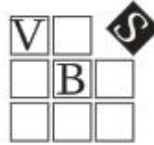


Východoslovenský
BIOPTICKÝ SEMINÁR



***Minisymposium:
Pathology of Melanocytic Lesions-***

Melanocytic Lesions on Genital Skin

*Thomas Brenn, MD, PhD
Western General Hospital
University of Edinburgh
Scotland*



Genital Melanocytic Lesions

-Introduction-

- **Pigmentary abnormalities of genital area present in ~10% of patients at routine GYN examination**
- **Mostly on vulval skin and mucosa**
- **Rare in vagina**
- **Melanocytic and non-melanocytic
(e.g. squamous lesions and inflammatory conditions)**

Genital Melanocytic Lesions

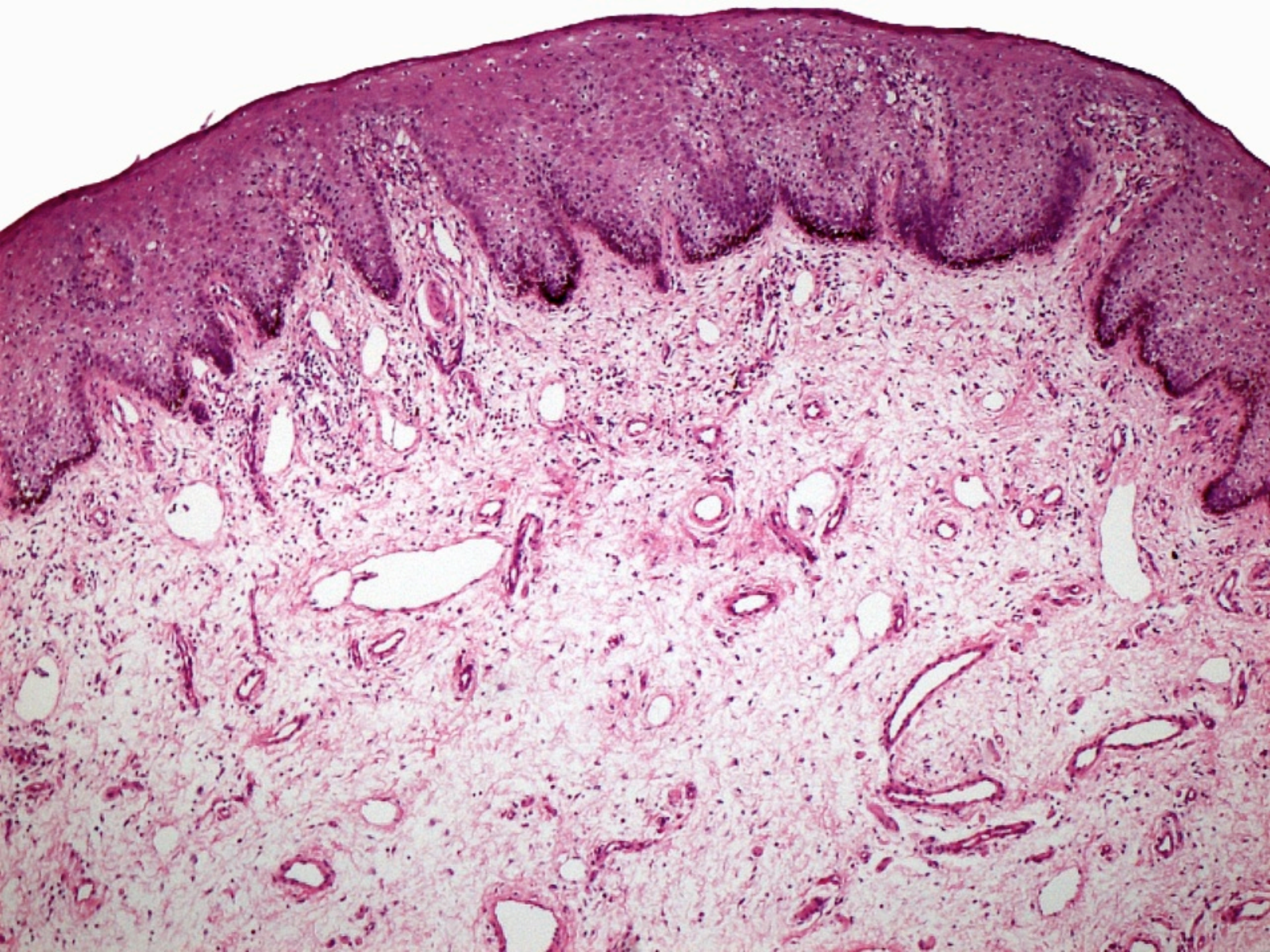
-Overview-

- **Vulval melanocytic tumours are rare**
- **Wide morphological spectrum**
- **Benign to frank malignant**
 - **“Genital Melanosis (Genital Melanotic Macule)”**
 - **Melanocytic Naevi**
 - **Melanoma**
- **Vast majority benign but distinction may be difficult**

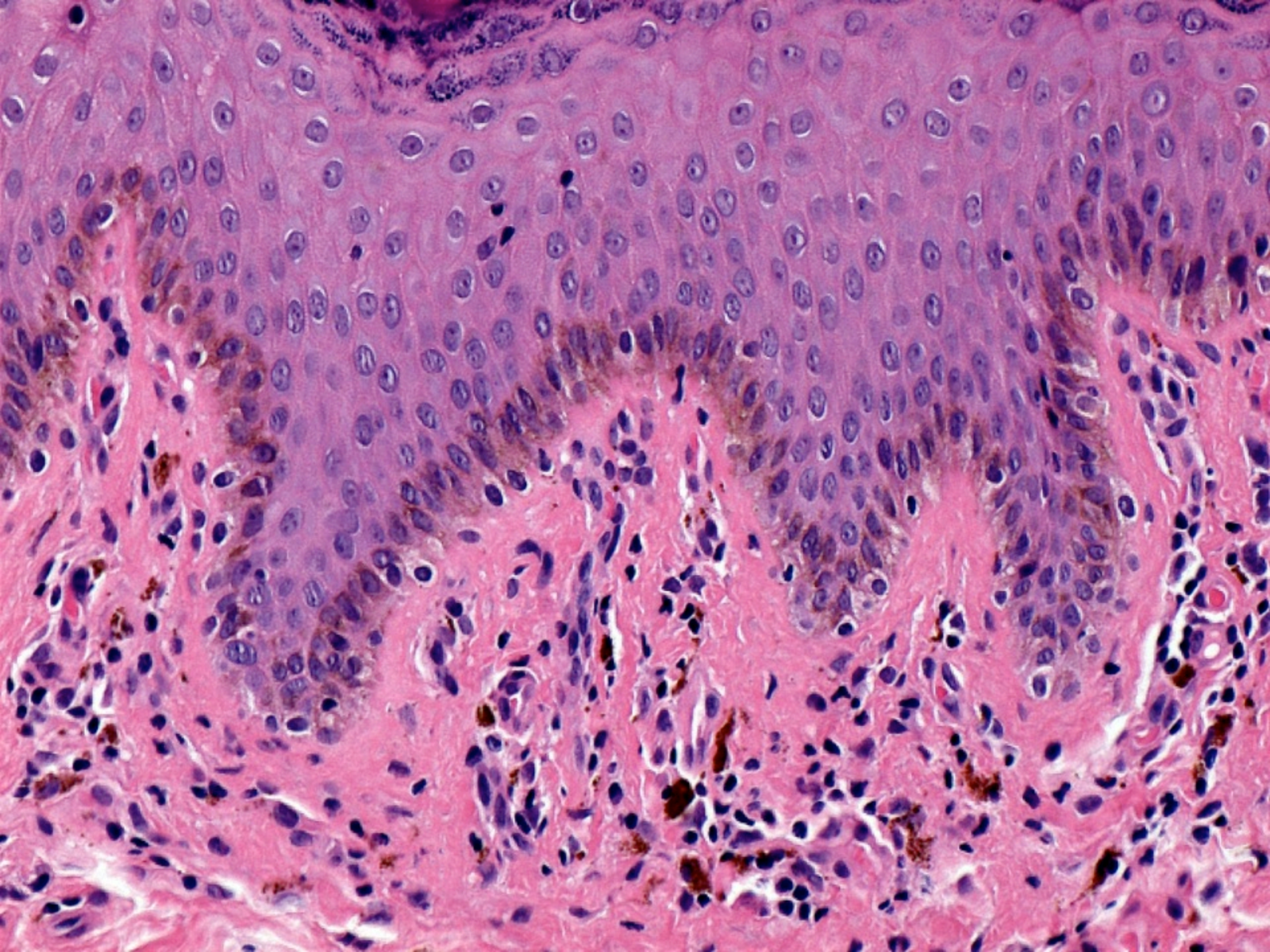
Genital Melanotic Macule

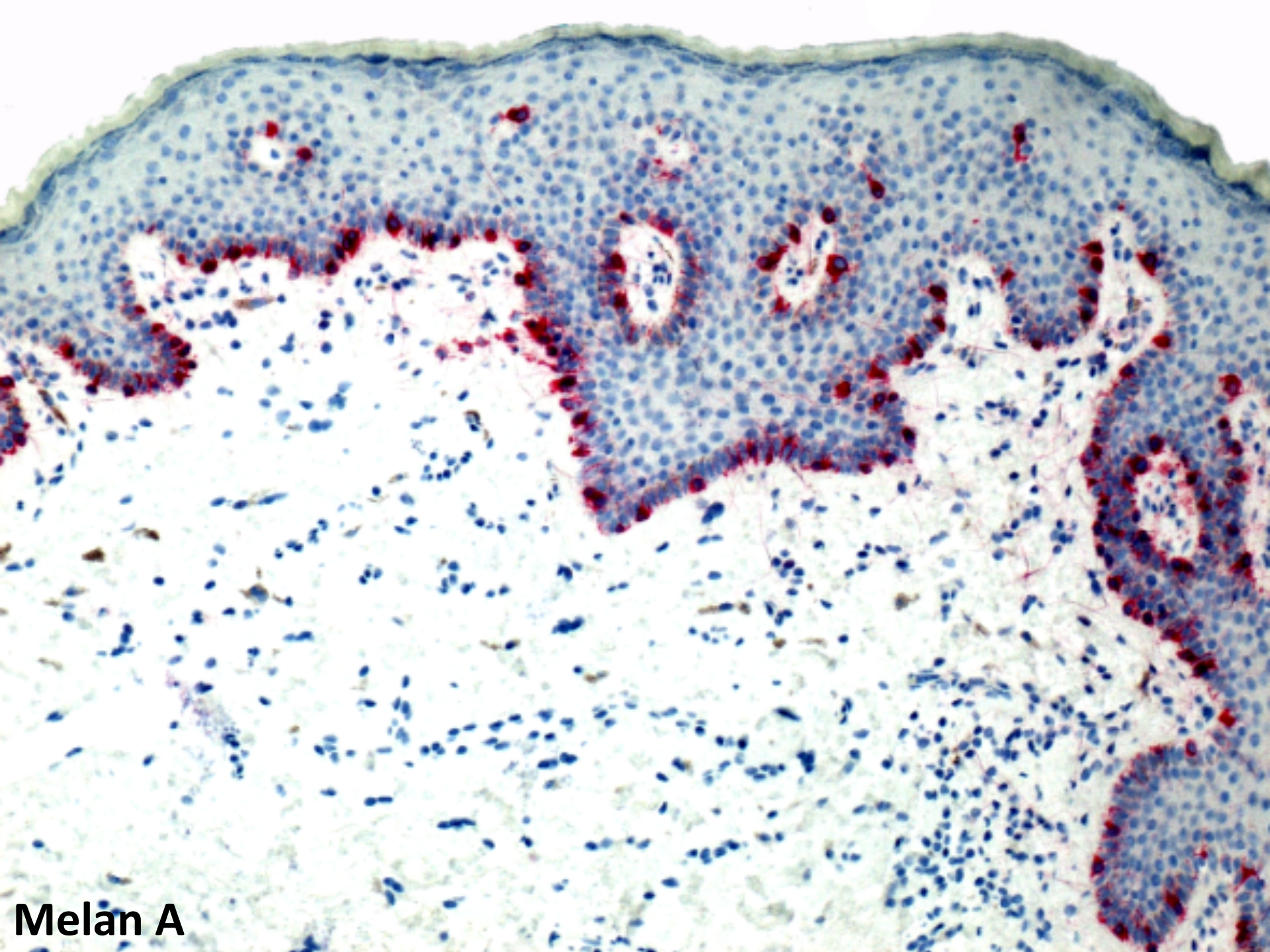
-Clinical Features-

- **Relatively frequently encountered**
- **Similar to mucosal melanoses at other sites;
e.g. labial melanotic macule**
- **Solitary, multiple or confluent macules and patches of tan to dark brown or bluish hyperpigmentation (0.5-2cm)**
- **Vulva most frequently affected**
- **Both cutaneous and mucosal surfaces**
- **Adulthood presentation (around 40 yrs)**
- **Irregular borders, variable pigmentation and large size are clinically alarming features**









Melan A

Genital Melanotic Macule

-Behaviour-

- **Entirely benign**
- **Recognition important as clinical picture may be worrying**
- **Association with increased melanoma risk likely anecdotal**

Genital Melanocytic Naevi

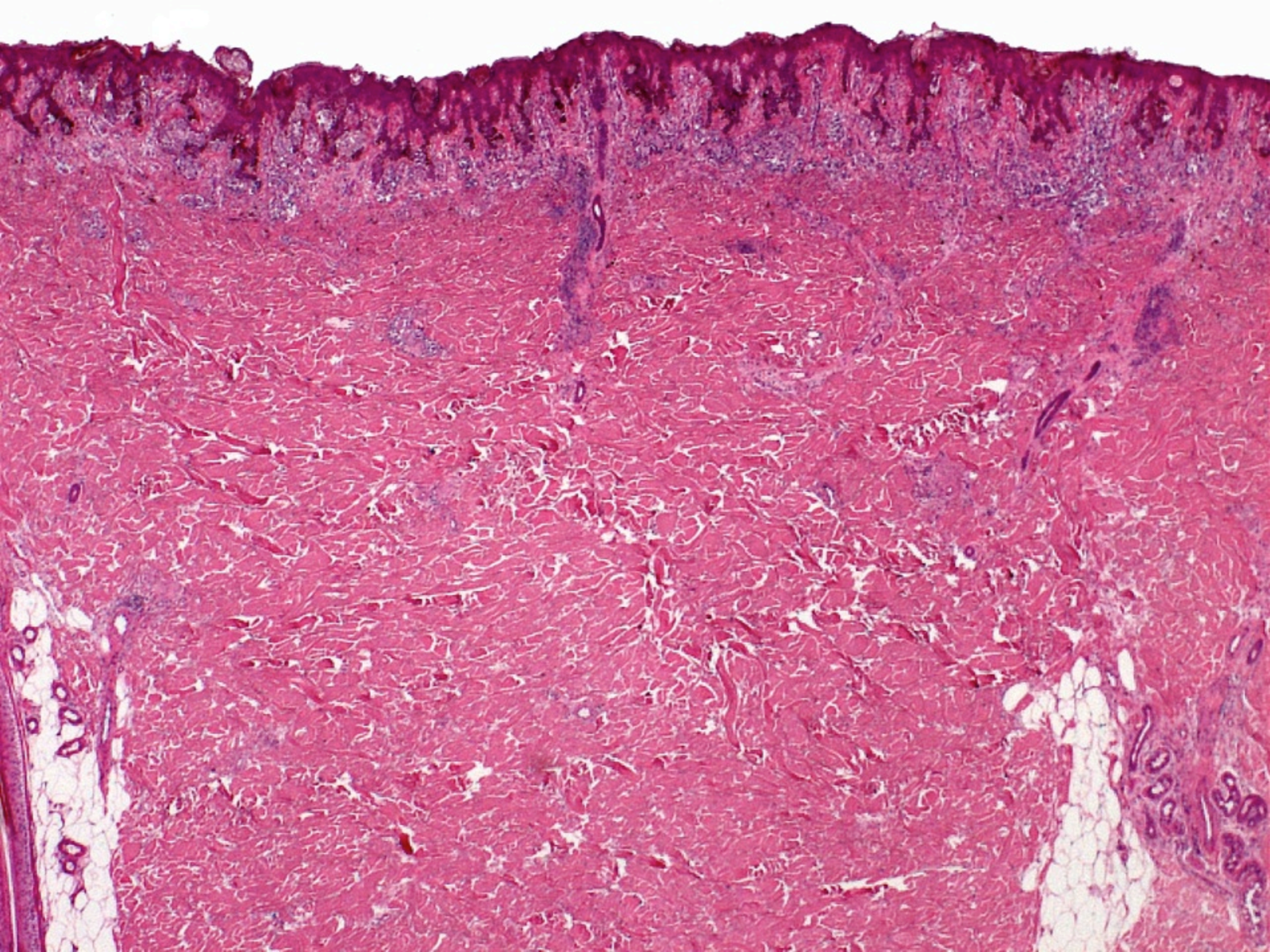
-Overview-

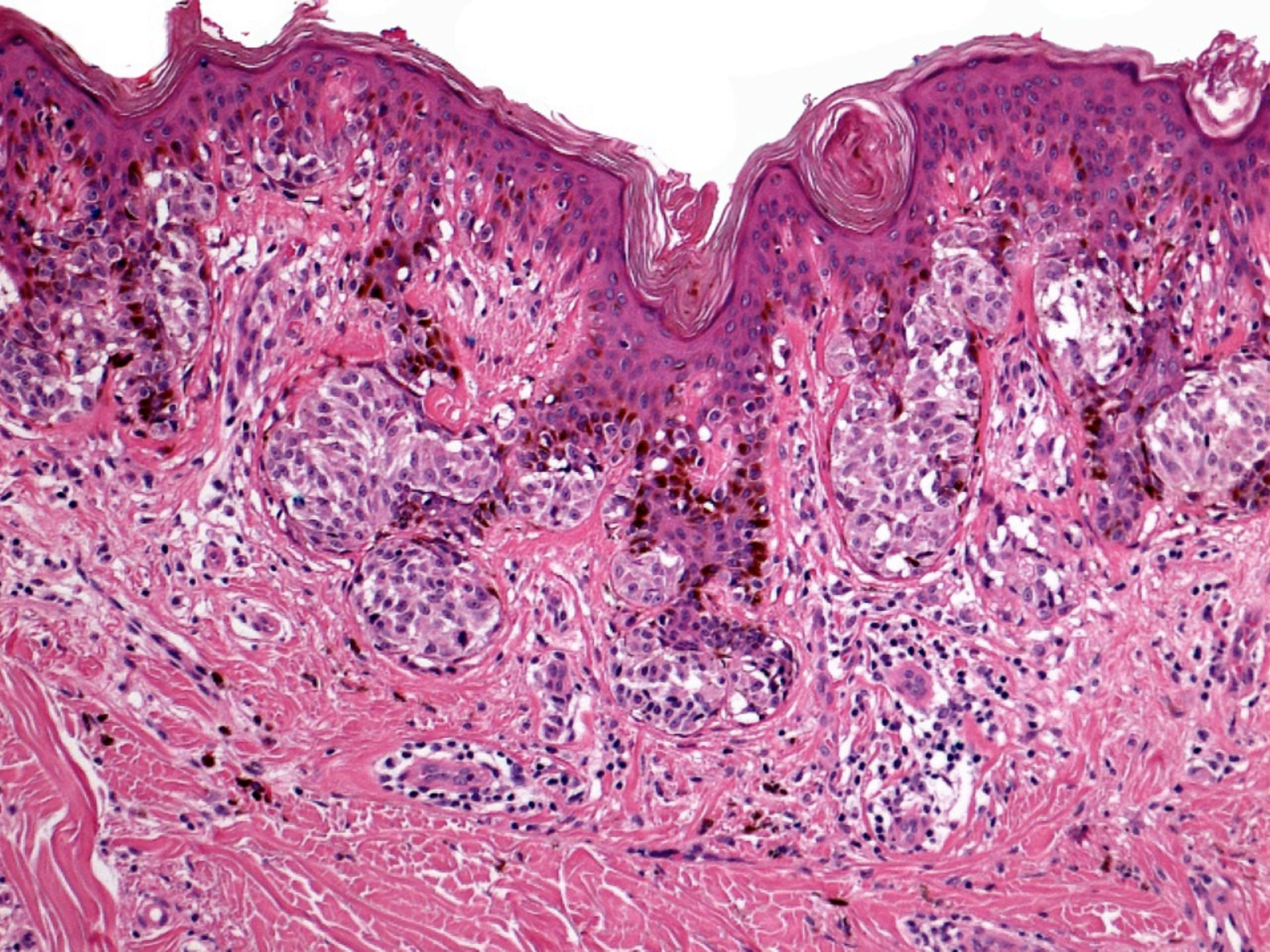
- **Congenital naevi**
- **Common acquired naevi**
- **Spitz naevi**
- **Blue naevi**
- **Dysplastic naevi**
- **Atypical Genital Naevi**

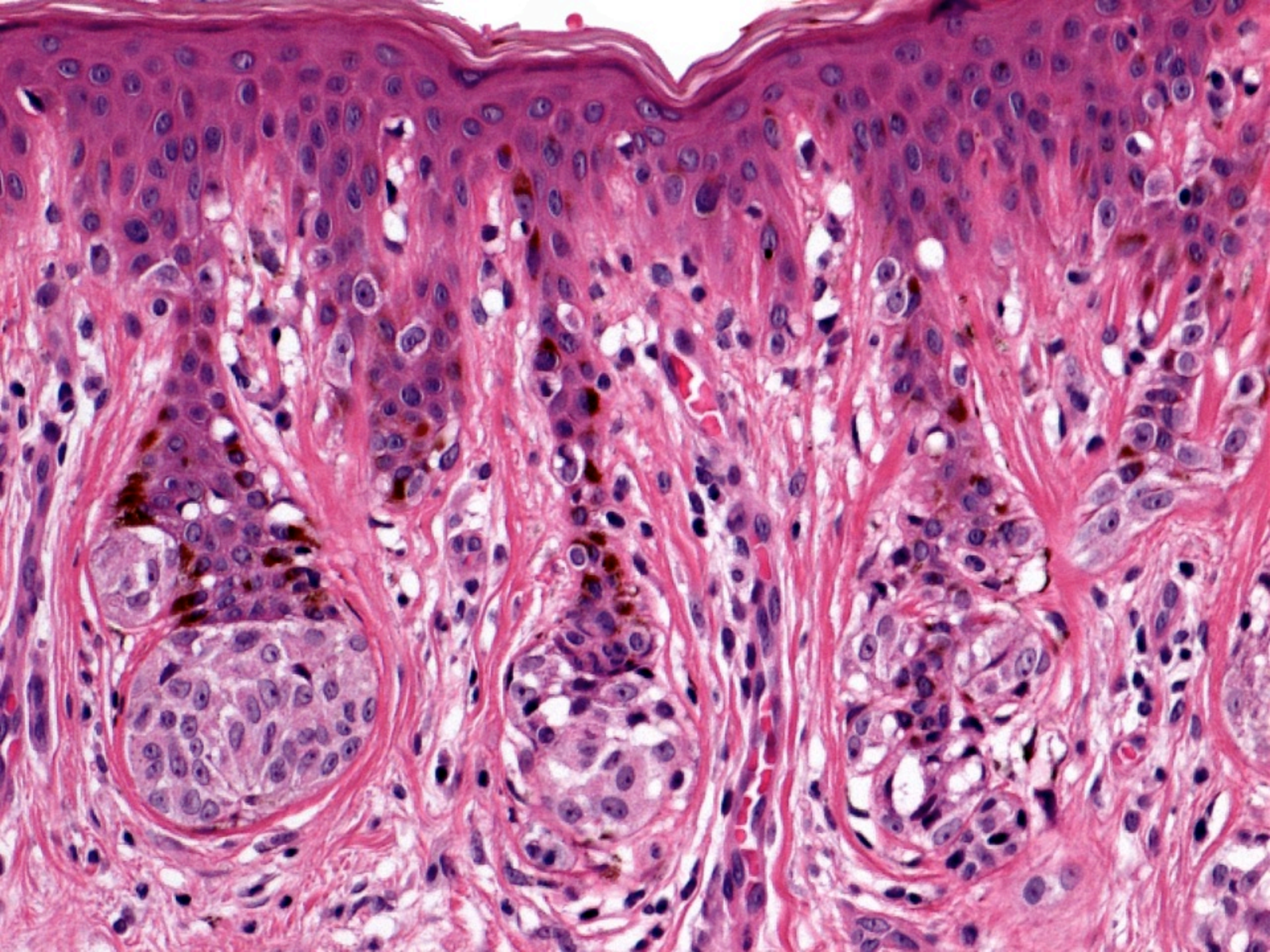
Dysplastic Naevi

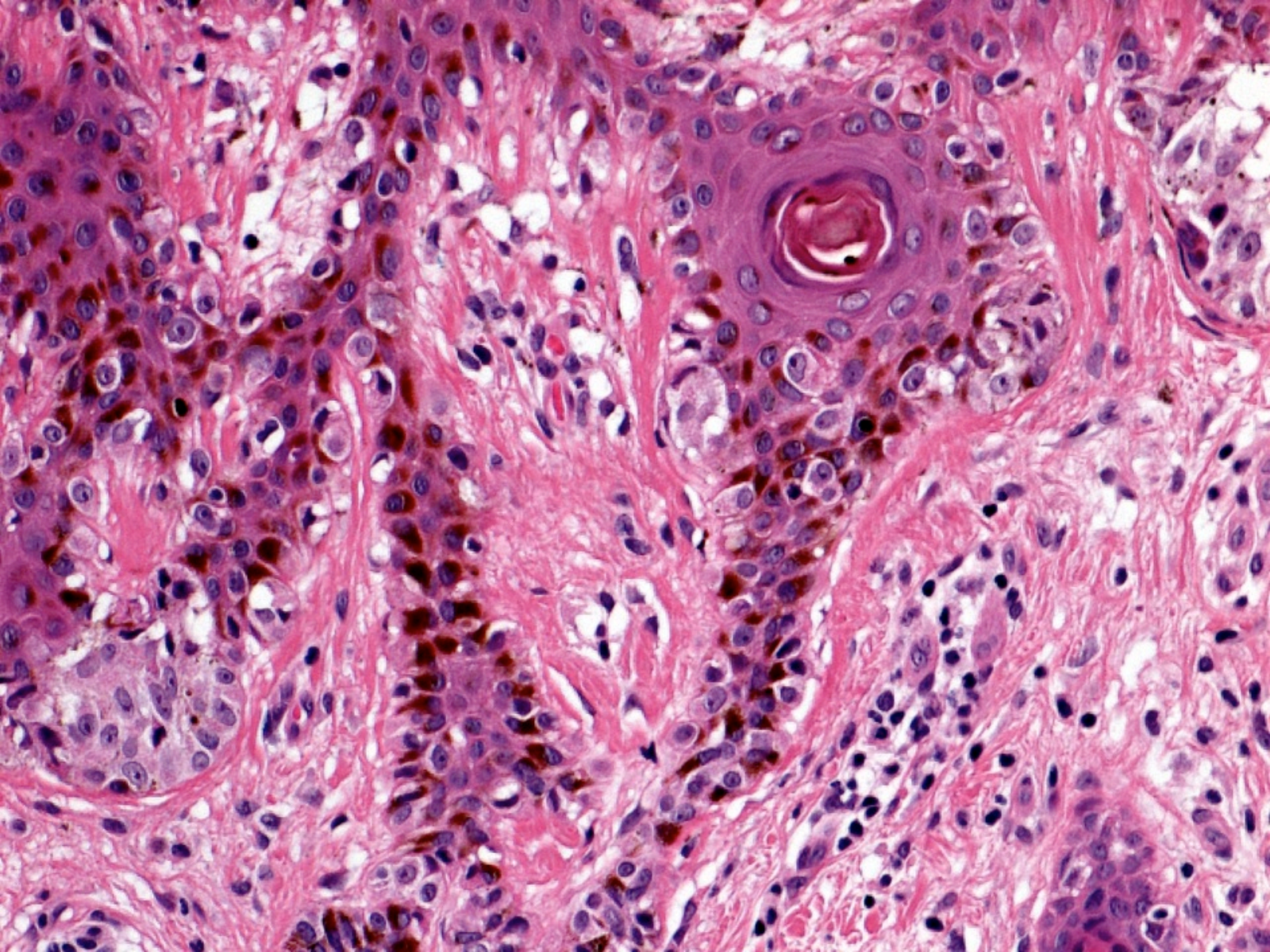
-Clinical-

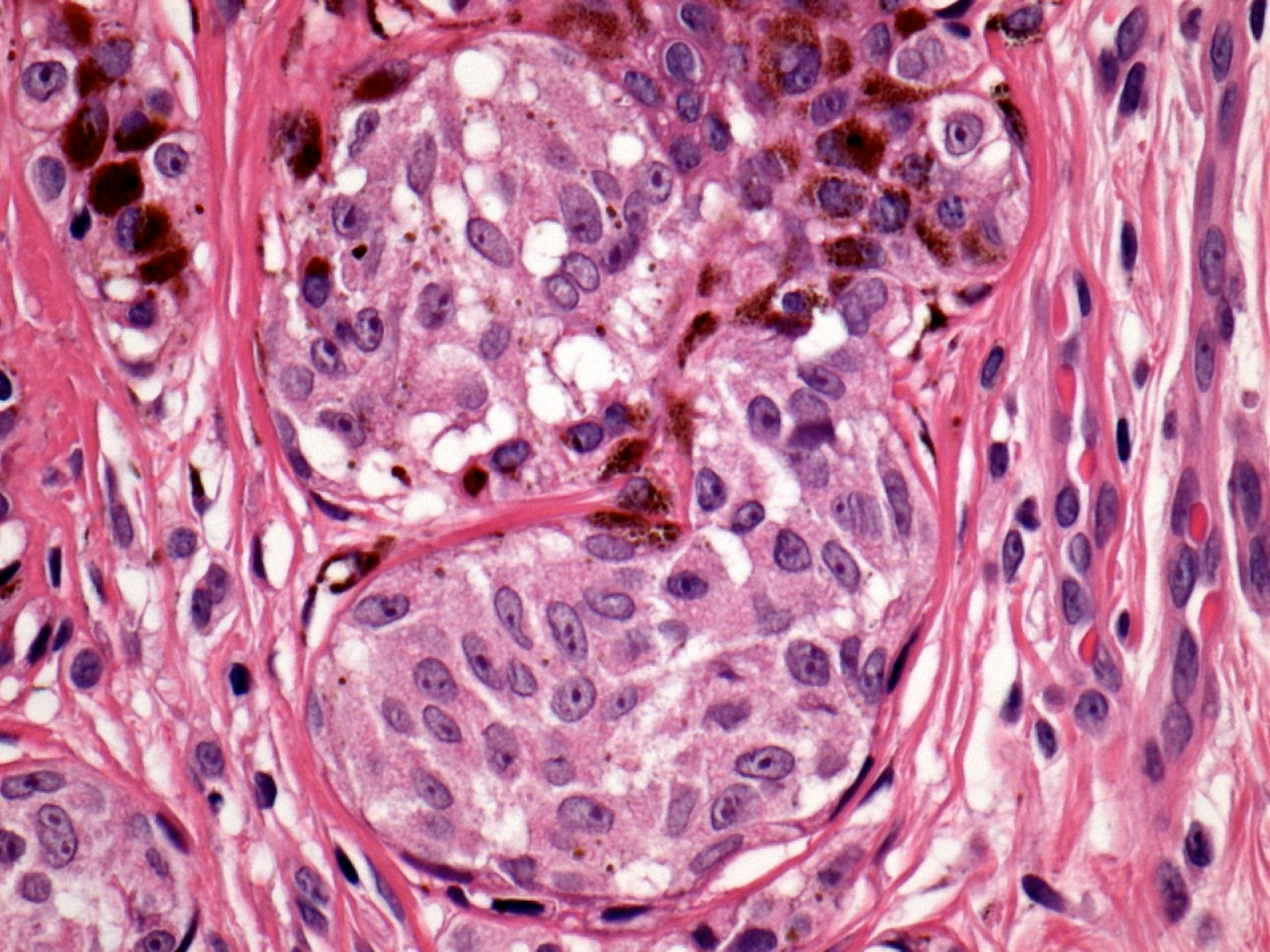
- **No precise incidence data**
- **Rare on genital skin**
- **Hair bearing skin of labia majora and perineum**
- **Young adulthood**
- **Clinical presentation similar to DN at other sites**
- **Sporadic or part of DN syndrome**

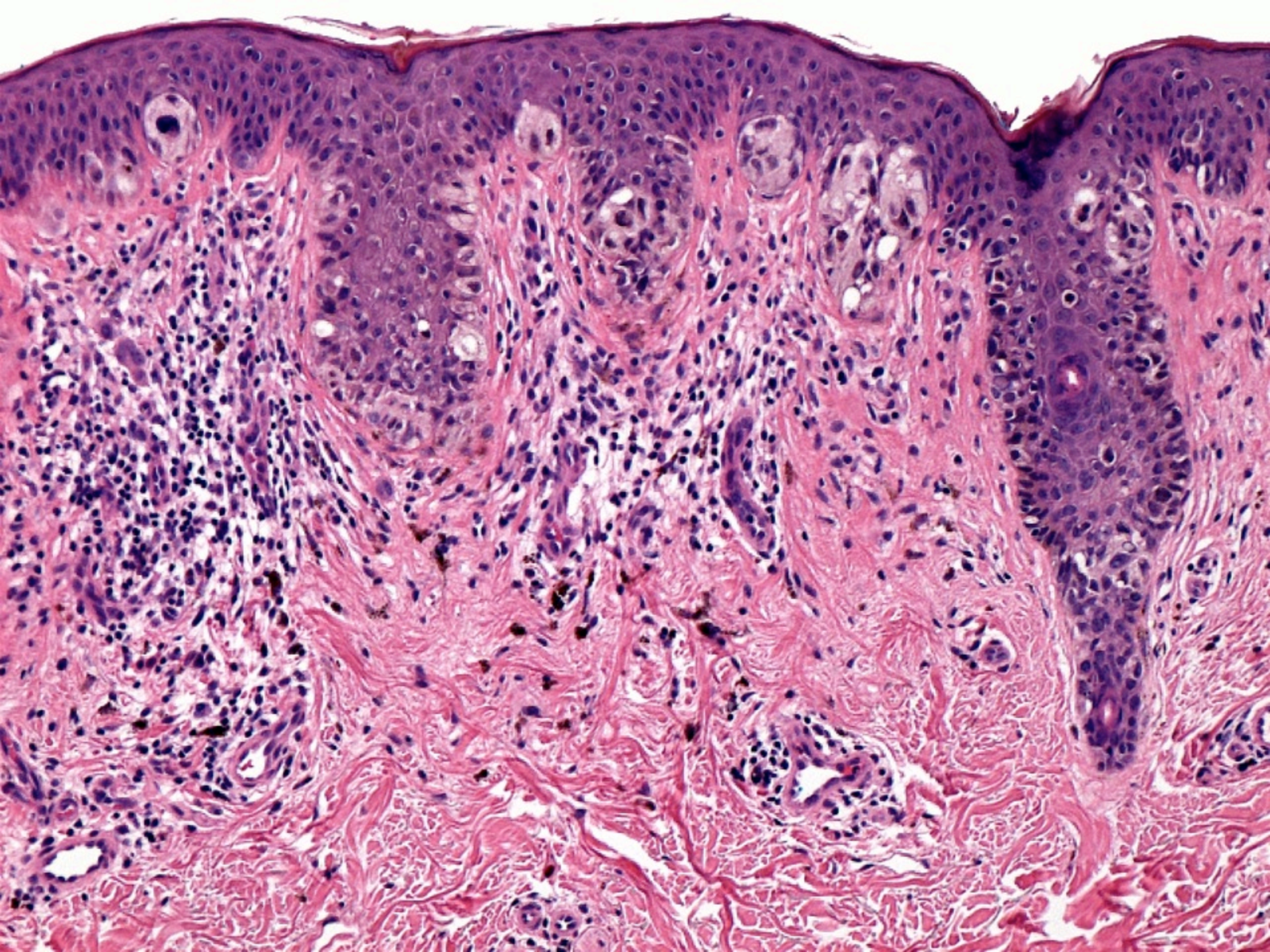


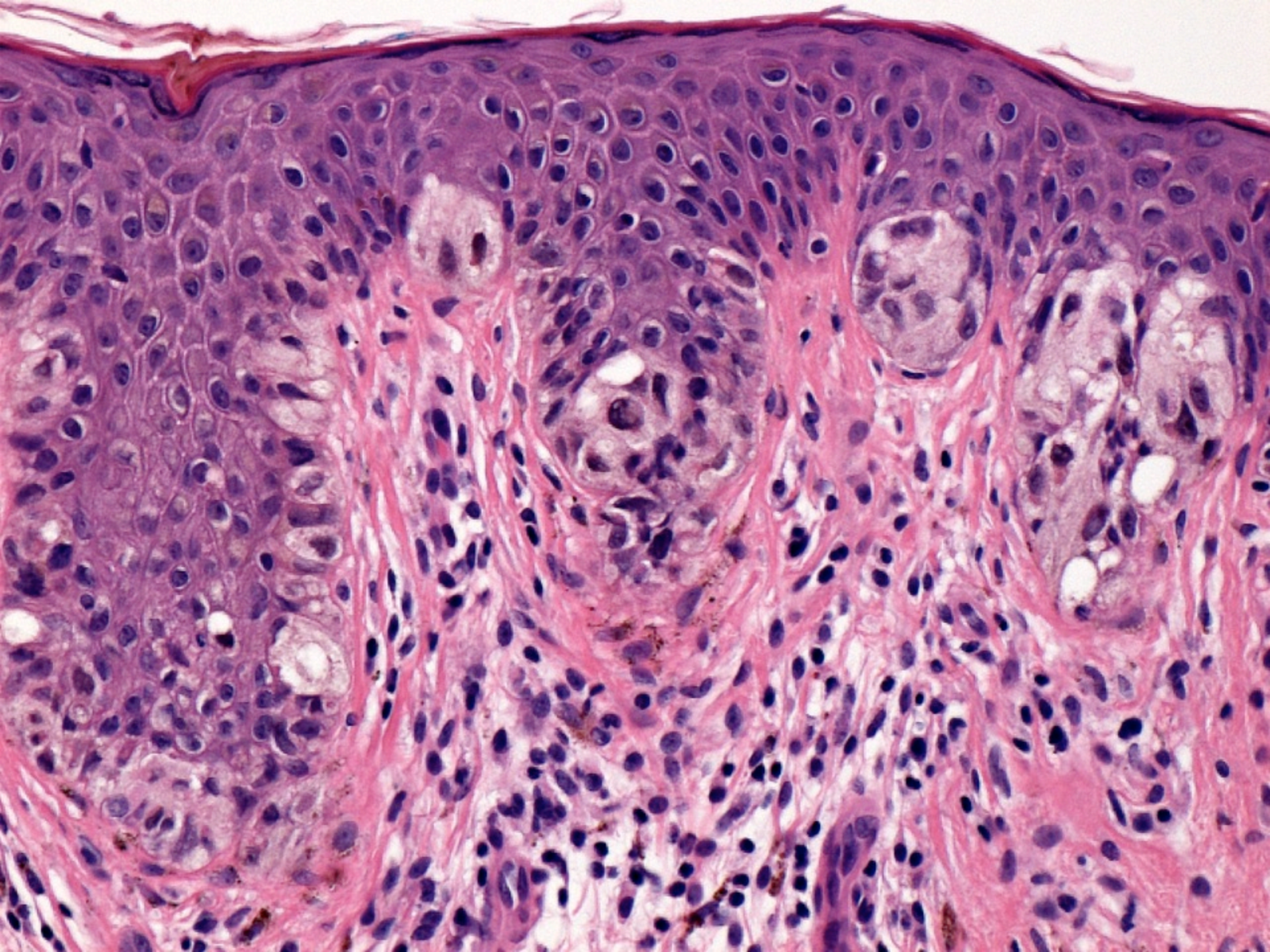












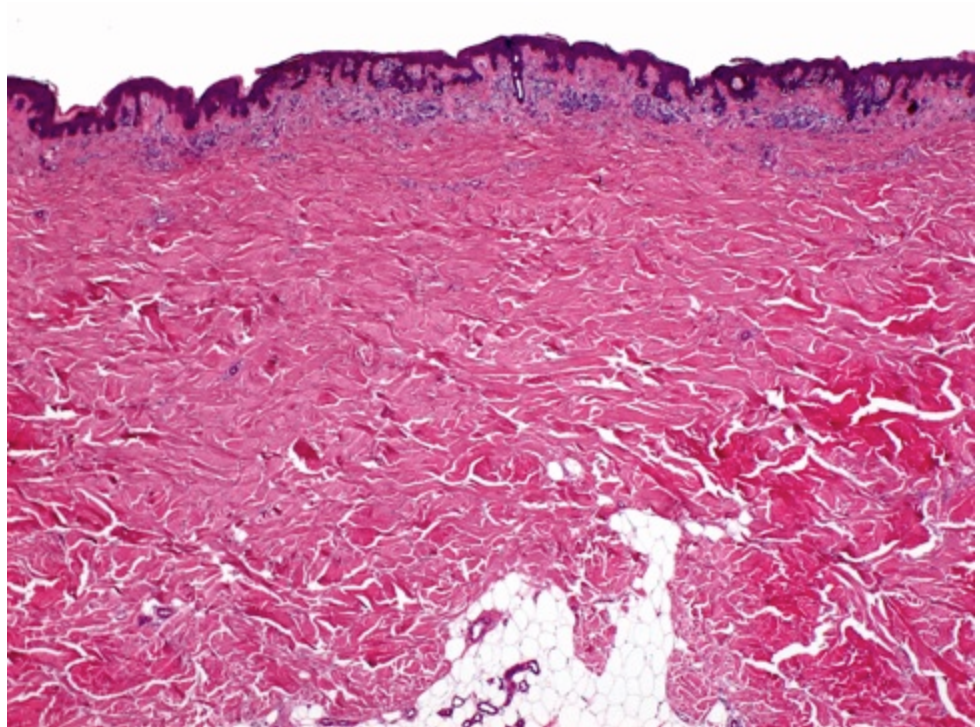
Dysplastic Naevus

-Histology-

- Slightly ill-defined and asymmetrical
- Lentiginous and nested
- Bridging and shoulder
- Cytological atypia

But

- No Pagetoid spread
- Epidermal hyperplasia
- No Dermal expansile growth
- No Dermal mitotic activity



Atypical Genital-Type Naevi

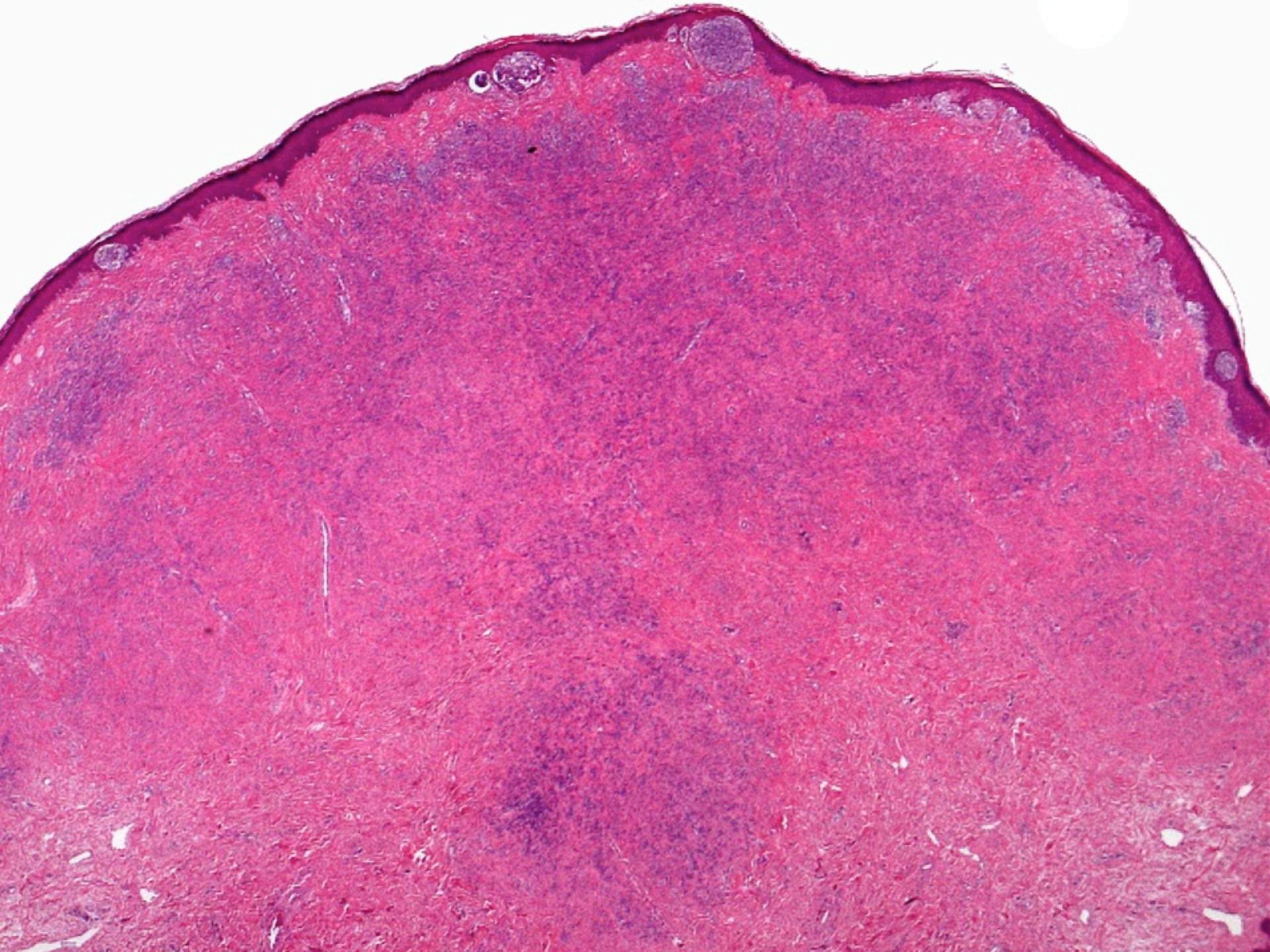
-General-

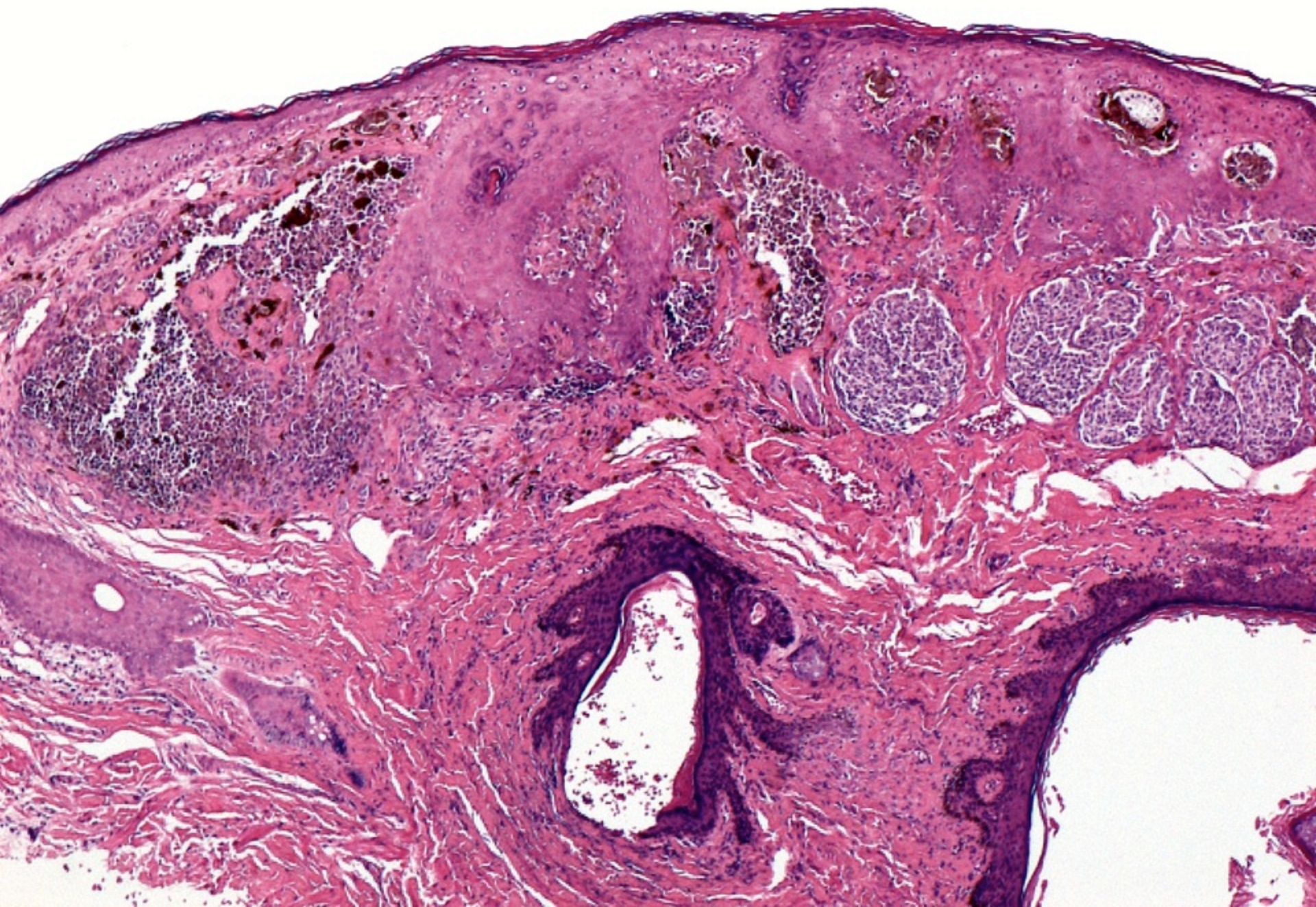
- **Original report in 1981 (Friedman and Ackerman)**
- **First series in 1998 (Clark et al. 1998, Hum Pathol)**
- **Rare and poorly documented**
- **2.3% patients at routine GYN exam**
- **10% of vulval melanocytic lesions**
- **“Special site naevus”**
- **Worrying clinical and histological features**
- **1/3 proposed histological dx: melanoma (Clark et al.)**
- **Benign behaviour (Gleason et al. 2008, Am J Surgical Pathol)**

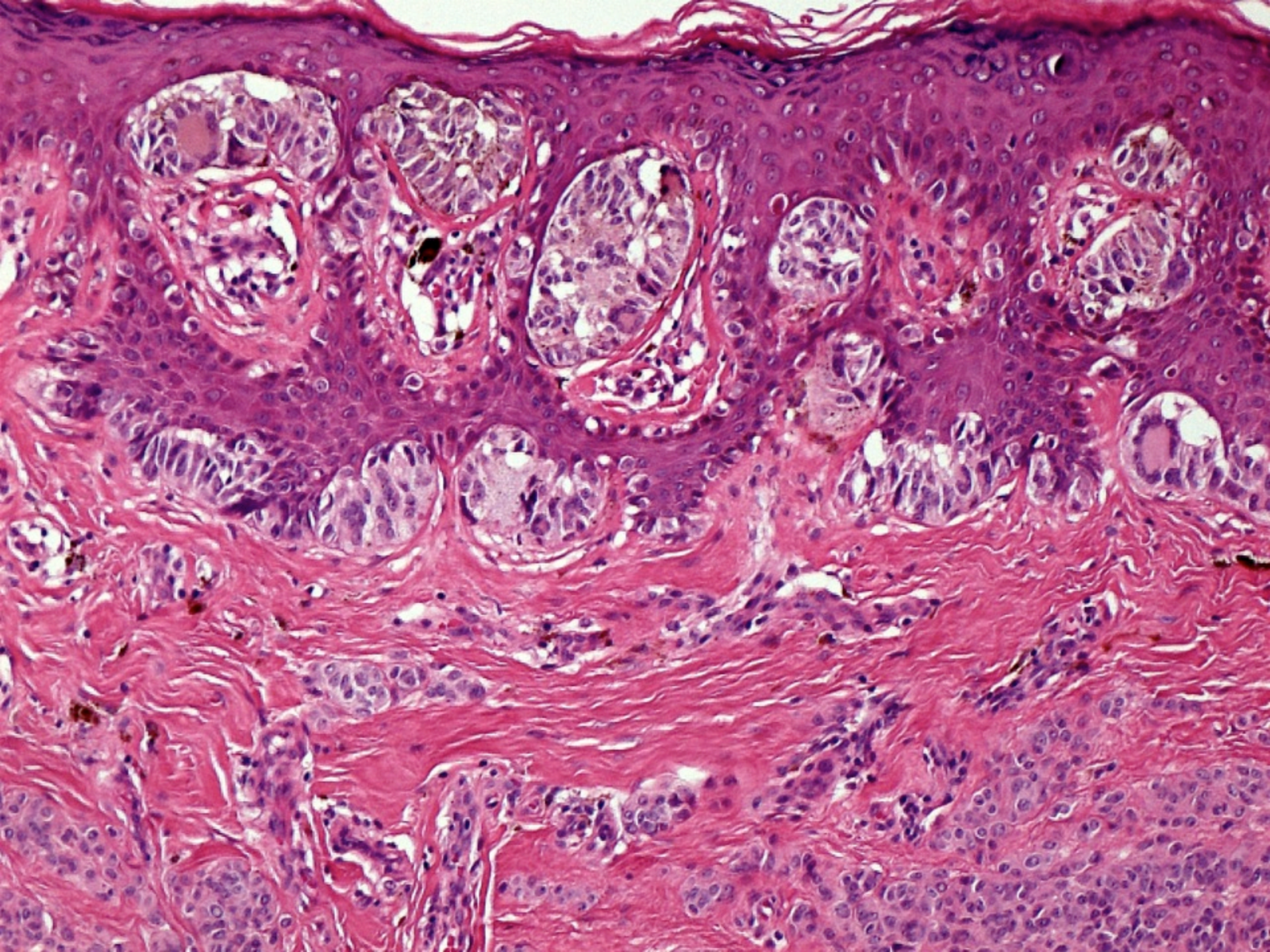
Atypical Genital-Type Naevi

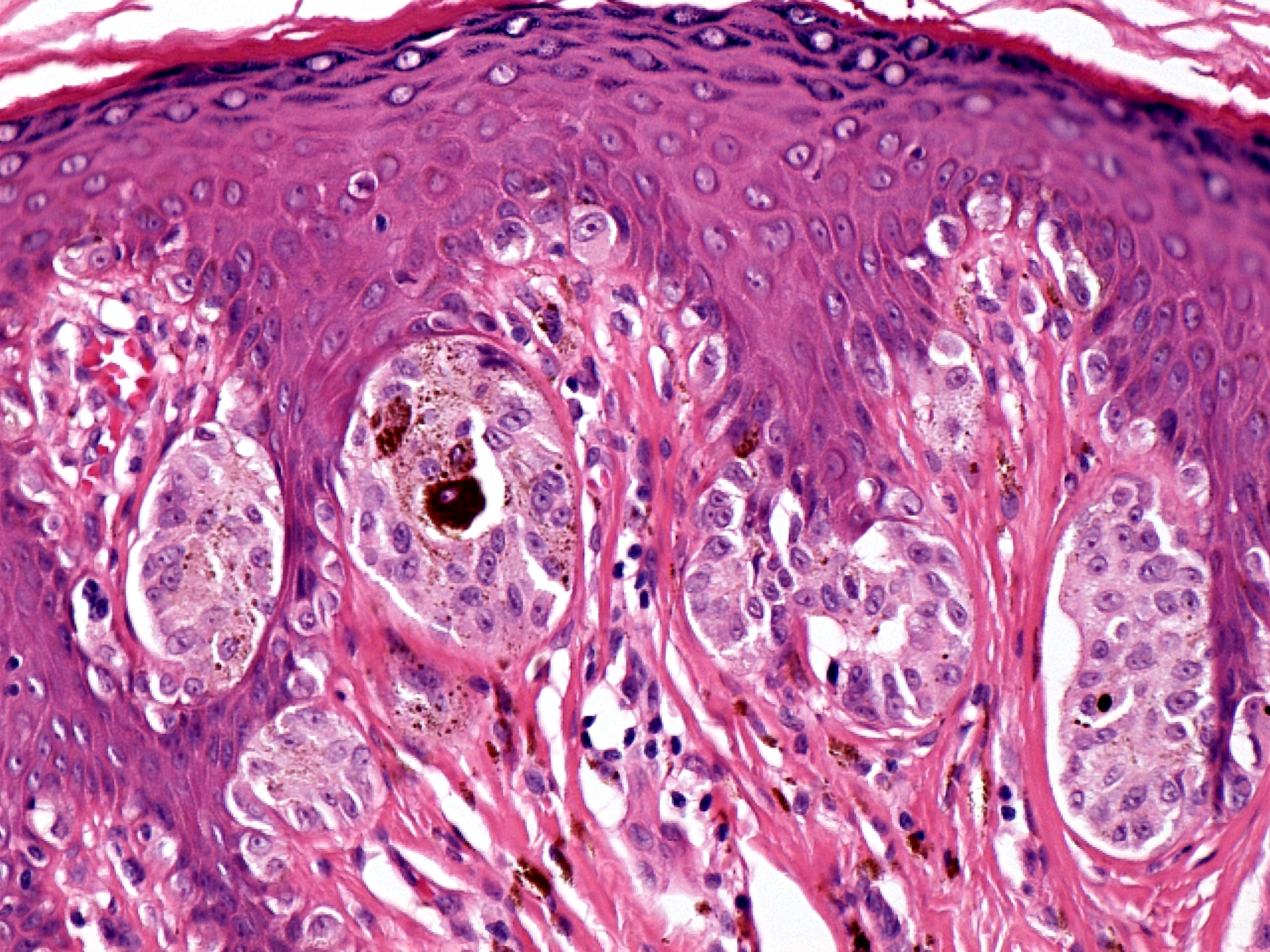
-Clinical-

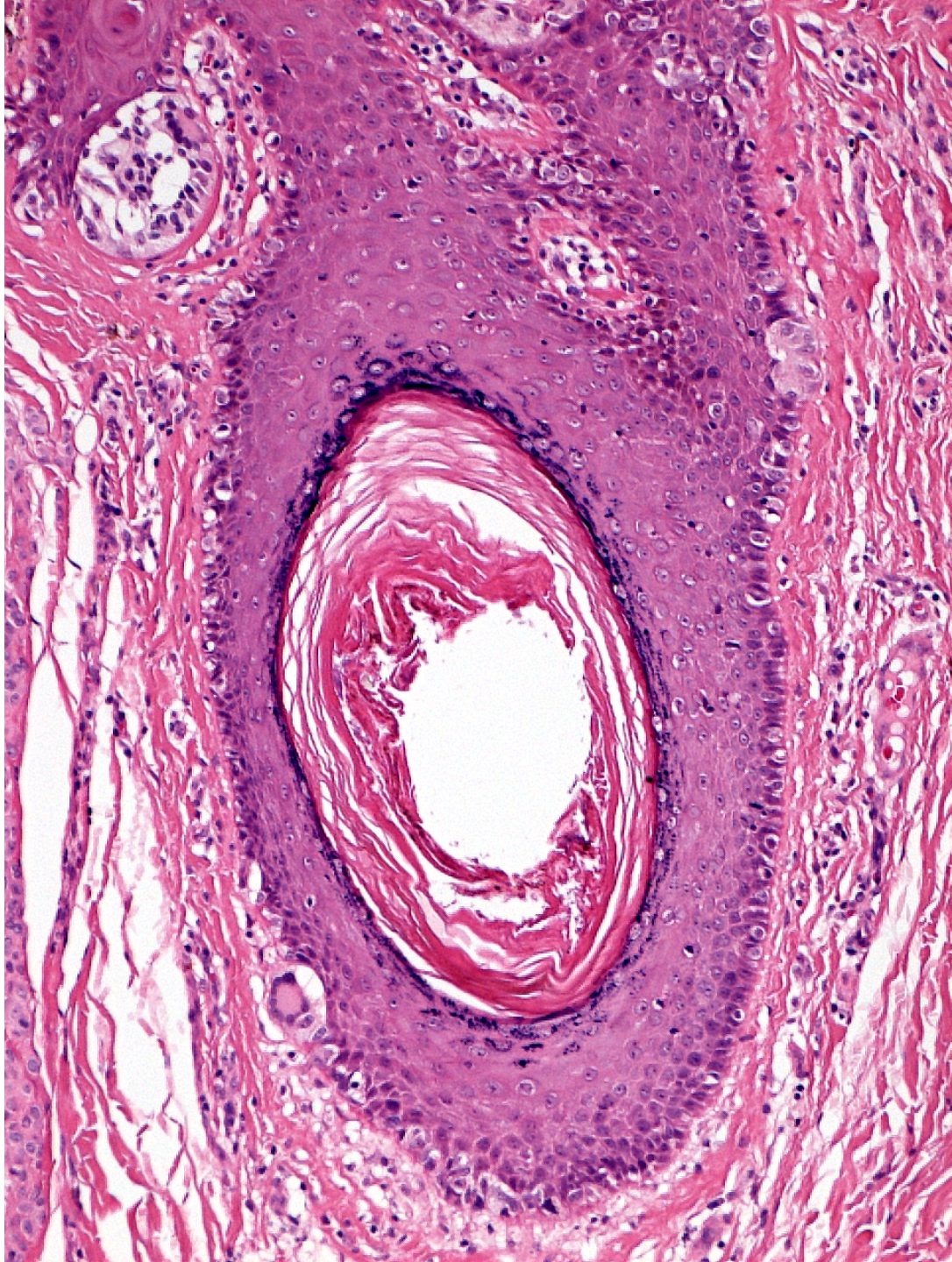
- **Adolescents and young adults (median age:26years)**
- **Strong female predilection**
- **Vulva (mucosa and skin)**
- **Mons pubis, perineum**
- **Clinically atypical**
(large, hyperpigmented, irregular)
- **Mean size: 6 mm (range: 2-20mm)**

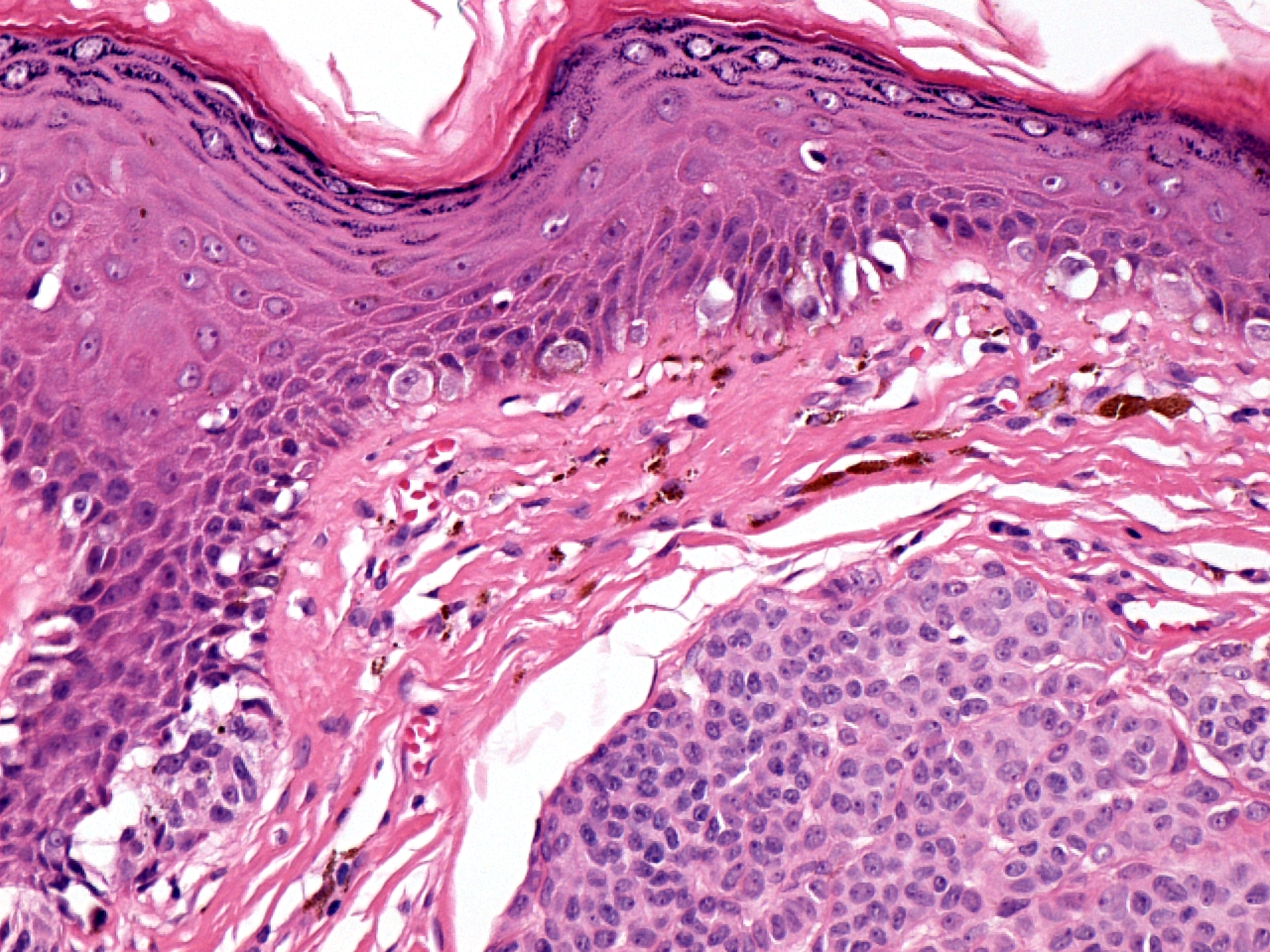


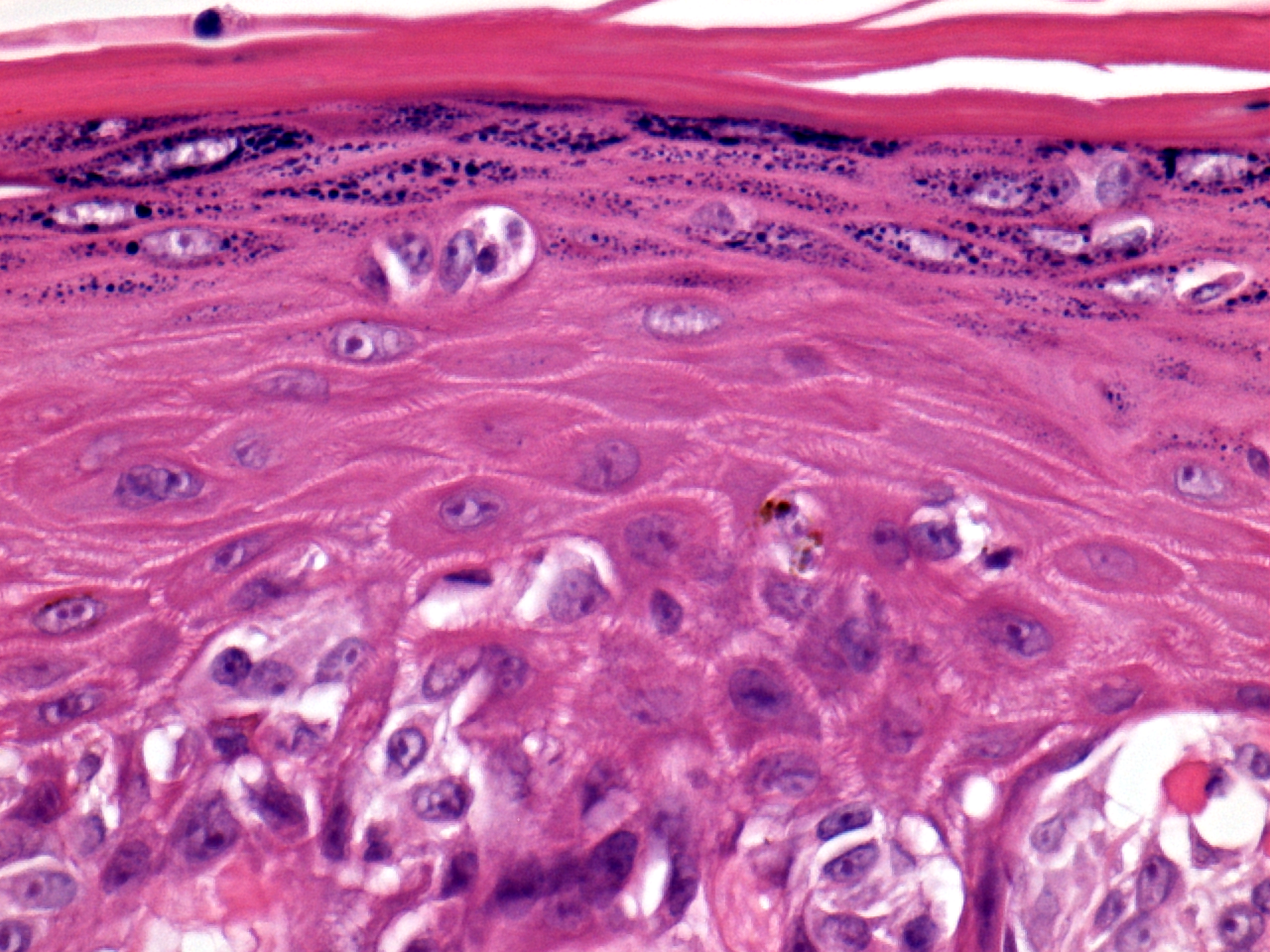


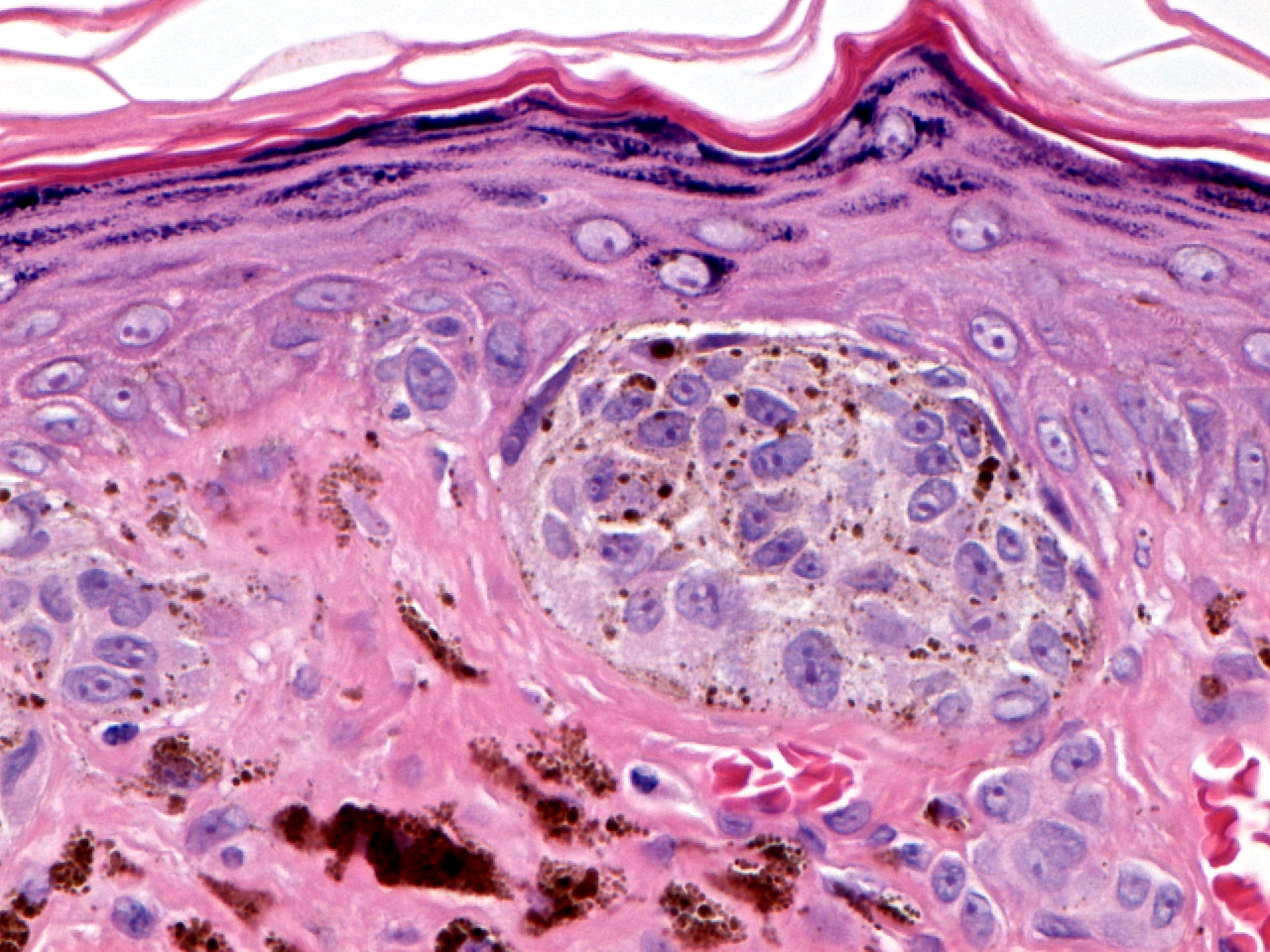


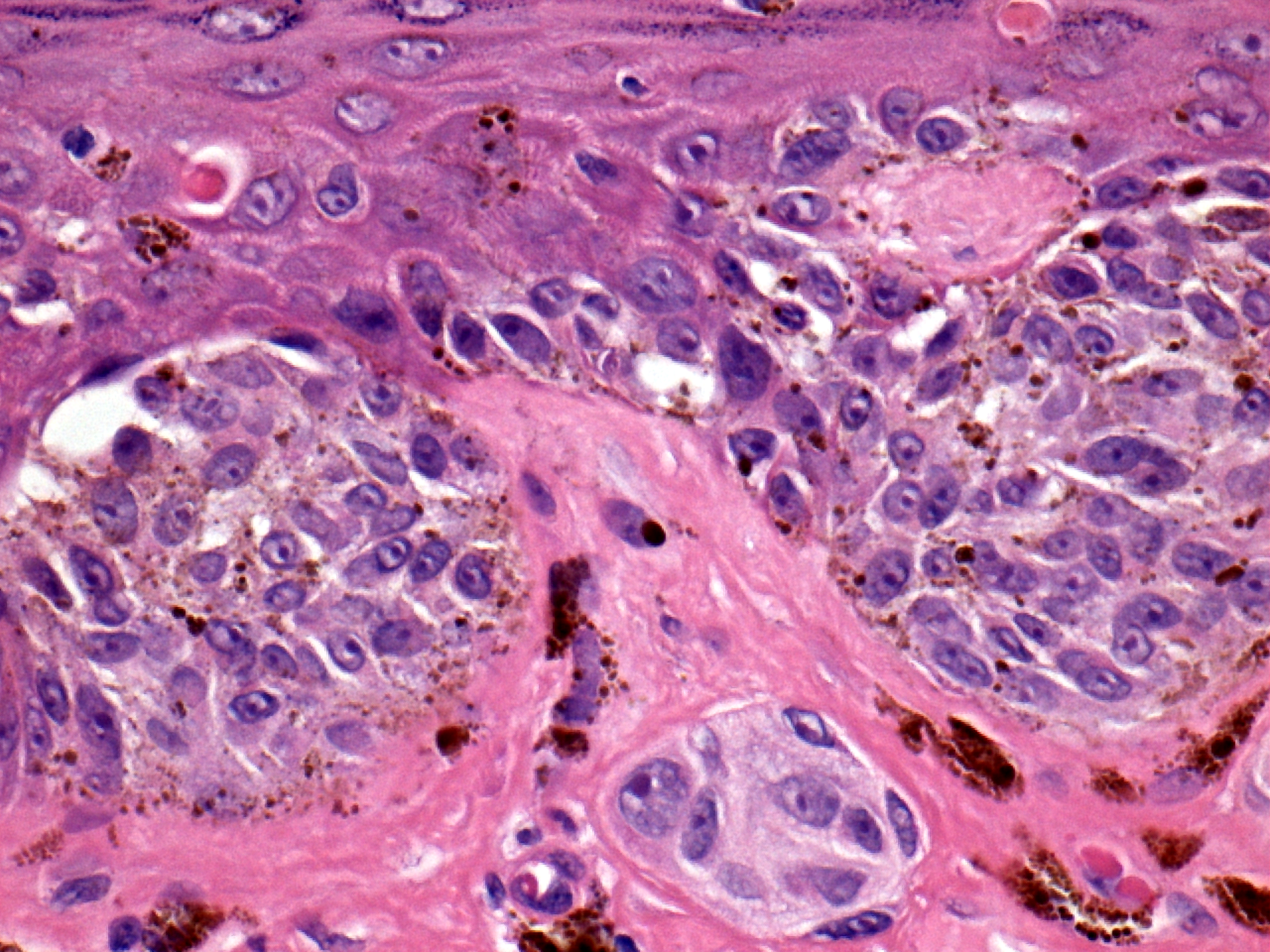


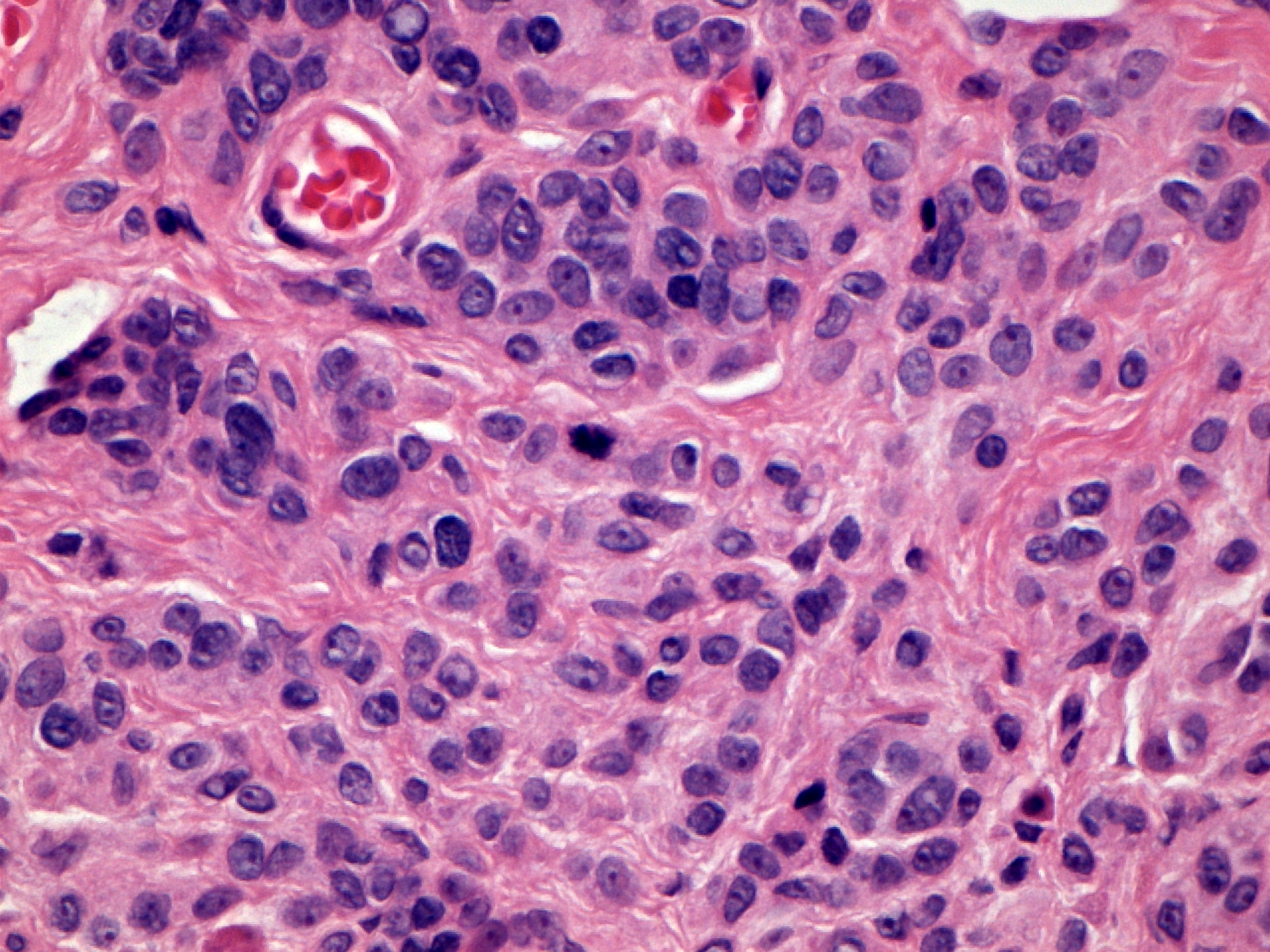


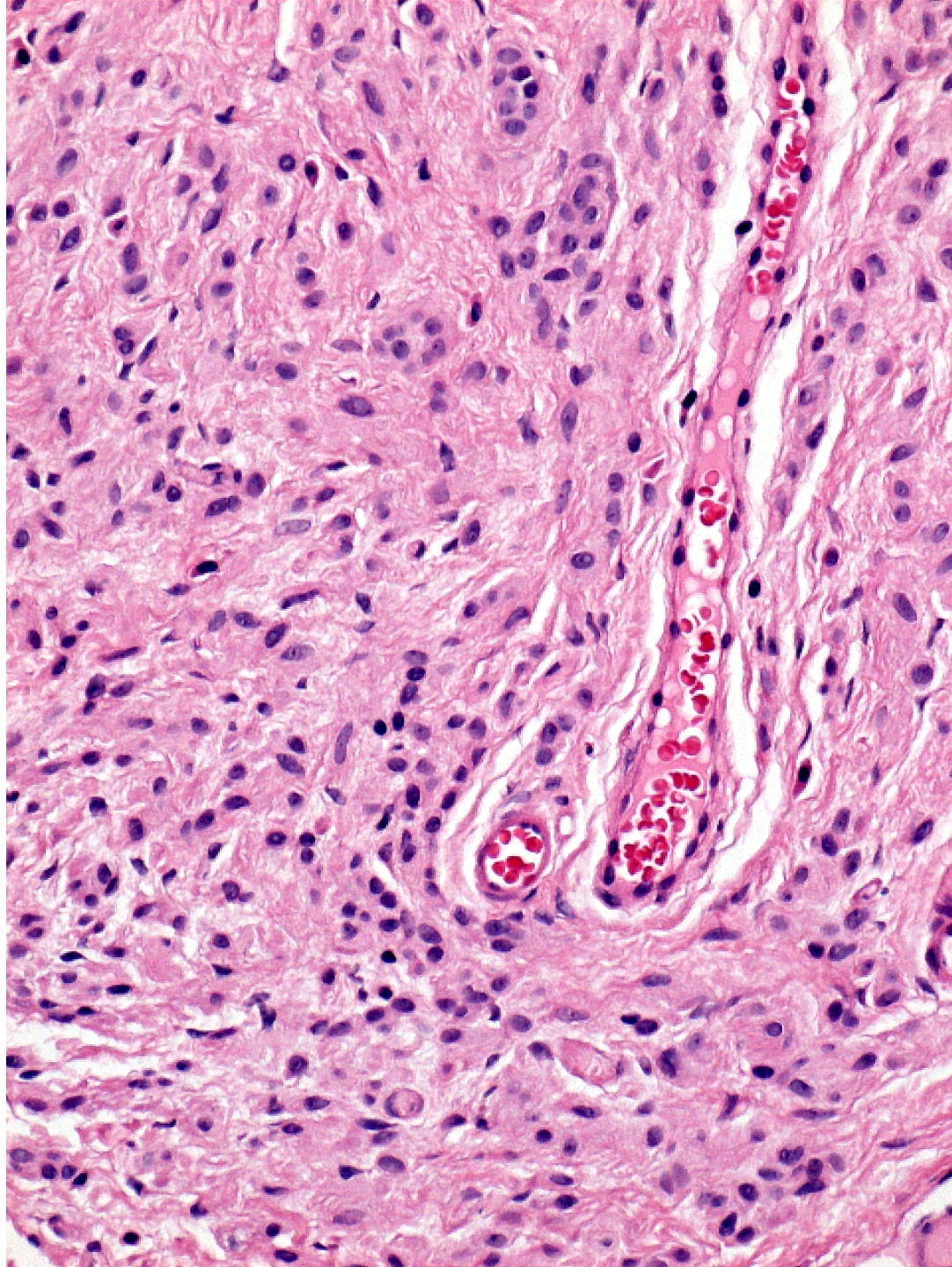


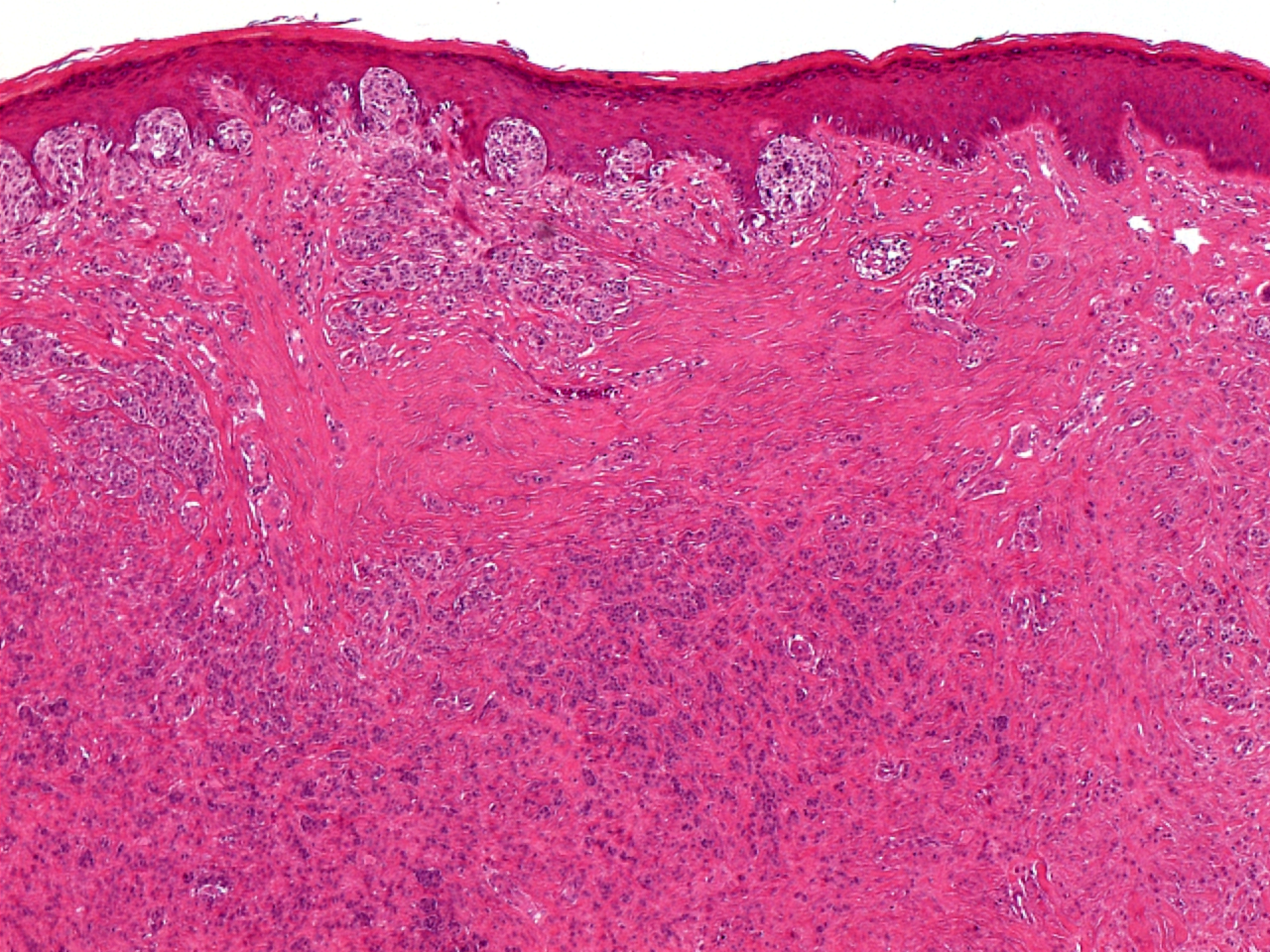


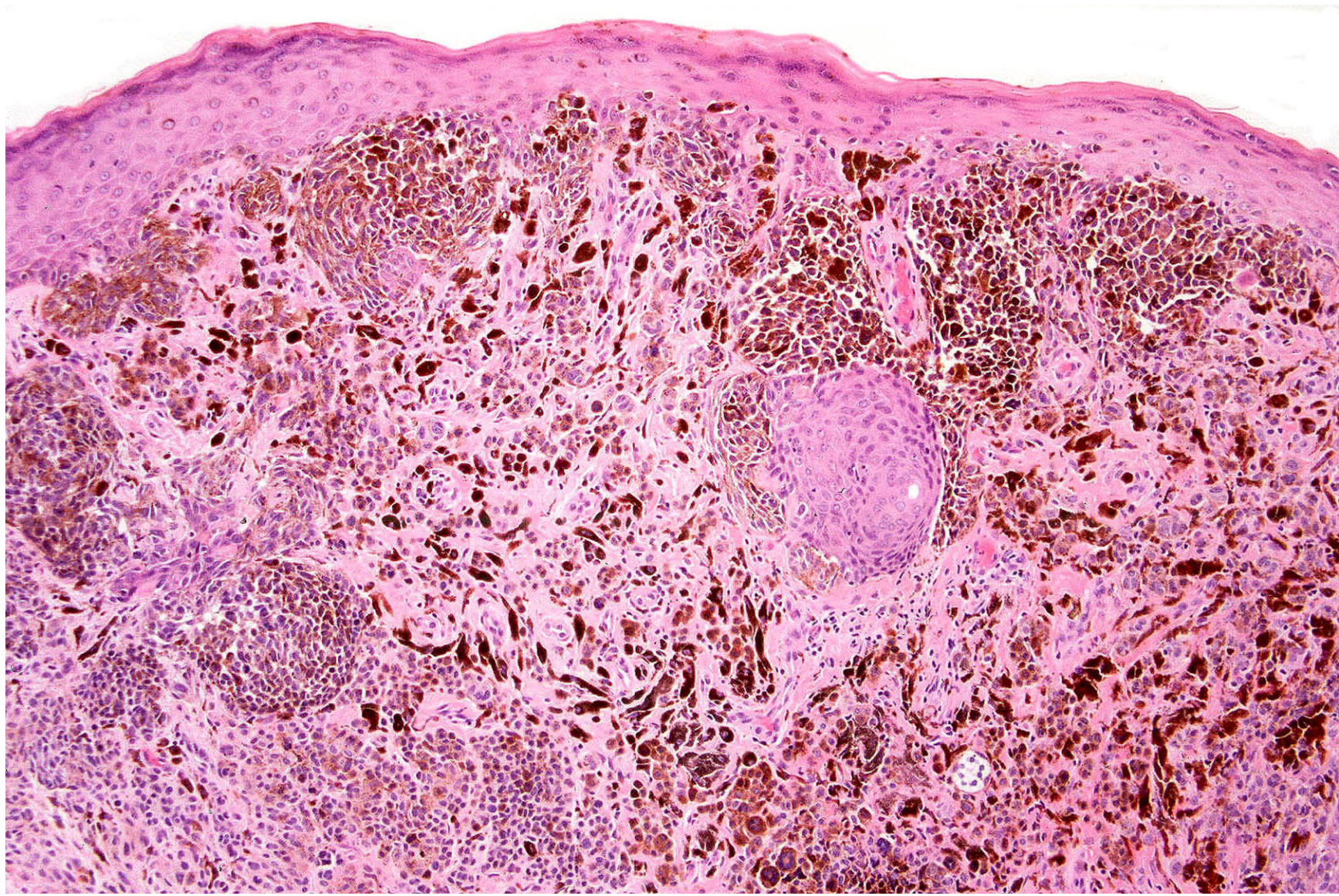


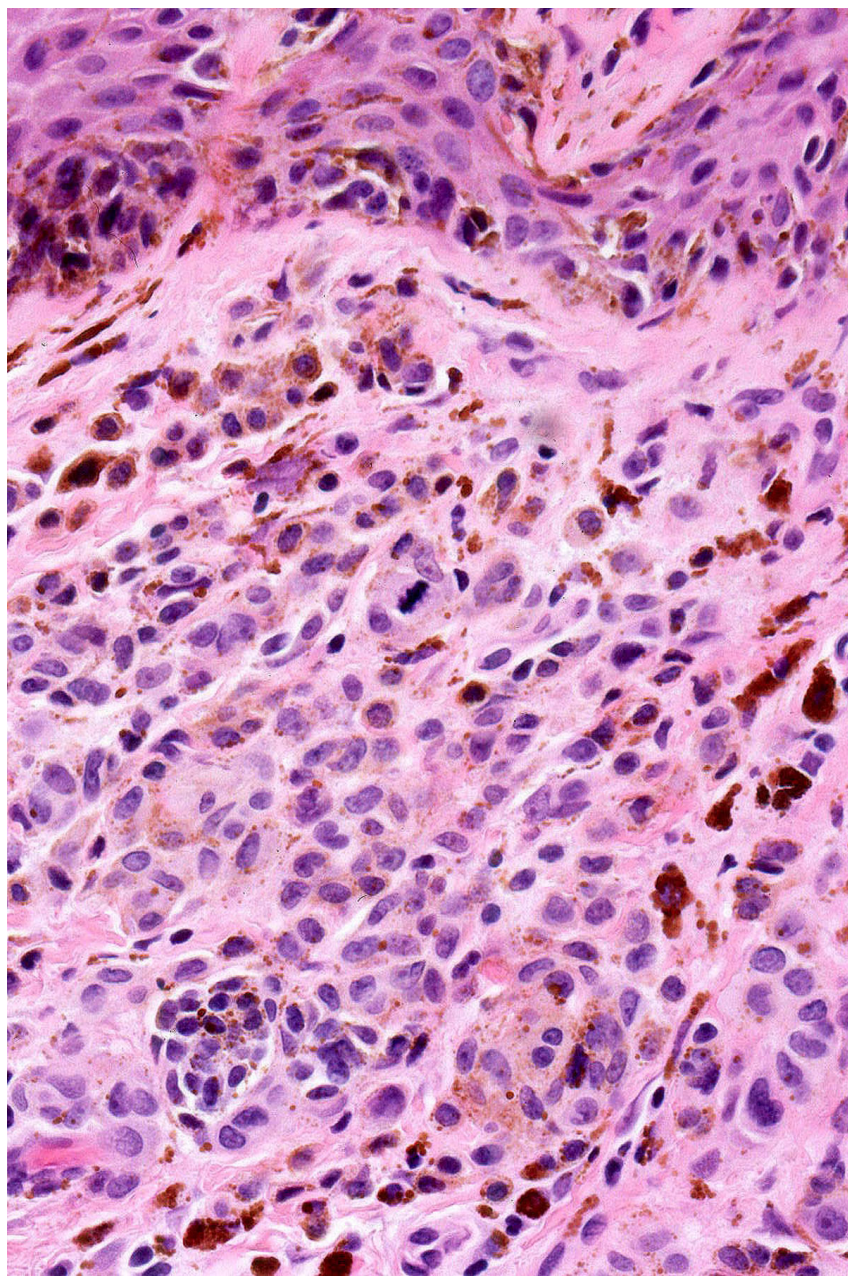


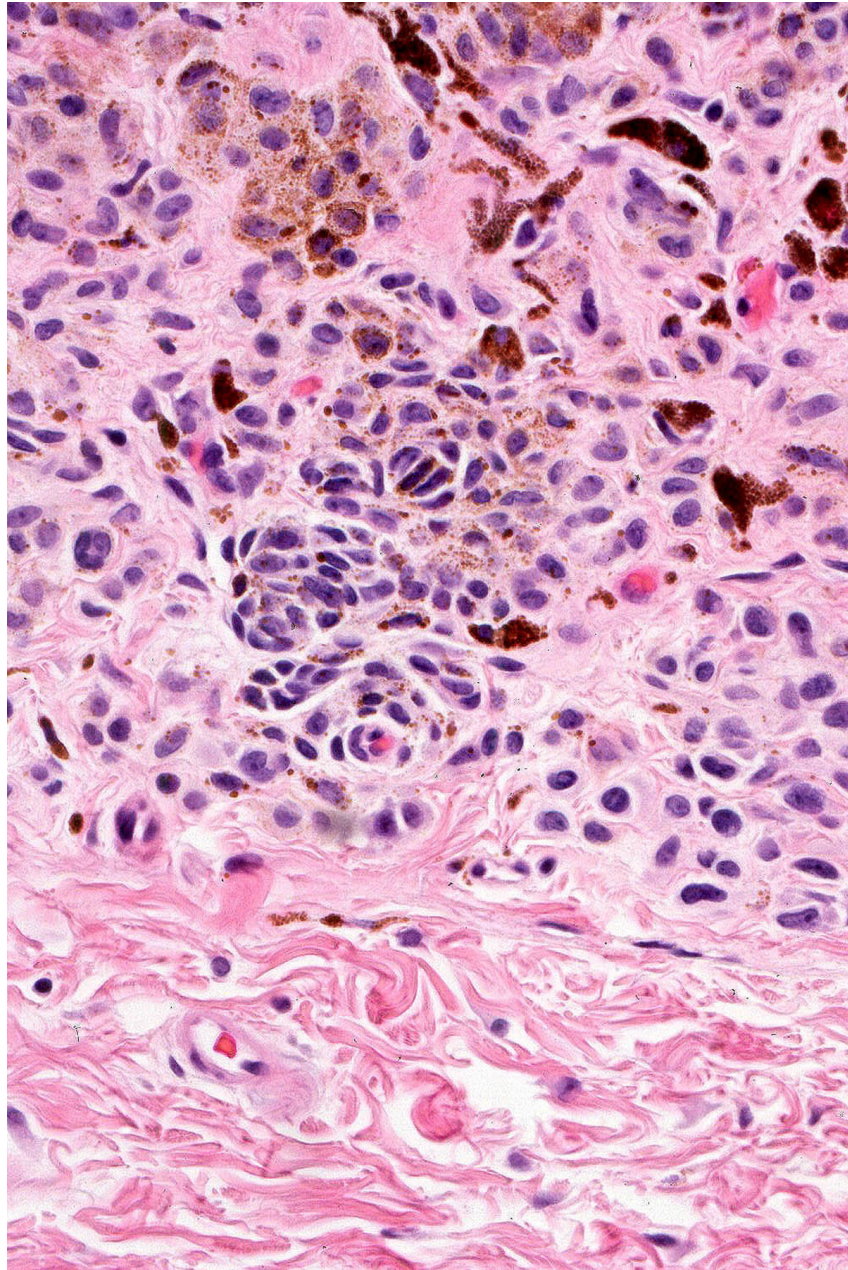


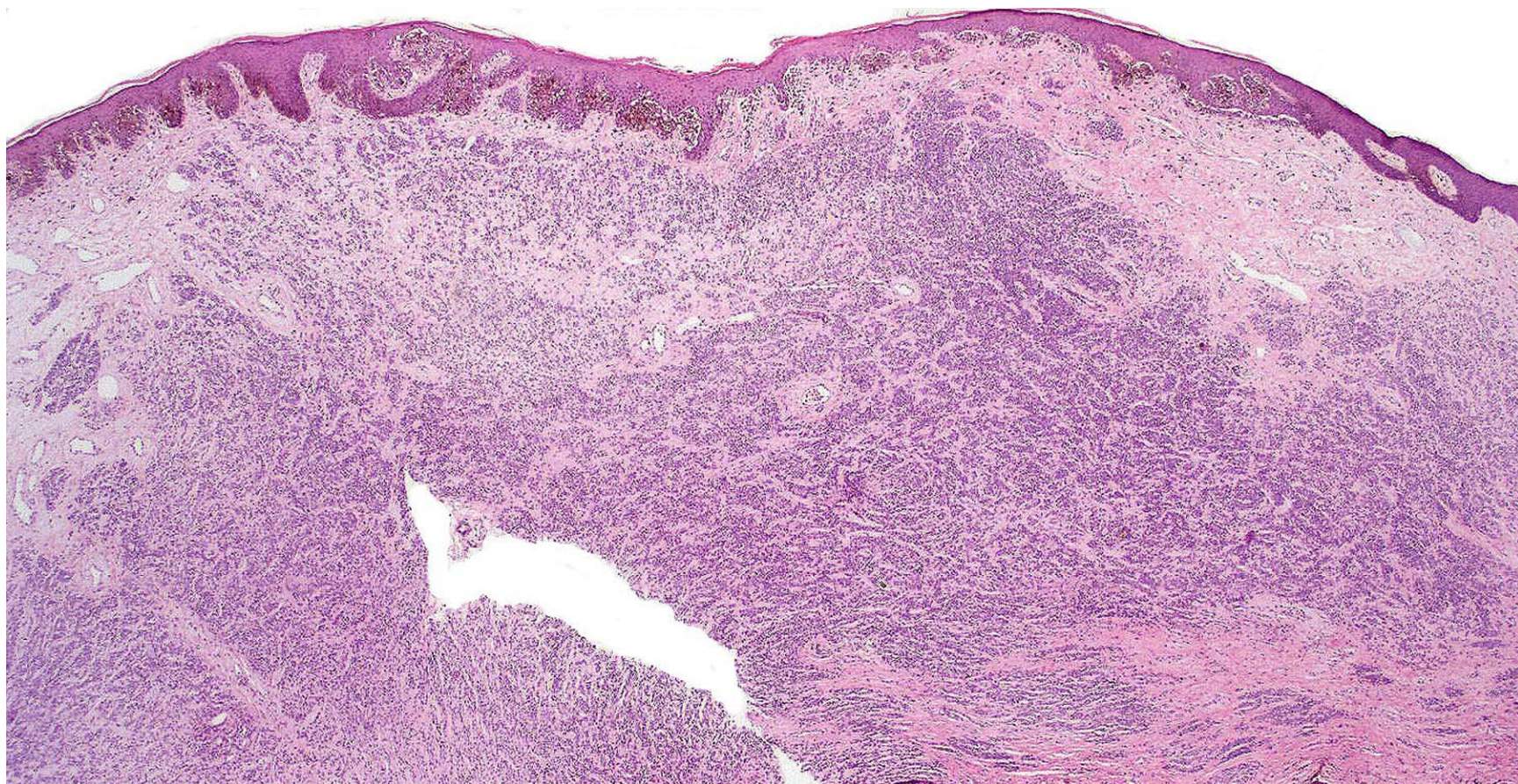


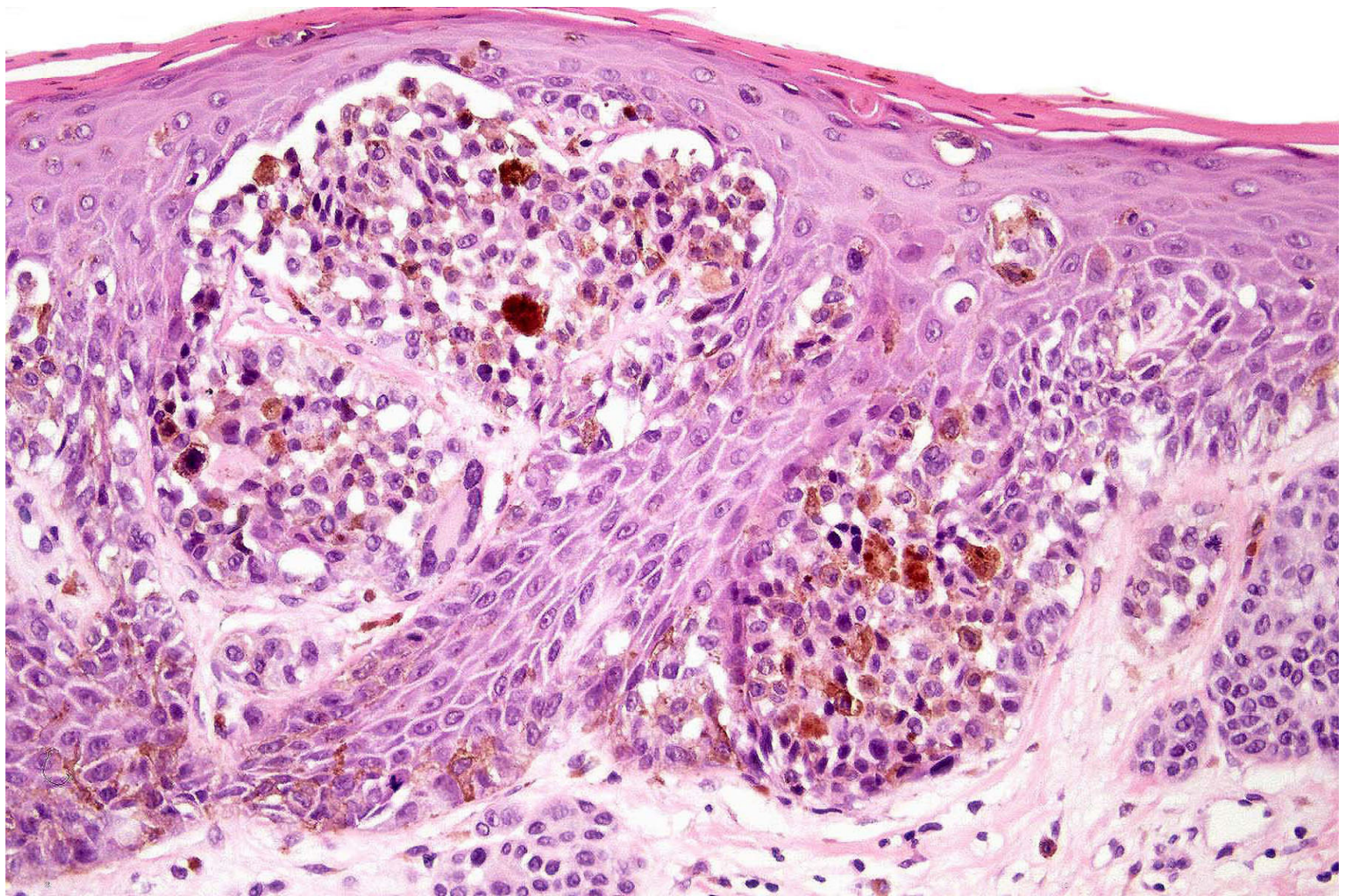


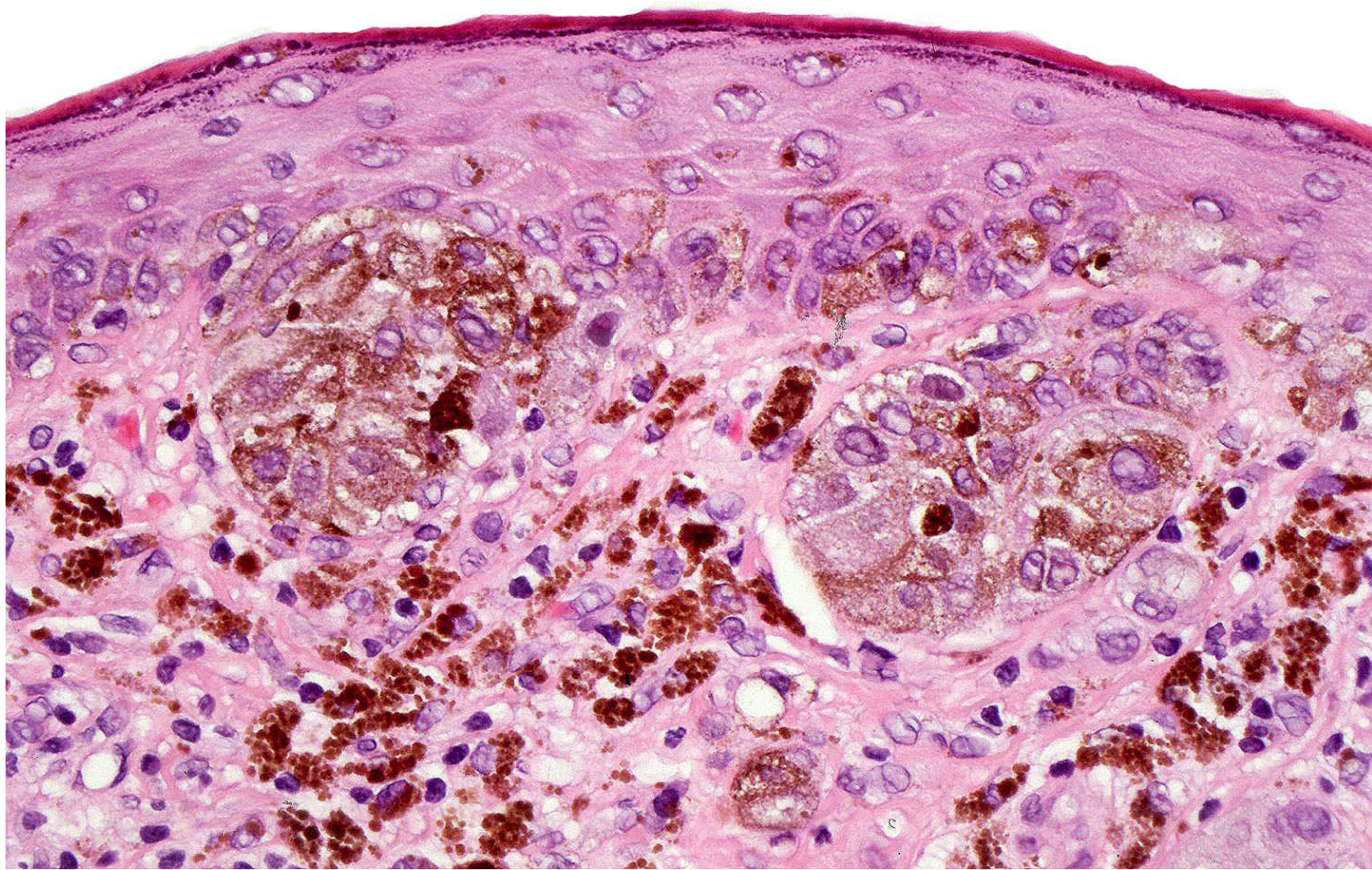


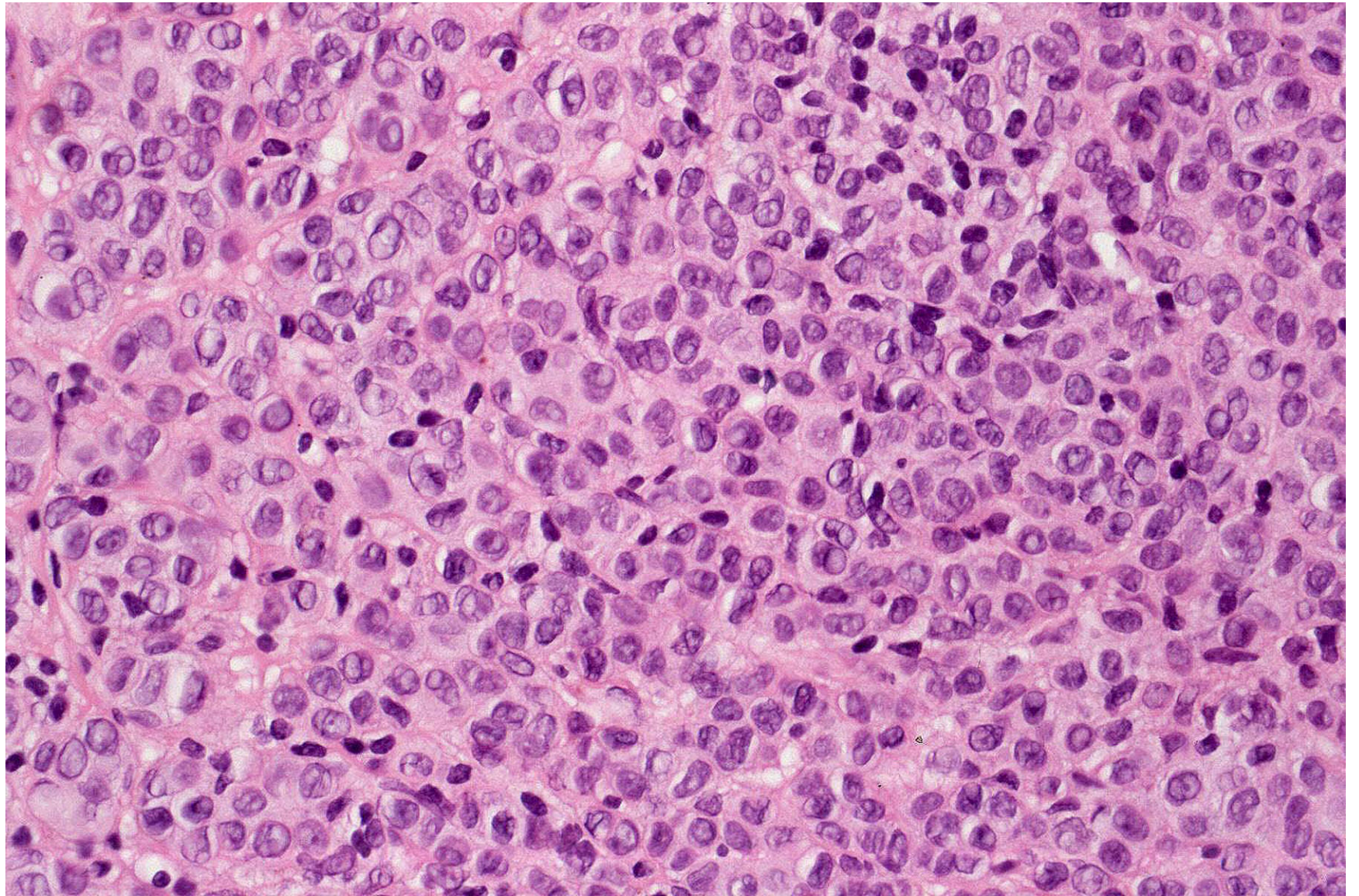


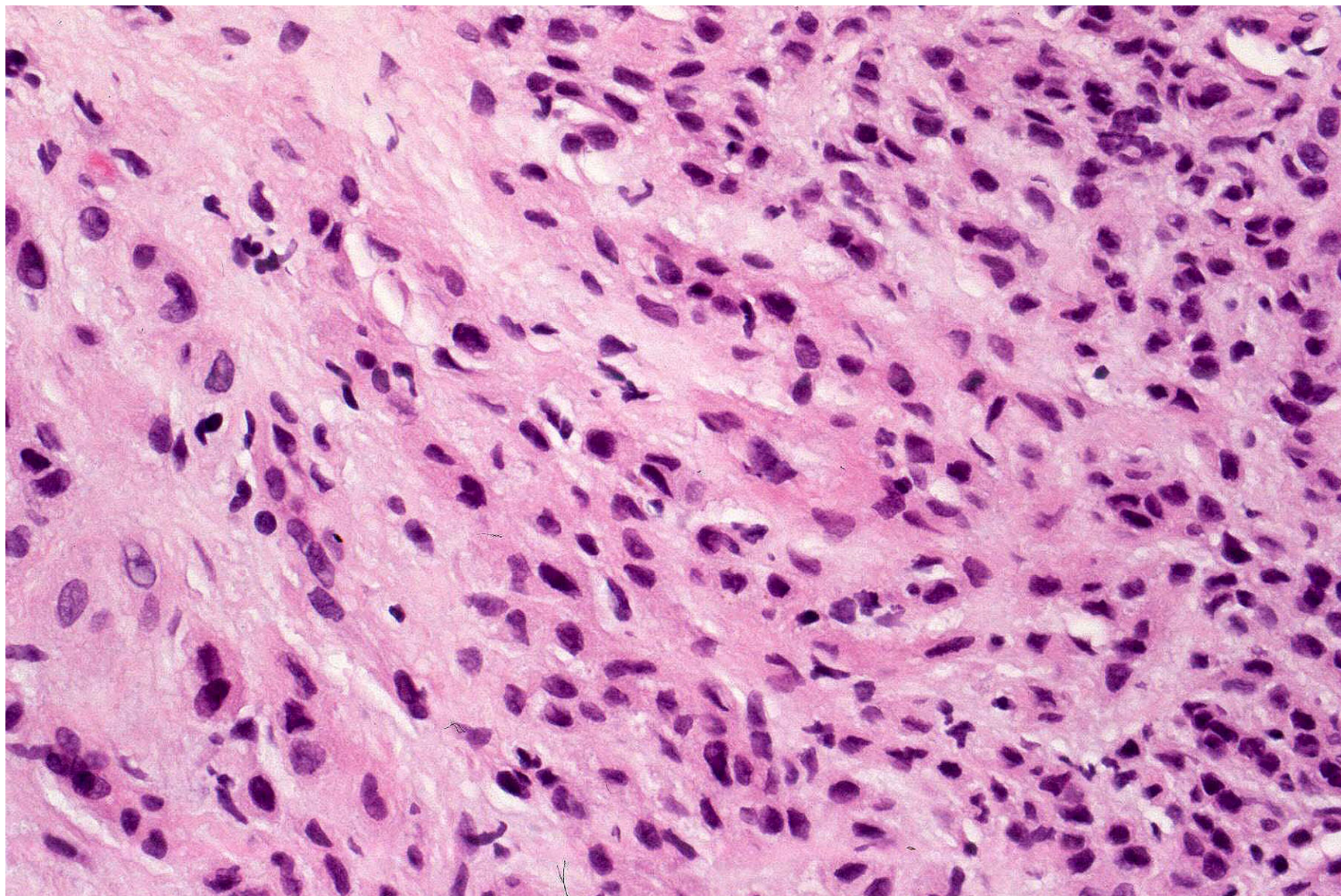


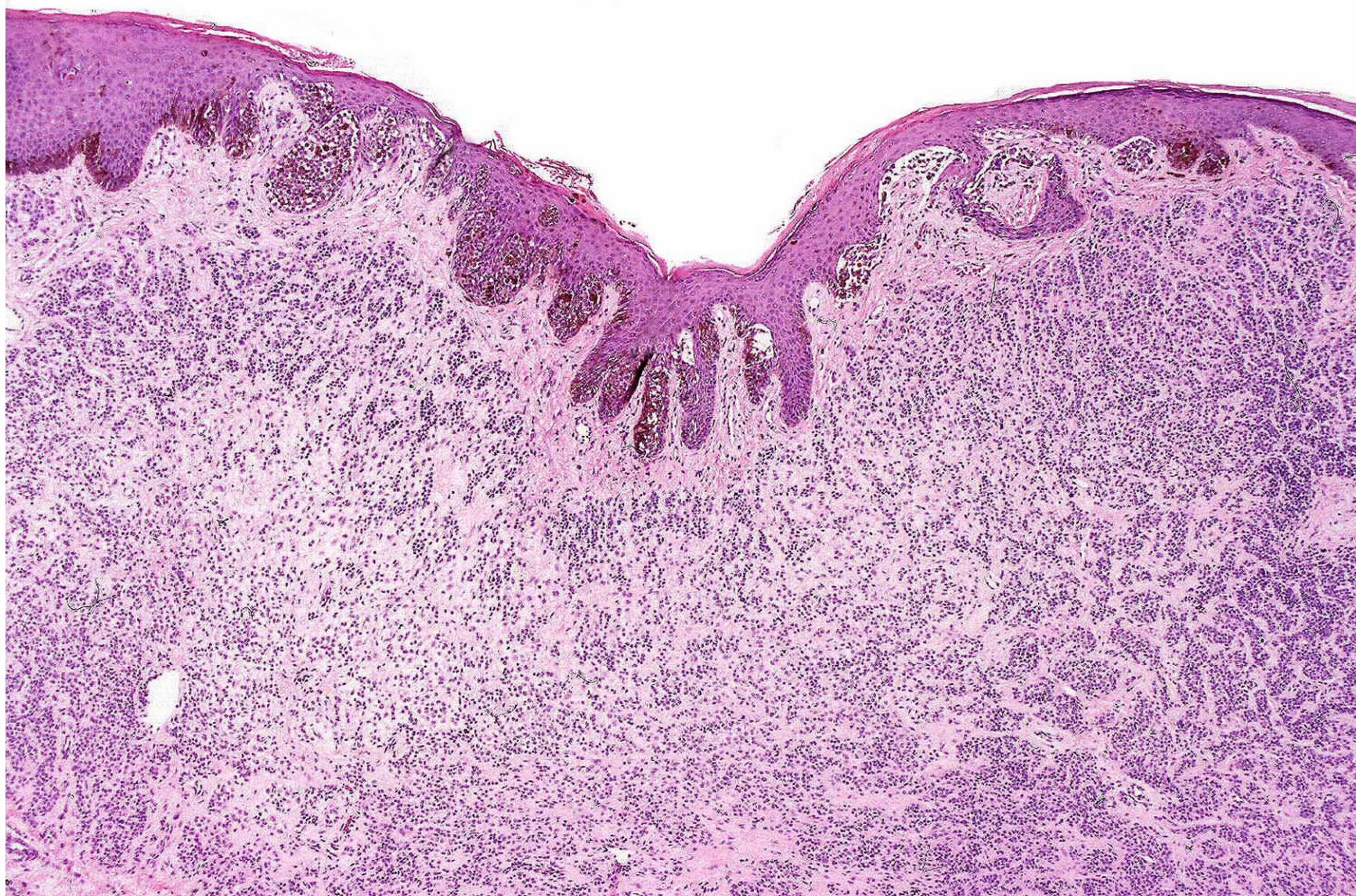


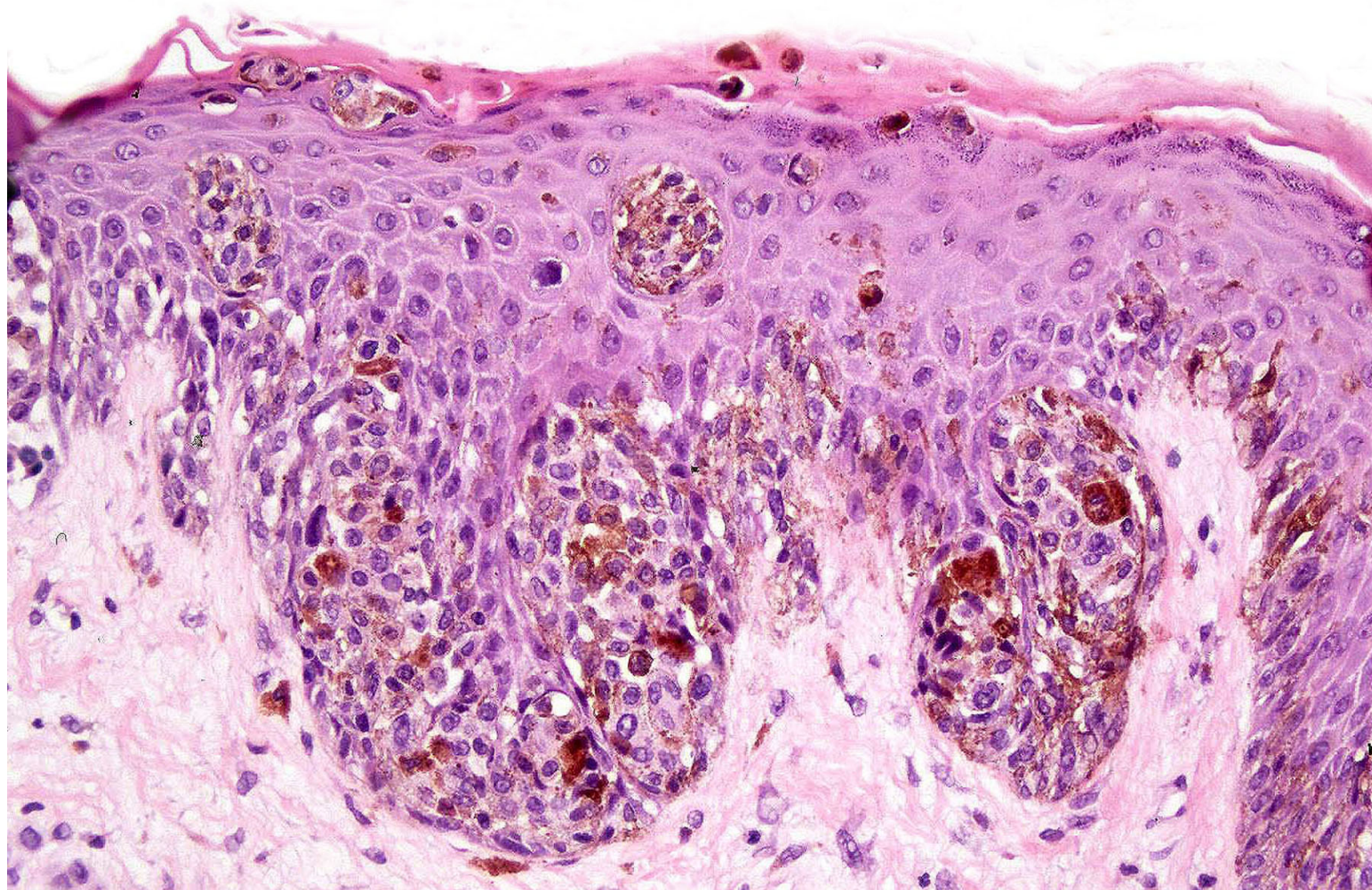


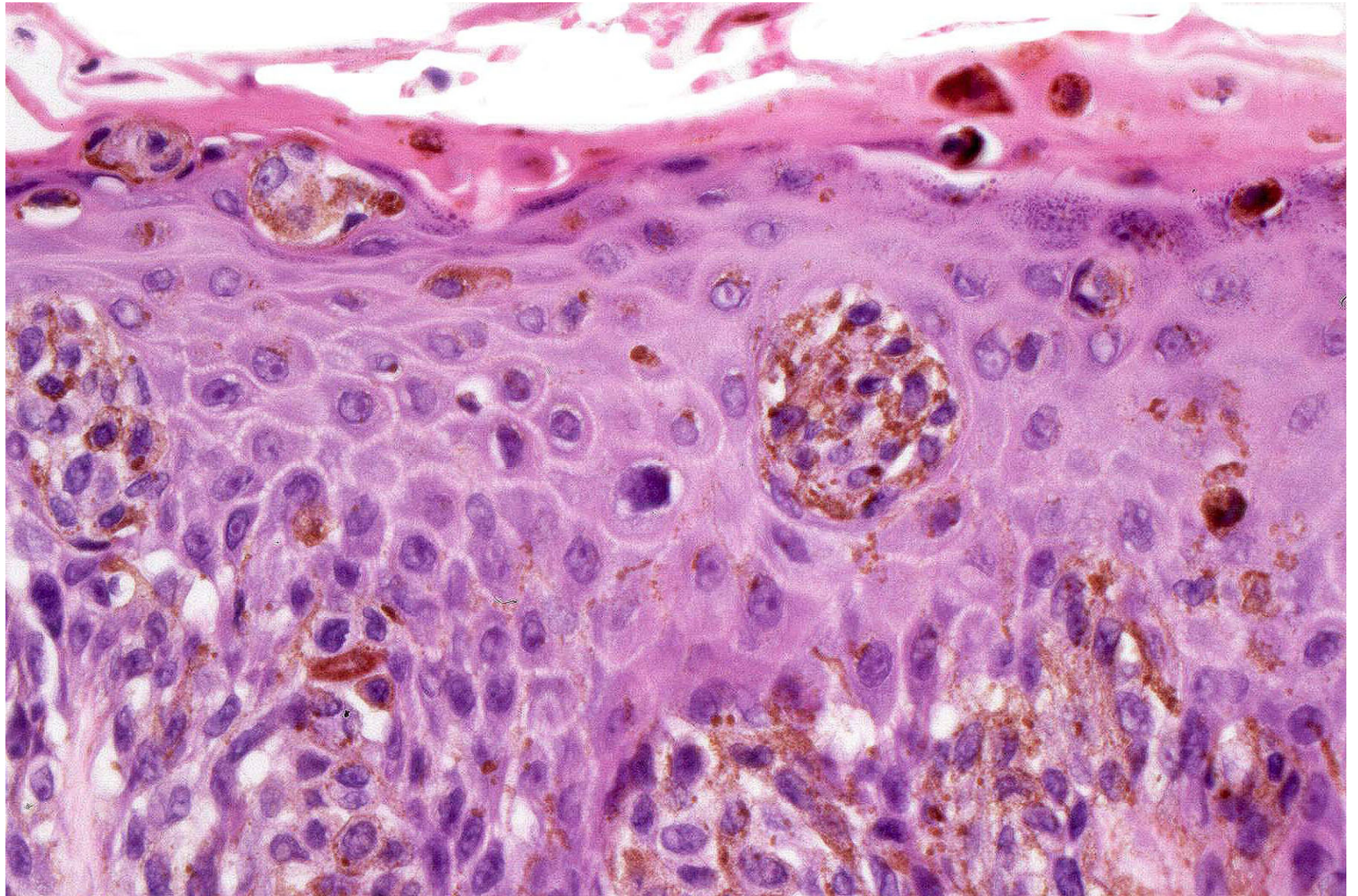


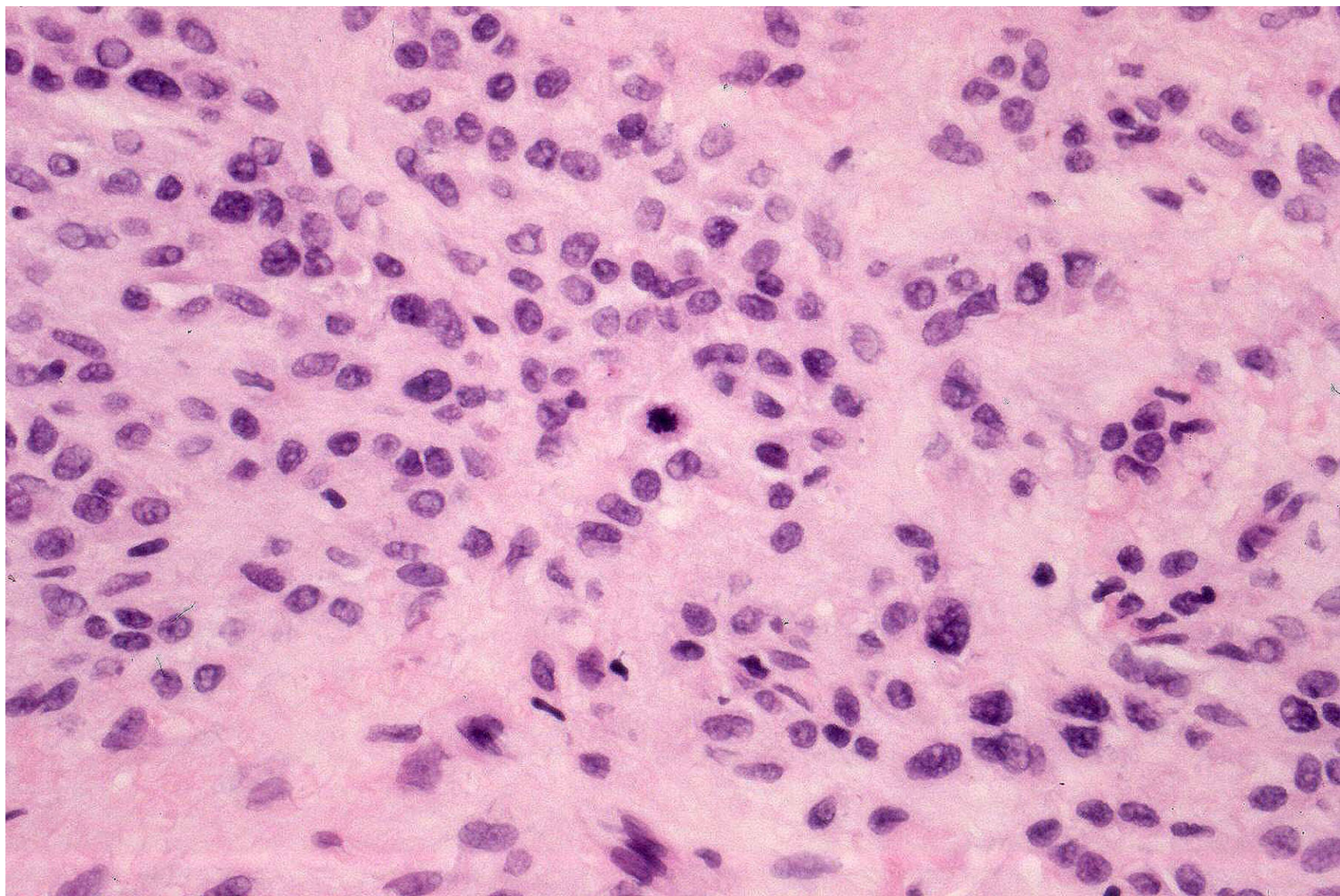


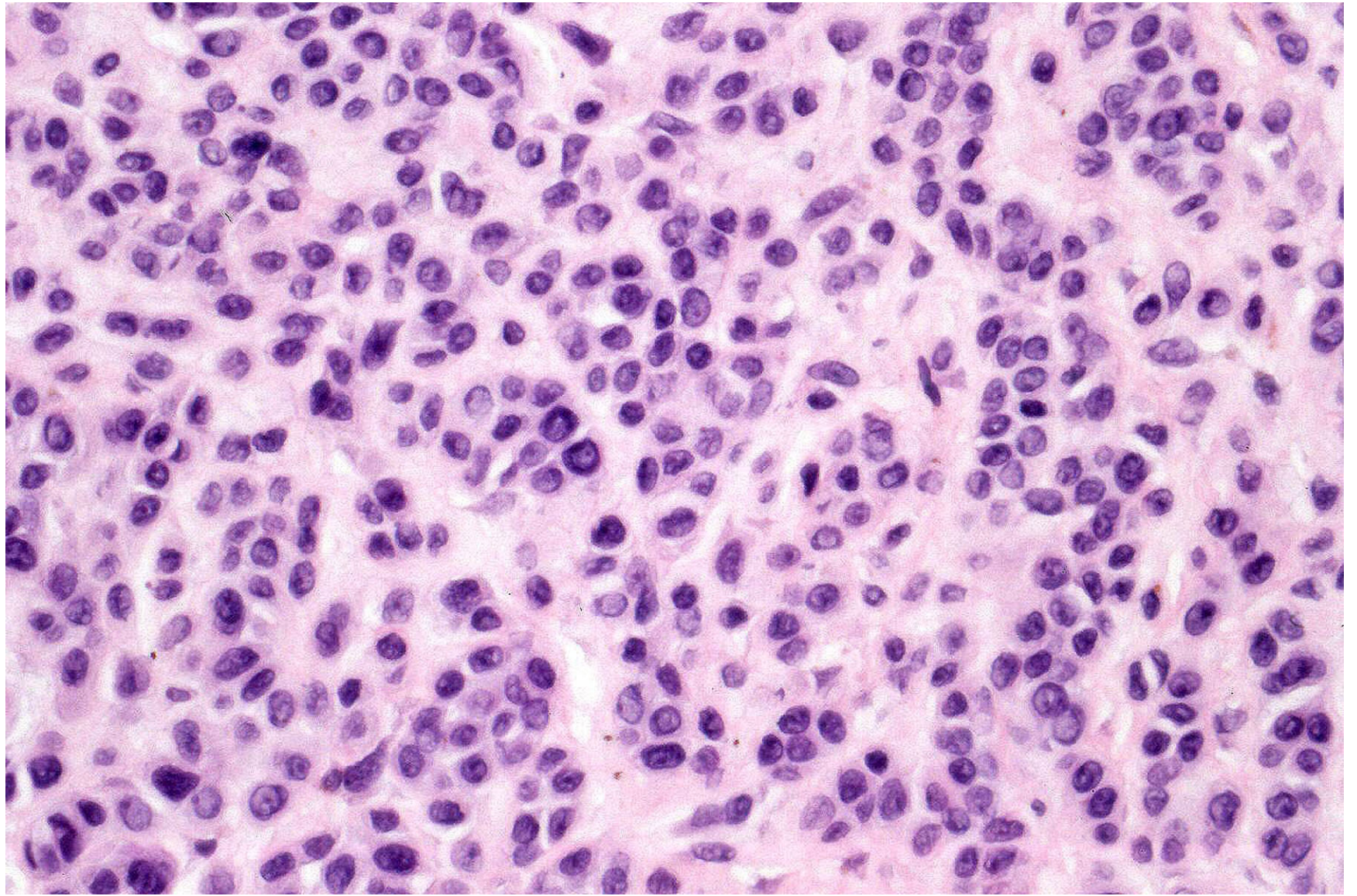


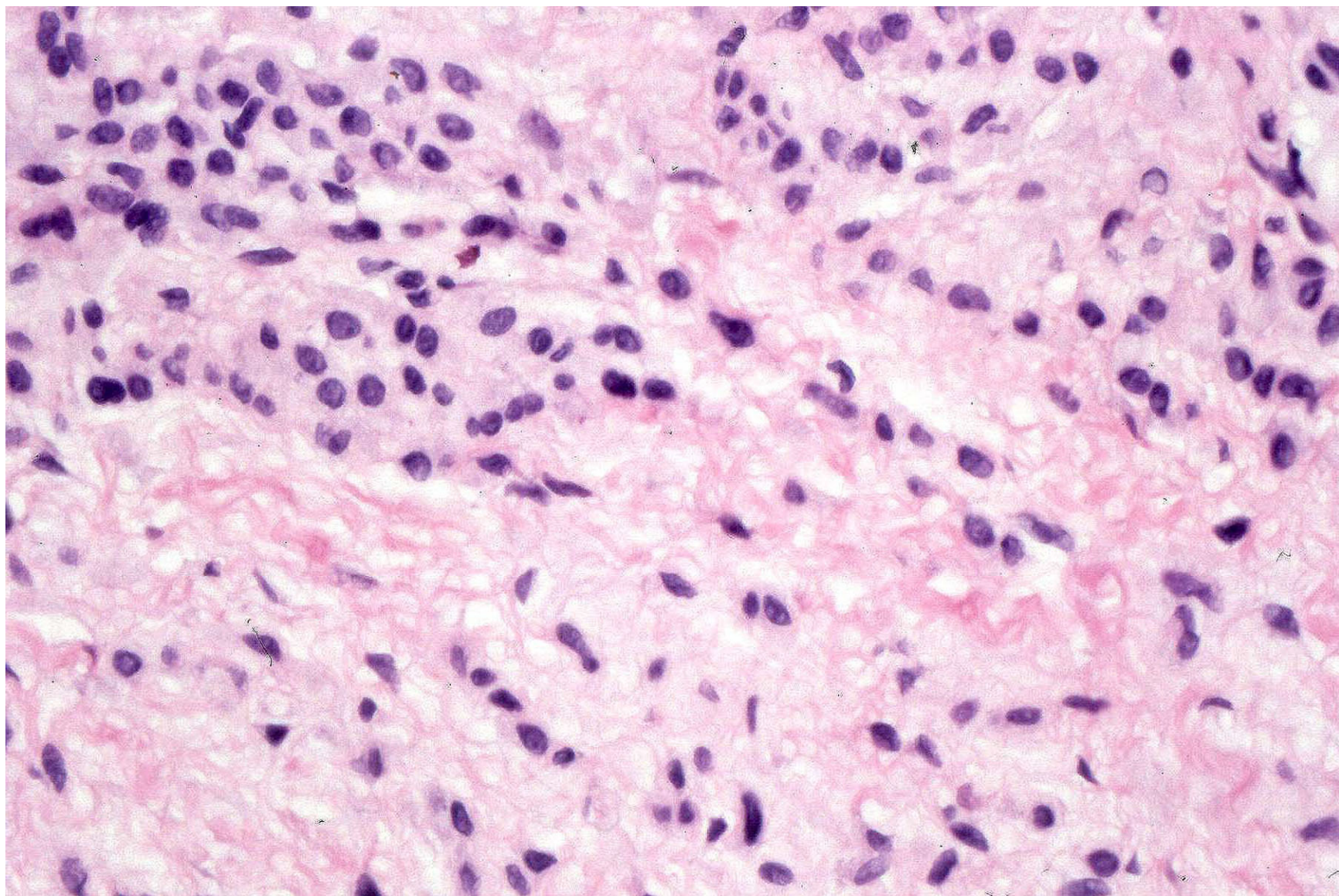












Atypical Genital-Type Naevi

-Concerning features-

Clinical presentation

- **Size**
- **Shape**
- **Pigmentation**

Histological features

- **Size**
- **Cytological atypia**
(mod-severe in 80%)
- **Confluent atypia**
- **Dermal atypia**
- **Suprabasilar and rarely**
Pagetoid spread
- **Adnexal involvement**
- **Dermal mitoses (up to 4)**

Atypical Genital-Type Naevi

-Reassuring features-

BUT:

- Lesional circumscription and symmetry**
- No significant shoulder formation and radial growth**
- Cytological atypia confined to junctional and superficial dermal component**
- Maturation with depth**
- Lack of expansile growth**
- No deep dermal or atypical mitoses**

Atypical Genital-Type Naevi

-Outcome-

- **Benign behaviour**
- **Rare local recurrence after incomplete removal**
- **No adverse outcome reported so far**

Atypical Genital-Type Naevi

-Treatment-

No firm recommendation

Insufficient experience

?Complete removal

Melanoma of the Vulva

-Clinical Features-

- **Rare, estimated incidence 0.15/100.000**
- **2-4% of all melanomas in women;**
- **3-10% of all primary vulval malignancies**
- **Second most common malignancy of vulva**

Vulval Melanoma

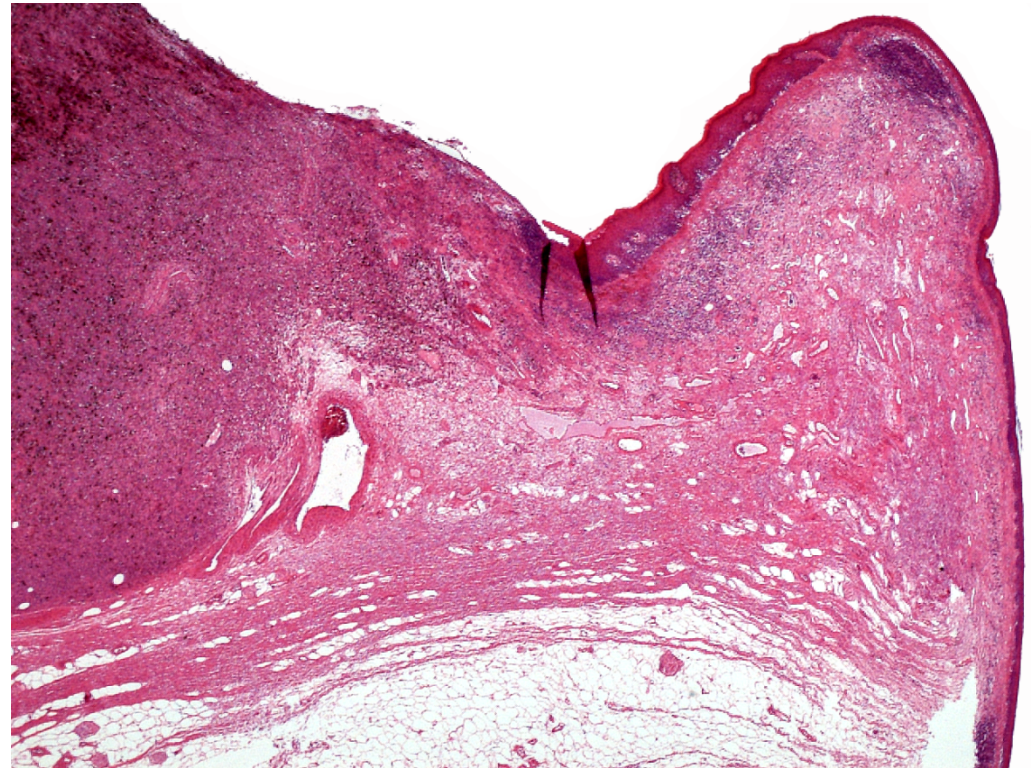
-Clinical Features-

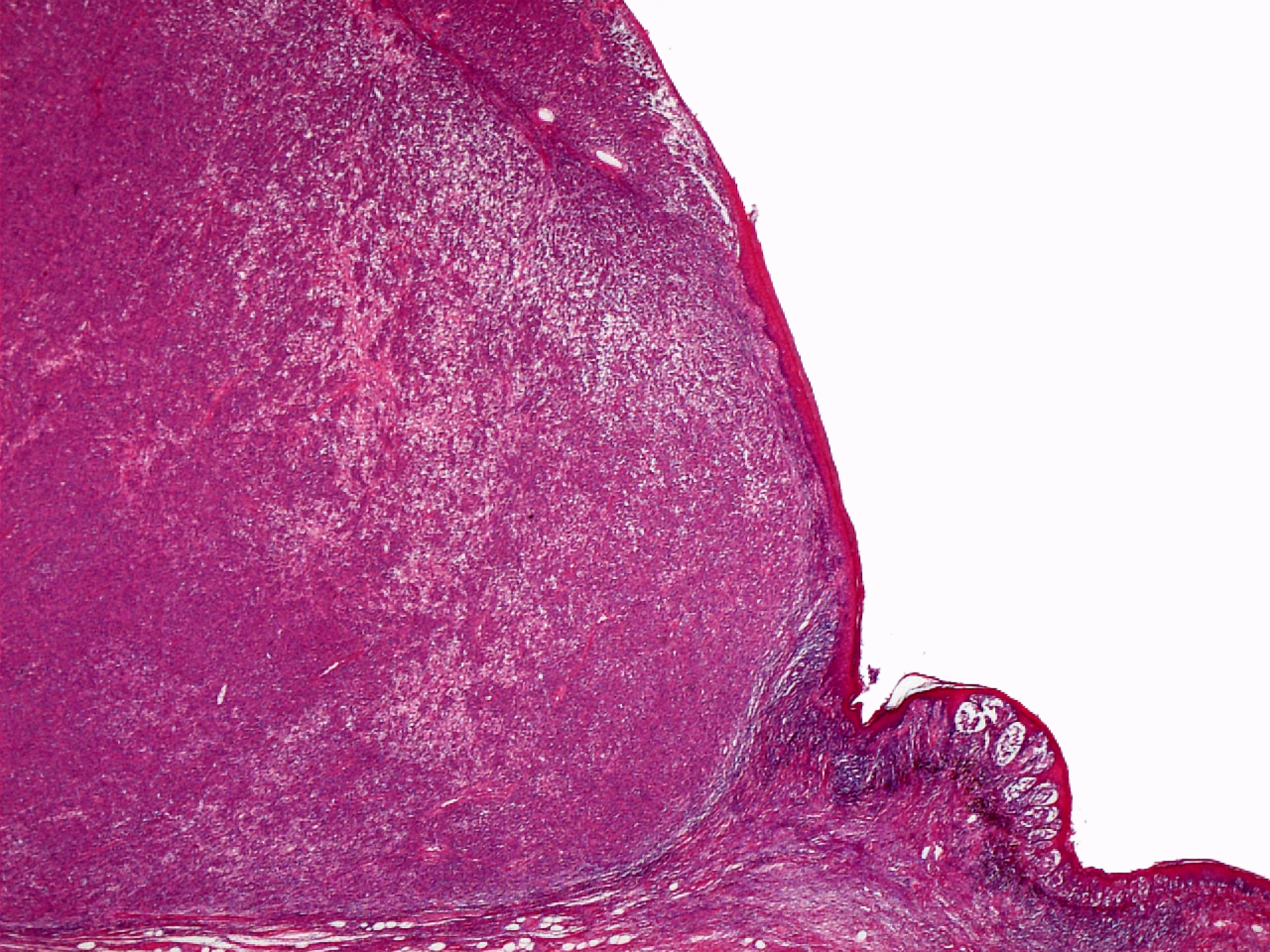
- **Postmenopausal women**
- **Mean age 60-70 years**
- **20% of vulval melanoma before age 50**
- **Predominantly involving mucosal surfaces**
- **Large size (~2cm)**
- **Irregular shape and pigment distribution**
- **Amelanotic, multicentric**
- **Presenting signs: Mass, pain, bleeding, itch, mole**

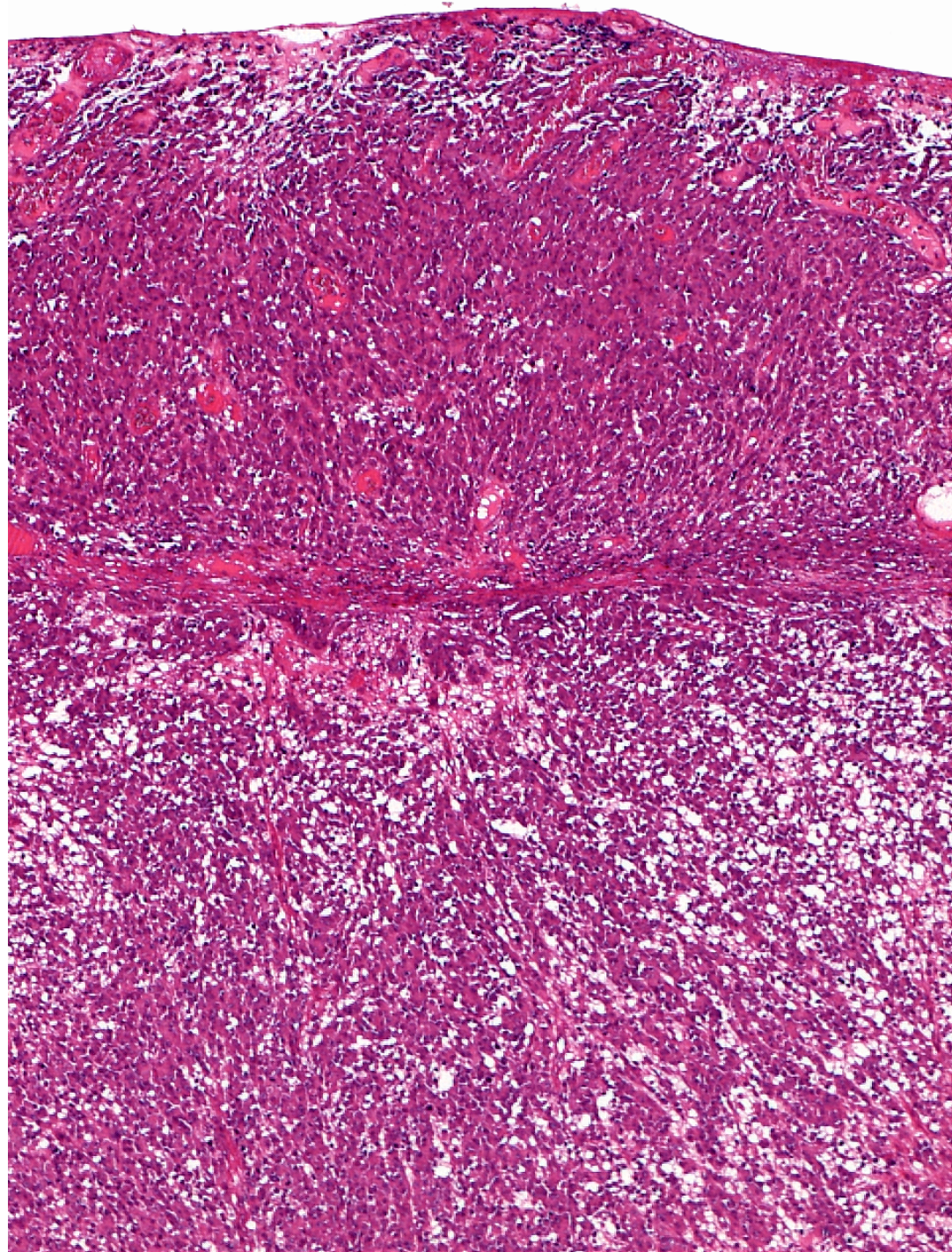
Vulval Melanoma

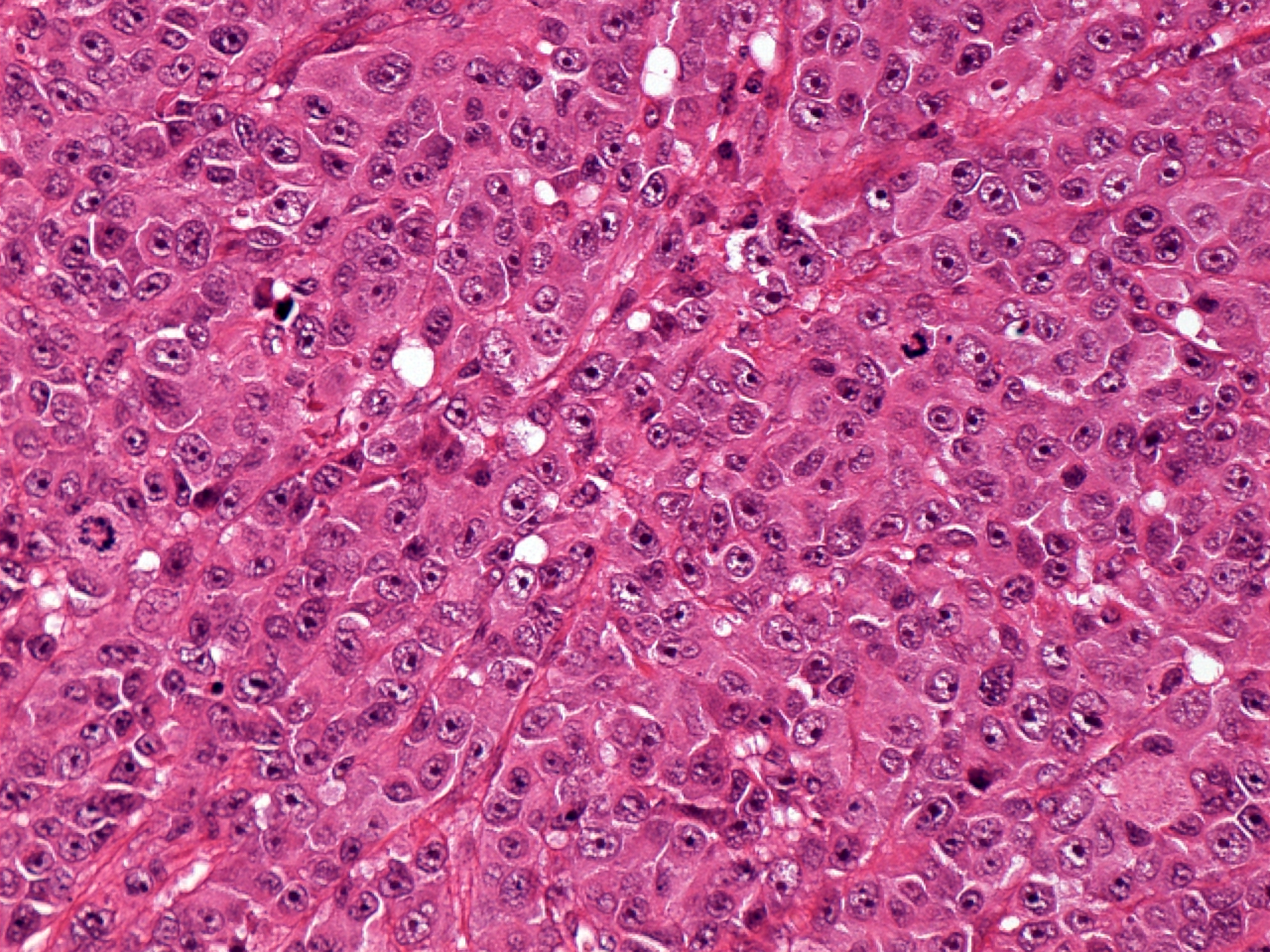
-Histology-

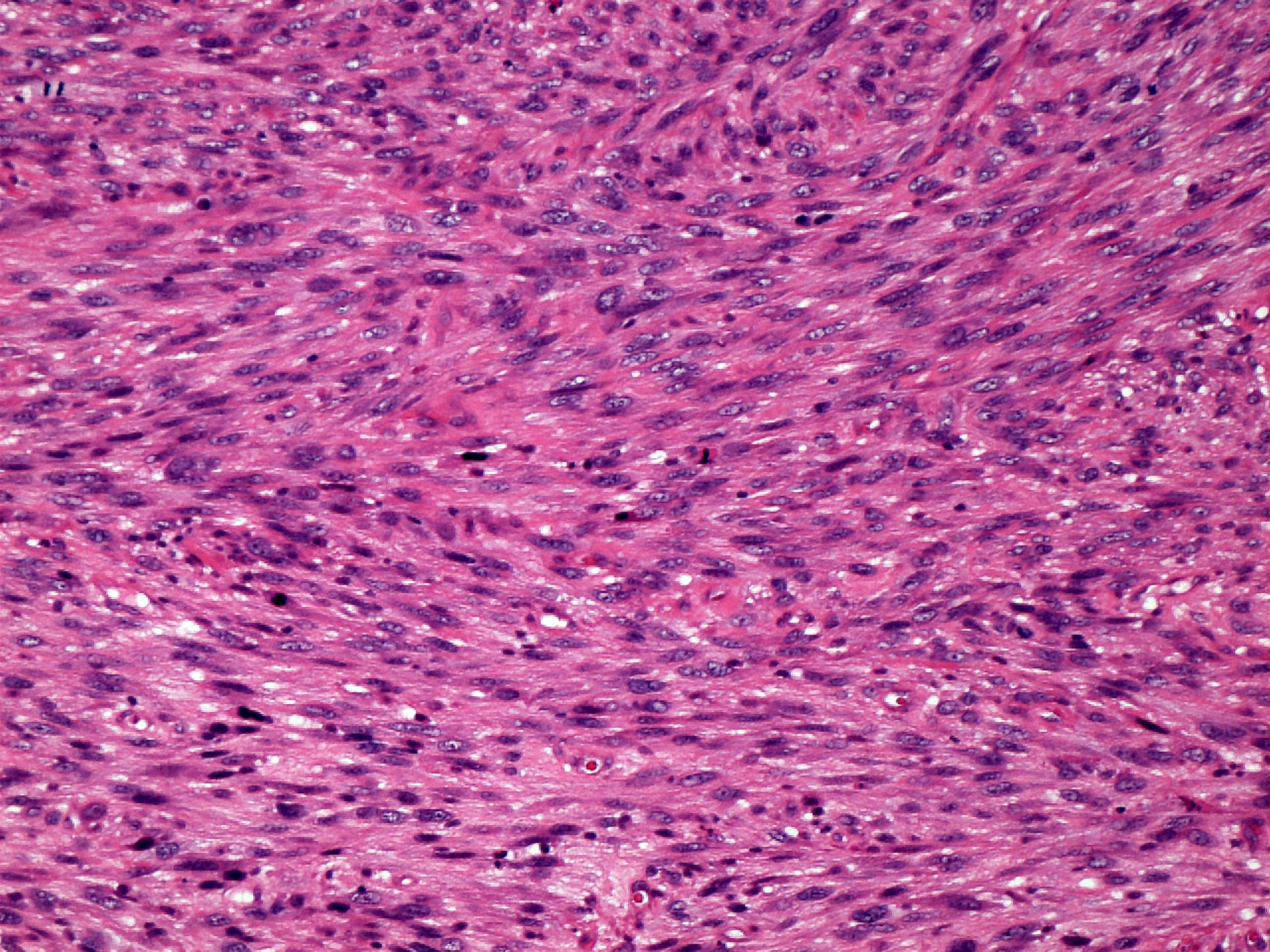
- **Lentiginous Mucosal Melanoma**
- **Superficial Spreading Melanoma**
- **Nodular Melanoma**
- **Rare types**

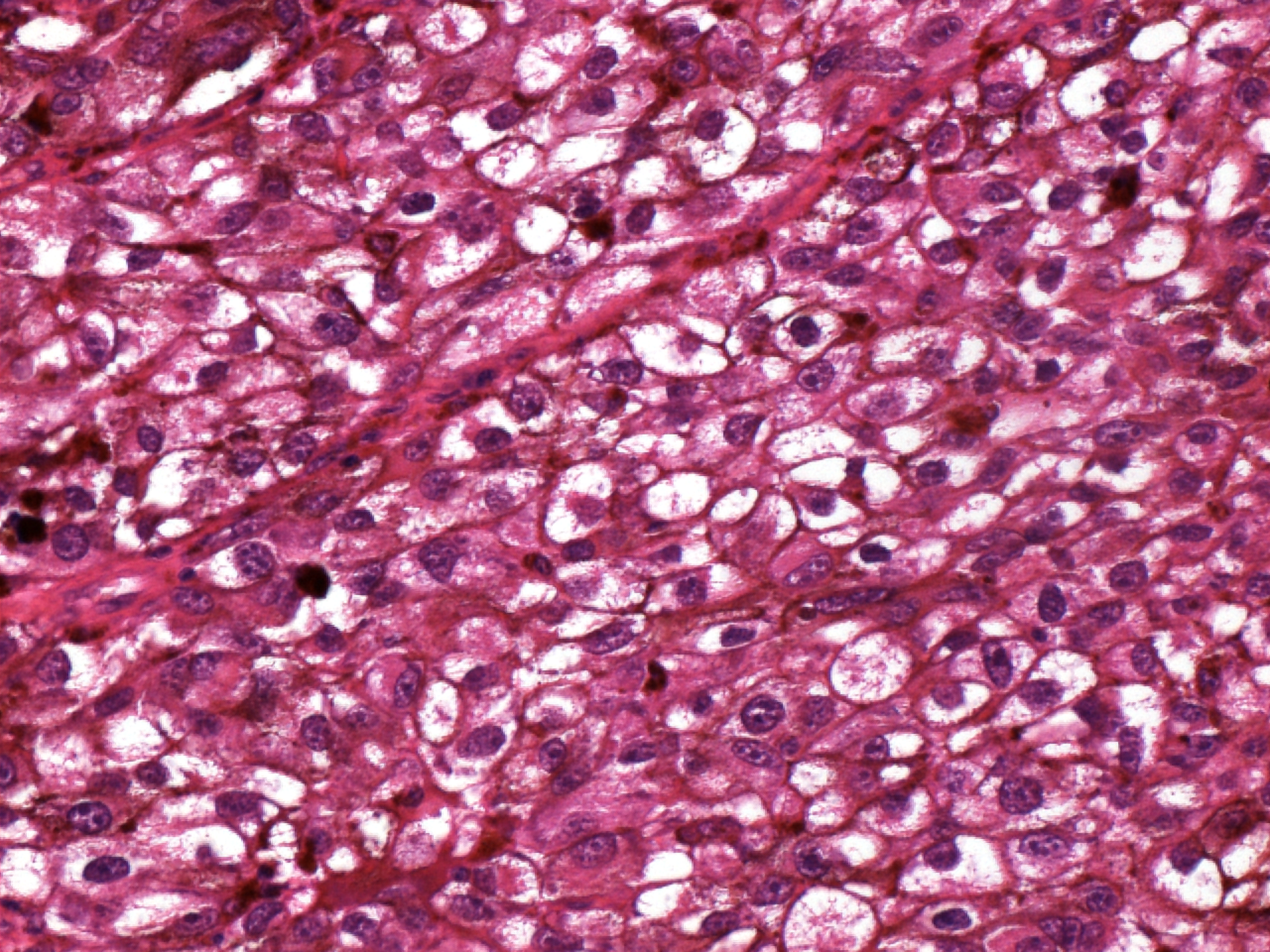


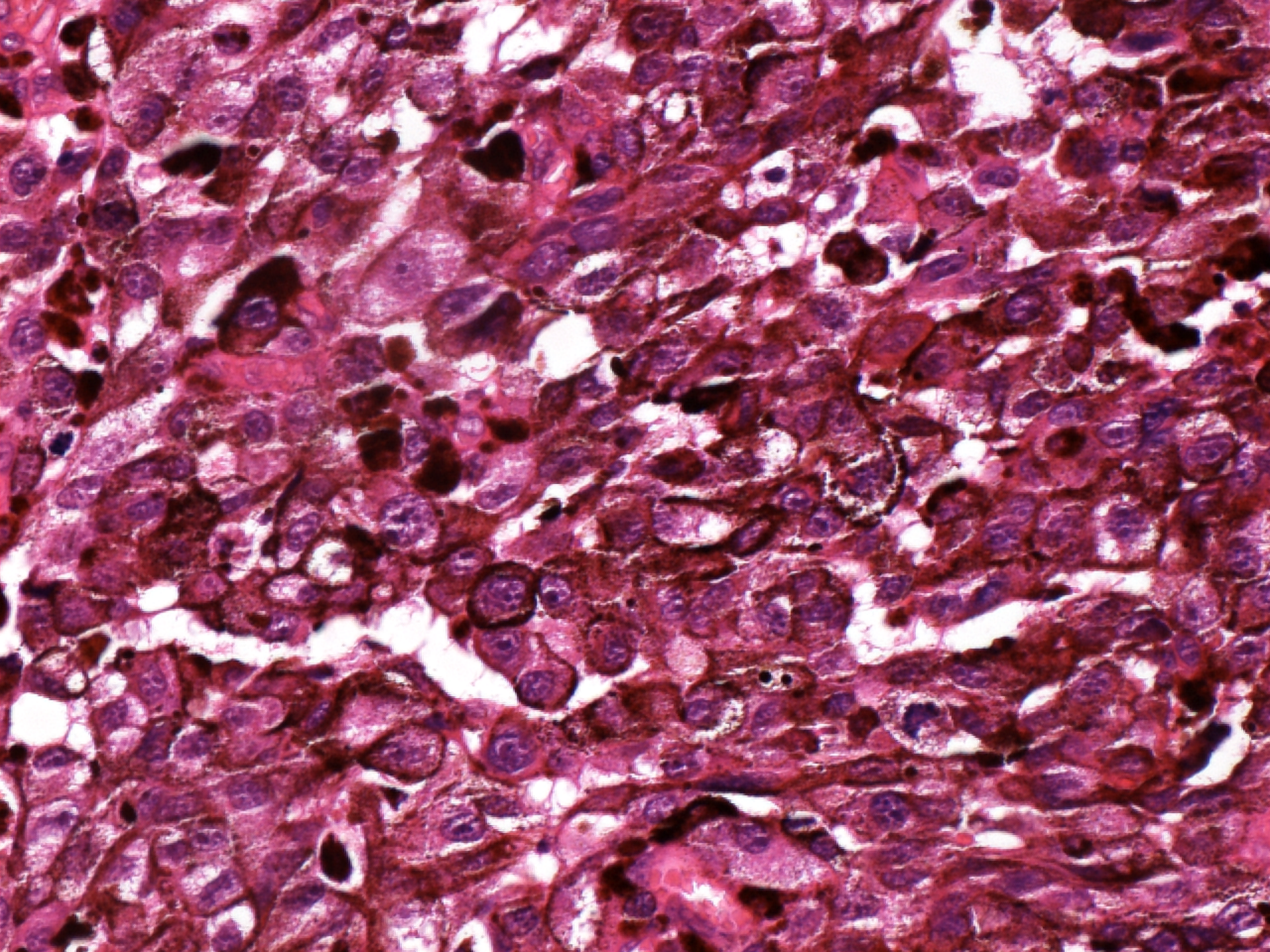


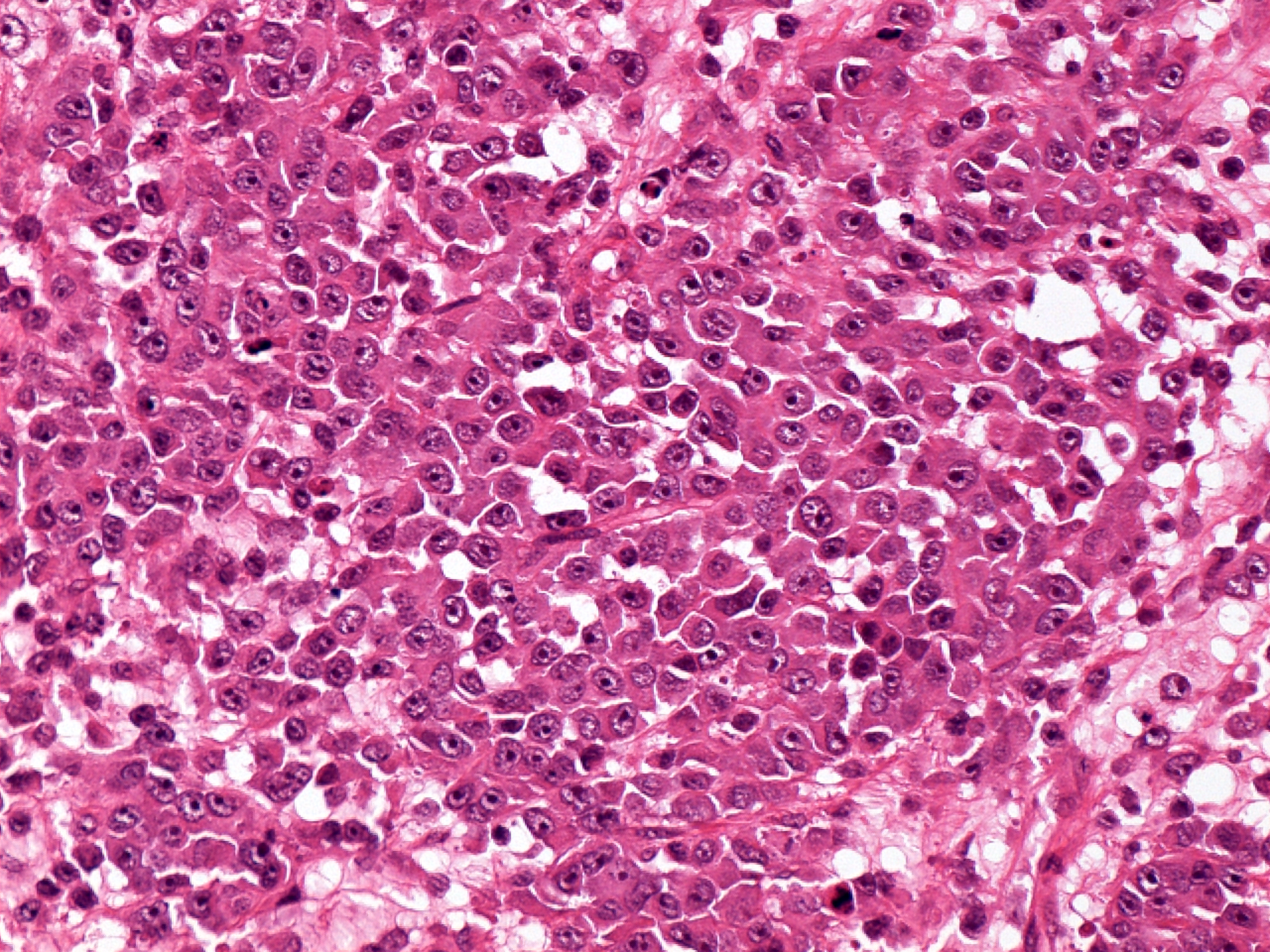


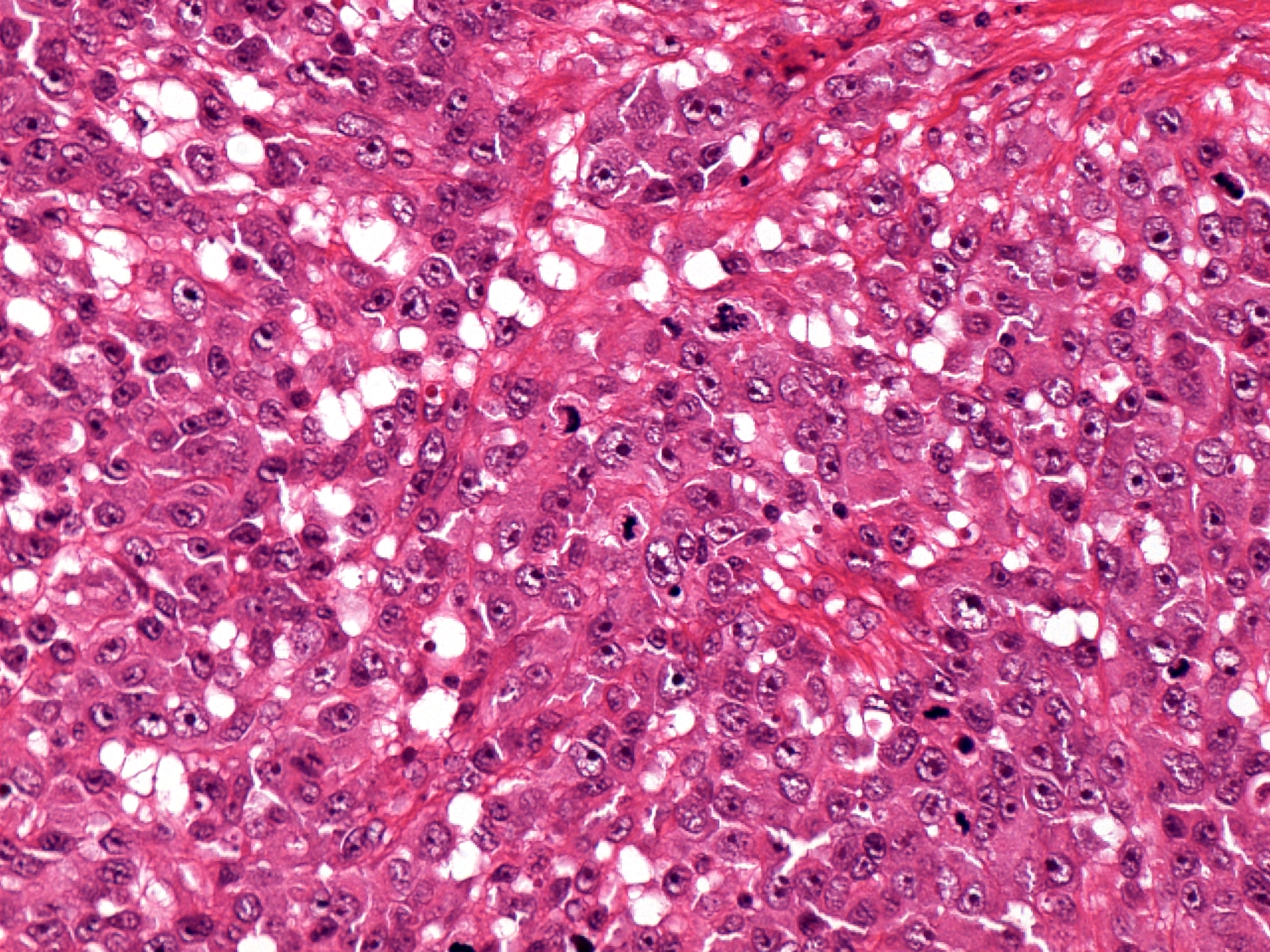


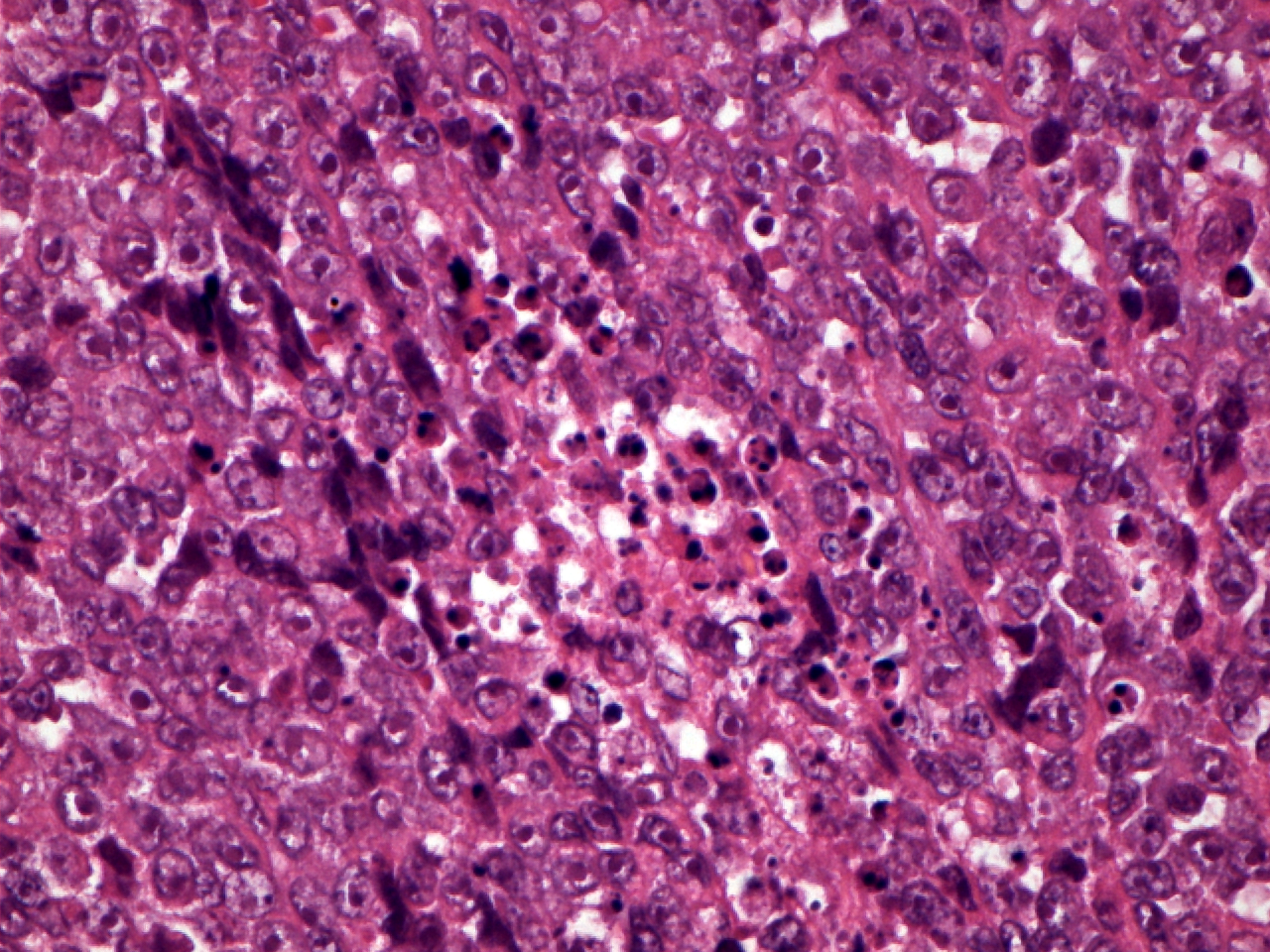


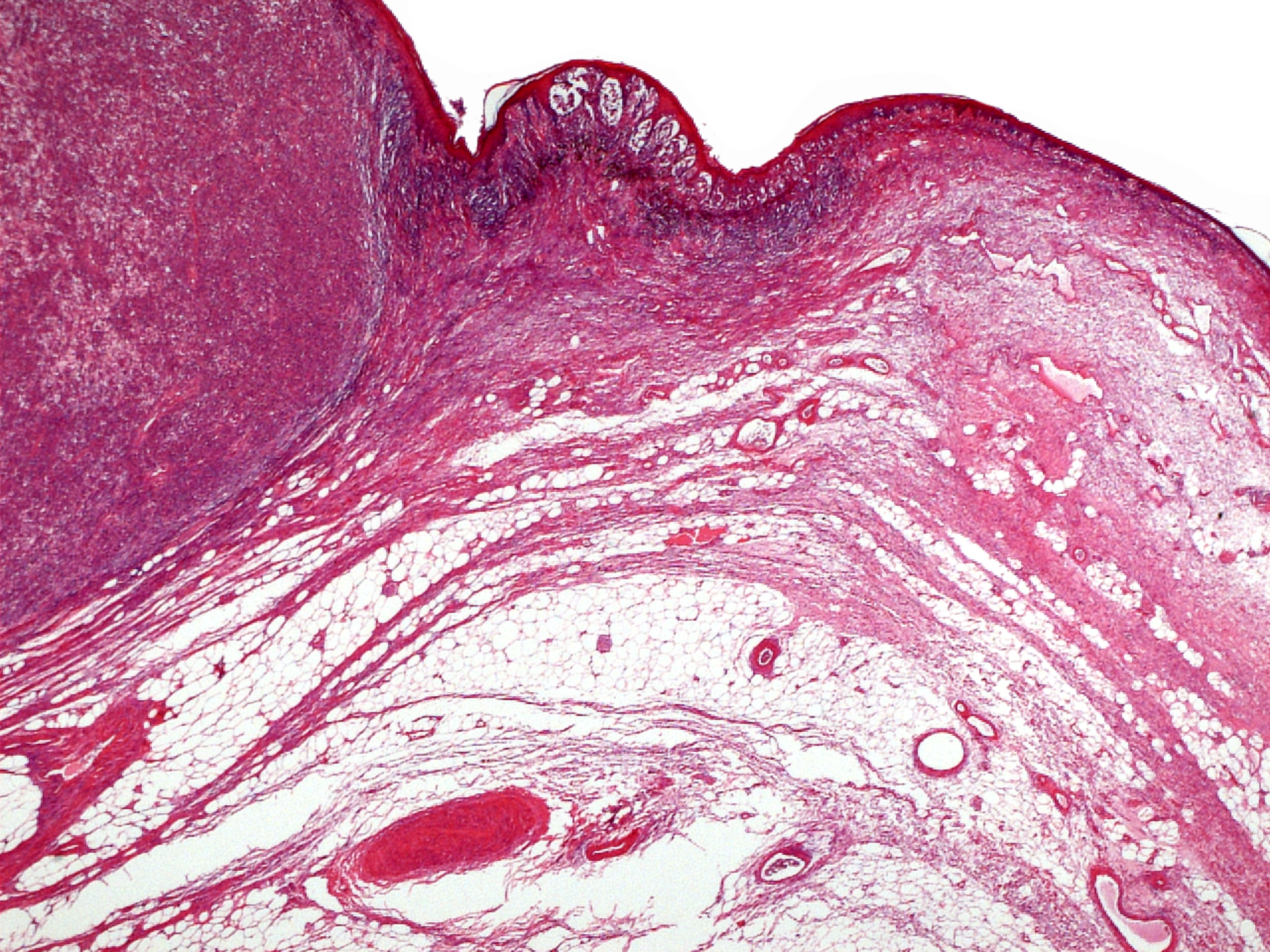


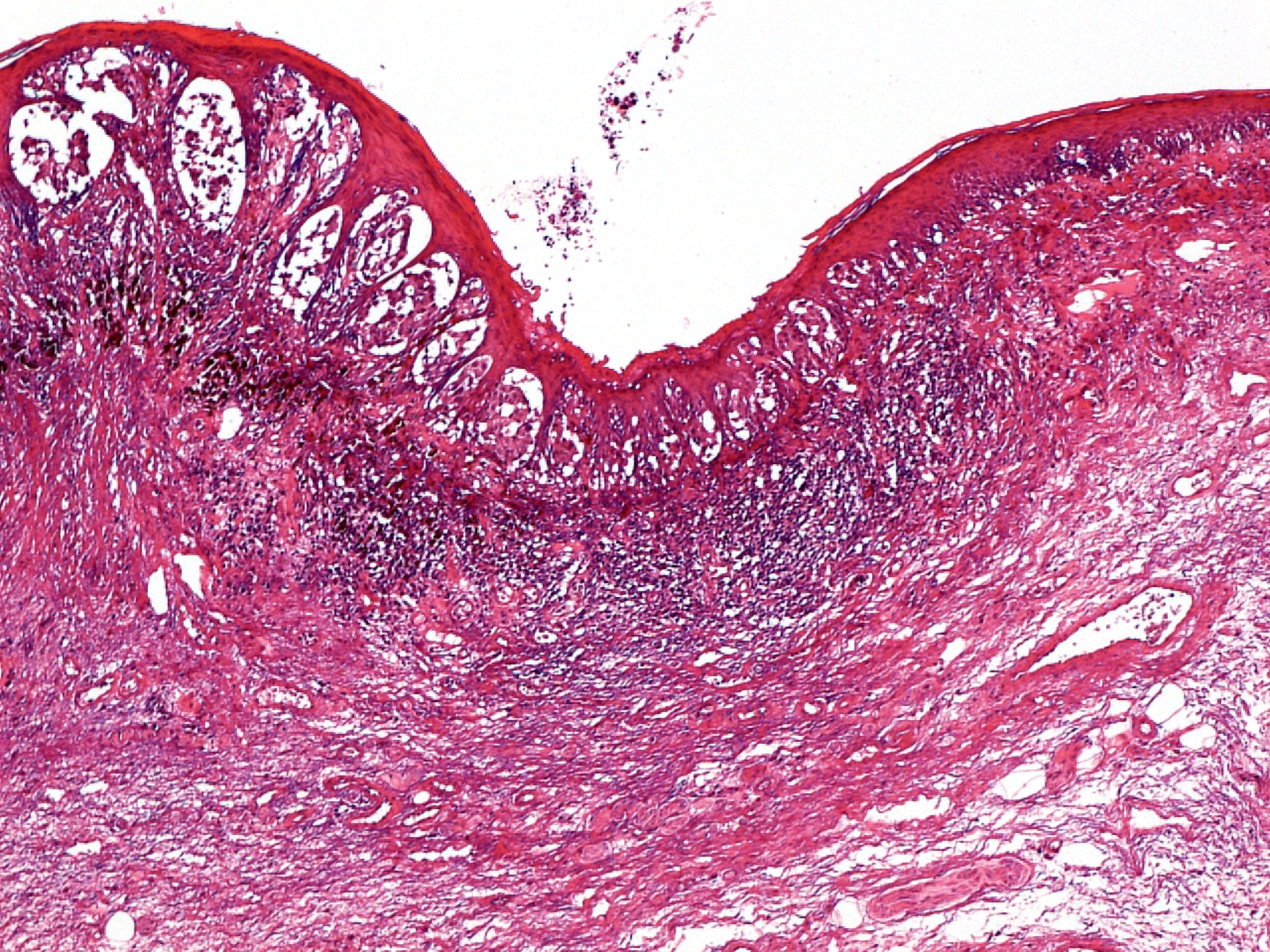


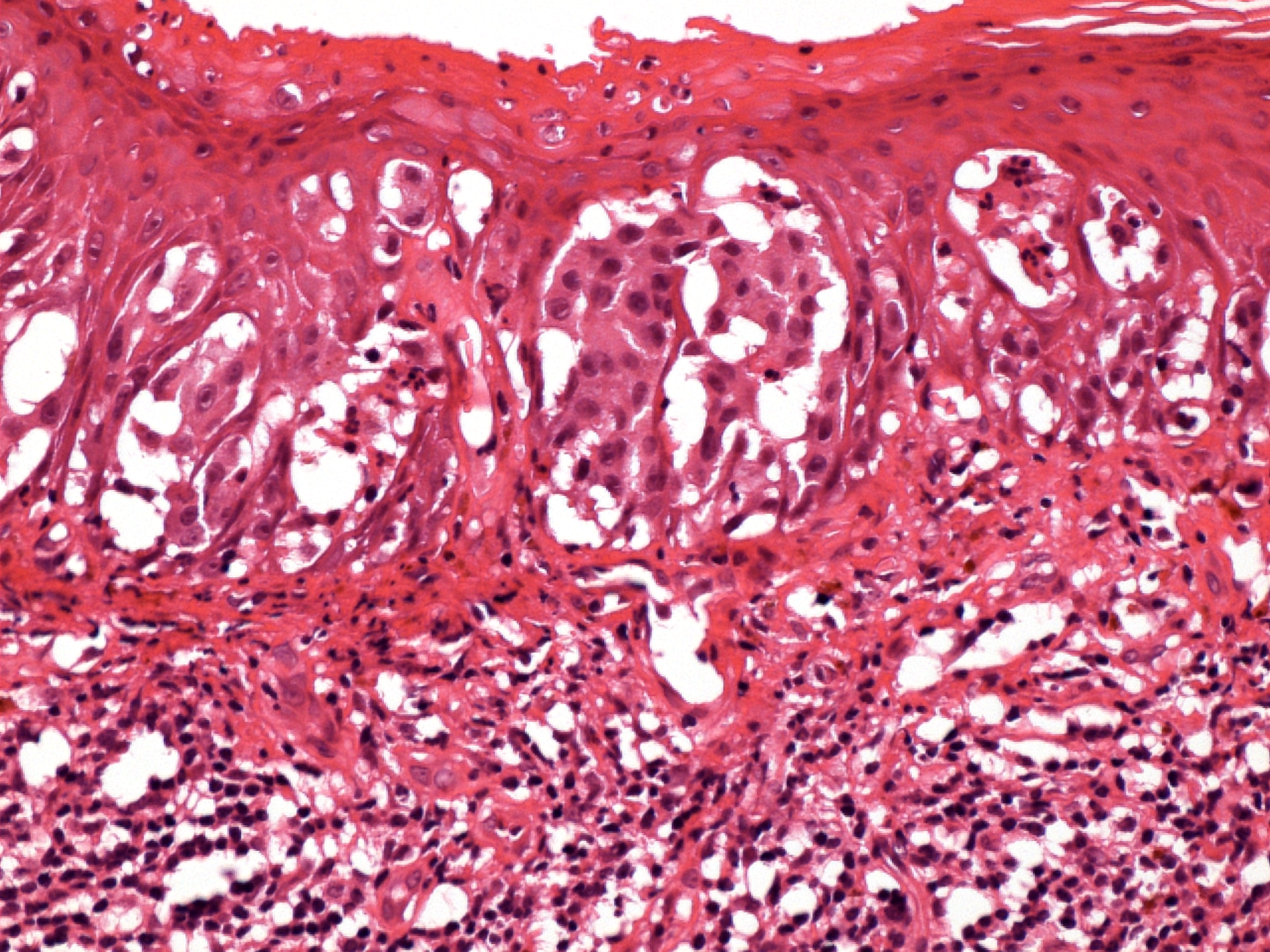


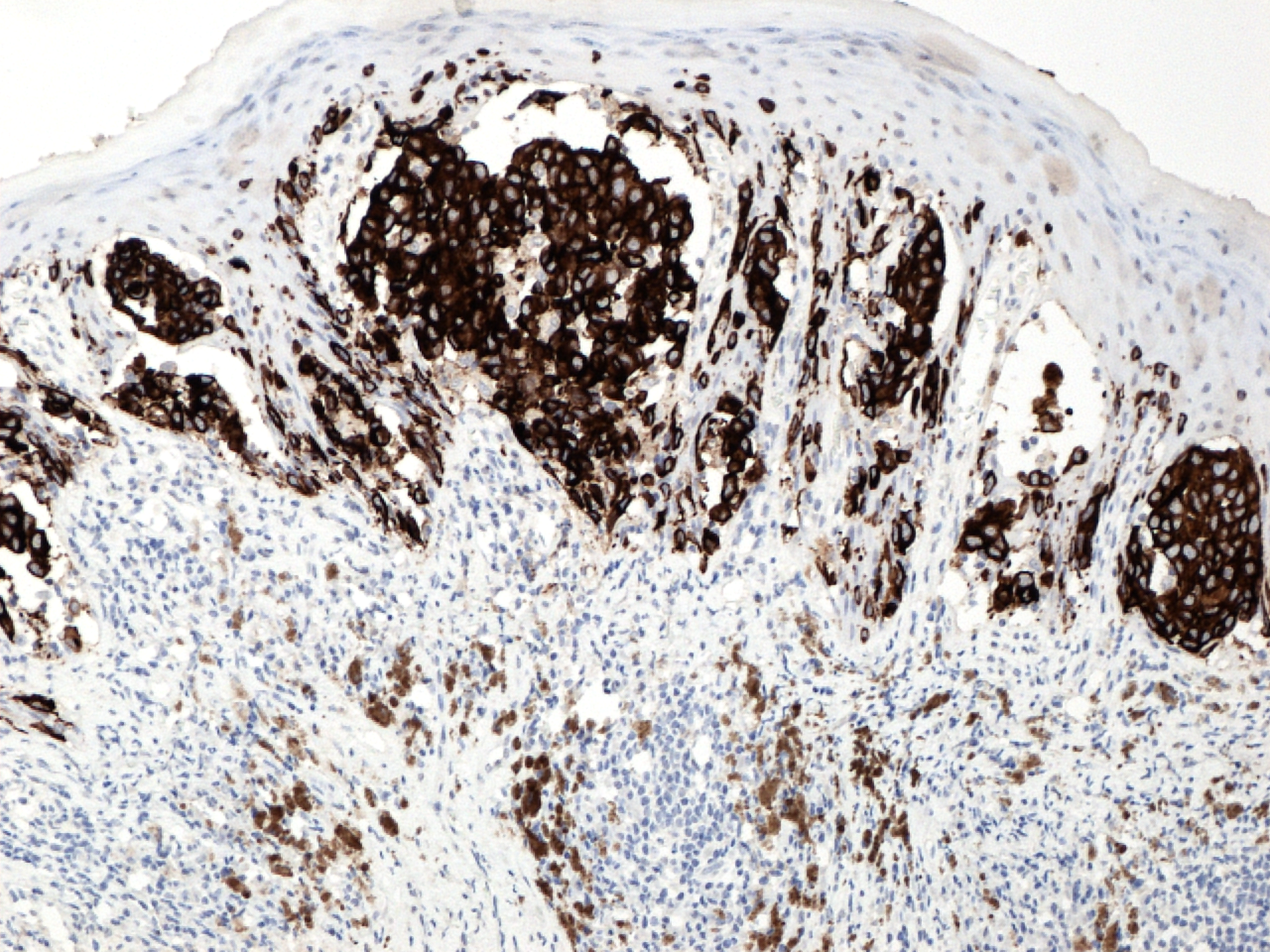


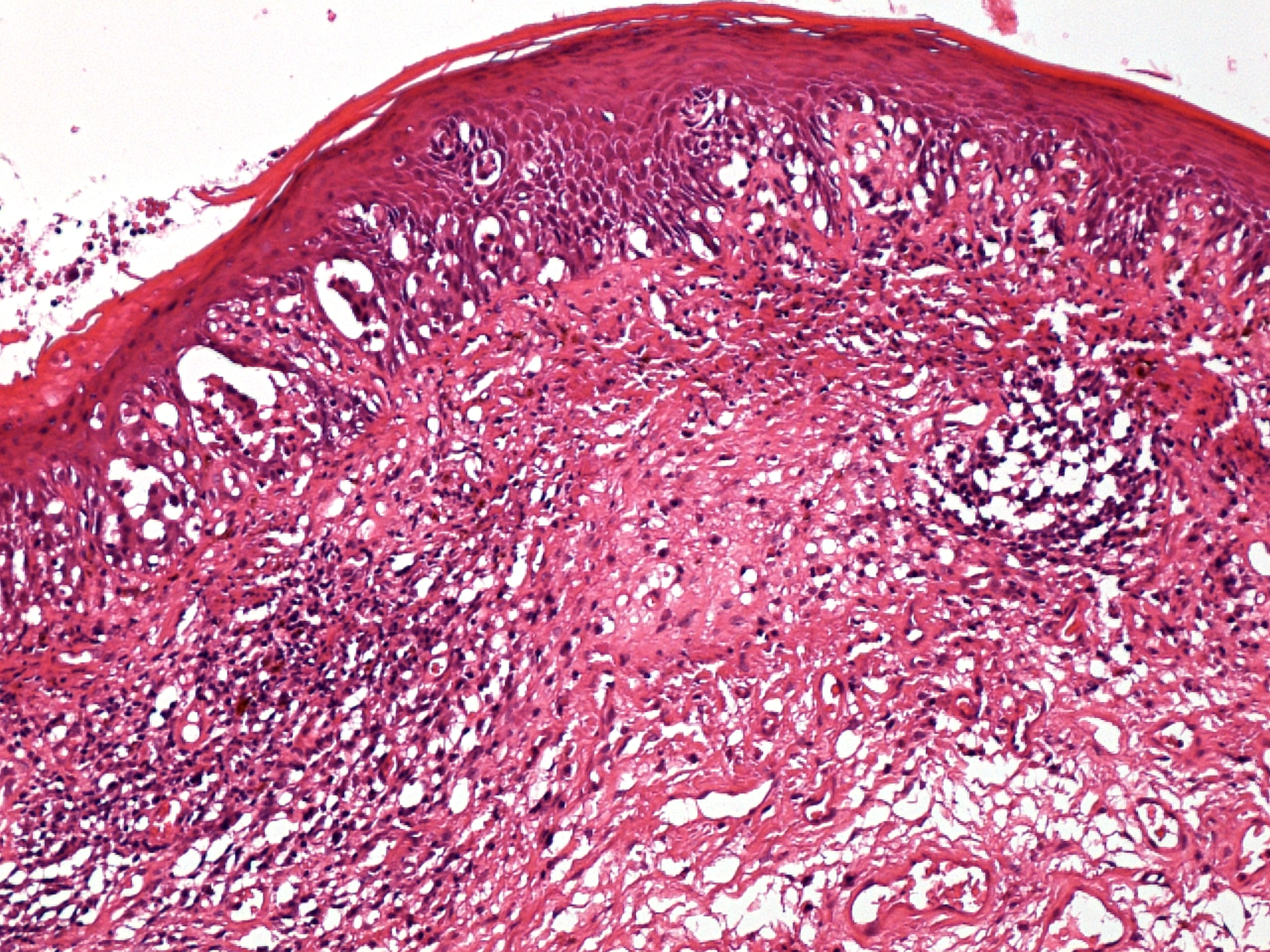


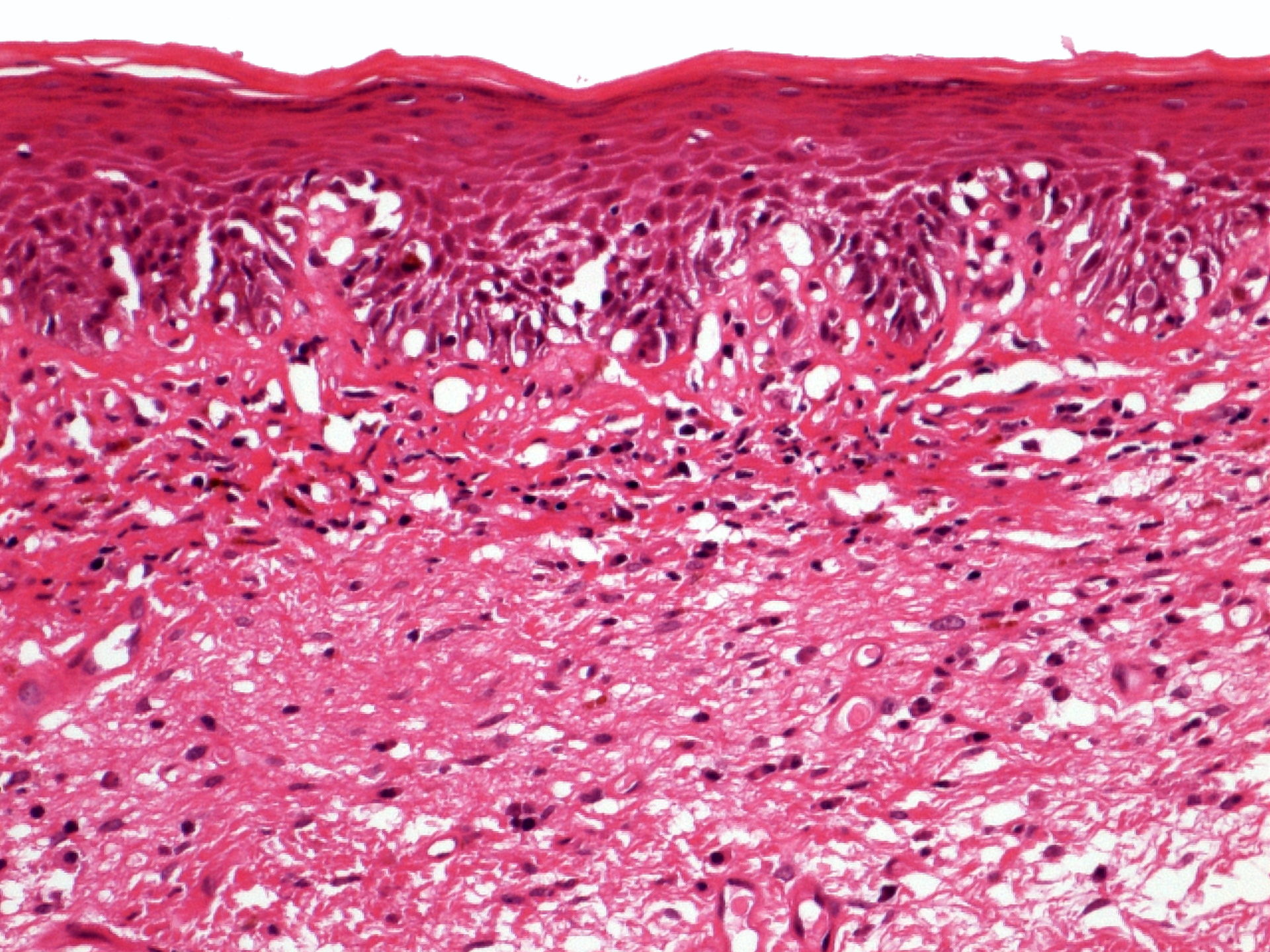


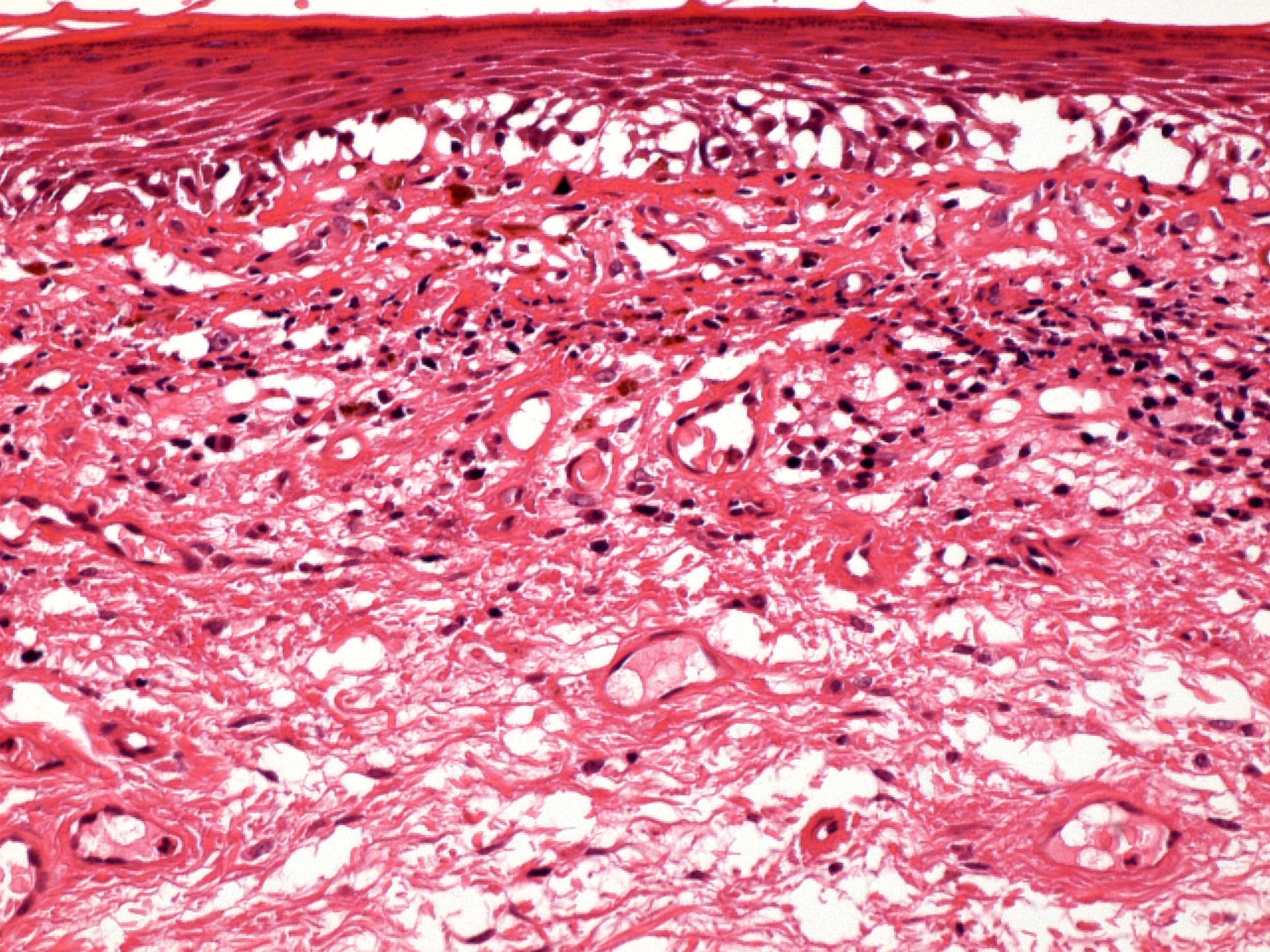


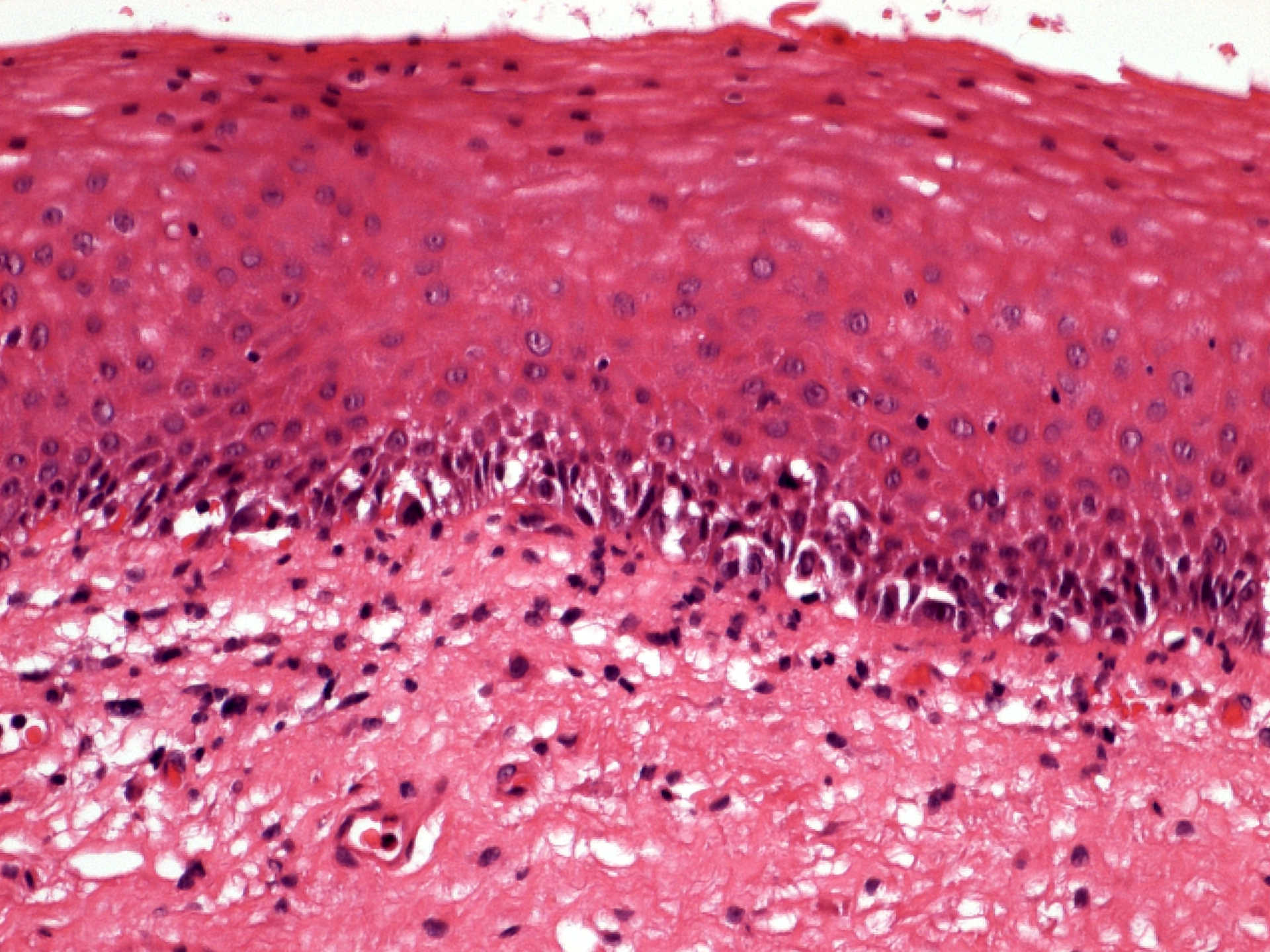


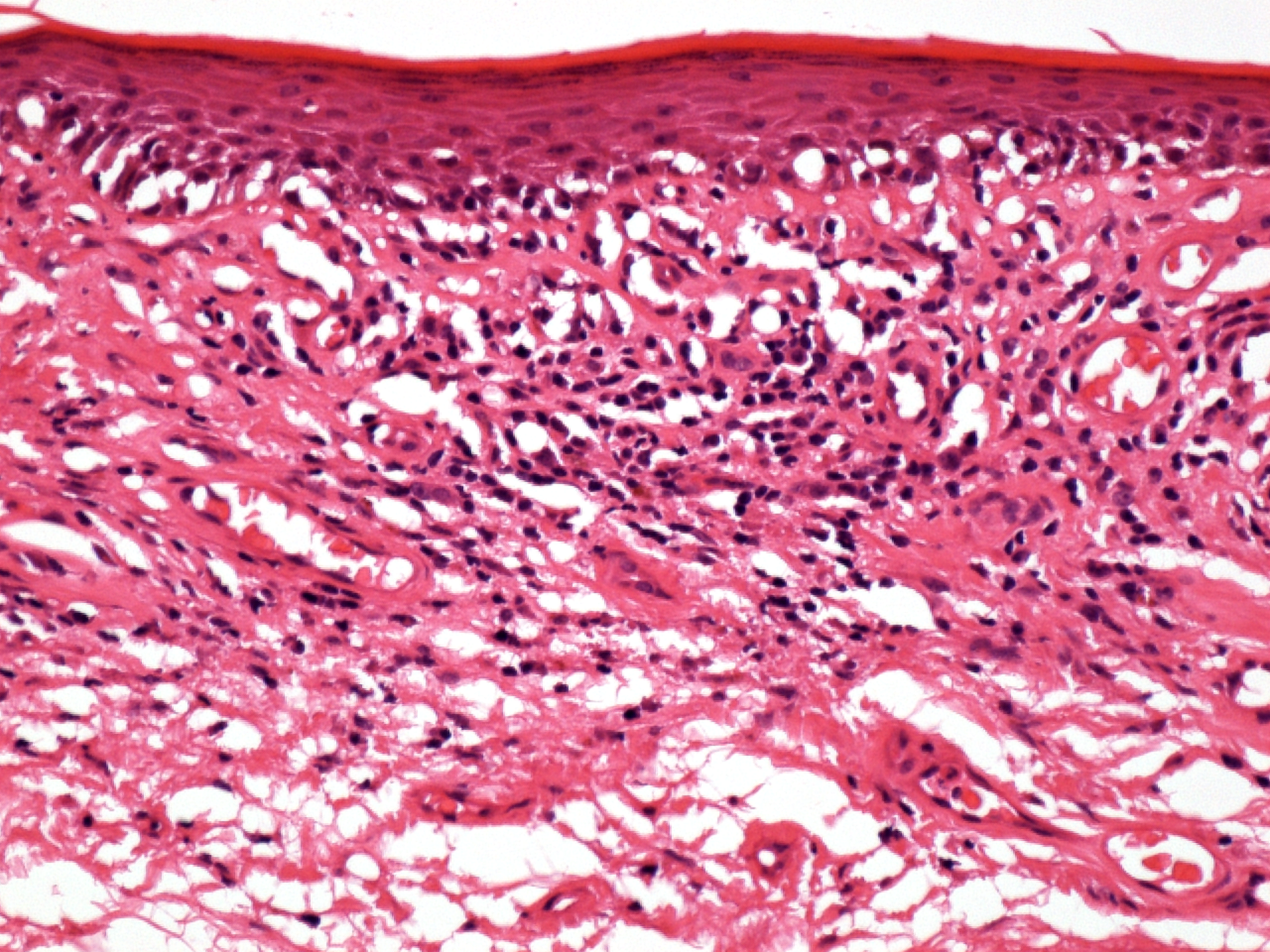


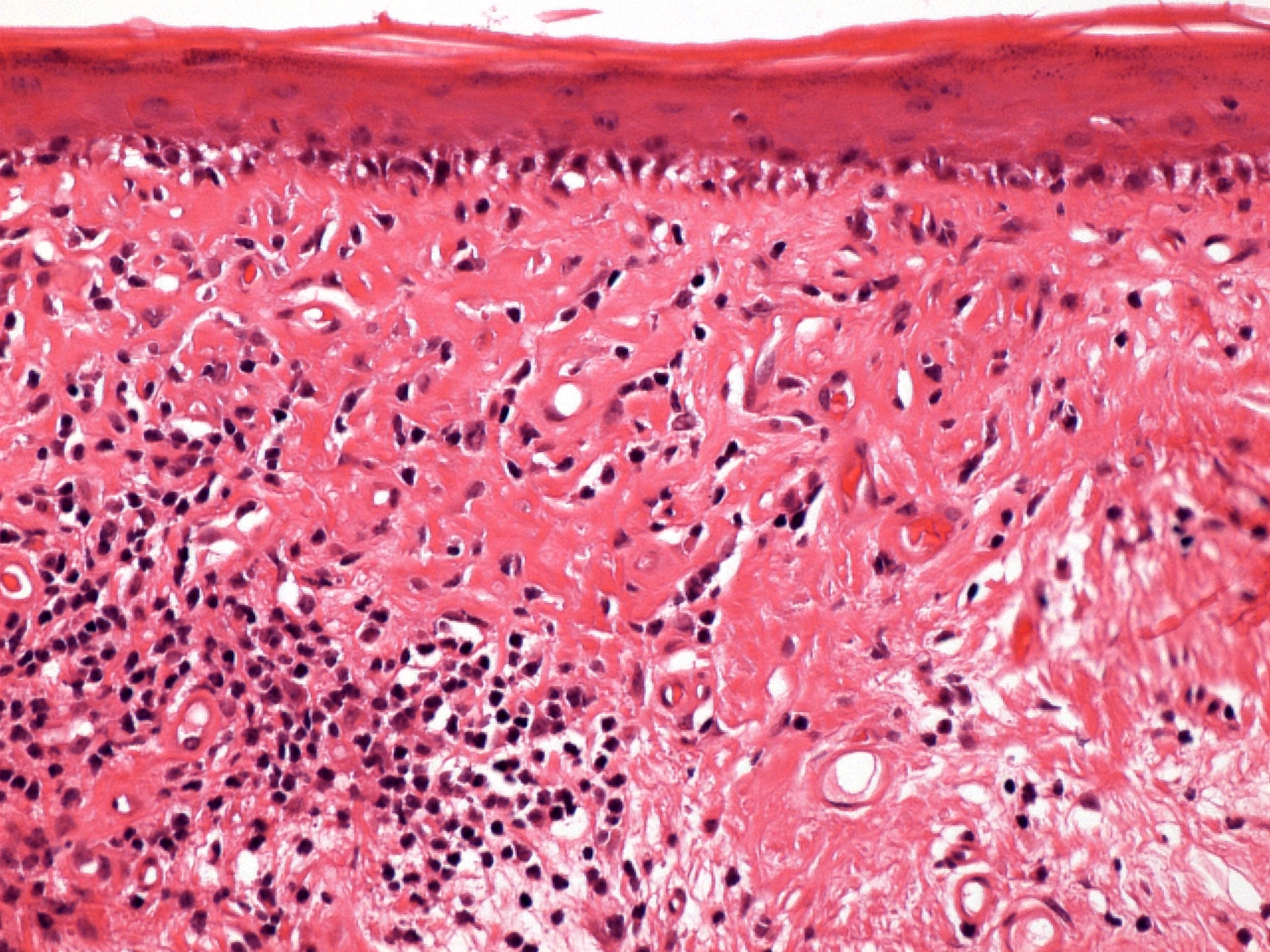


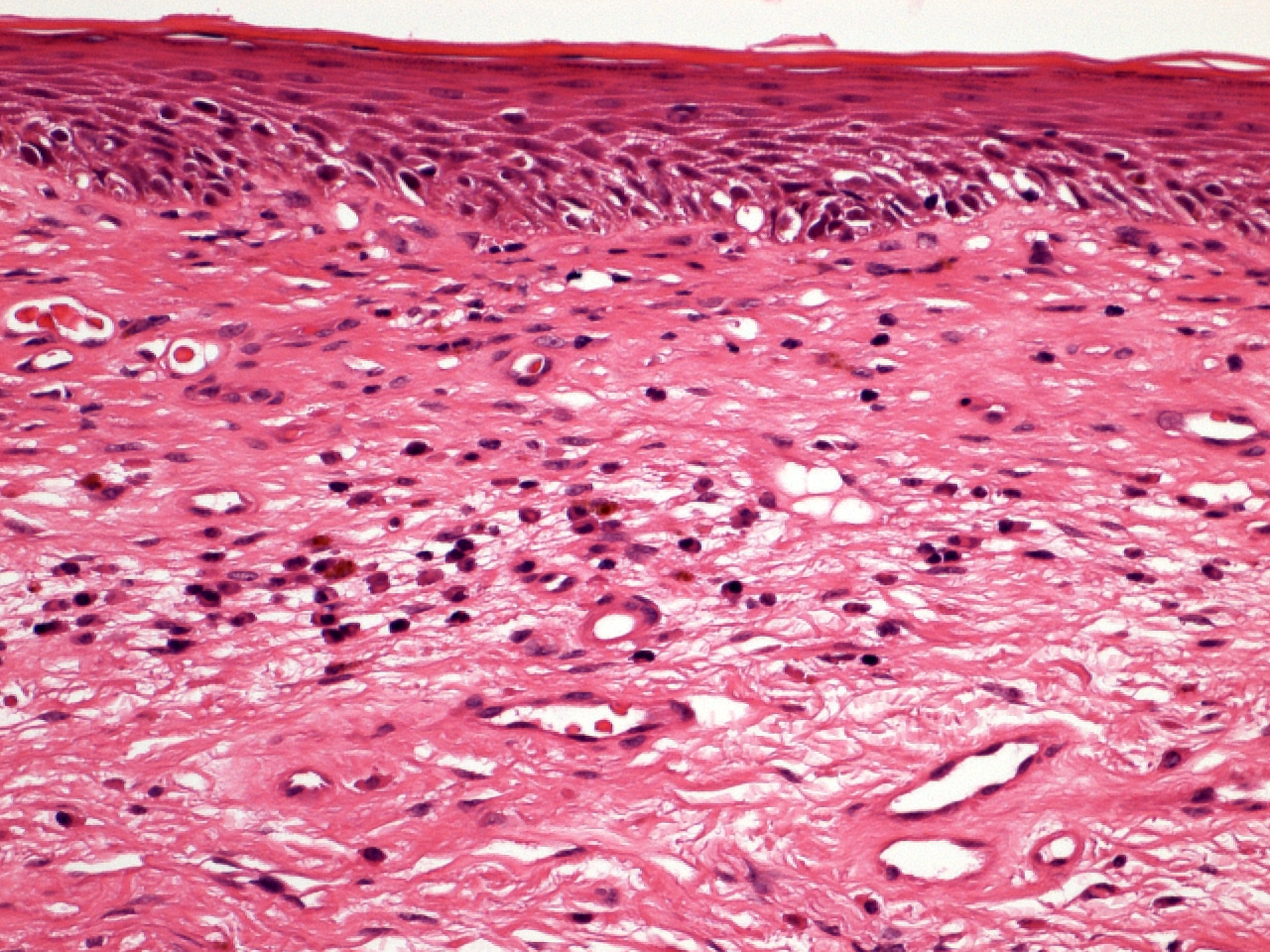


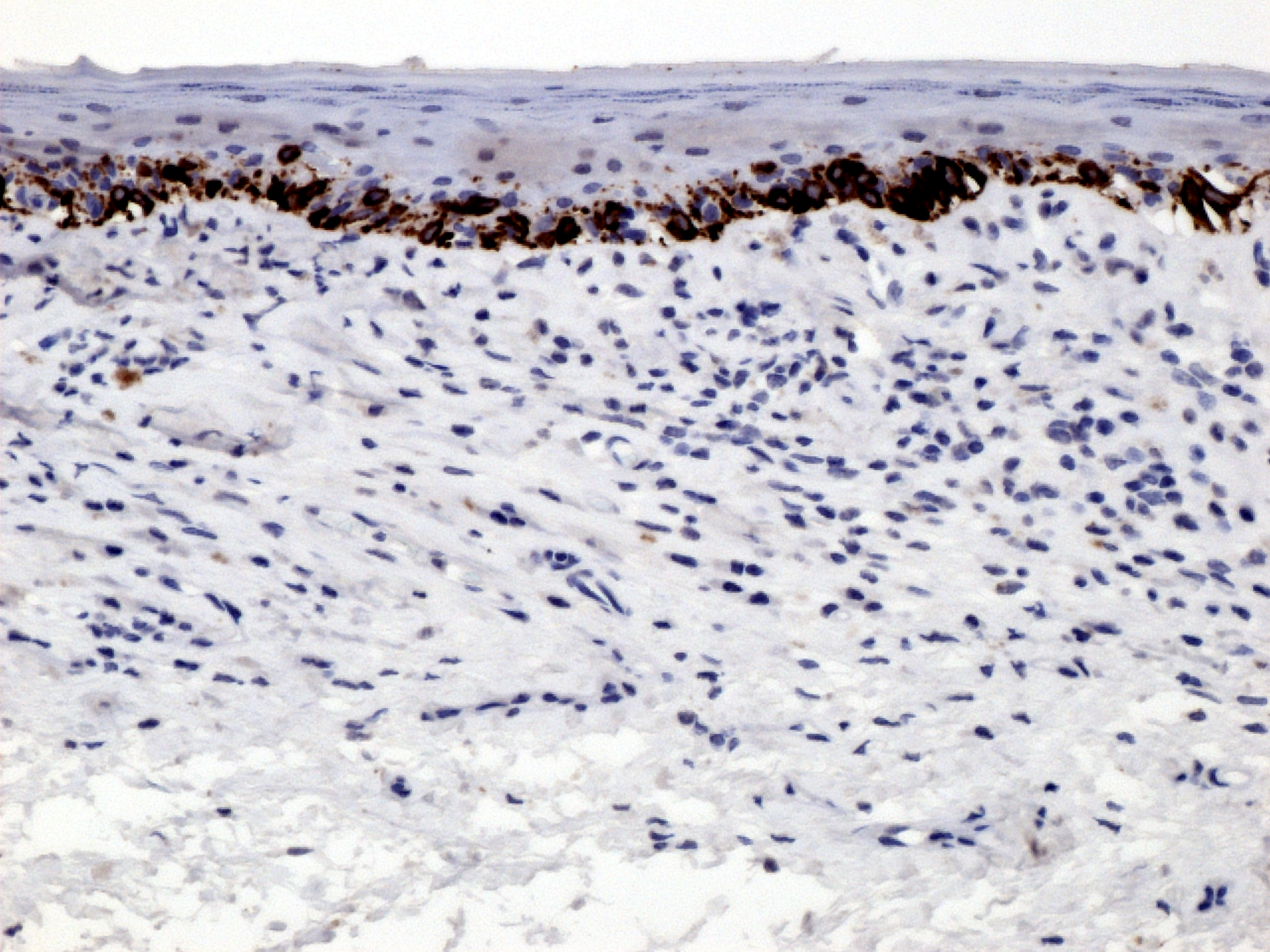








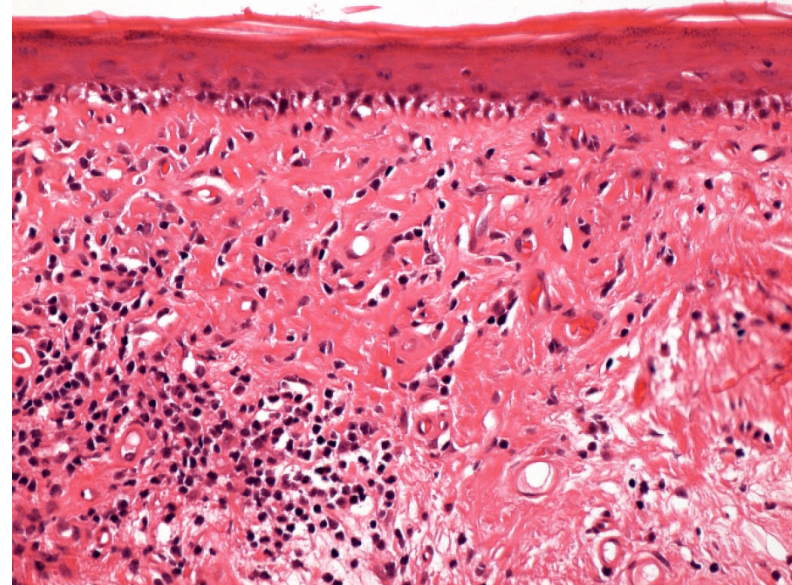
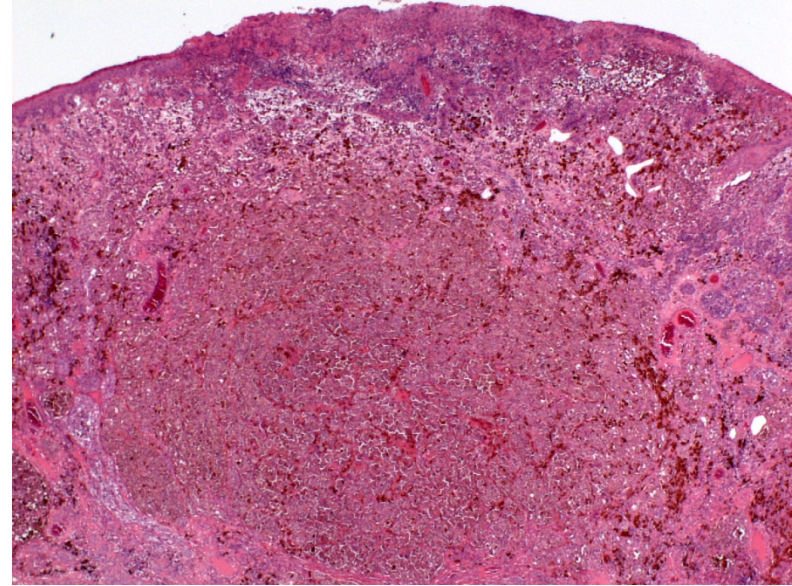




Vulval Melanoma

-Histology-

- Deeply invasive tumours
- Median Breslow 2-4mm
- Frequently ulcerated
- Broad radial growth
- Subtle histological features



Vulval Melanoma

-Prognosis-

- **Advanced stage at presentation**
- **LN at involvement presentation in 30%**
- **Poor 5-year survival (30-60%)**
- **Adverse prognostic indicators**
 - **LN metastasis**
 - **Tumour thickness (>3mm)**
 - **Ulceration**

Vulval Melanoma

-Prognosis-

**10-year survival
(Trimble et al 1992):**

- **68% -<0.75mm**
- **48% - 0.76-1.5mm**
- **44% - 1.5-3mm**
- **22% - >3mm**

**5-year survival
(SEER 2007):**

- **75.5% – localized dx**
- **38.7% – regional dx**
- **22.1% - distant dx**

Vulval Melanoma

-Treatment-

Sentinel lymph node consideration: as for cutaneous melanoma

Wide local excision with:

1 cm margin for tumour thickness <1mm

2 cm margin for tumour thickness 1-4mm

Vulval Melanoma

-Treatment-

Activating mutations in c-kit in ~35%

Target therapies, i.e. imatinib

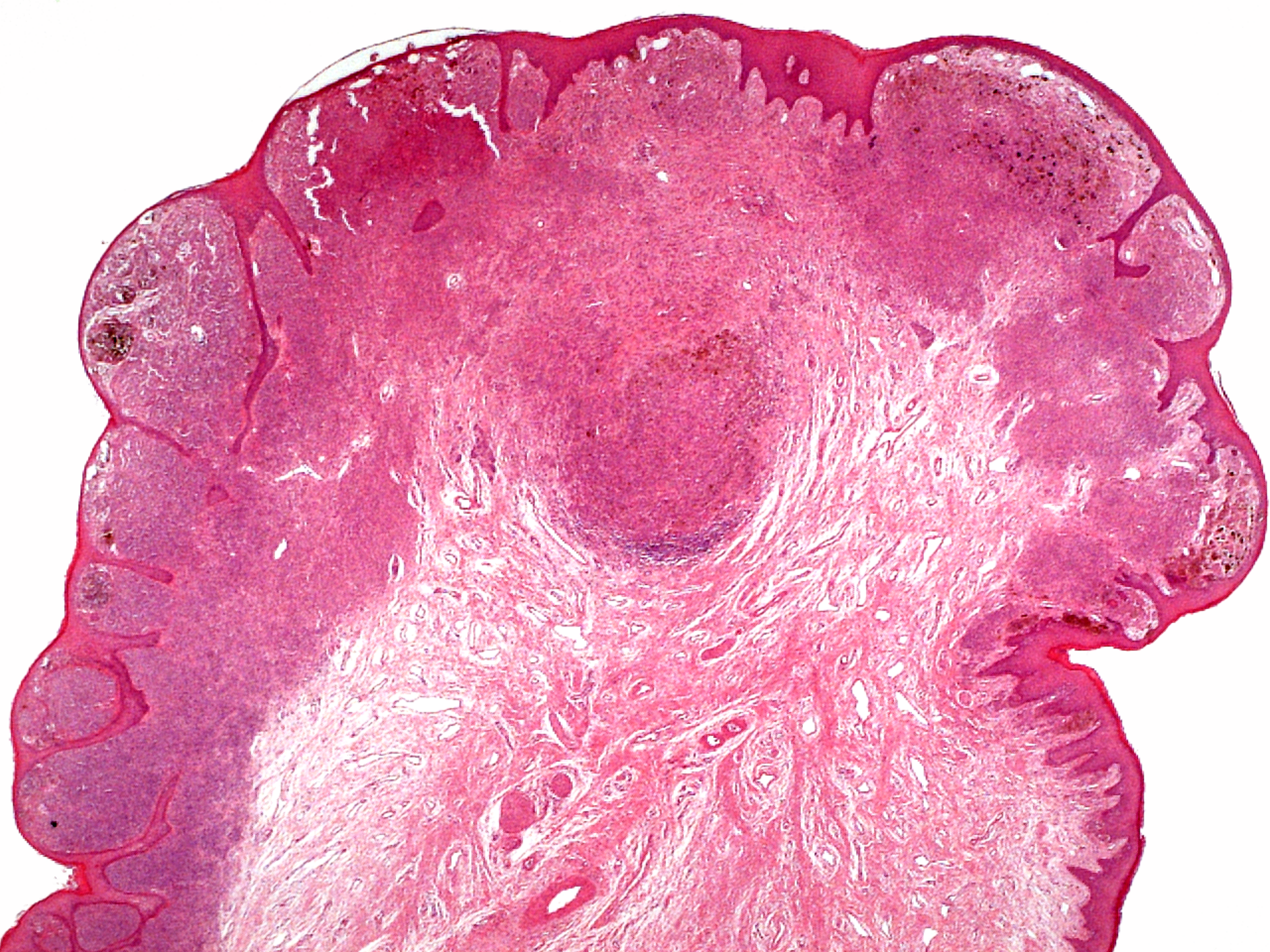
Vulval Melanoma

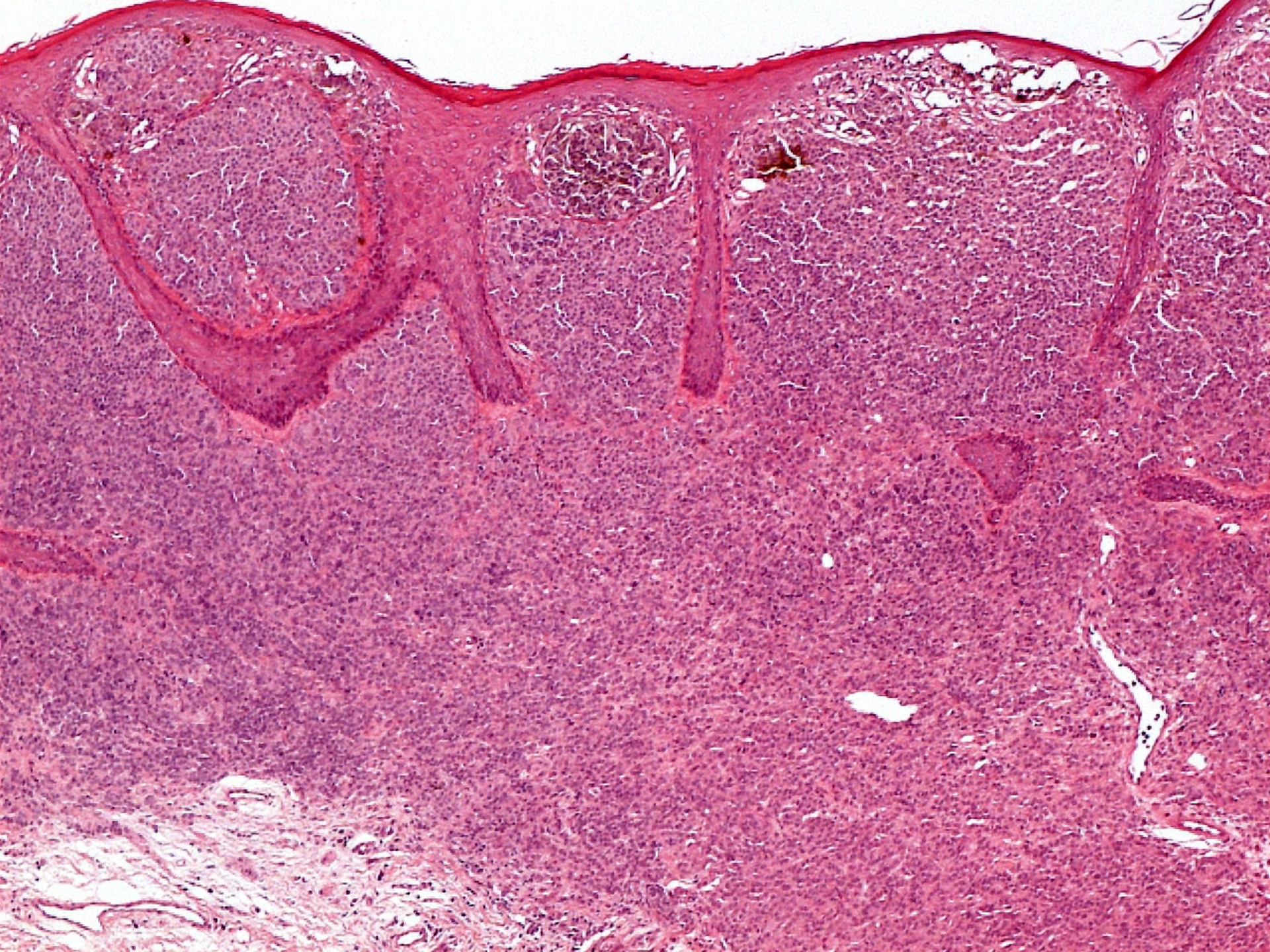
-Differential Diagnosis-

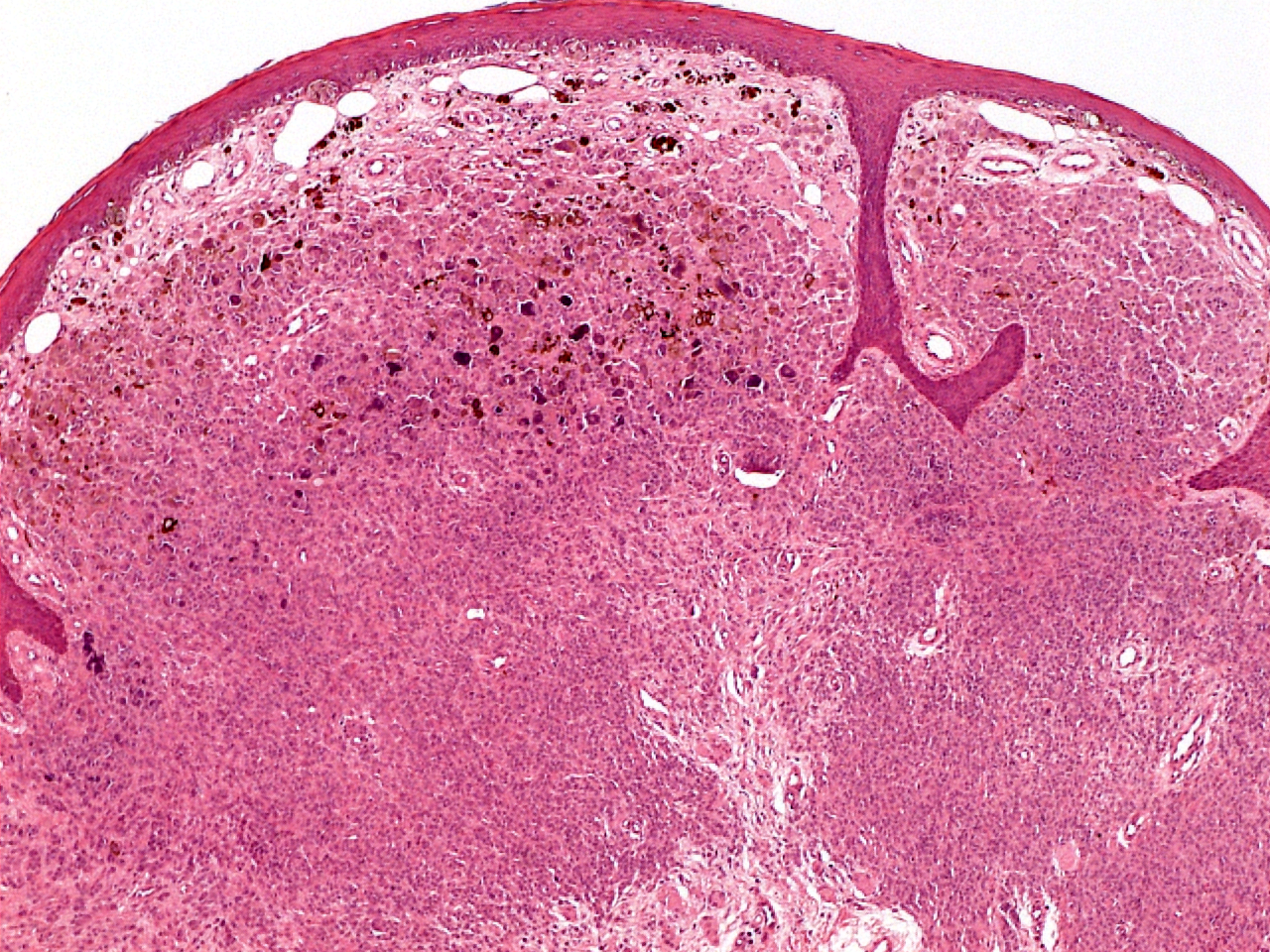
- **Dysplastic naevi**
- **Atypical genital naevi**
- **Vulval melanosis**
- **Pigmented Bowen's**
- **Extramammary Paget's**

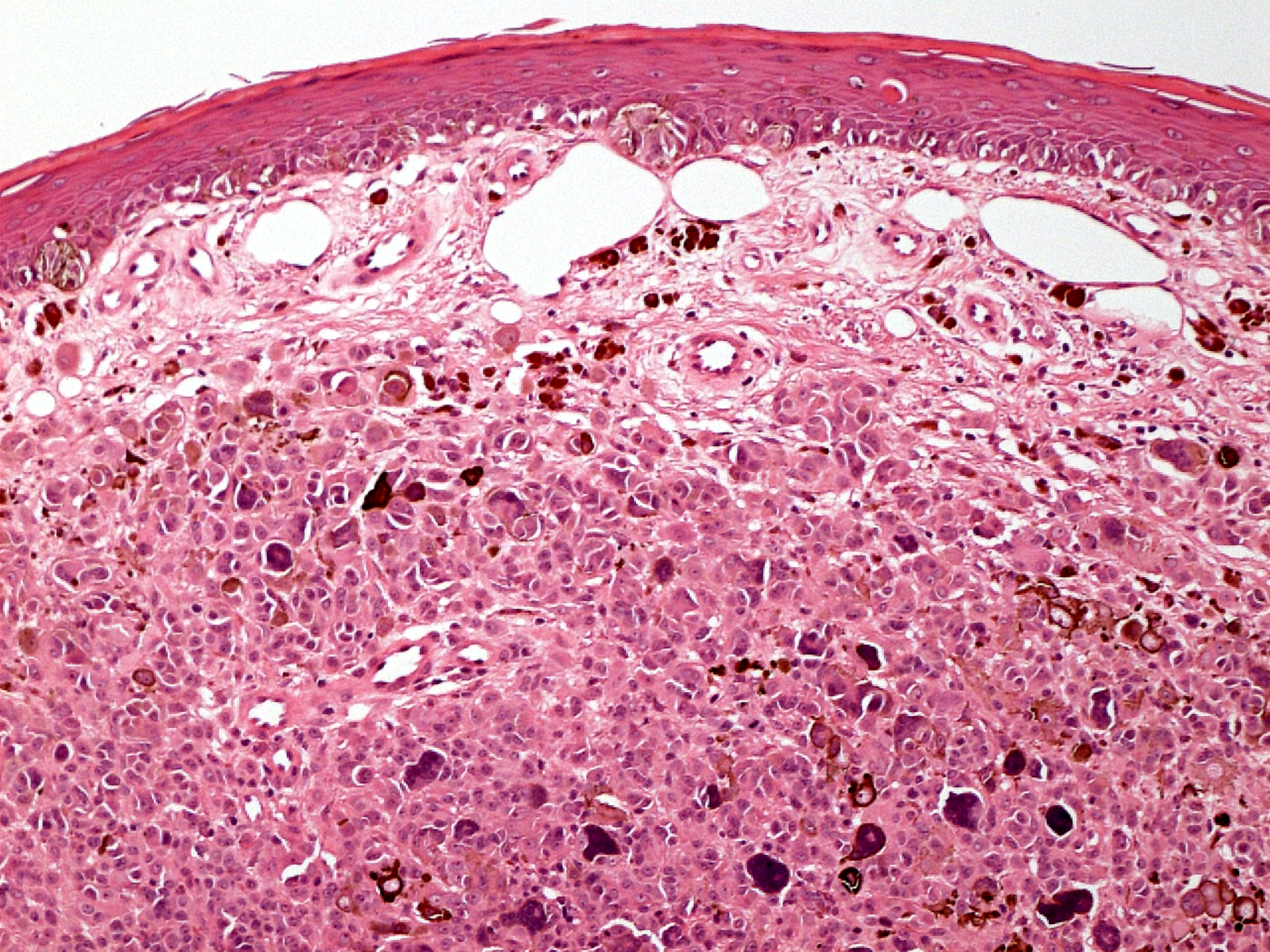
Atypical genital naevus, Dysplastic Naevus and Vulval Melanoma: Distinguishing Clinical and histological features

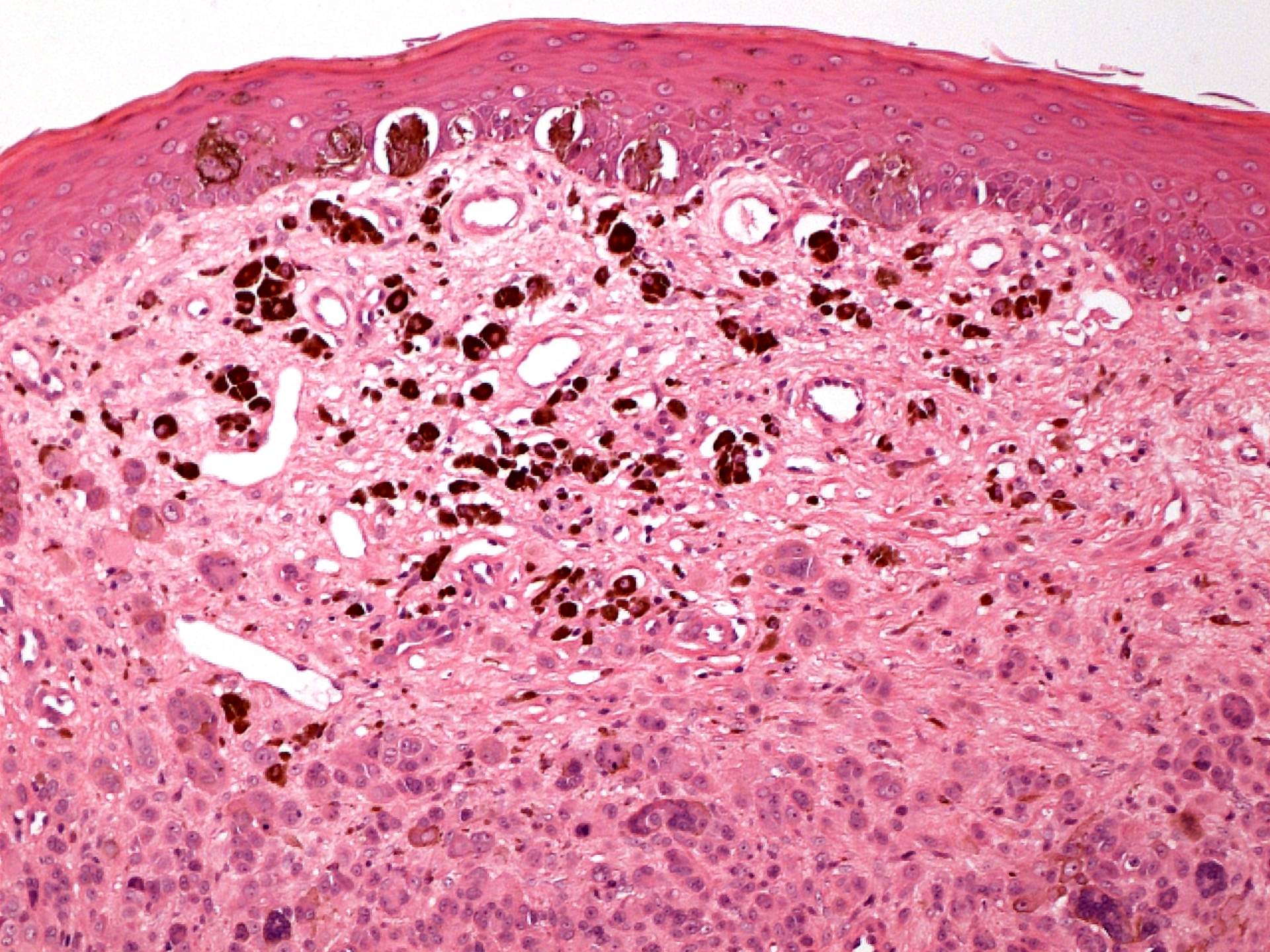
	Atypical Genital Naevus	Dysplastic Naevus	Vulval Melanoma
Age	Premenopausal	Premenopausal	Postmenopausal
Size, cm	<1cm	<1cm	>1cm
Symmetry	Preserved	Slight asymmetry	Absent
Lesional Contours	Well defined and circumscribed	Indistinct	Ill-defined and indistinct
Junctional Shoulder	Absent	present	Extensive
Lentiginous Growth	Minor component	present	Major component
Pagetoid Invasion	Focal and rare, confined to lesional center	Absent	Extensive and randomly distributed across the lesion
Epidermal Hyperplasia	Present	Pronounced rete ridge pattern	Absent
Ulceration	Absent	Absent	Present in majority of cases
Dermal Melanocyte Atypia	Limited to the superficial aspect	Absent	Prominent
Dermal Growth	Non-expansile	Non-expansile	Expansile
Dermal Maturation	Preserved	Preserved	Absent
Dermal Mitotic Activity	Rare; superficial aspect	Absent	Brisk
Necrosis	Absent	Absent	May be present
LVI	Absent	Absent	May be present

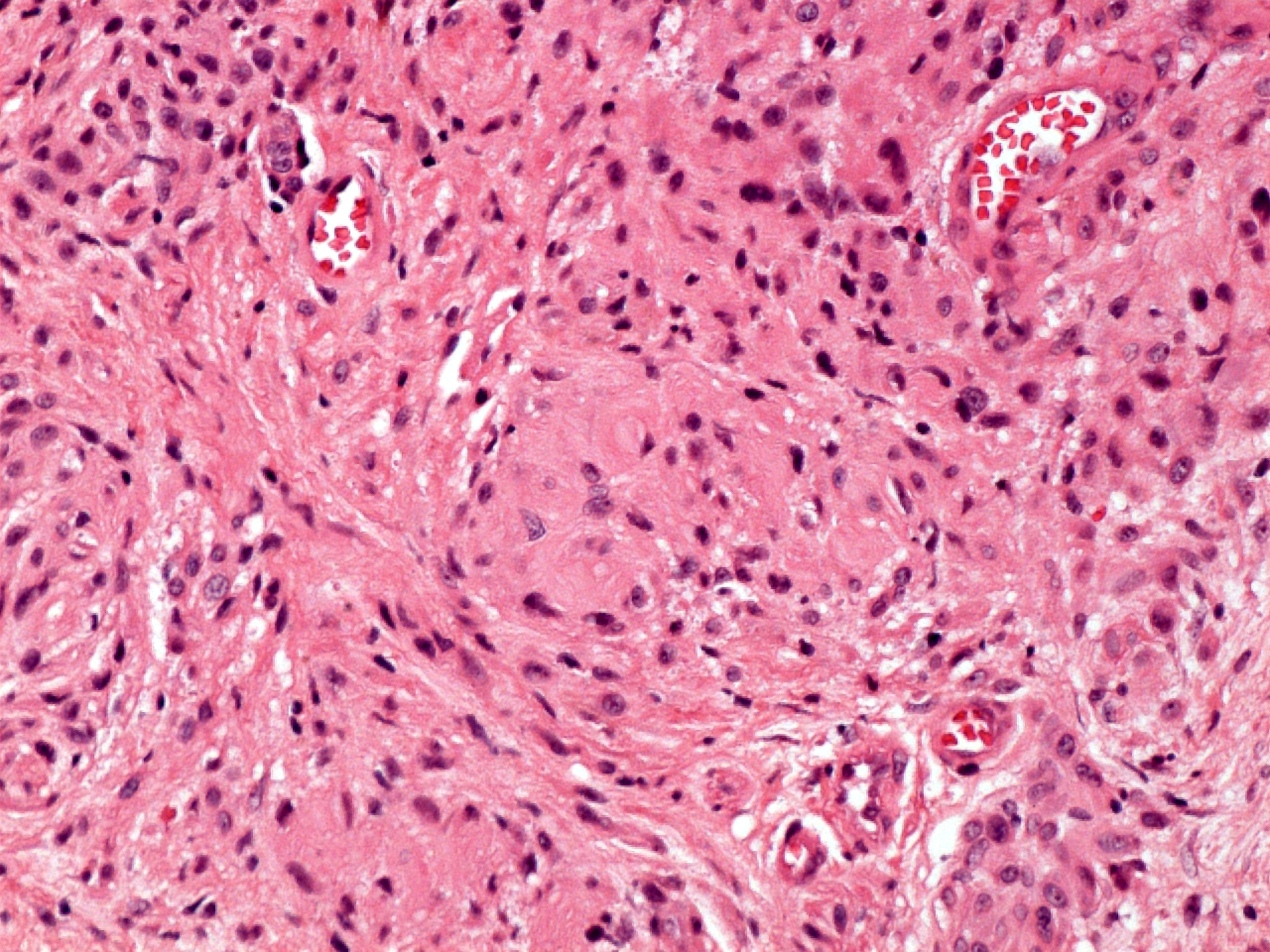


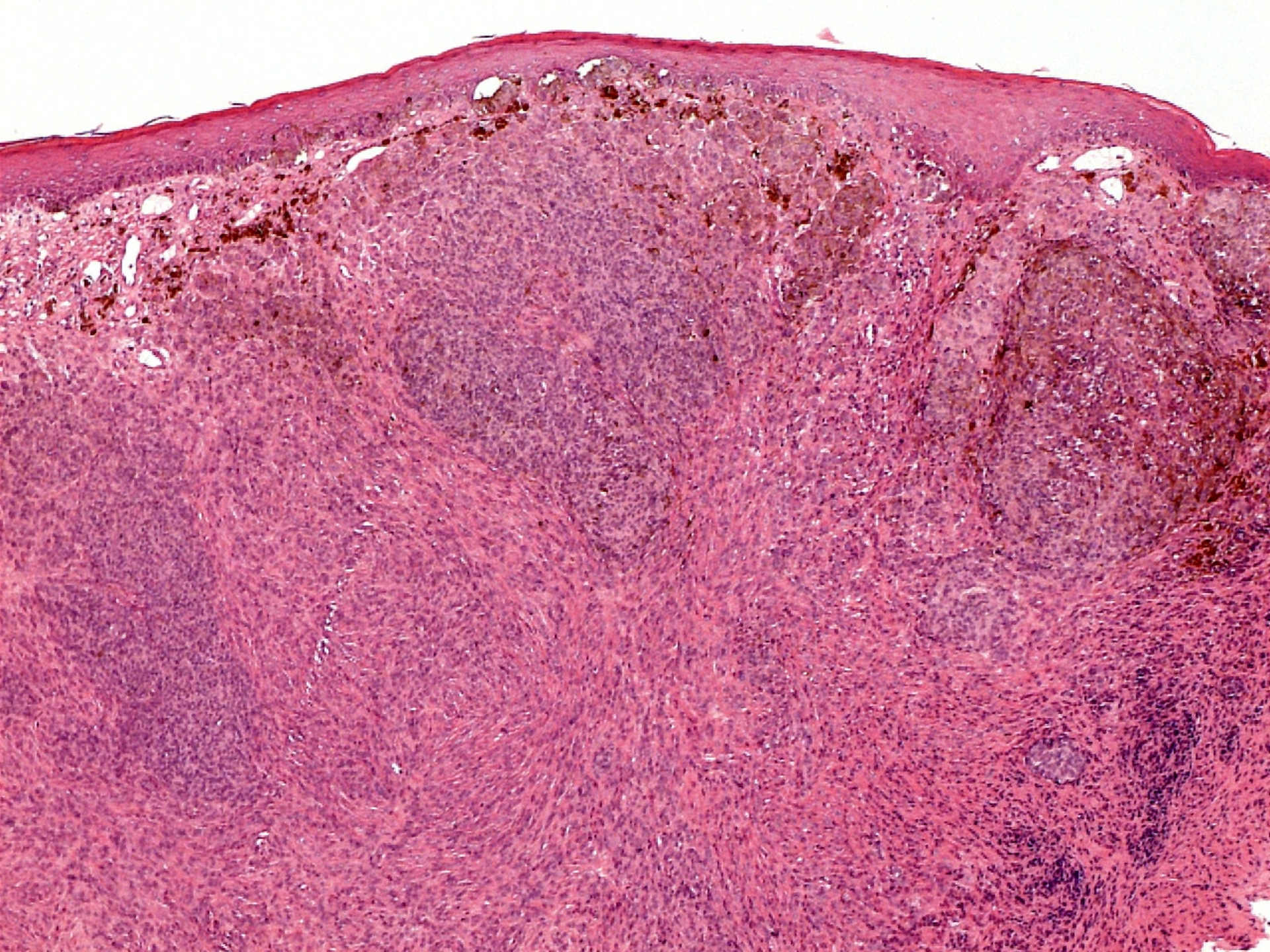


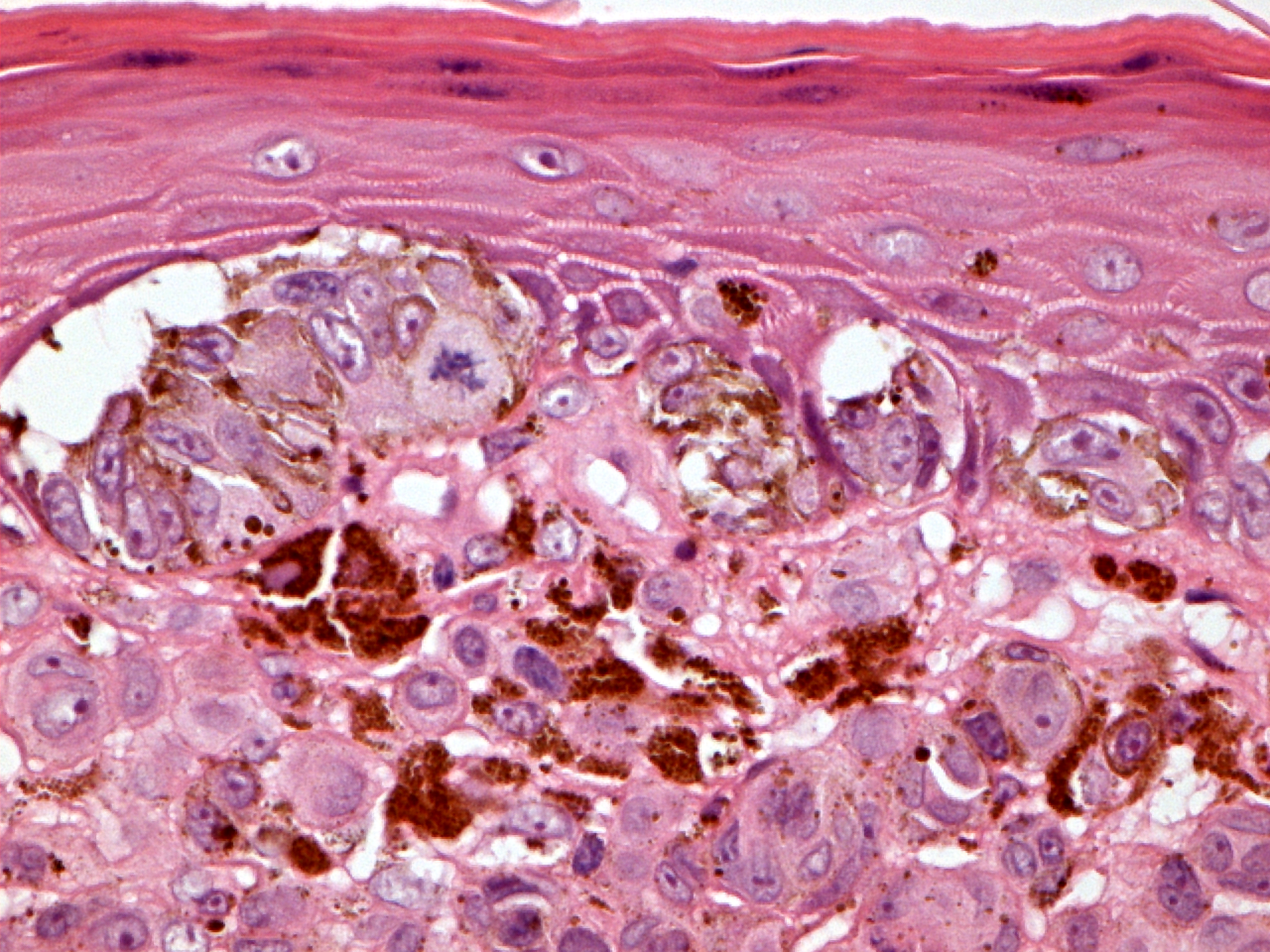


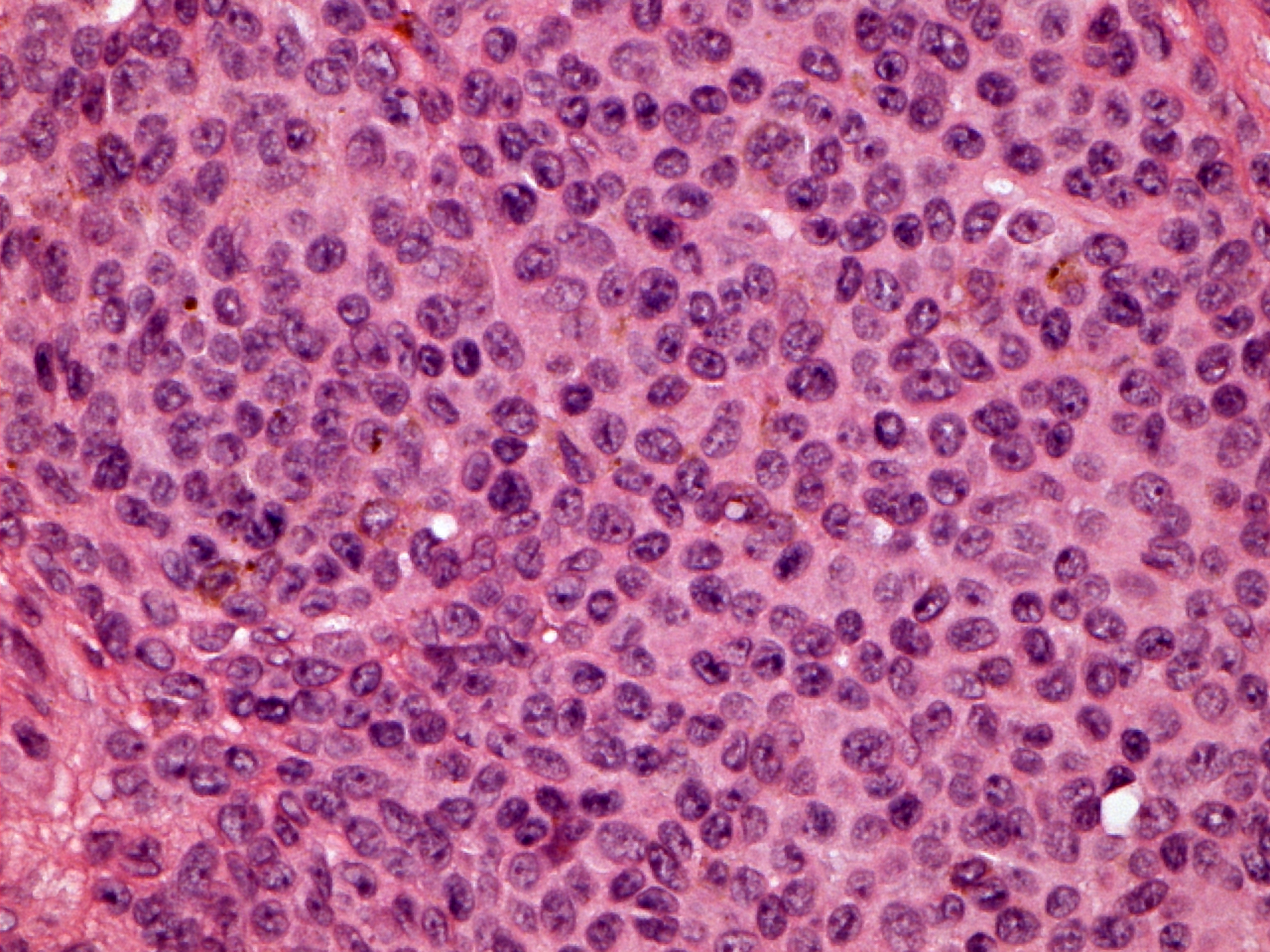


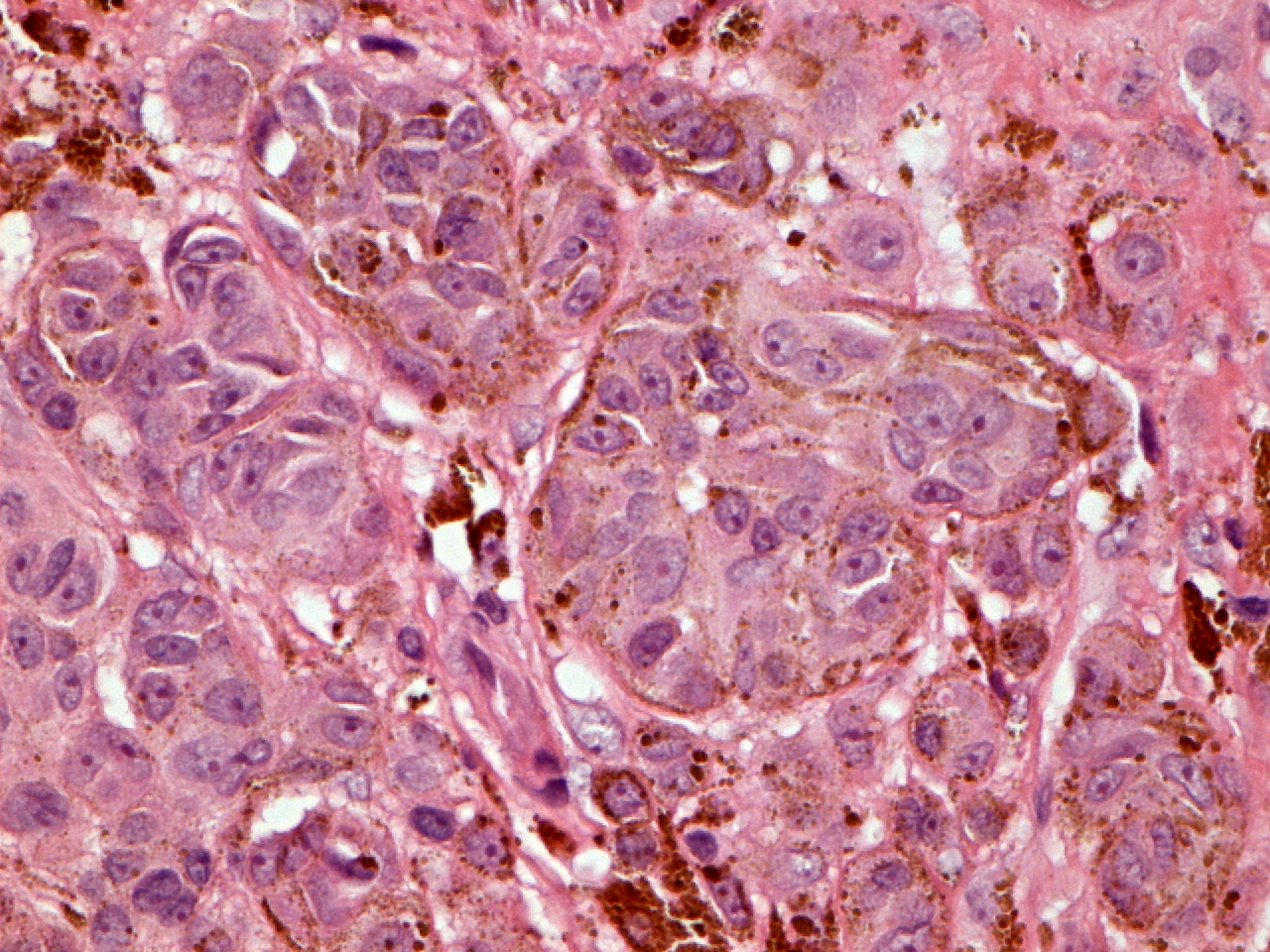


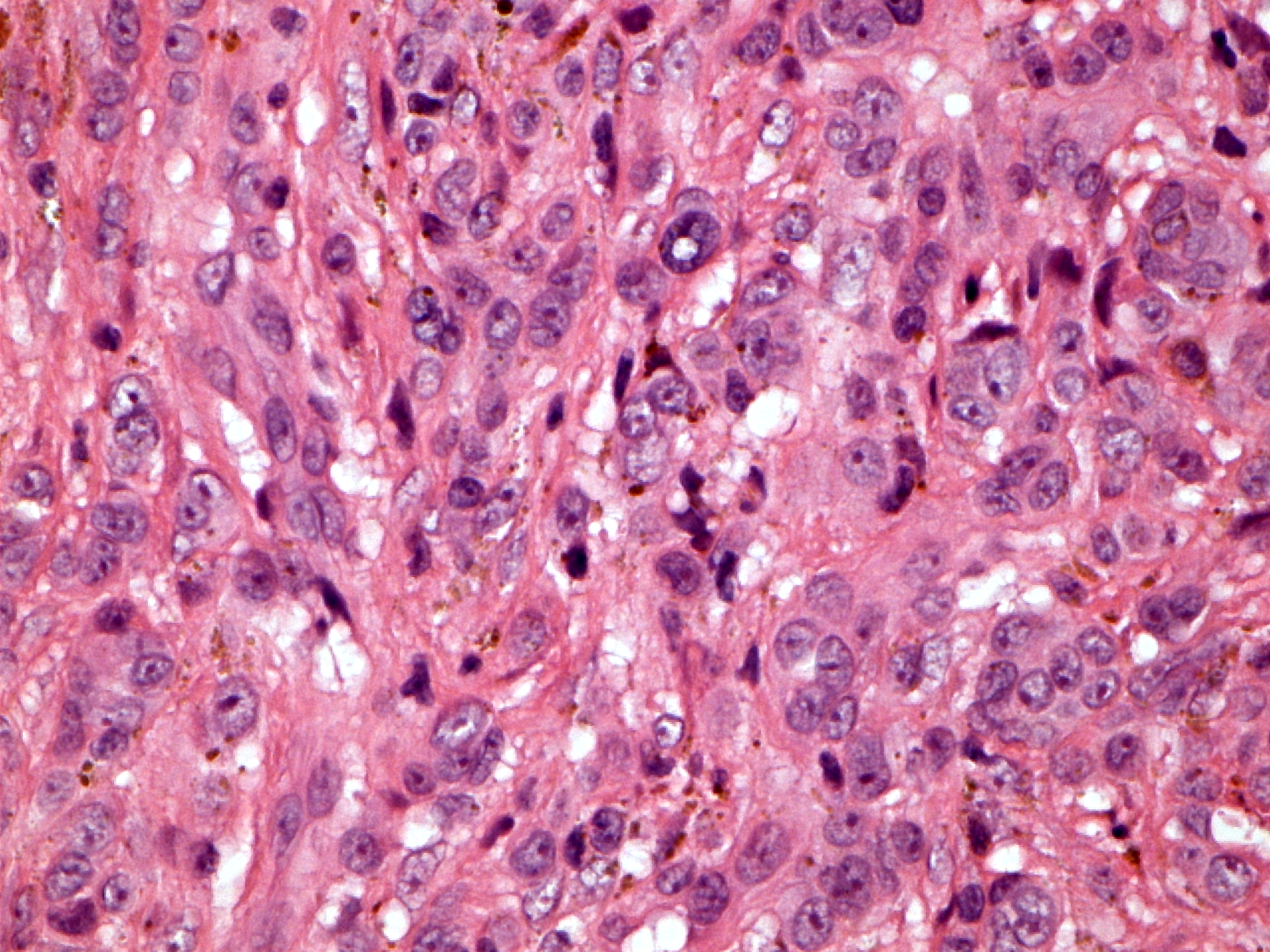


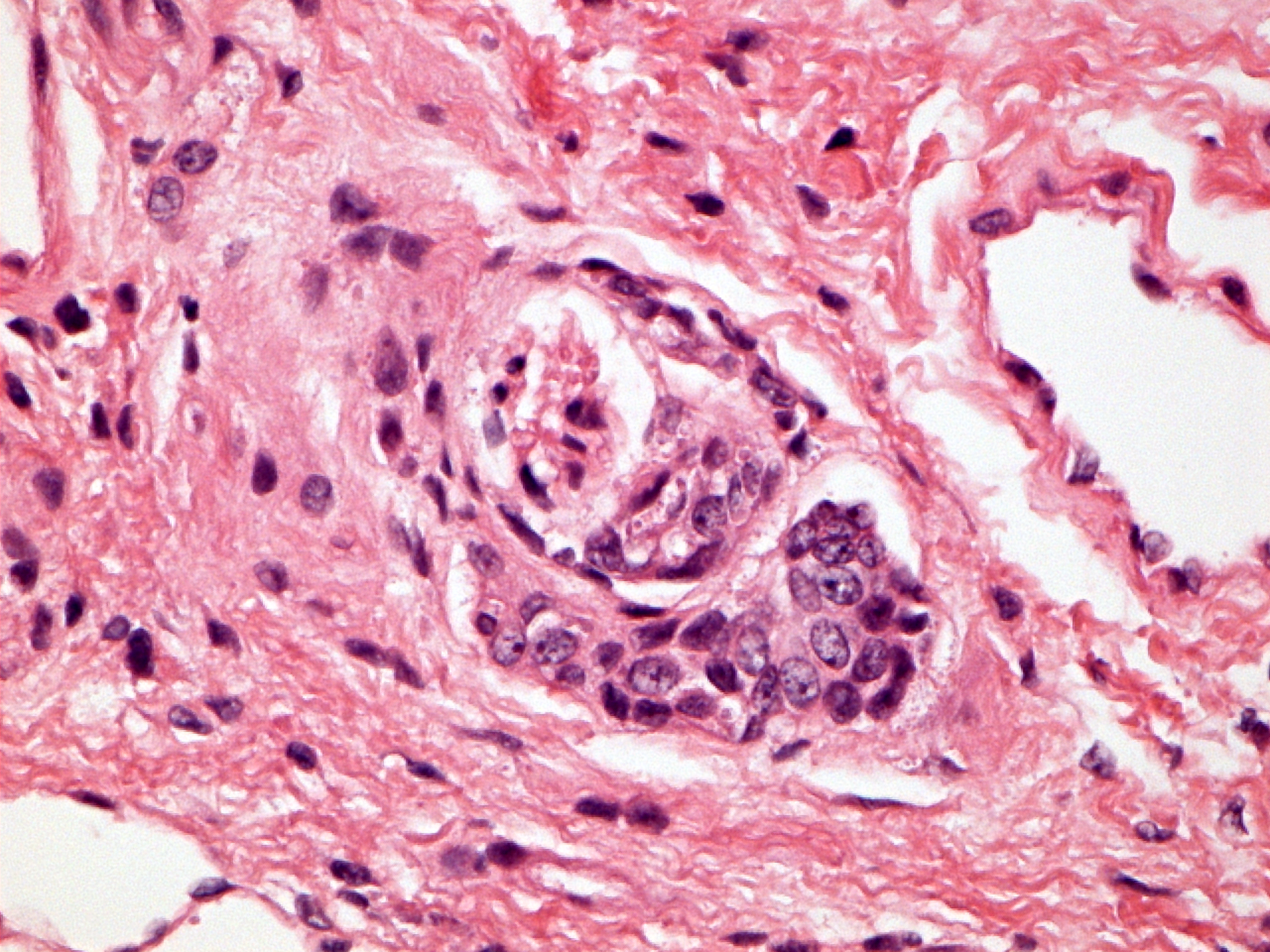


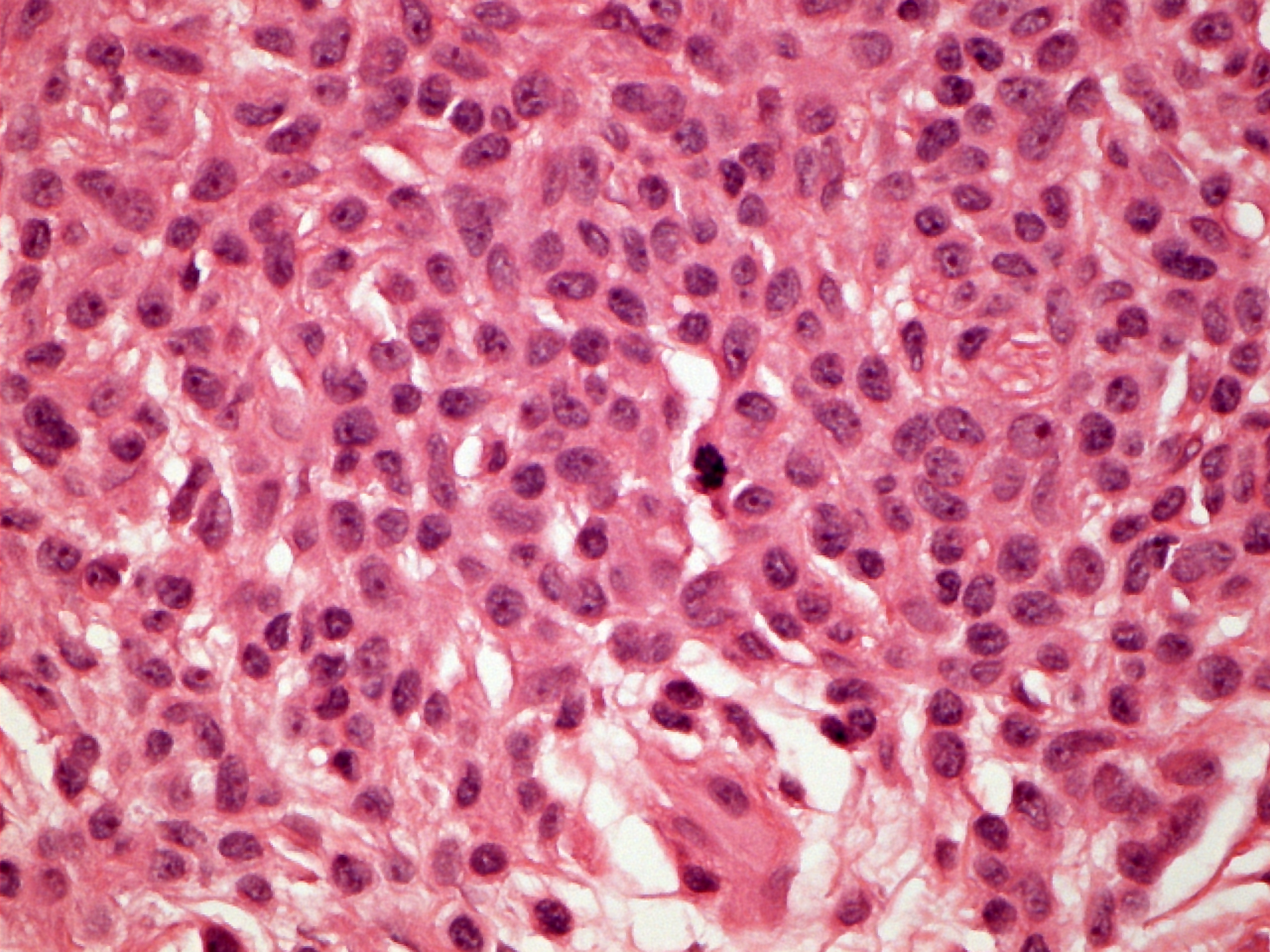


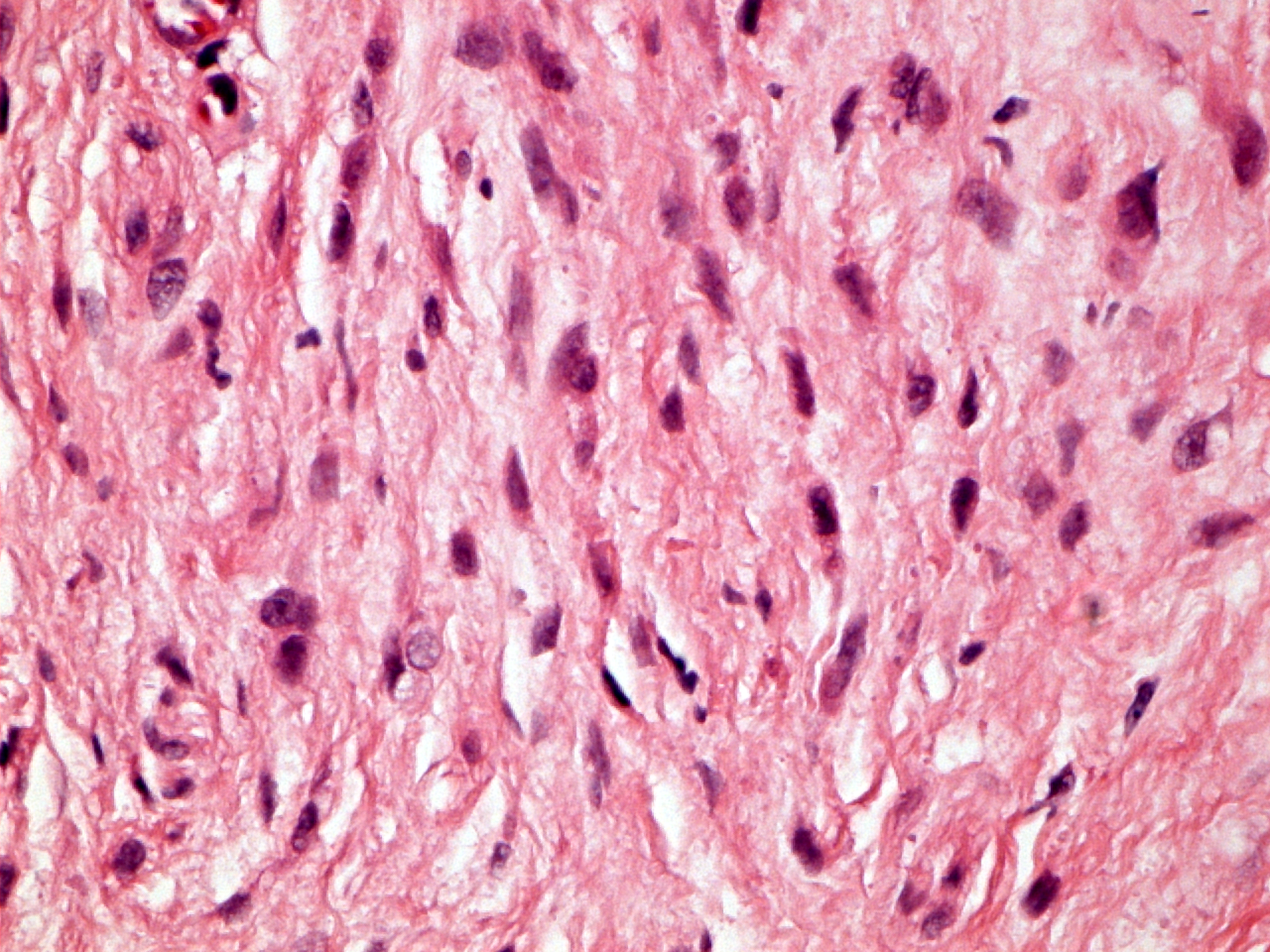








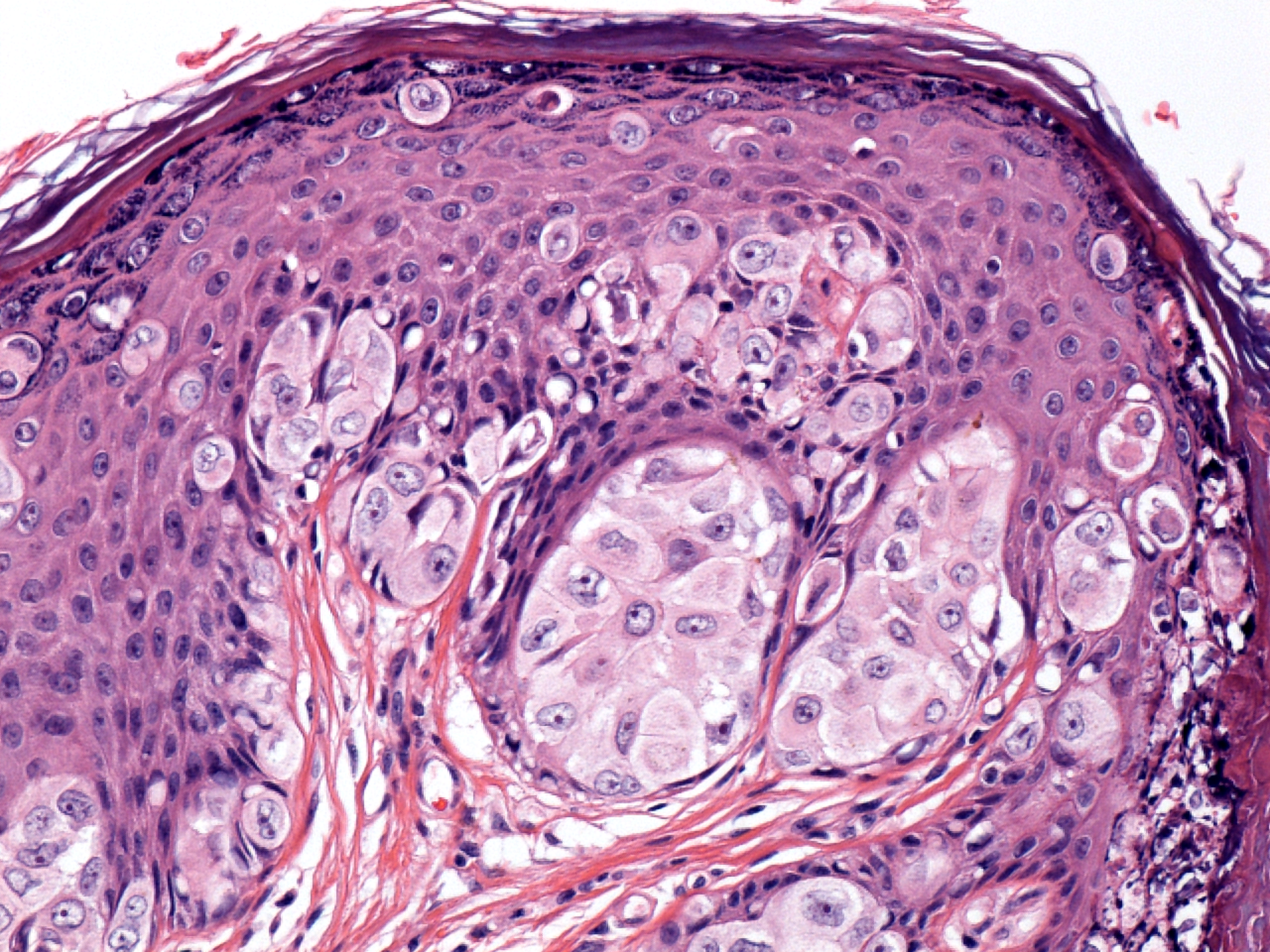


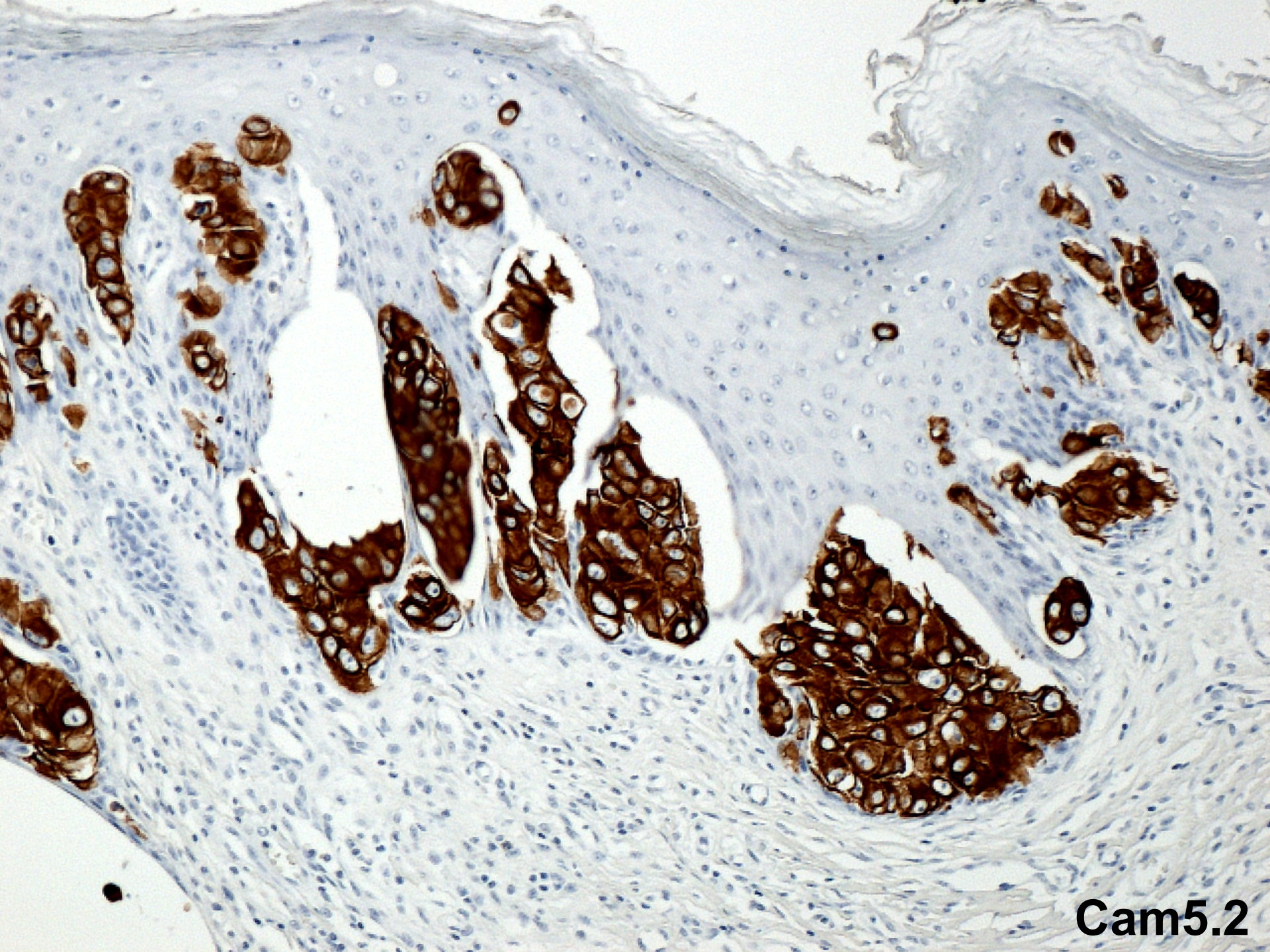


Extramammary Paget Disease

-Clinical-

- **Rare tumour**
- **Scaly plaques resembling eczema**
- **Occasionally pigmented**
- **Pruritus**
- **Anogenital area**
- **Elderly adults**
- **Female predominance**





Melanocytic Tumours of the Vulva

Diagnosis of melanoma may be challenging

- **Clinically undetected**
- **Subtle features of radial growth phase**
- **Significant morphological overlap with benign melanocytic tumours**
- **“Atypical genital-type naevus”**

