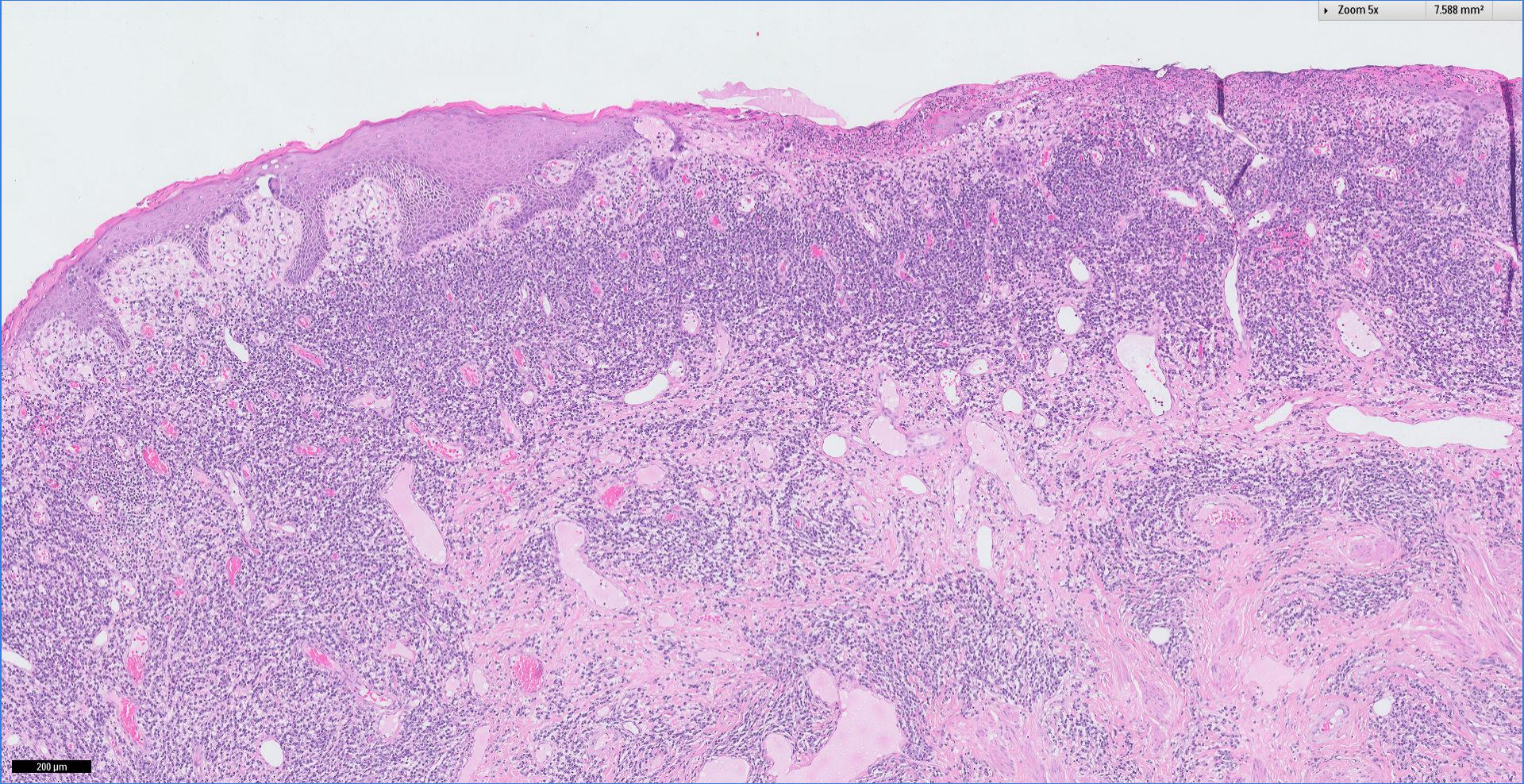


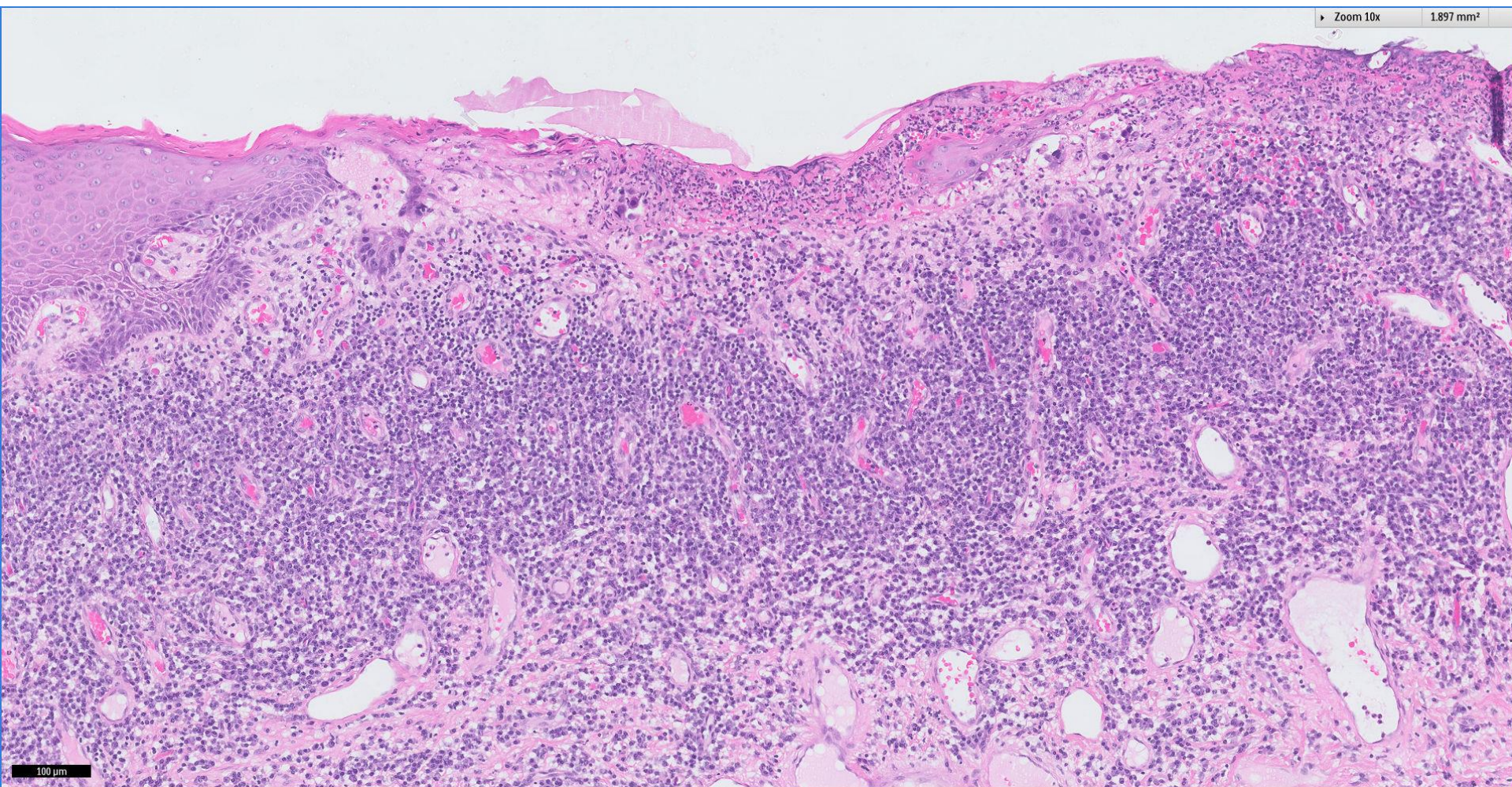


Previous punch biopsy of the nipple showed abnormal cells consistent with **Paget disease**

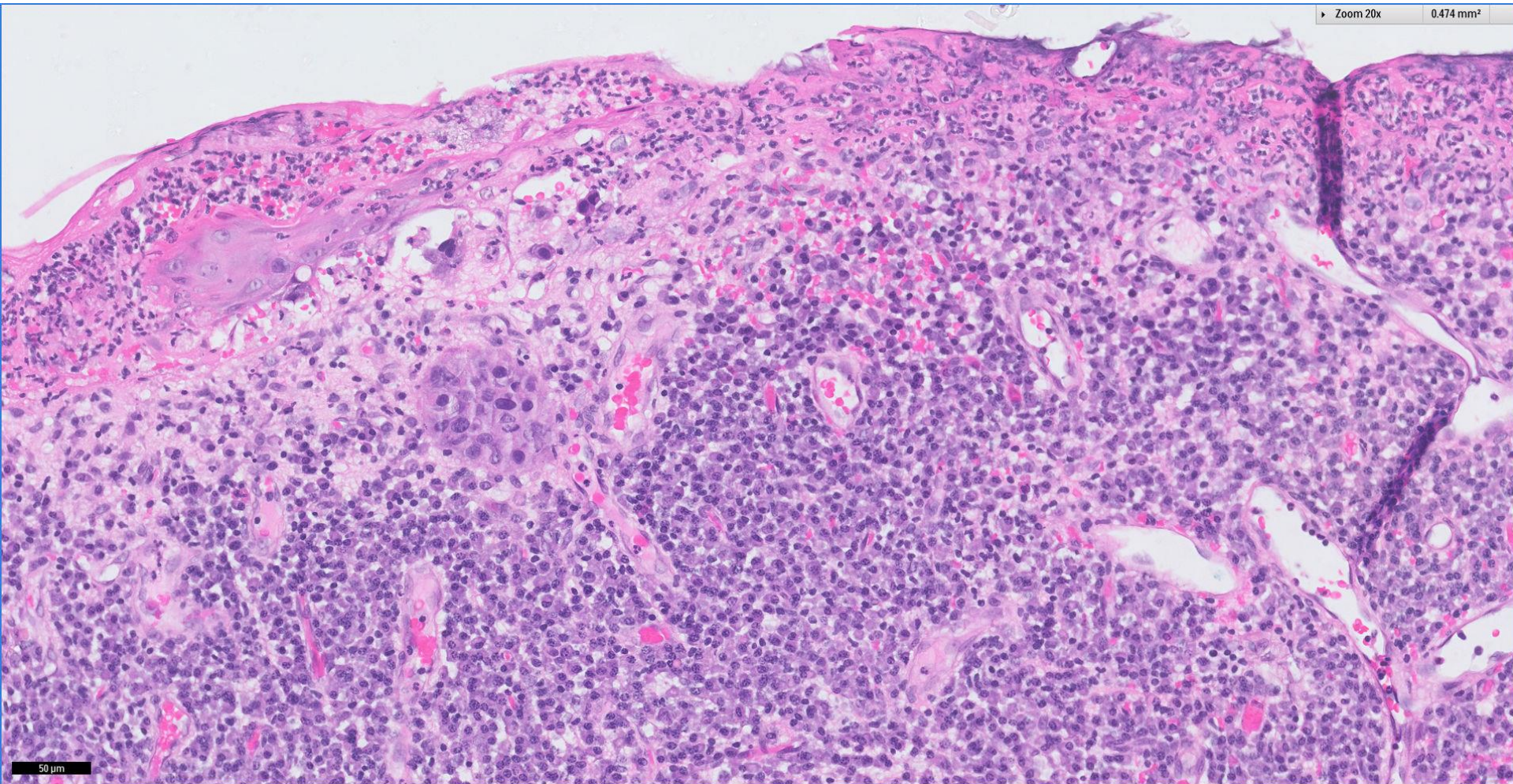




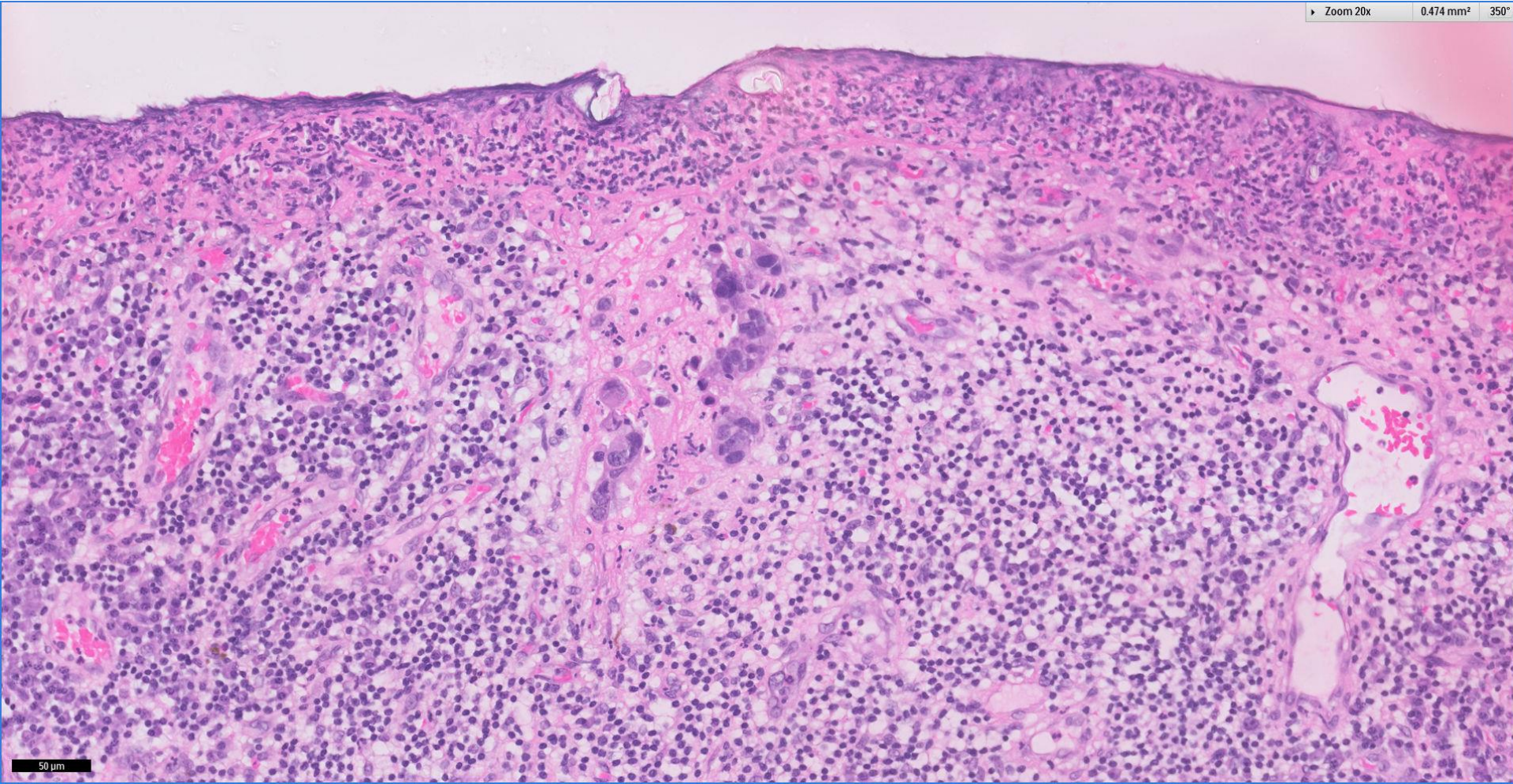




100  $\mu$ m

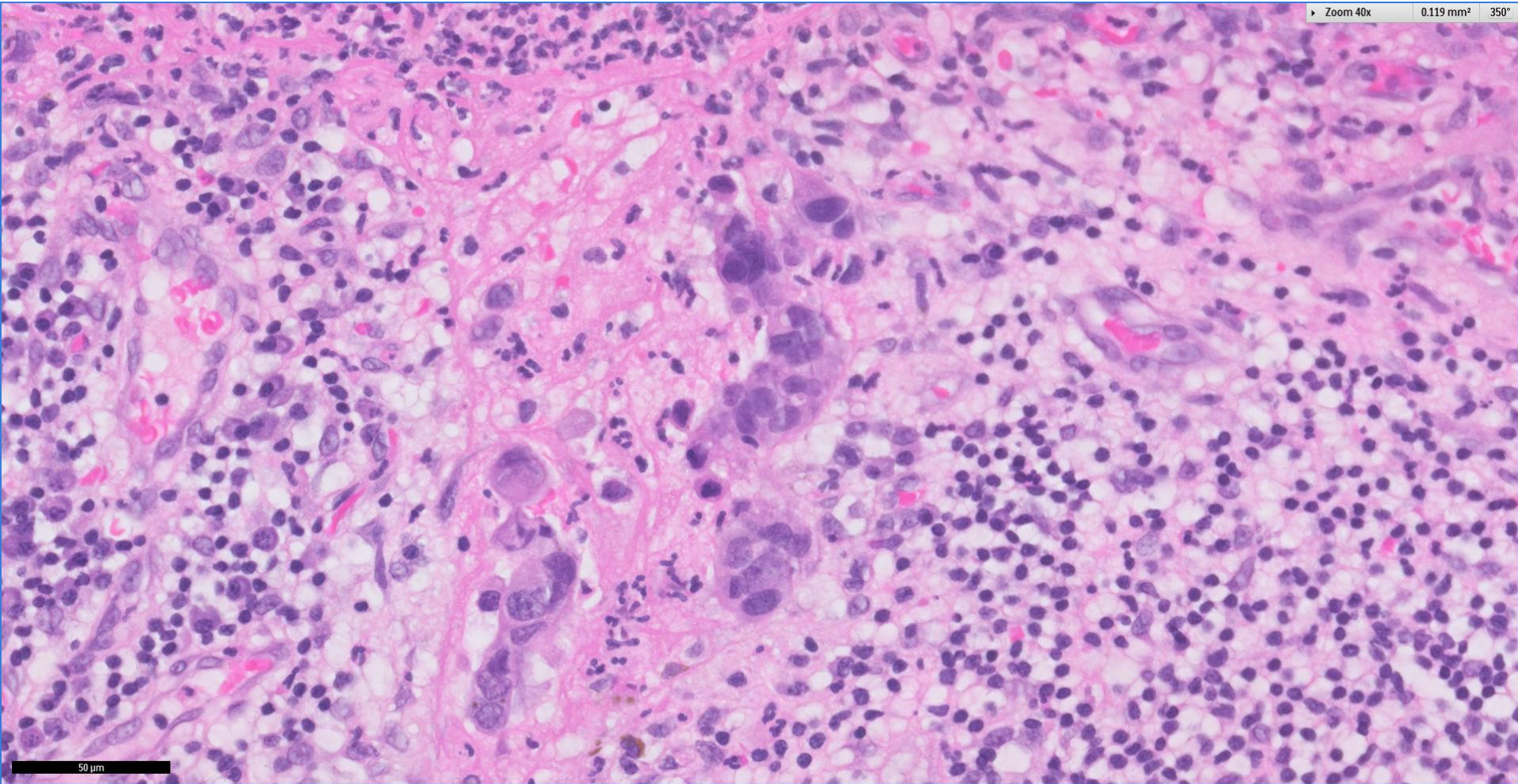


50 μm

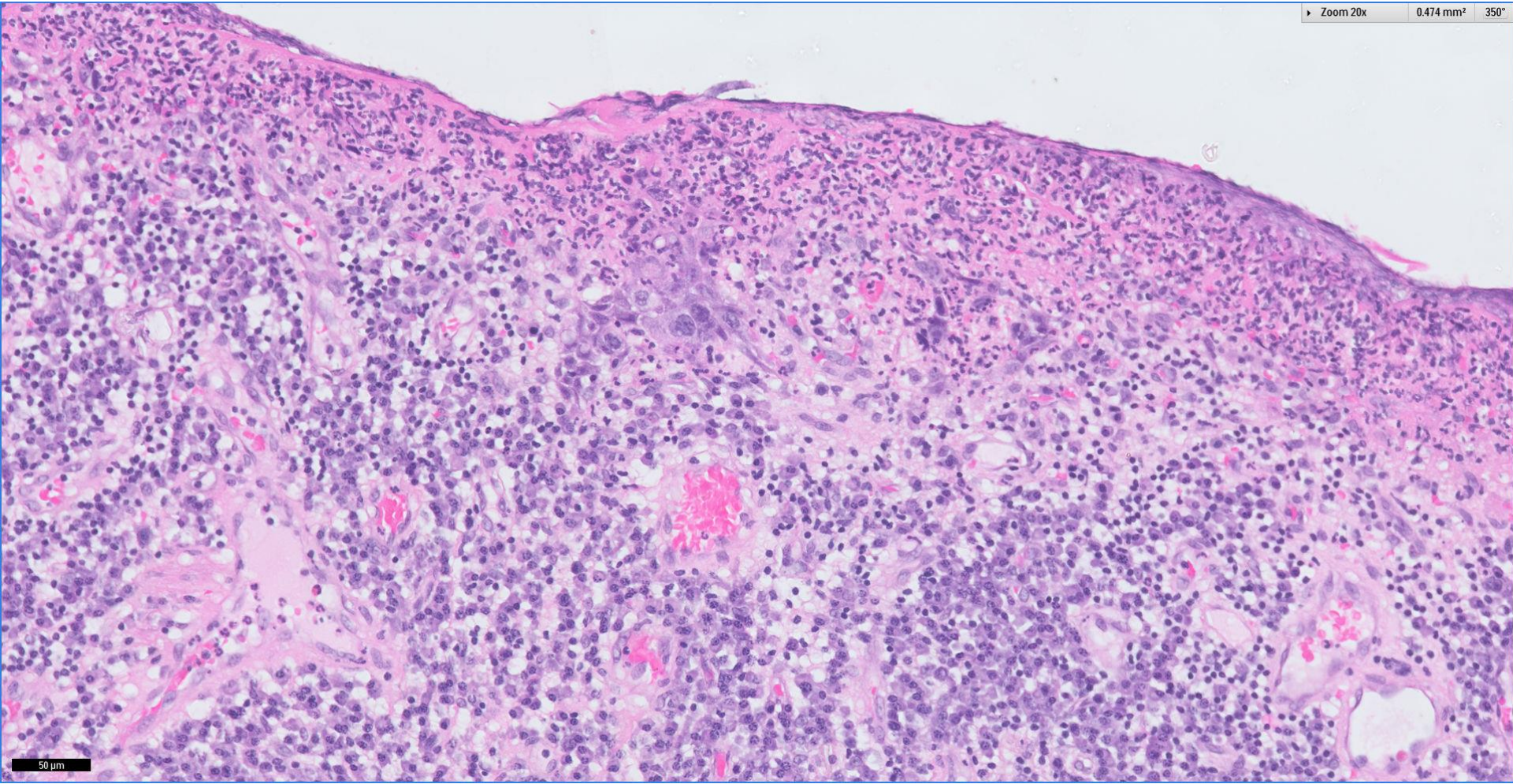


50 µm

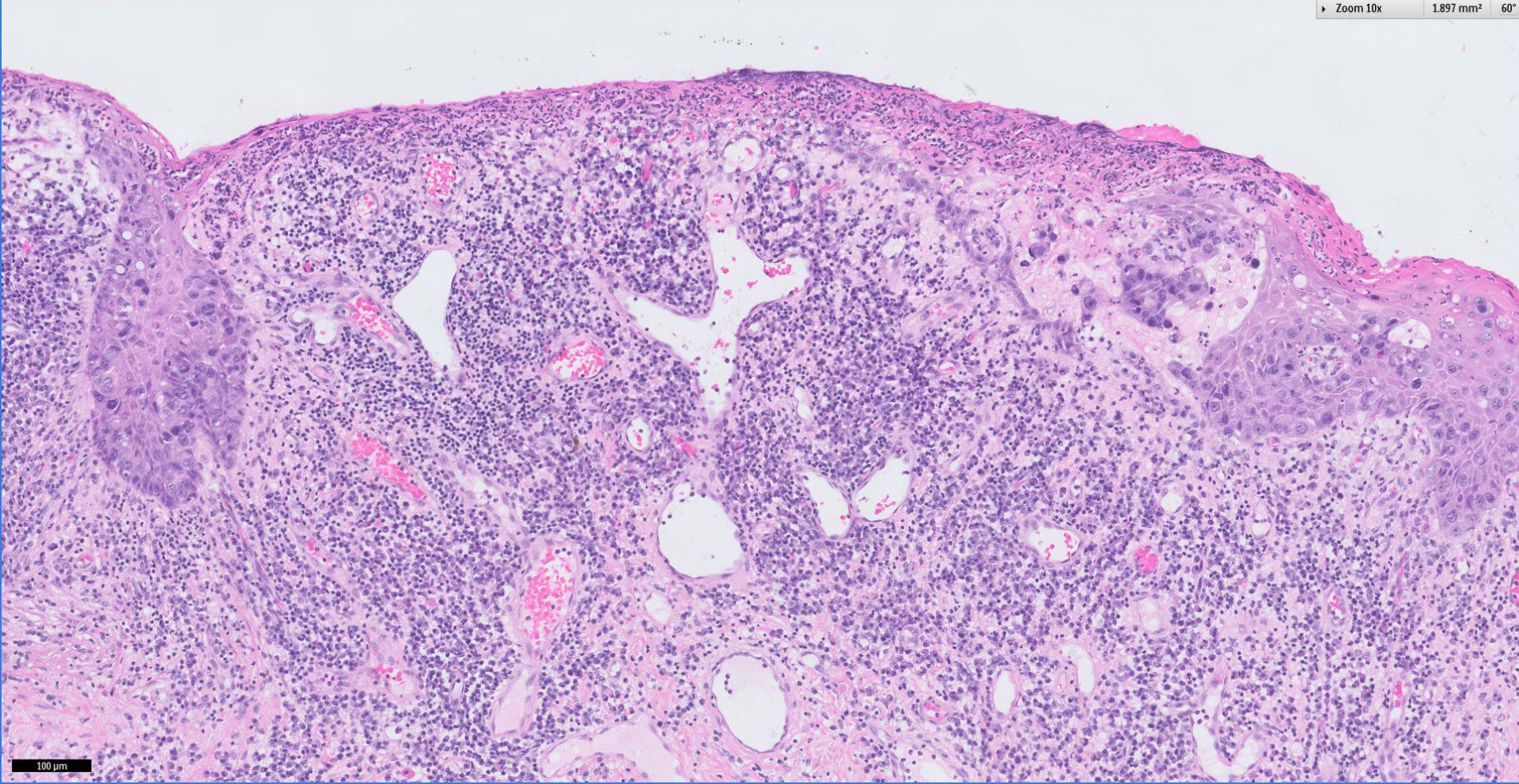




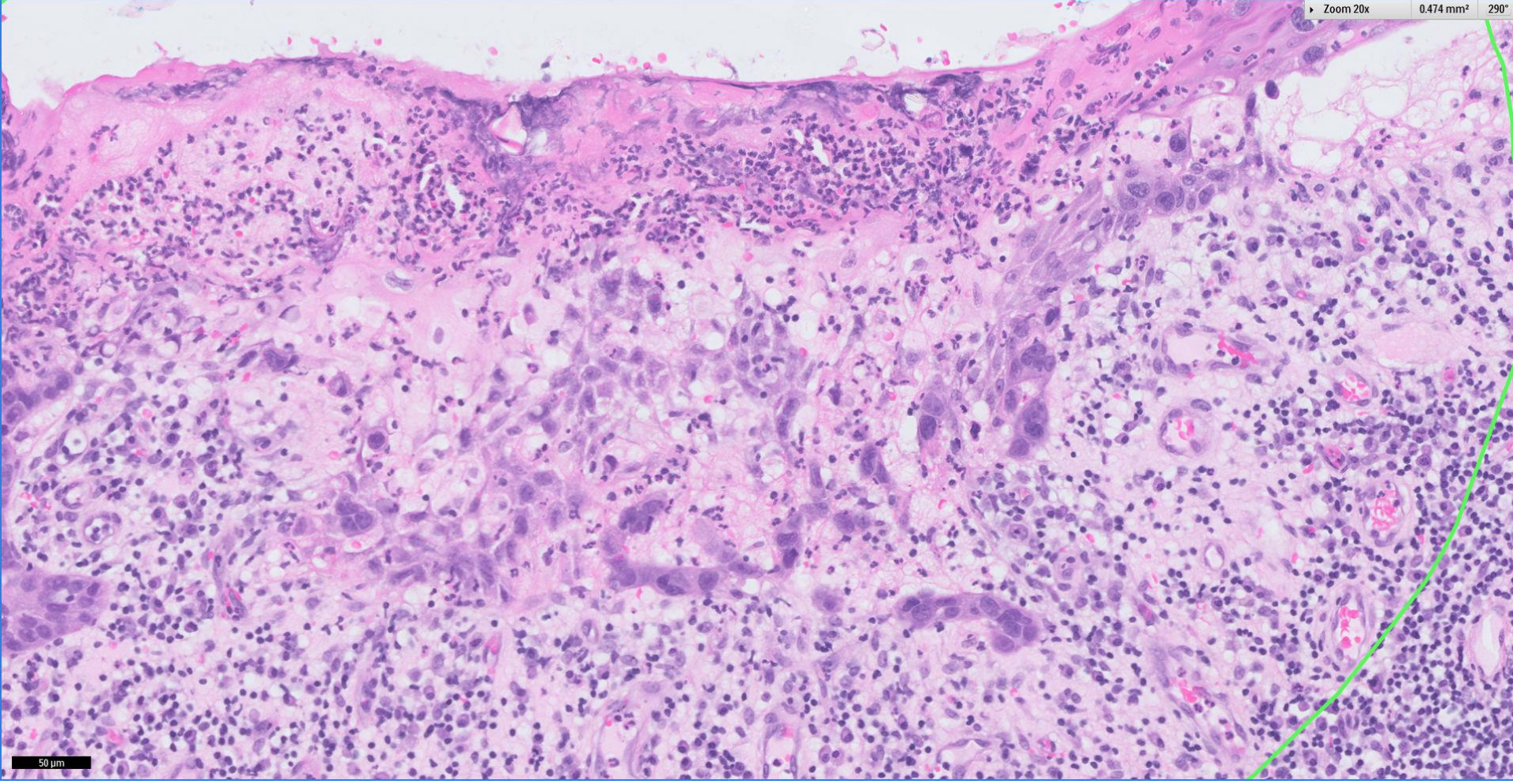
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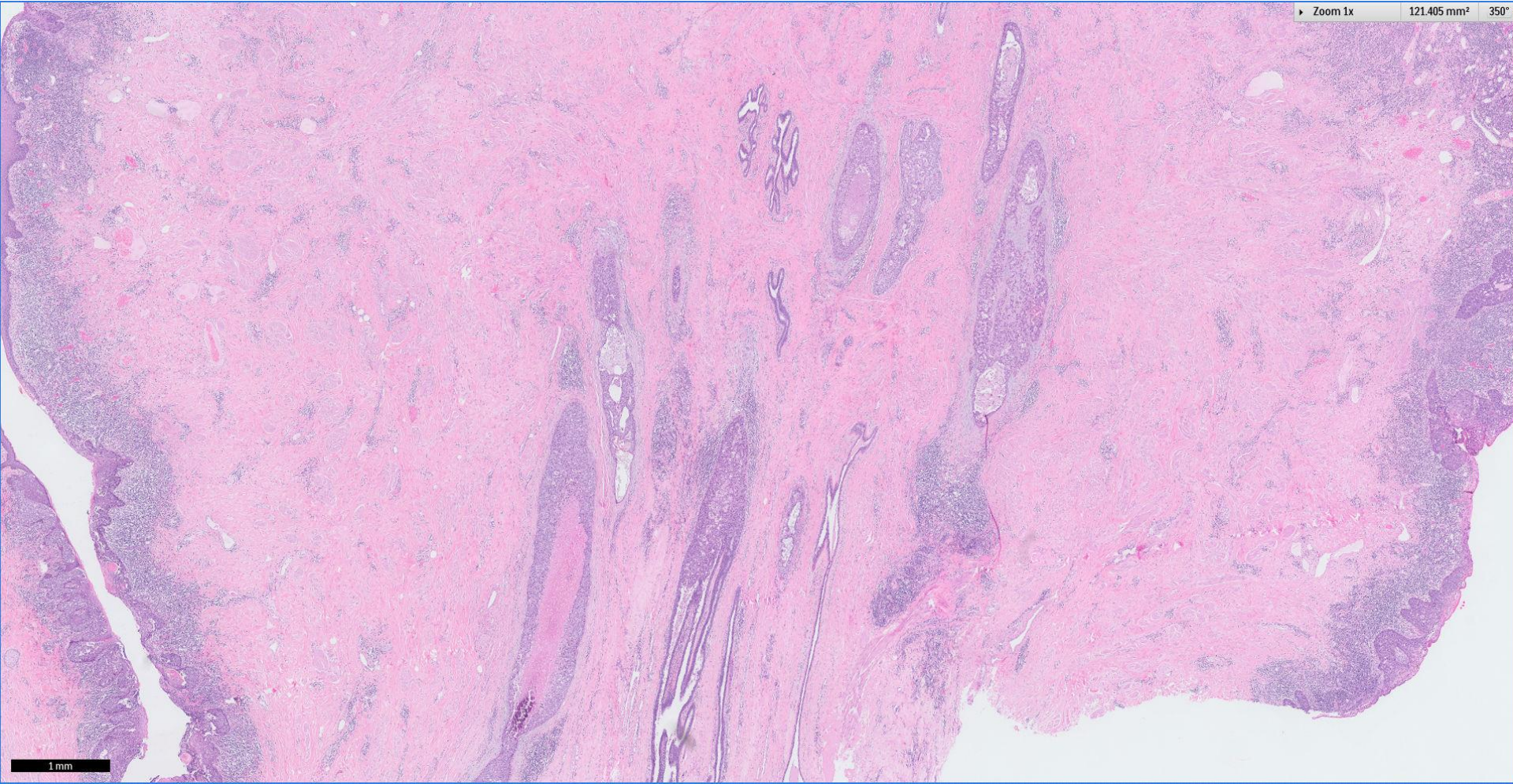
50 μm



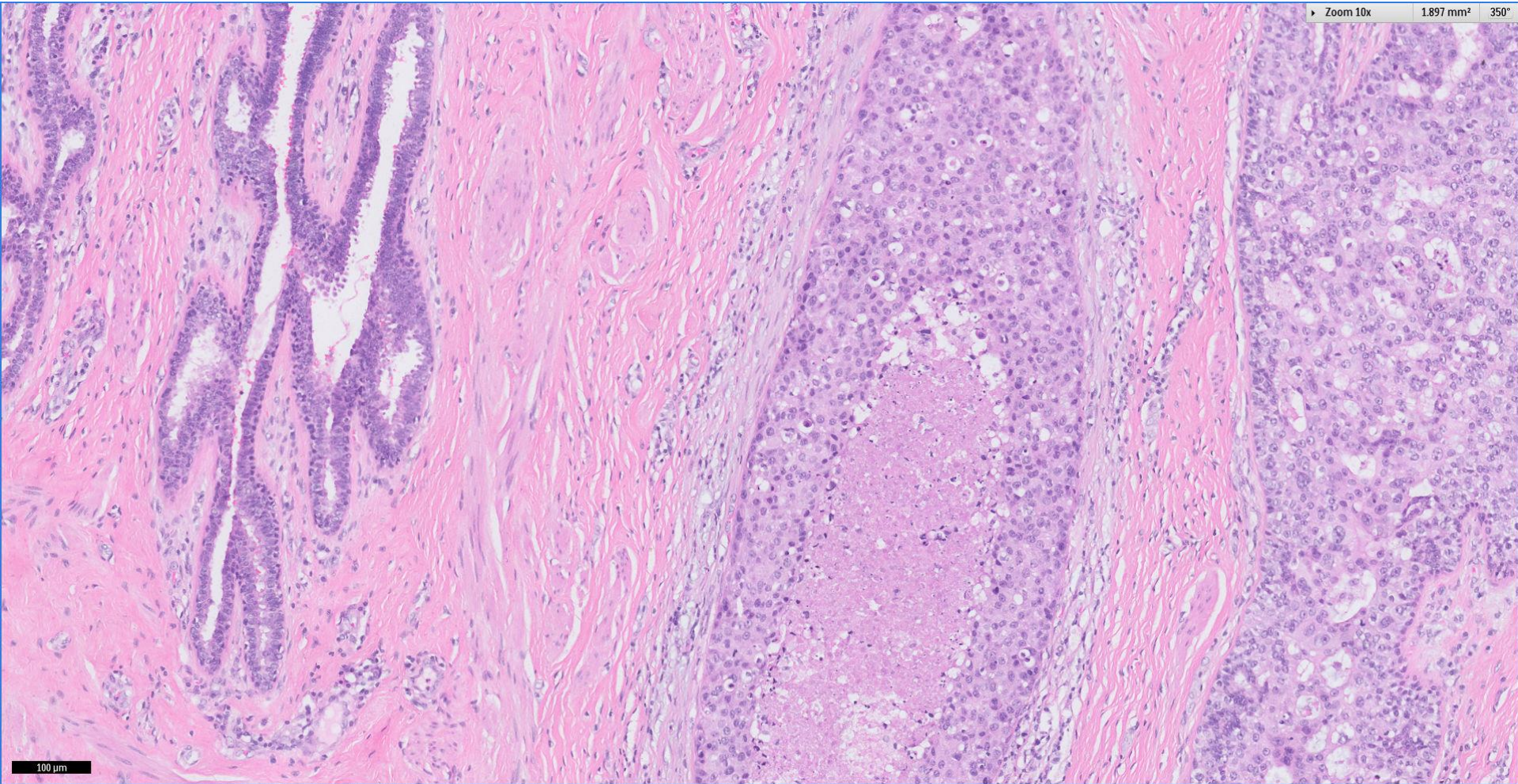
100 µm



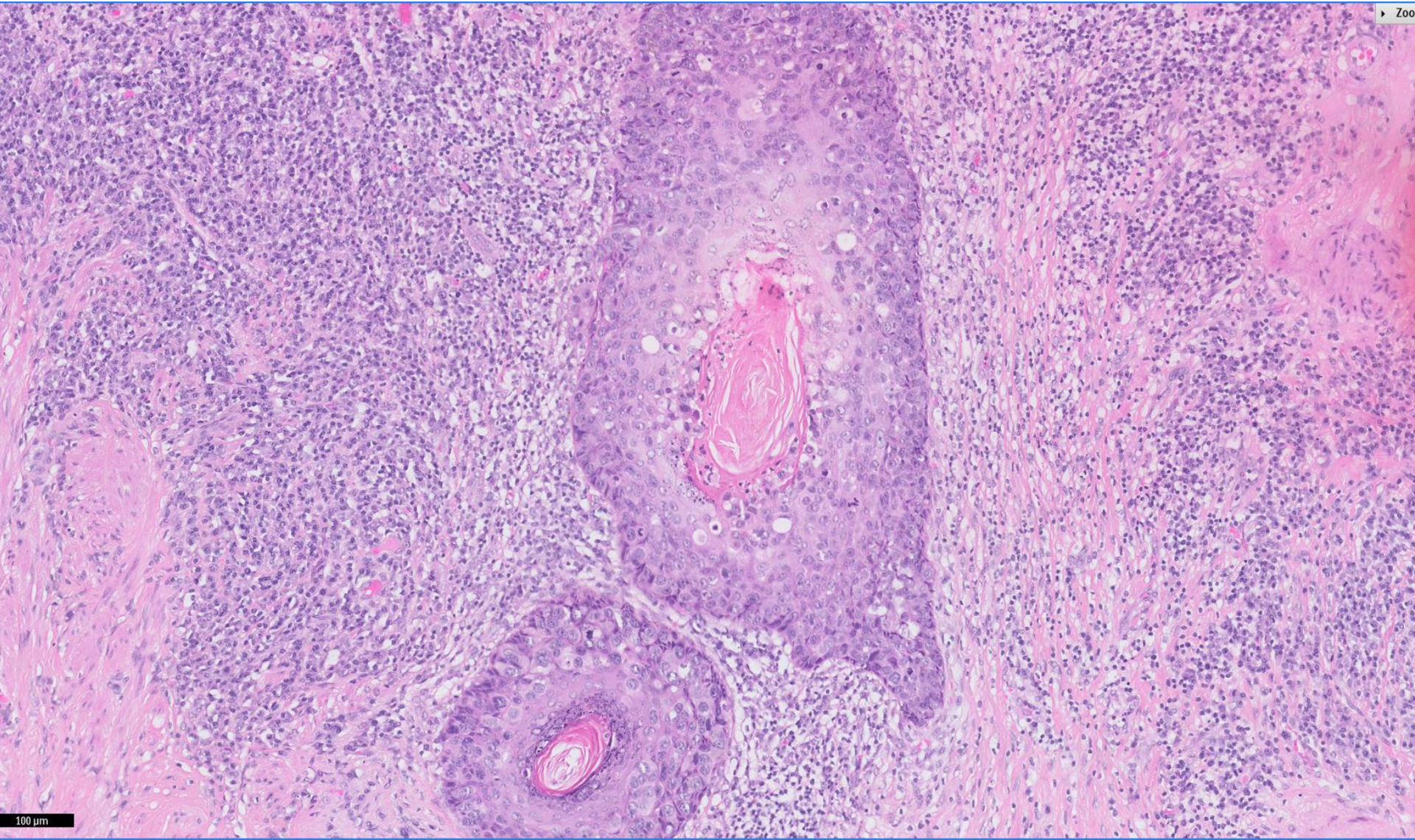
50 μm

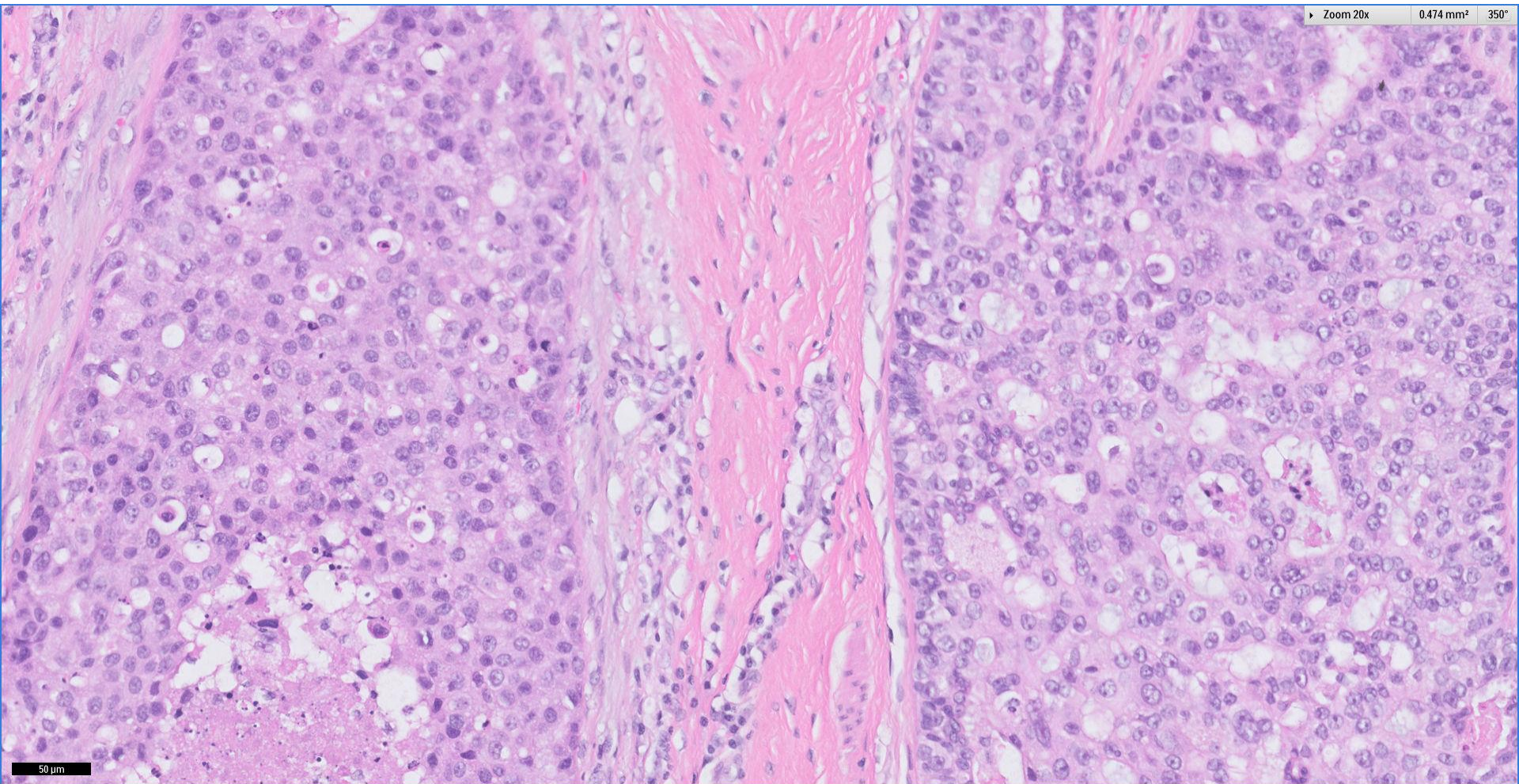


1 mm



100 μm







# Diagnosis:

## Left breast, simple mastectomy ~

Paget disease with microinvasion.

Ductal carcinoma in situ, high nuclear grade, with necrosis and calcifications.

## Left sentinel lymph nodes ~

3 benign nodes.



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# Paget disease

- Malignant glandular cells within the epidermis of the nipple-areolar complex.
- Believed to arise from malignant transformation of the intraepidermal portion of lactiferous ducts or from malignant cells migrating into the epidermis from underlying breast carcinoma.
- Paget disease is associated with underlying in situ and/or invasive ductal carcinoma in a large majority of cases.



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# Paget disease

- Encountered in about 1–4 % of all breast carcinomas.
- Clinically presenting as pain, discharge, eczematous rash, itch, or erosion of the nipple.
- It may also be occult and discovered only upon microscopic examination of the nipple in mastectomies performed for breast carcinoma.
- Paget disease without an underlying in situ or invasive breast carcinoma is rare, reported in 1.4–13 % of all cases of Paget disease.



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# Paget disease ~ imaging

- Nipple changes of Paget disease are commonly nonspecific or normal appearing on imaging.
- There may be nipple retraction, areolar skin thickening, or dermal microcalcifications.
- Presence of subareolar microcalcifications or mass is suggestive of an underlying associated malignancy.



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# Paget disease ~ microscopy

- Malignant cells punctuate the nipple epidermis in a pagetoid fashion, with cytologically high-grade, abnormal cells placed singly or in clusters among benign epidermal cells.
- Malignant cells sometimes show gland formation.
- Ductal carcinoma in situ (DCIS), usually of high nuclear grade, is frequently observed in the underlying lactiferous ducts.
- Overexpression and amplification of c-erbB-2 are seen in 80–90% of cases.
- Invasive carcinoma (often of a ductal subtype) is found in 53–60% of cases.
- There is an isolated report of Paget disease associated with lobular carcinoma in situ, but this report has been challenged as possibly representing nipple Toker cells rather than Paget cells.



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# Paget disease ~ differential diagnosis

- Nipple toker cells.
- Clear cells of nipple epidermis.
- Squamous carcinoma in situ (Bowen disease).
- Malignant melanoma.



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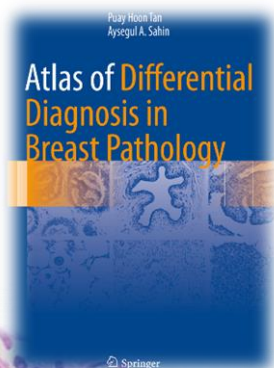
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**Table 13.1** Immunohistochemical comparison between Toker cells, Paget disease, squamous carcinoma in situ, and malignant melanoma

|          | Toker cells | Paget disease | Squamous CIS | Melanoma |
|----------|-------------|---------------|--------------|----------|
| CK7      | +           | +             | –            | –        |
| Cam 5.2  | +           | +             | –            | –        |
| CK5/6    | –           | –             | +            | –        |
| 34BE12   | –           | –             | +            | –        |
| p63      | –           | –             | +            | –        |
| S100     | –/+         | –/+           | –            | +        |
| HMB45    | –           | –             | –            | +        |
| MelanA   | –           | –             | –            | +        |
| ER, PR   | +           | –/+           | –            | –        |
| c-erbB-2 | –           | +             | –            | –        |
| Ki67     | –/low +     | +             | +            | +        |

*CIS* carcinoma in situ, *ER* oestrogen receptor, *PR* progesterone receptor



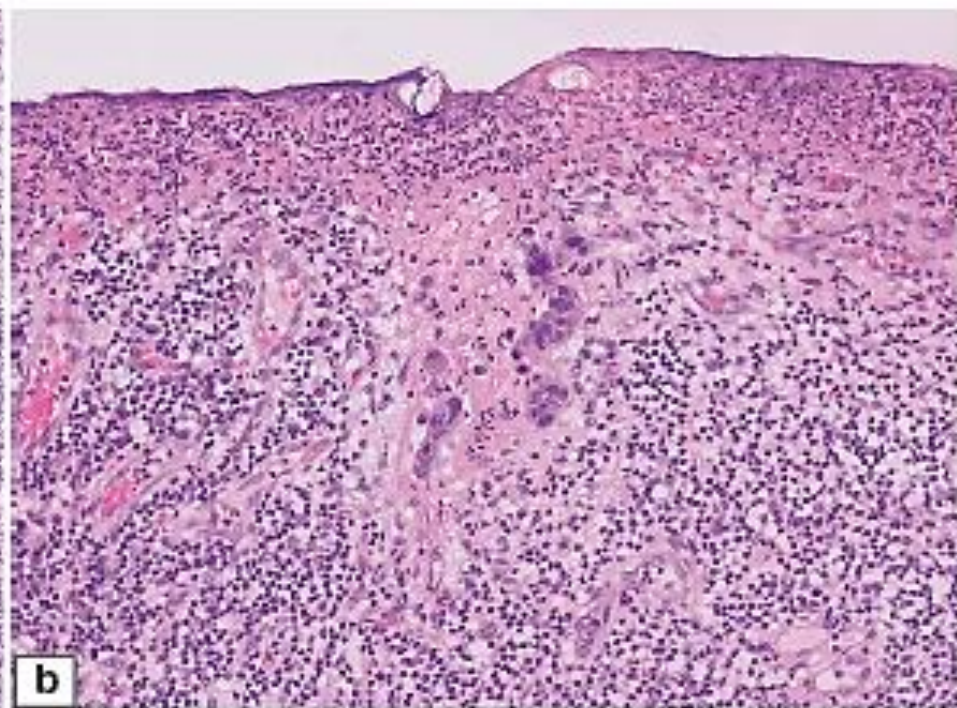
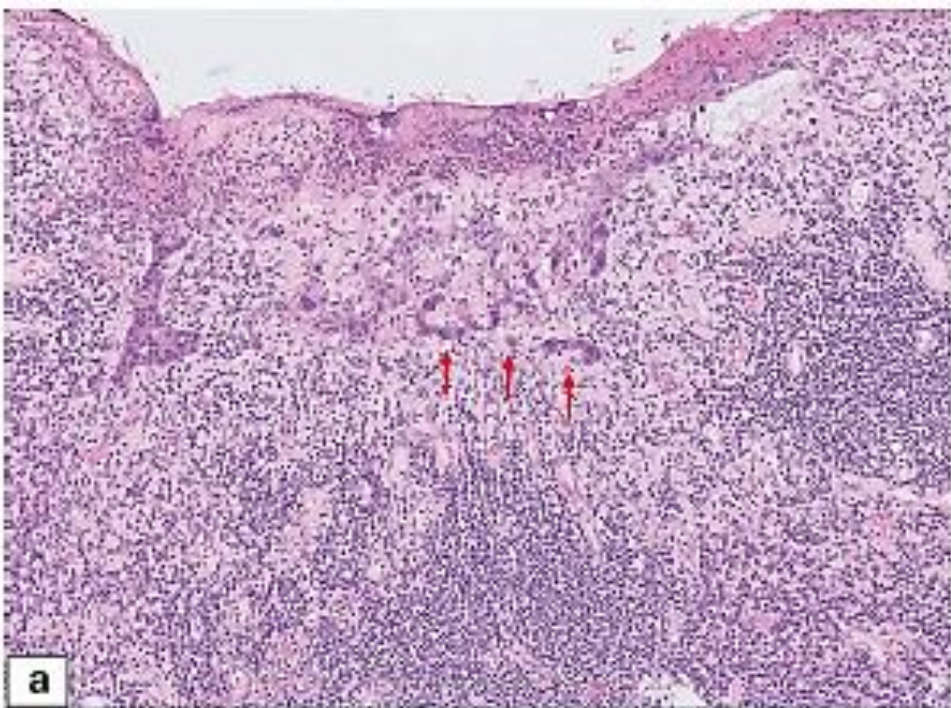
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**Fig. 13.83** Paget disease with direct dermal invasion. (a) The nipple epidermis is eroded, with remnant rete pegs variably harbouring intraepidermal malignant cells. A few small cords and narrow trabeculae of tumour cells are detached from the epidermis, lying within the oedematous inflamed stroma (*red arrows*). (b) Higher magnification shows the detached malignant epithelial aggregates within inflamed stroma. The overlying epidermis here is ulcerated. No invasive disease was found in the rest of the mastectomy specimen which contained ductal carcinoma in situ. It may be difficult to distinguish early invasive disease from Paget cells that are still contained within rete pegs that are

sectioned at a tangent. What can be helpful is to determine if the detached malignant epithelial island is connected with rete pegs in adjacent levels, in which case invasion is unlikely. Alternatively, immunohistochemistry for high molecular weight keratins or p63 may highlight a peripheral rim of squamous cells around the malignant Paget cells confirming absence of invasion. In this example, assessment is made challenging by the ulceration. However, the presence of individual malignant cells within the inflamed stroma, and persistence of such foci after deeper levels, support the conclusion of direct dermal invasion from Paget disease

*Direct dermal invasion from Paget disease has a more favourable outcome than skin invasion from underlying breast carcinoma and must therefore be distinguished from the latter, which represents pT4b disease*



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