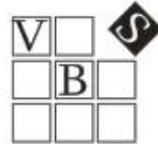


Východoslovenský
BIOPTICKÝ SEMINÁR



*Minisymposium:
Pathology of Melanocytic Lesions-*

Melanocytic Lesions on Children



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



Melanocytic Lesions in Children

-Introduction-

- Wide range from entirely benign to outright malignant
- Vast majority benign
- Wide morphological spectrum, some with concerning histological features
- Distinction from melanoma both critical and challenging

Melanocytic Lesions in Children

-Overview-

- **Congenital naevi in neonates and young children**
- **Proliferative nodules in CN**
- **Atypical Spitz Tumours and Spitzoid Melanoma**
- **“Childhood Melanoma”**

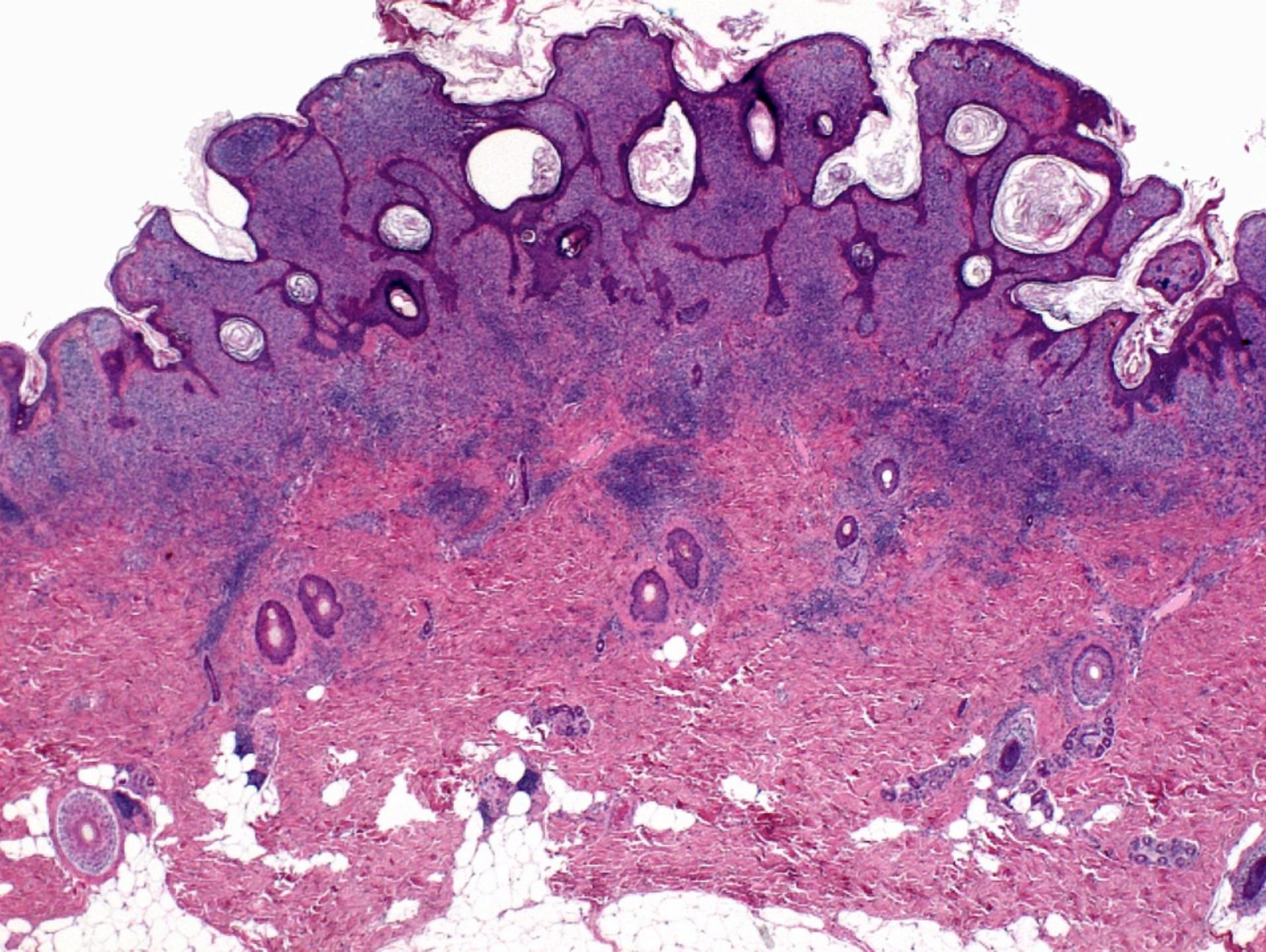
Congenital Naevi in Neonates and Young Children

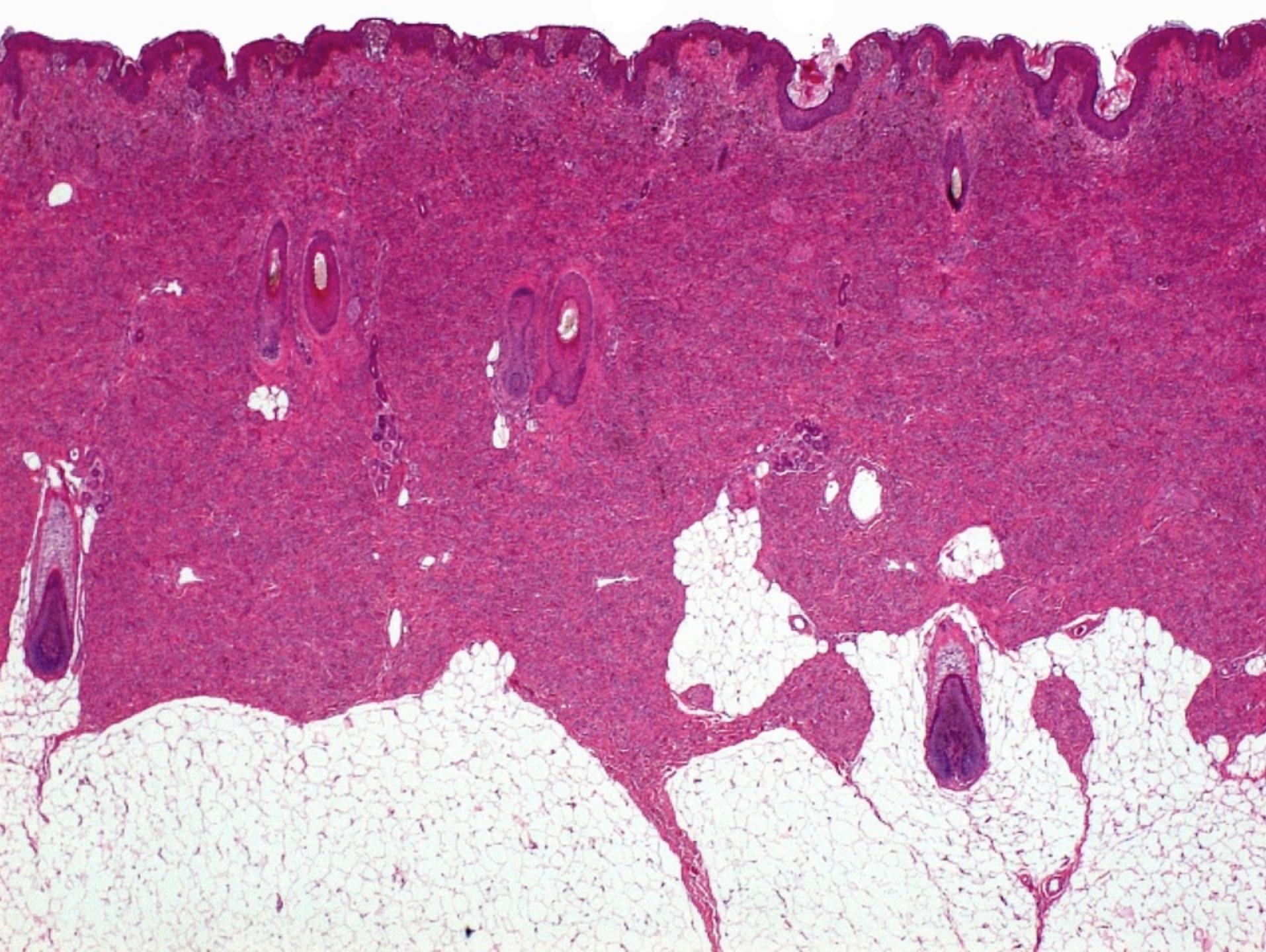
- **High incidence of Congenital Naevi (CMN)**
- **~1% of newborns**
- **Classified by size:**
 - Small (<1.5 cm)
 - Medium
 - Large/giant CMN (>20cm)

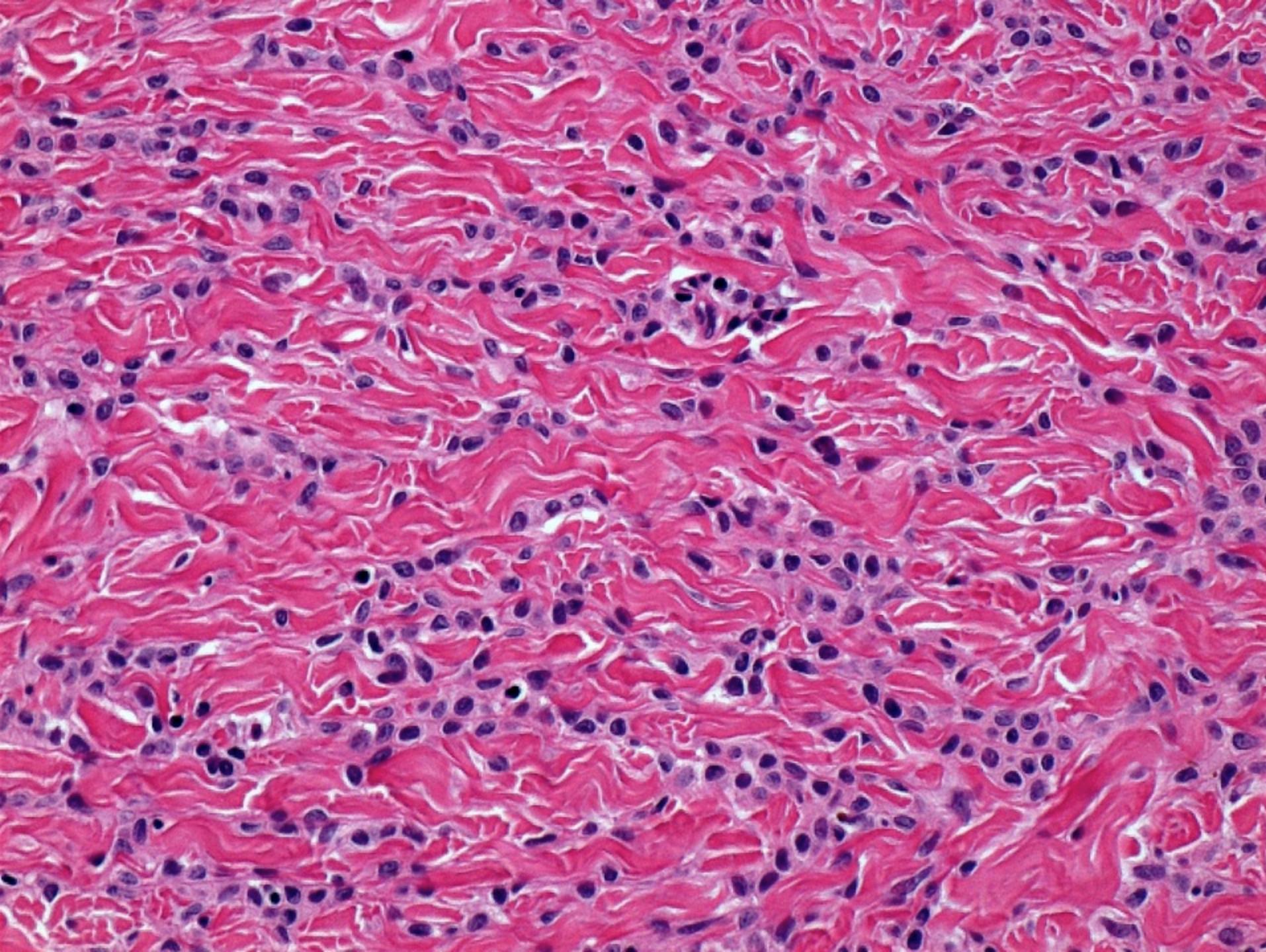
Congenital Naevi in Neonates and Young Children

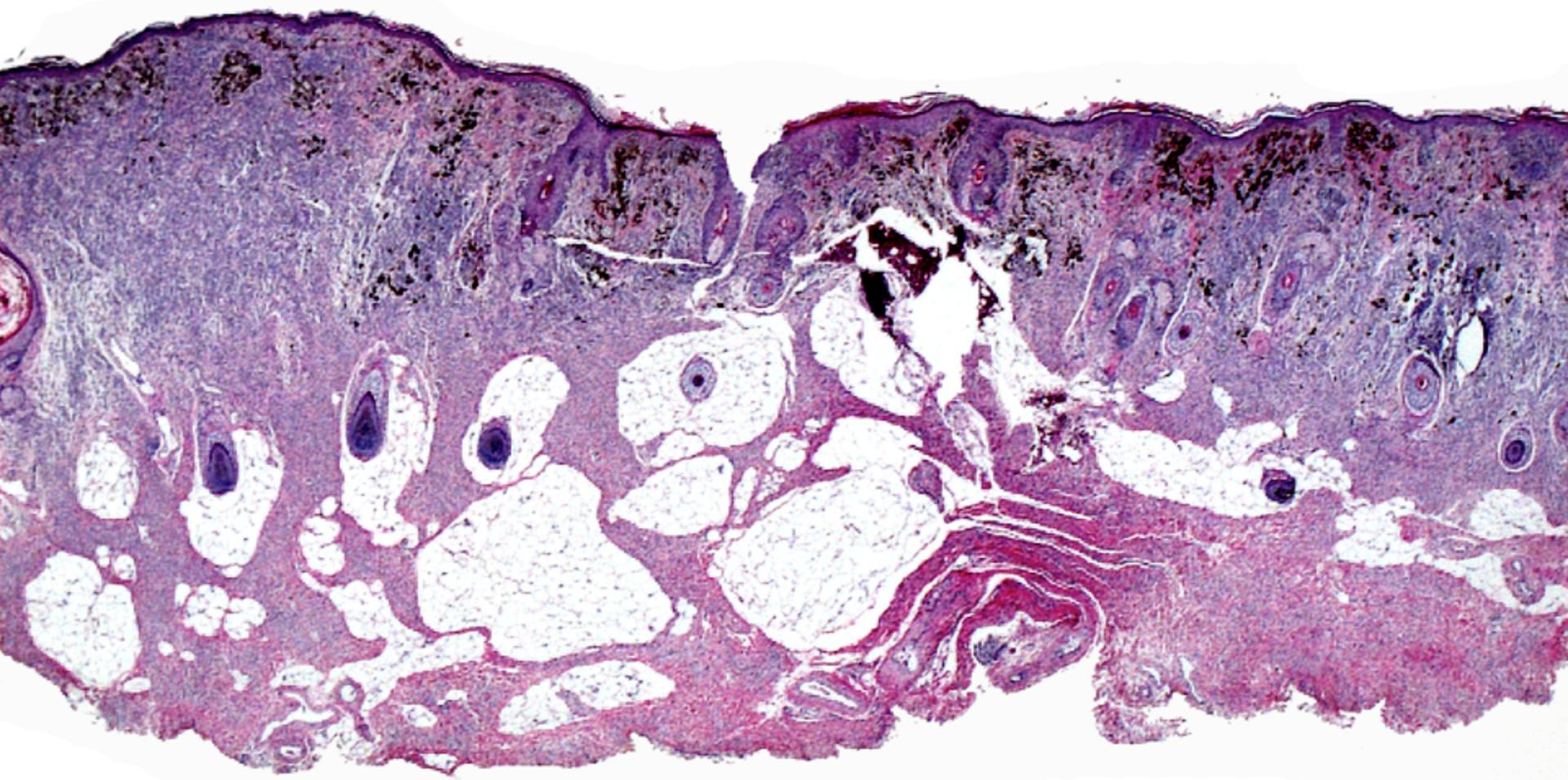
**Large CMN rare
(1:20,000 – 1:500,000)**

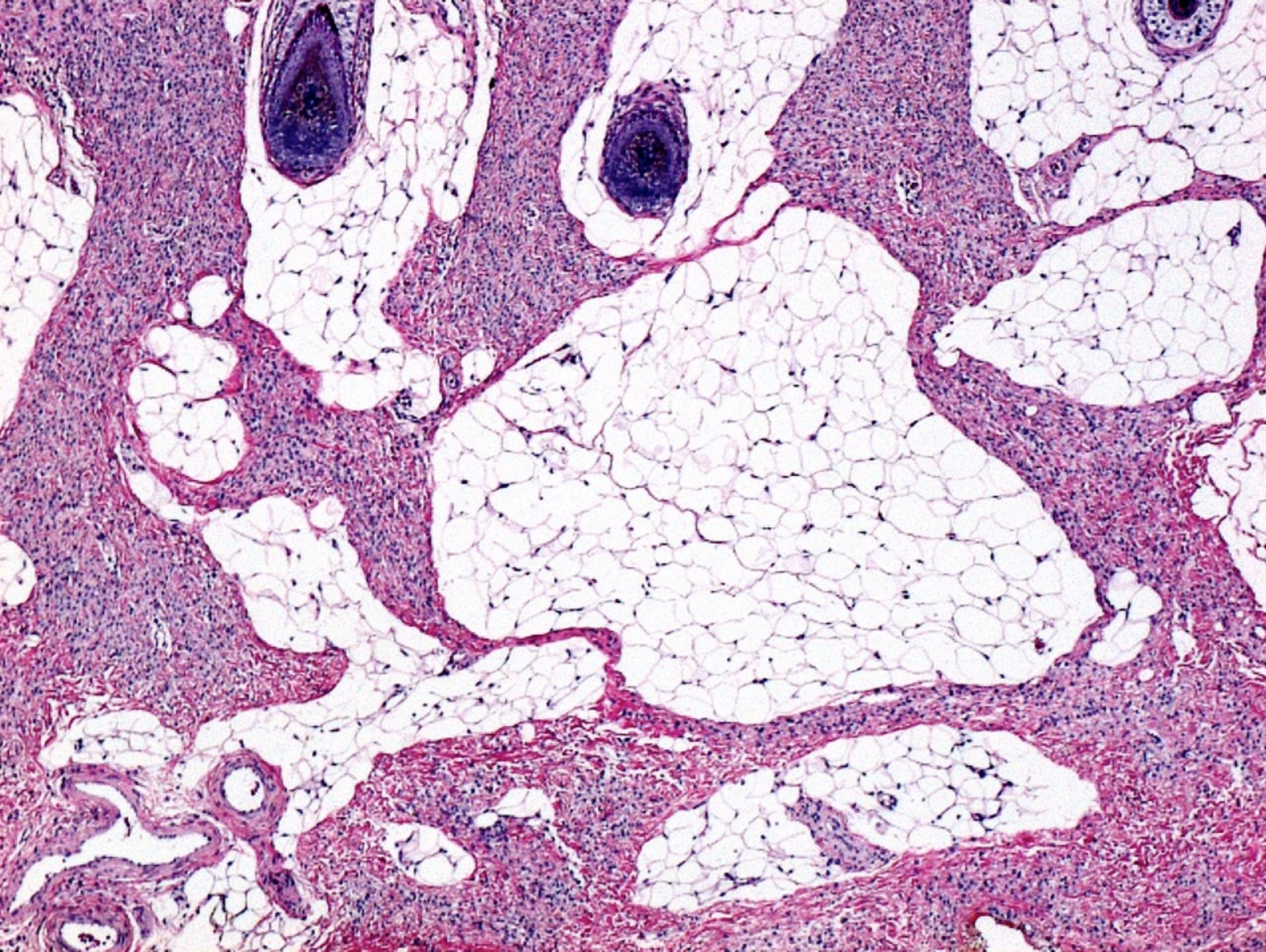
**Risk for development of
melanoma (3-4%)**

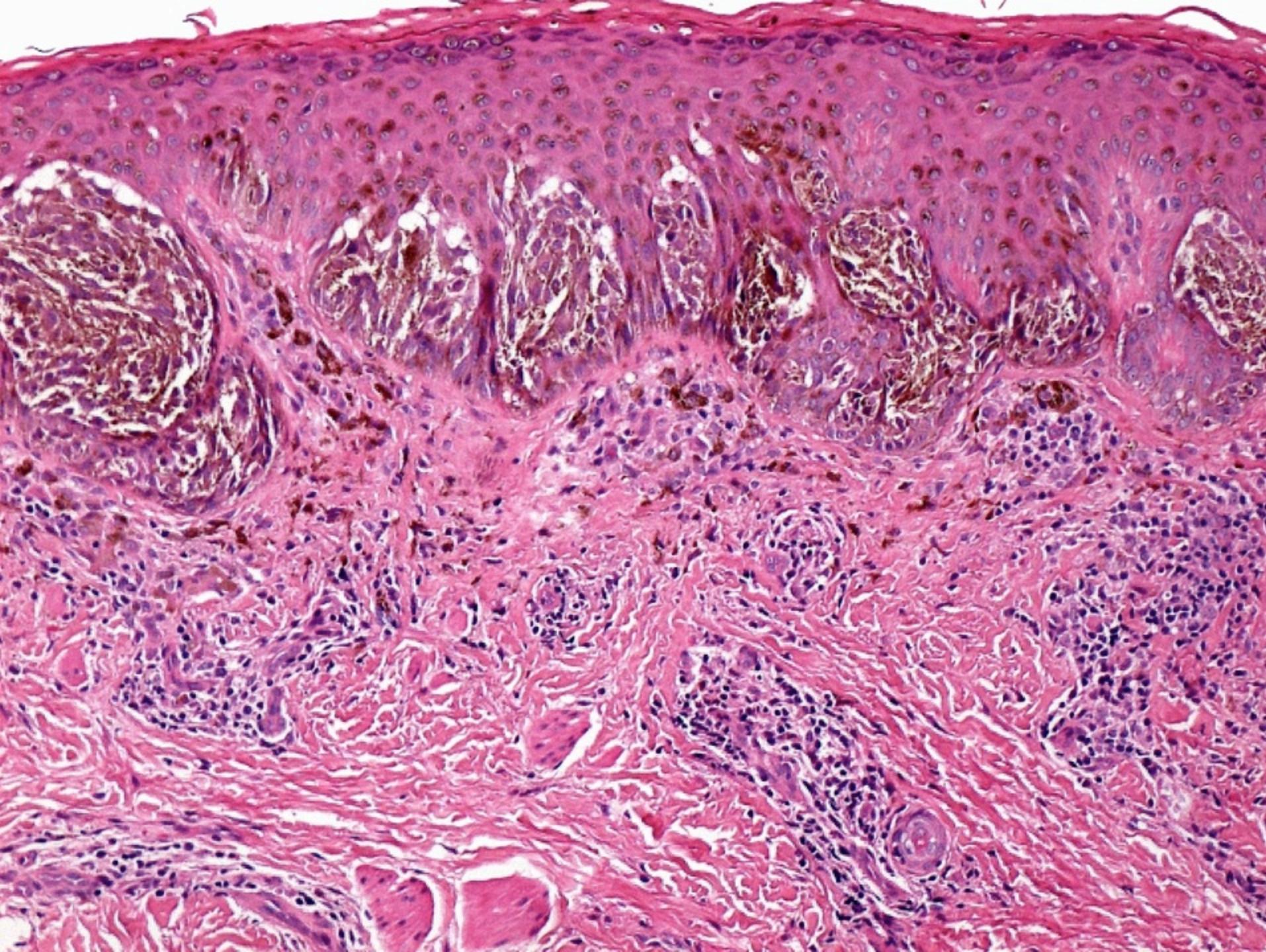


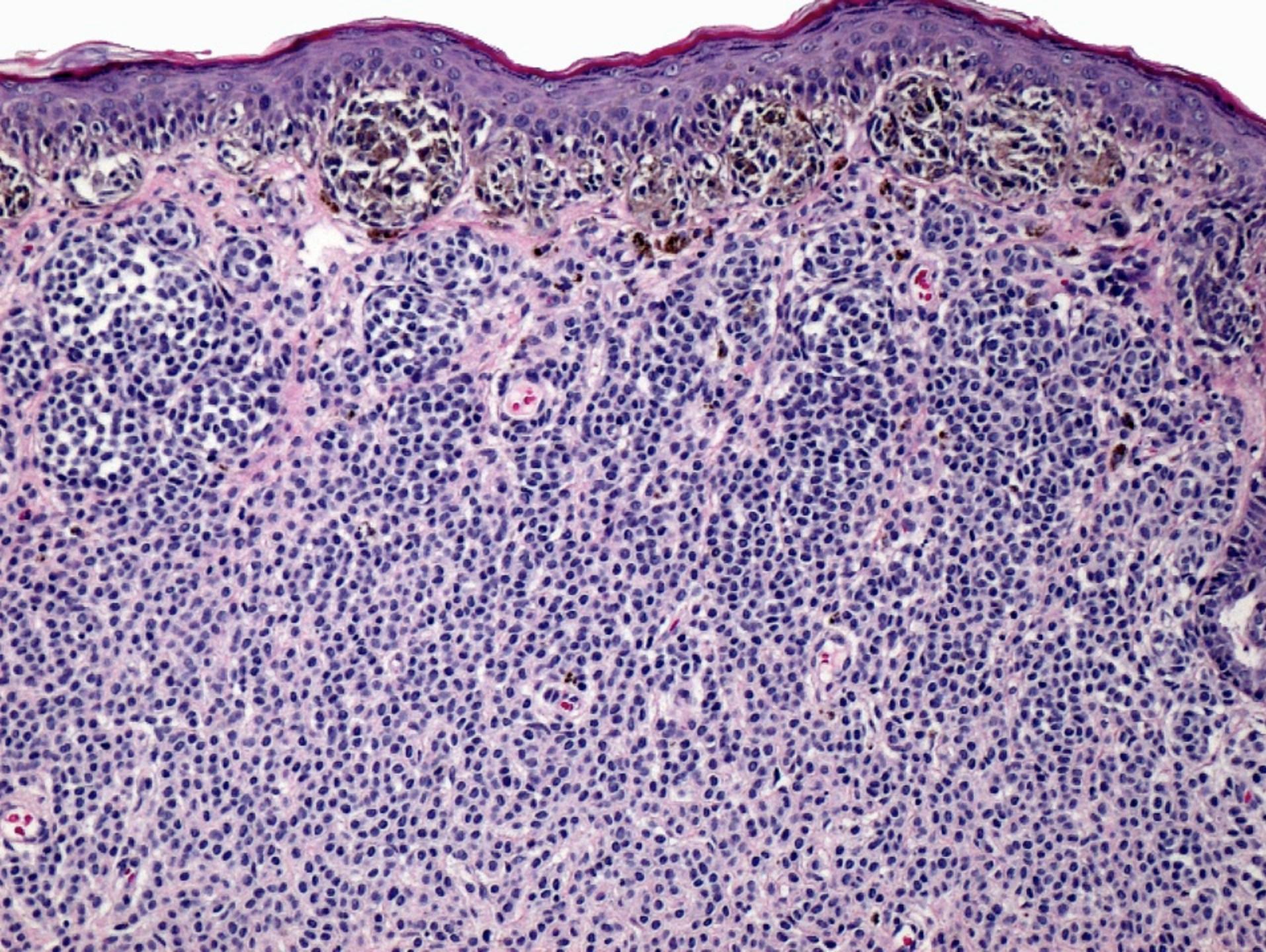


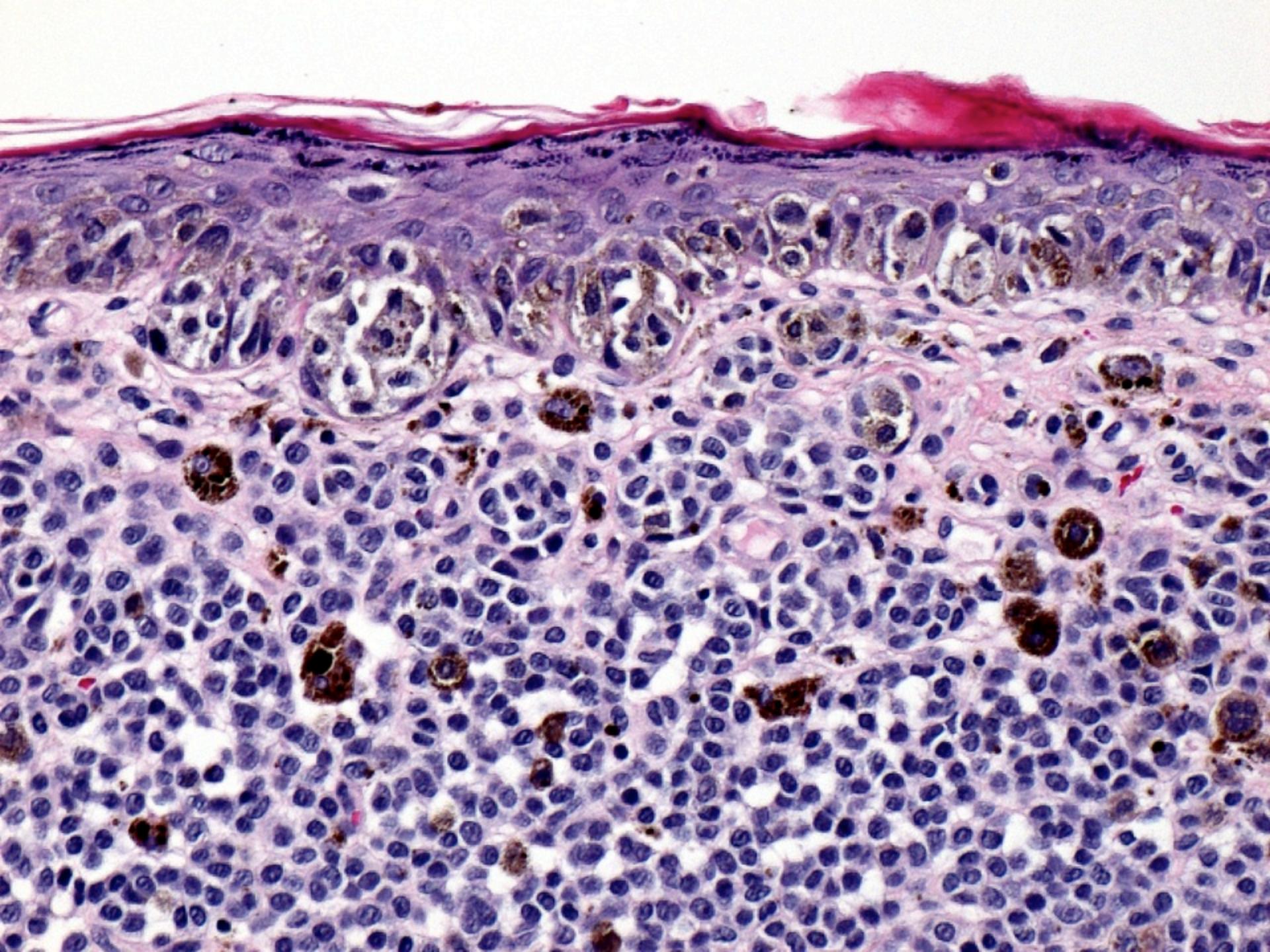


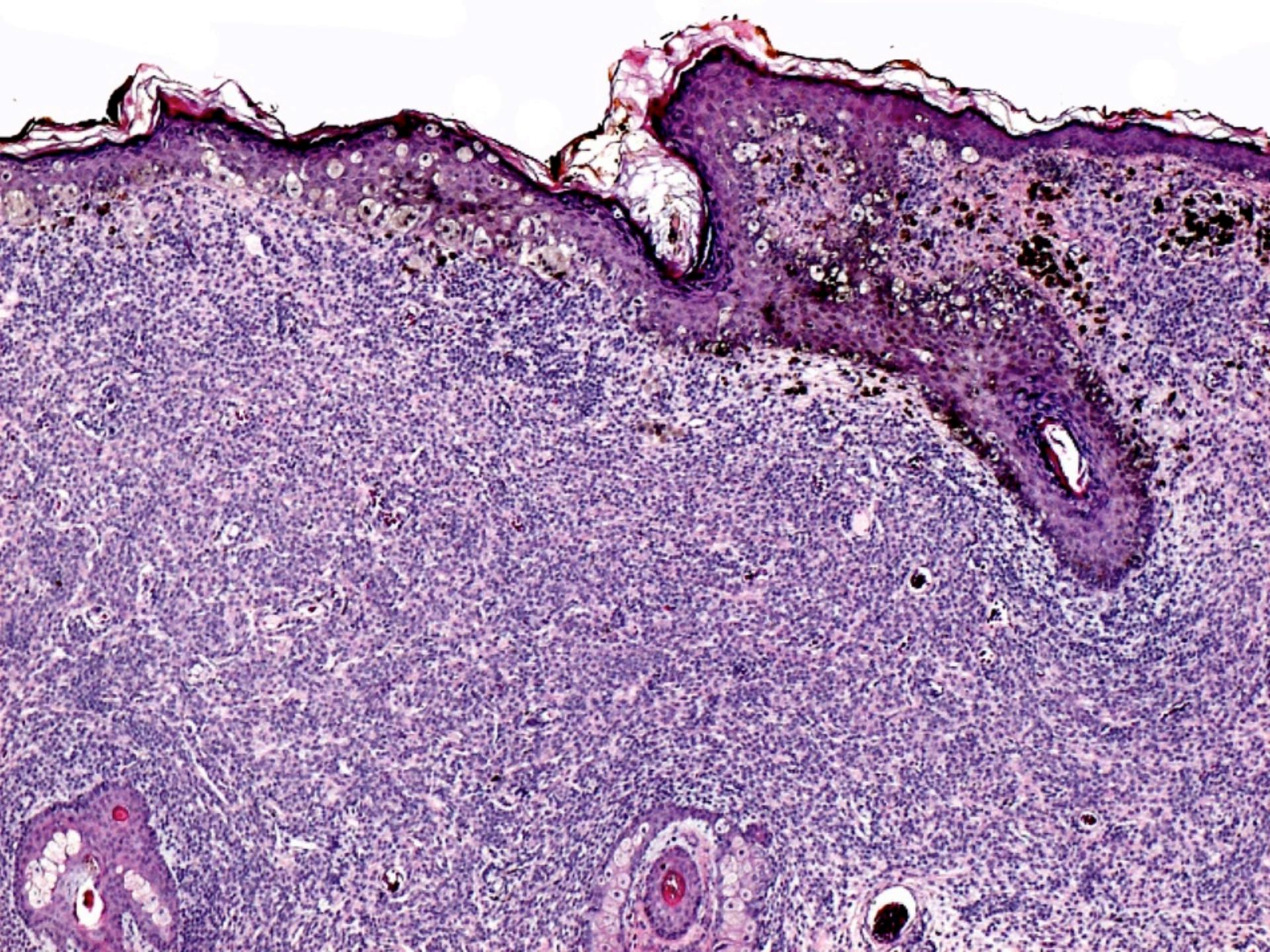


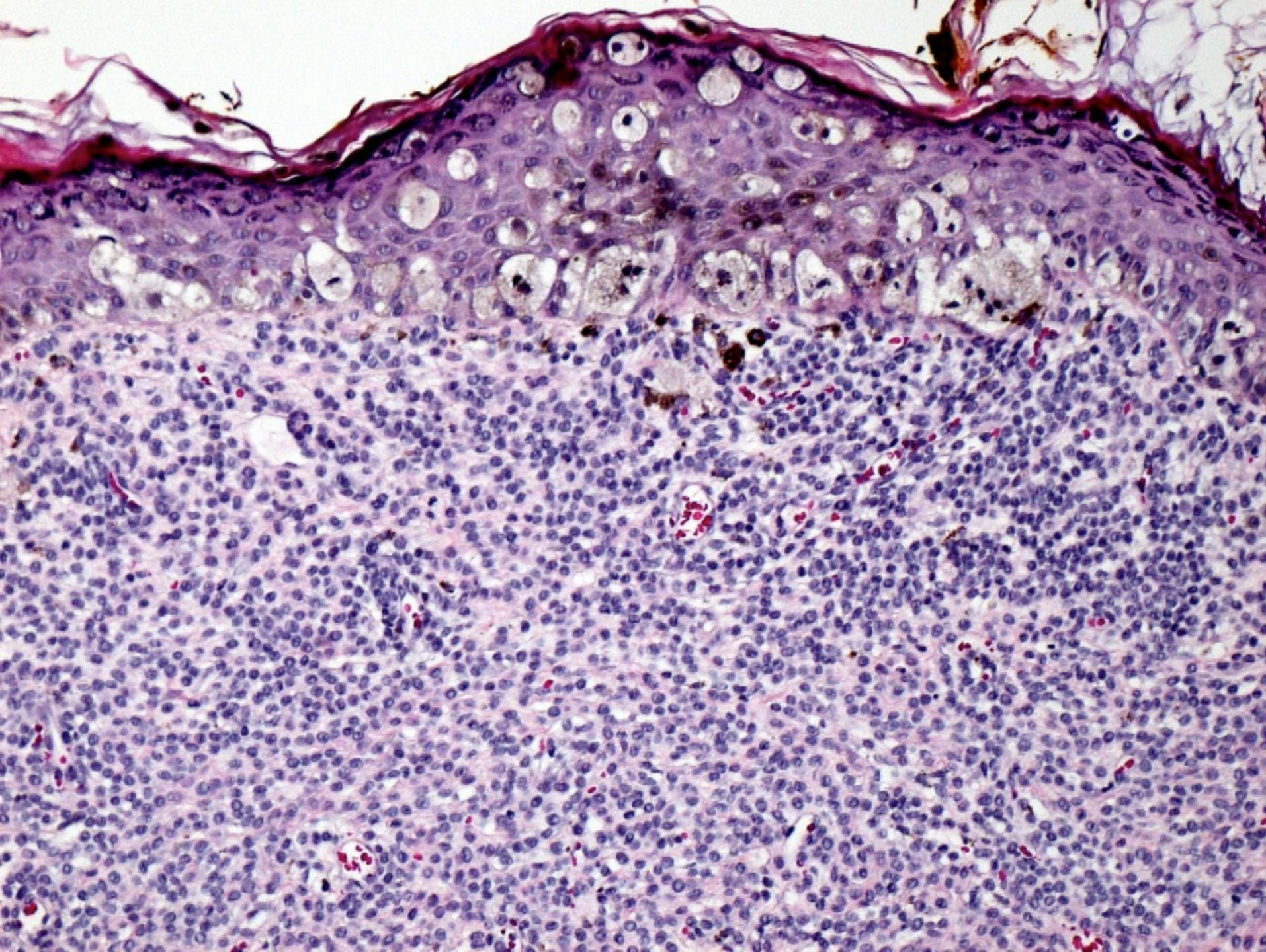


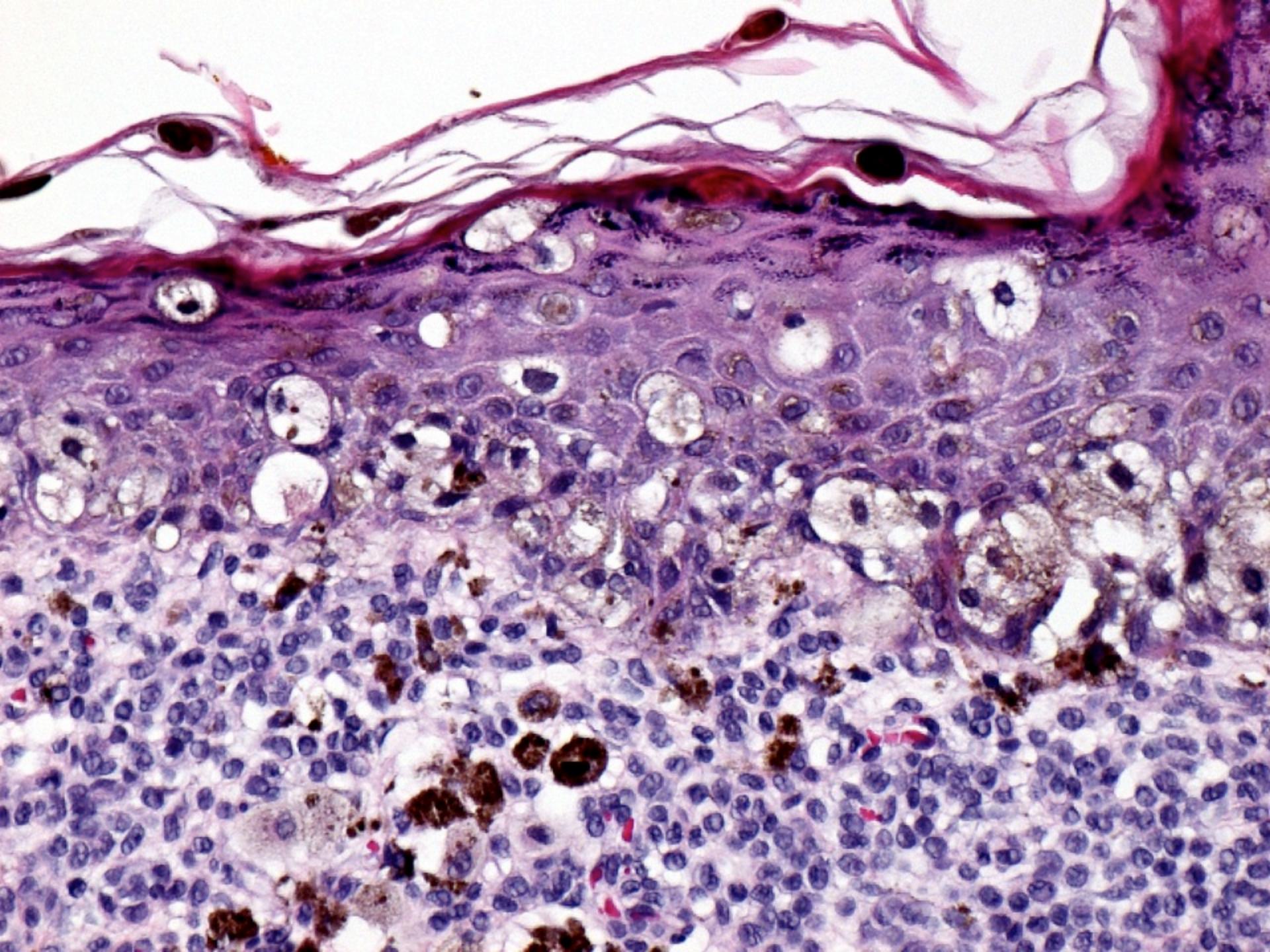


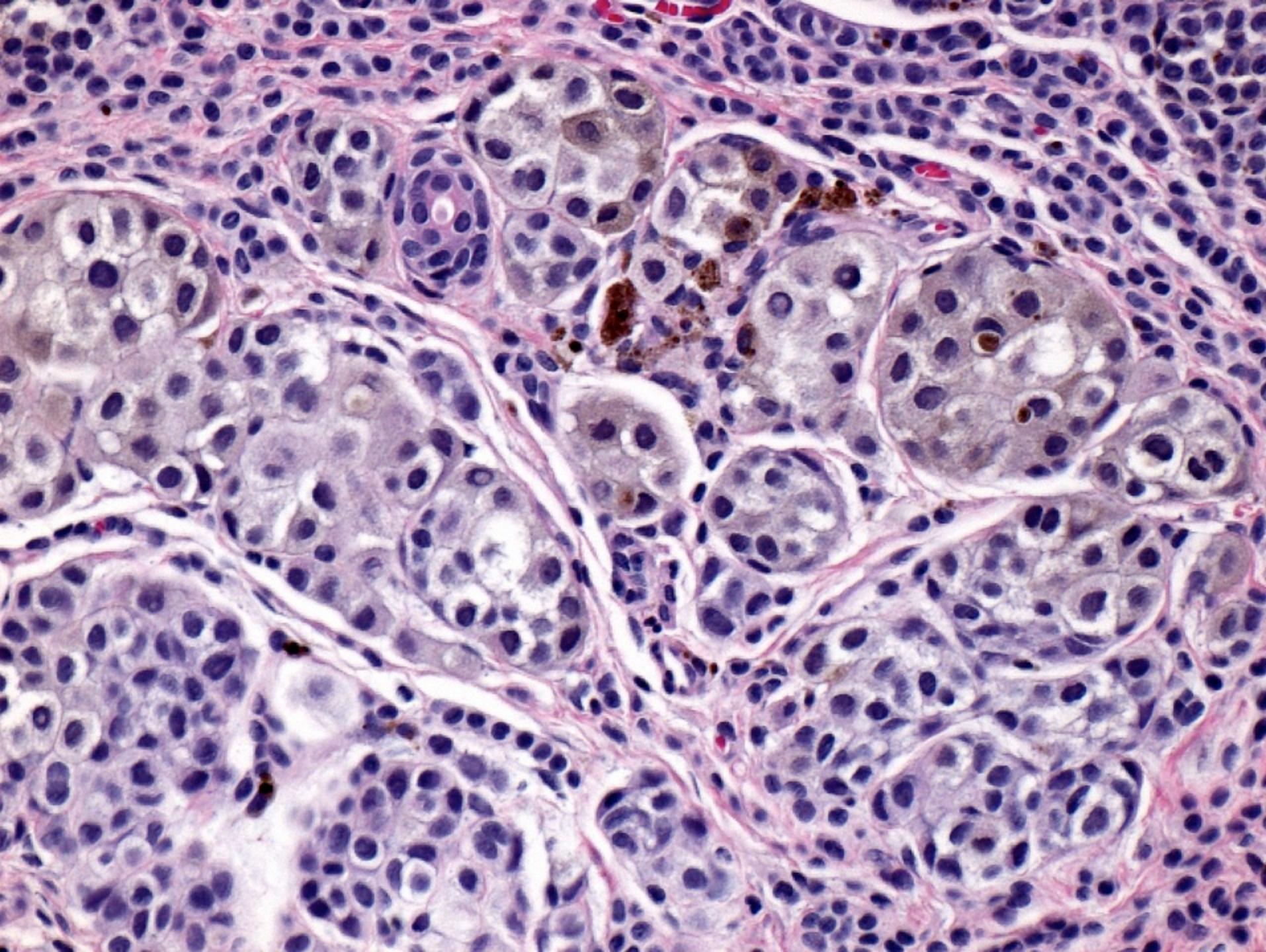


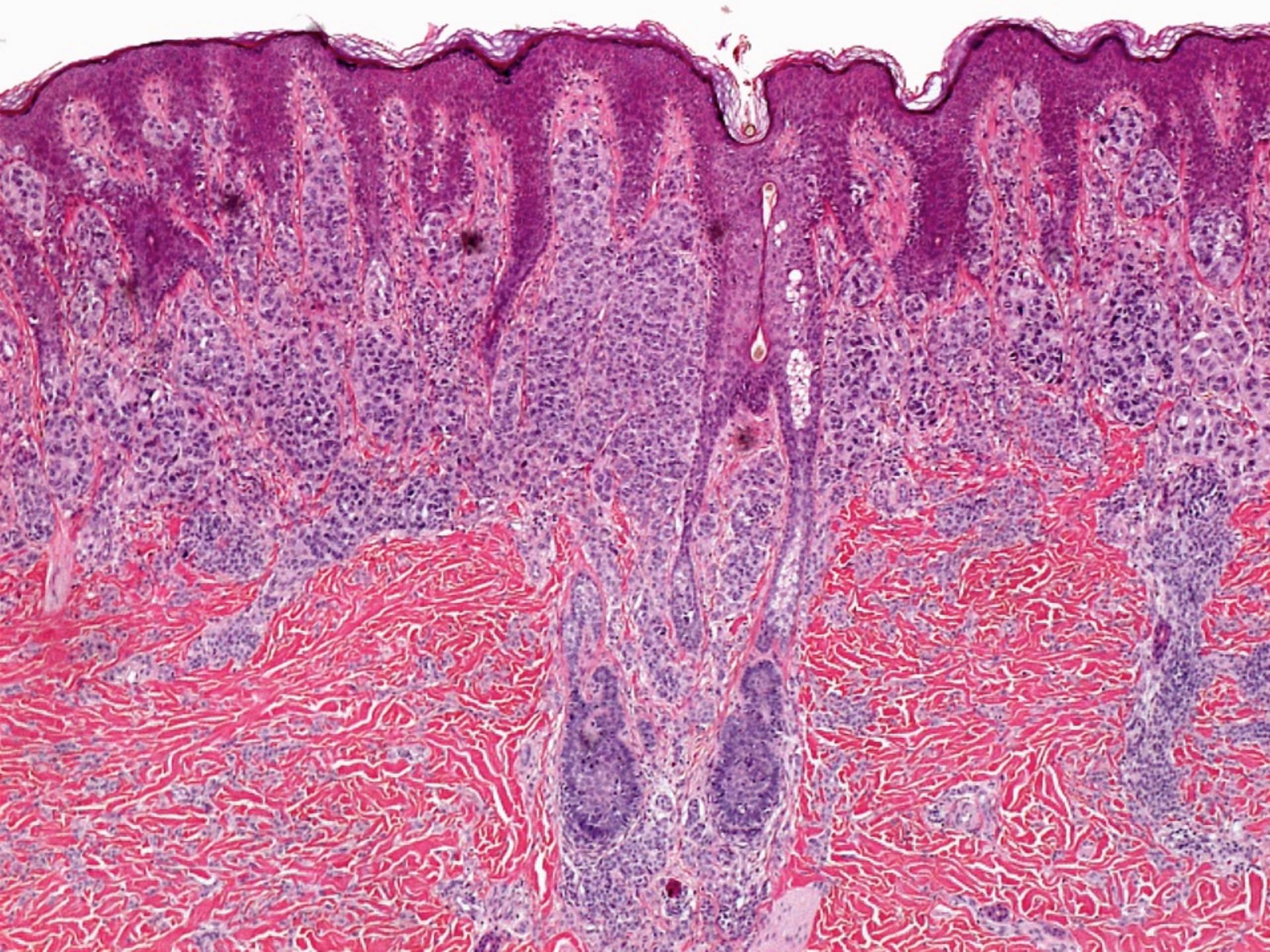


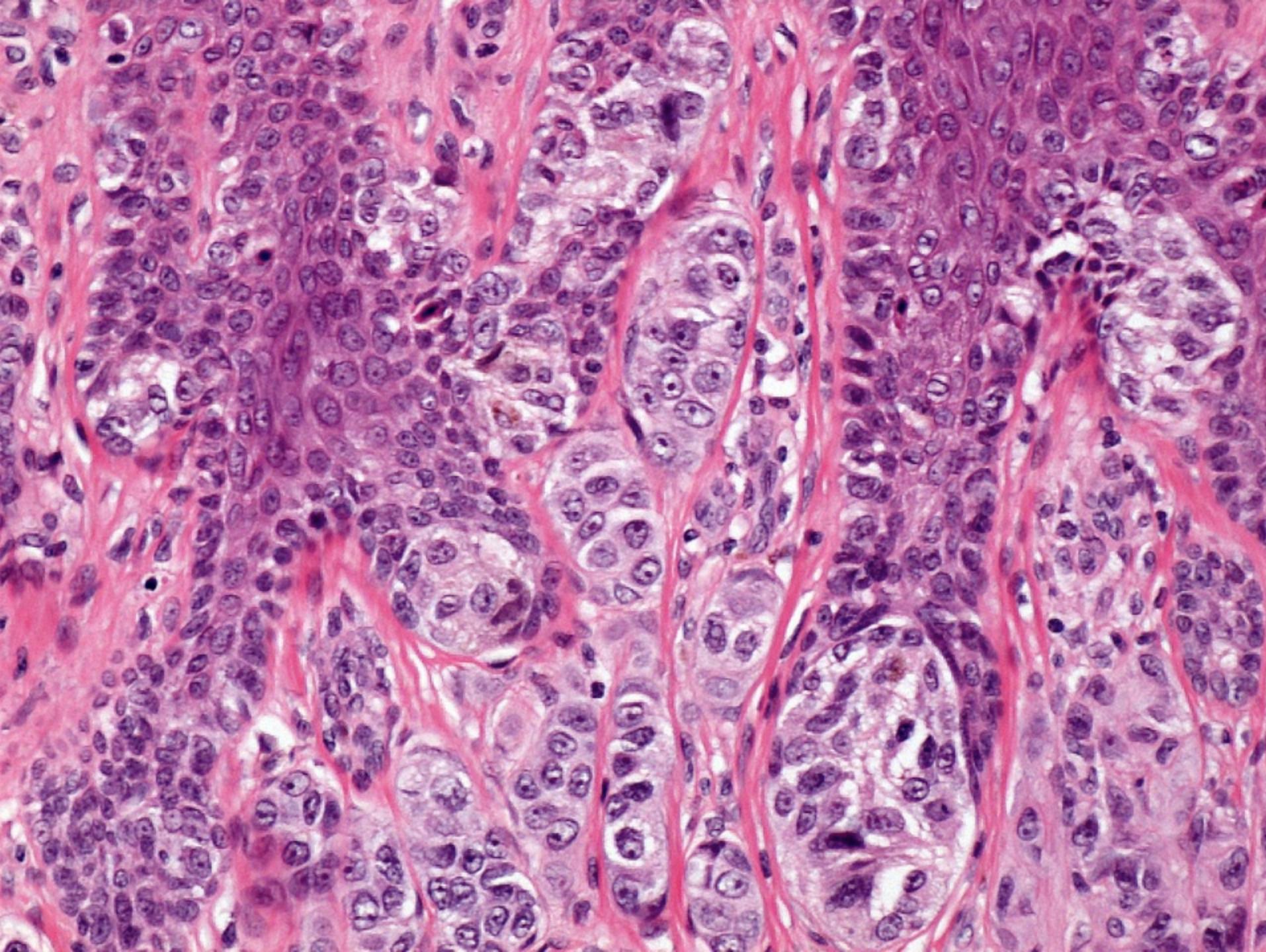


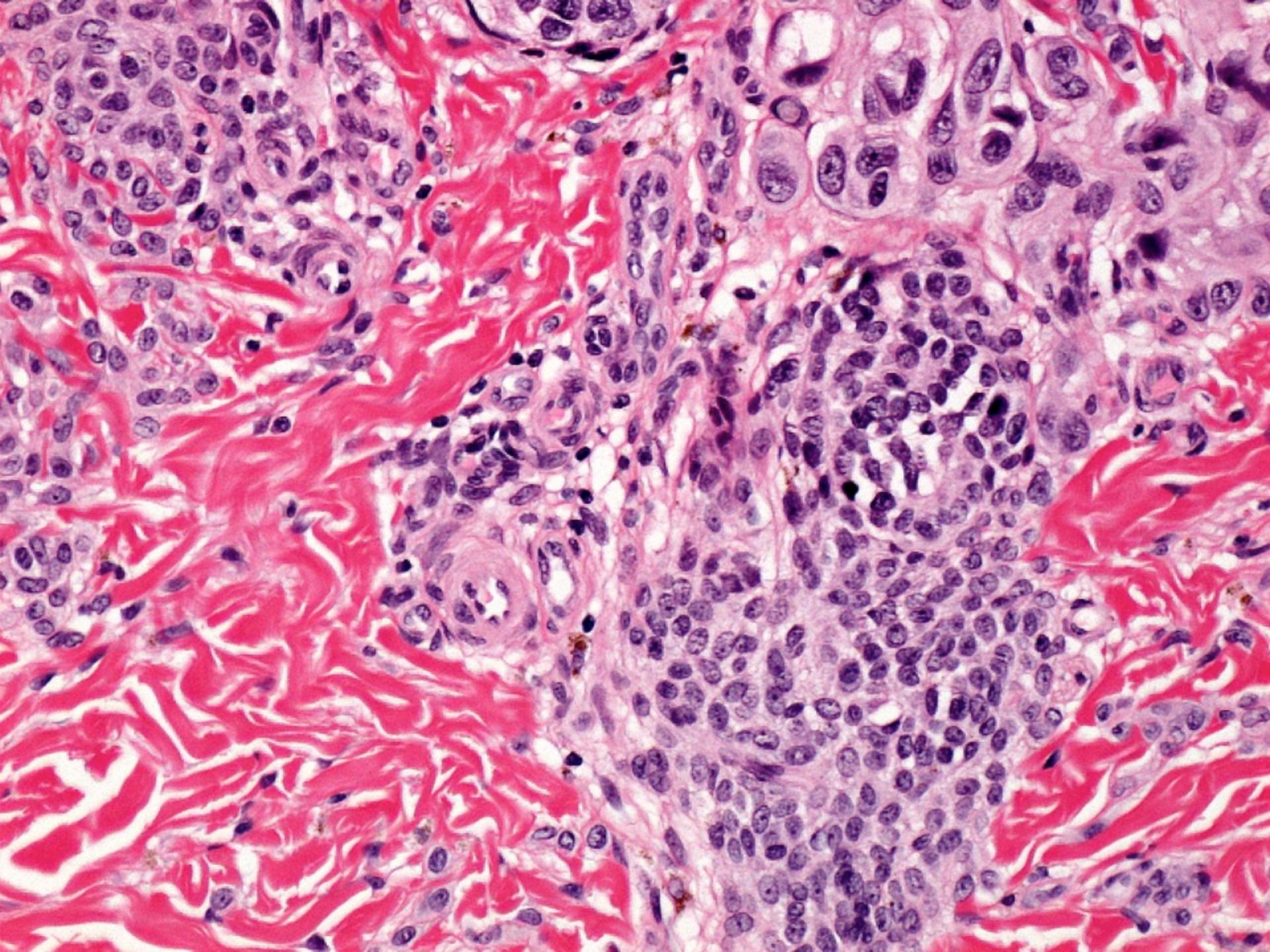


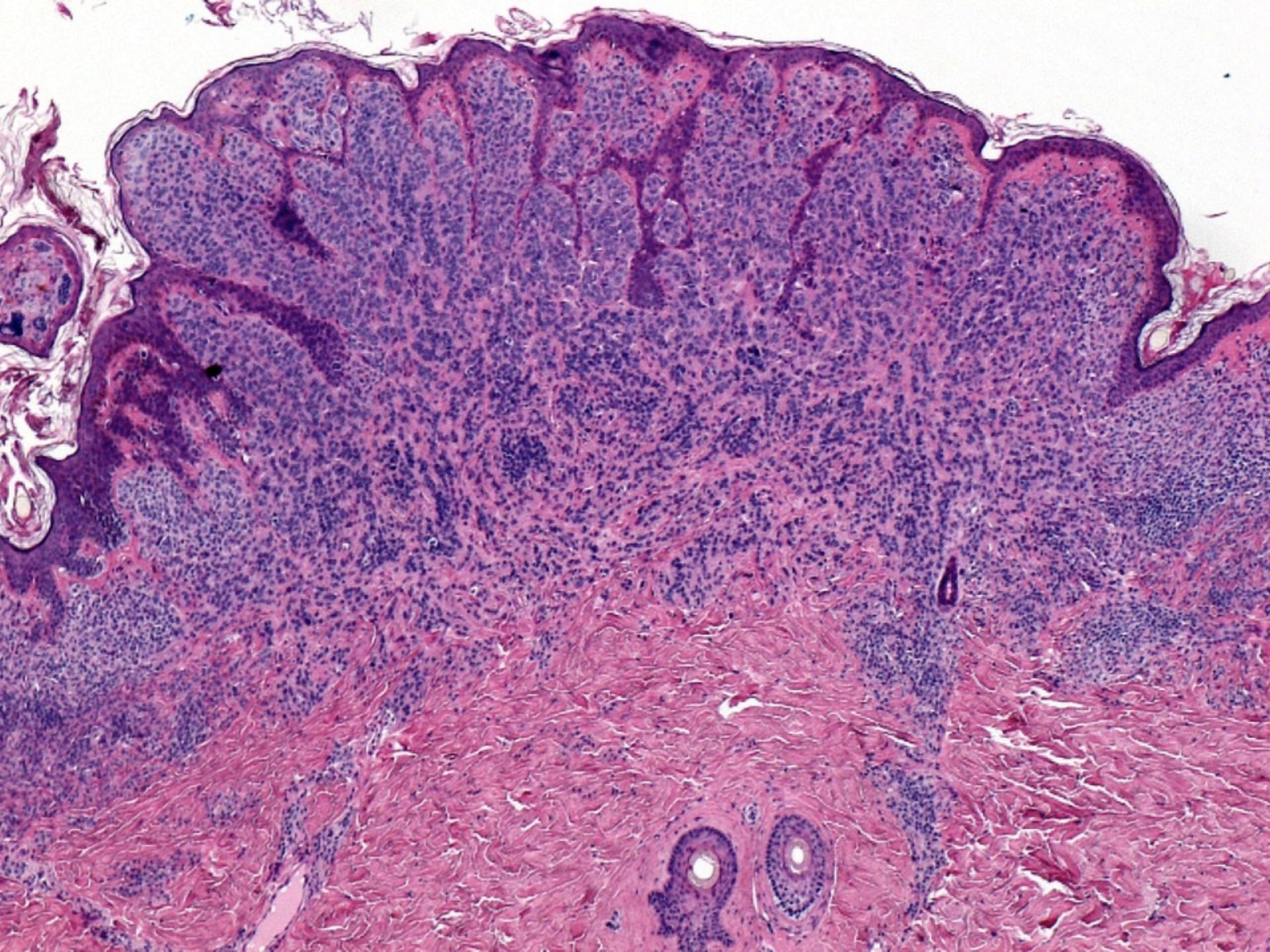


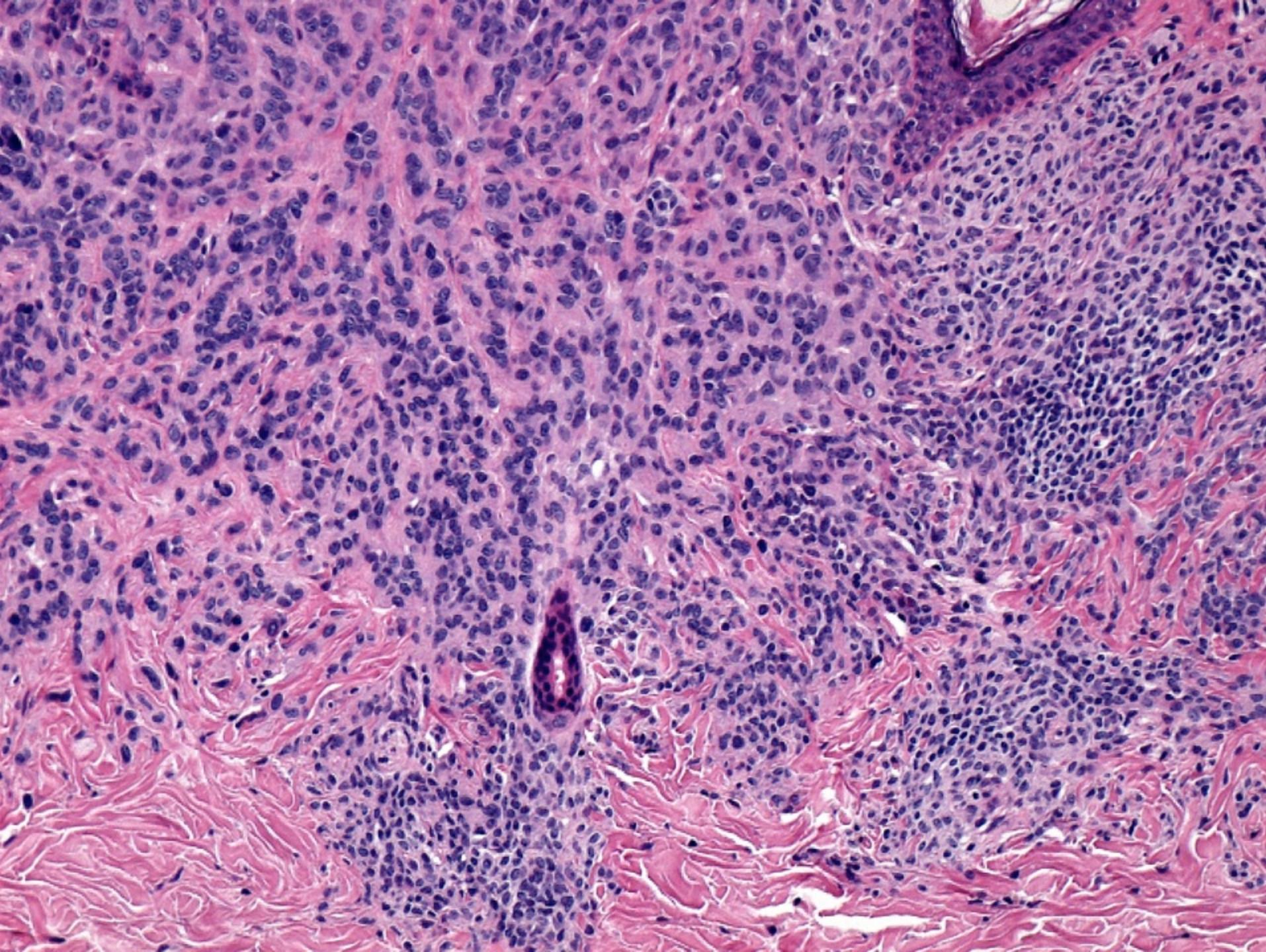


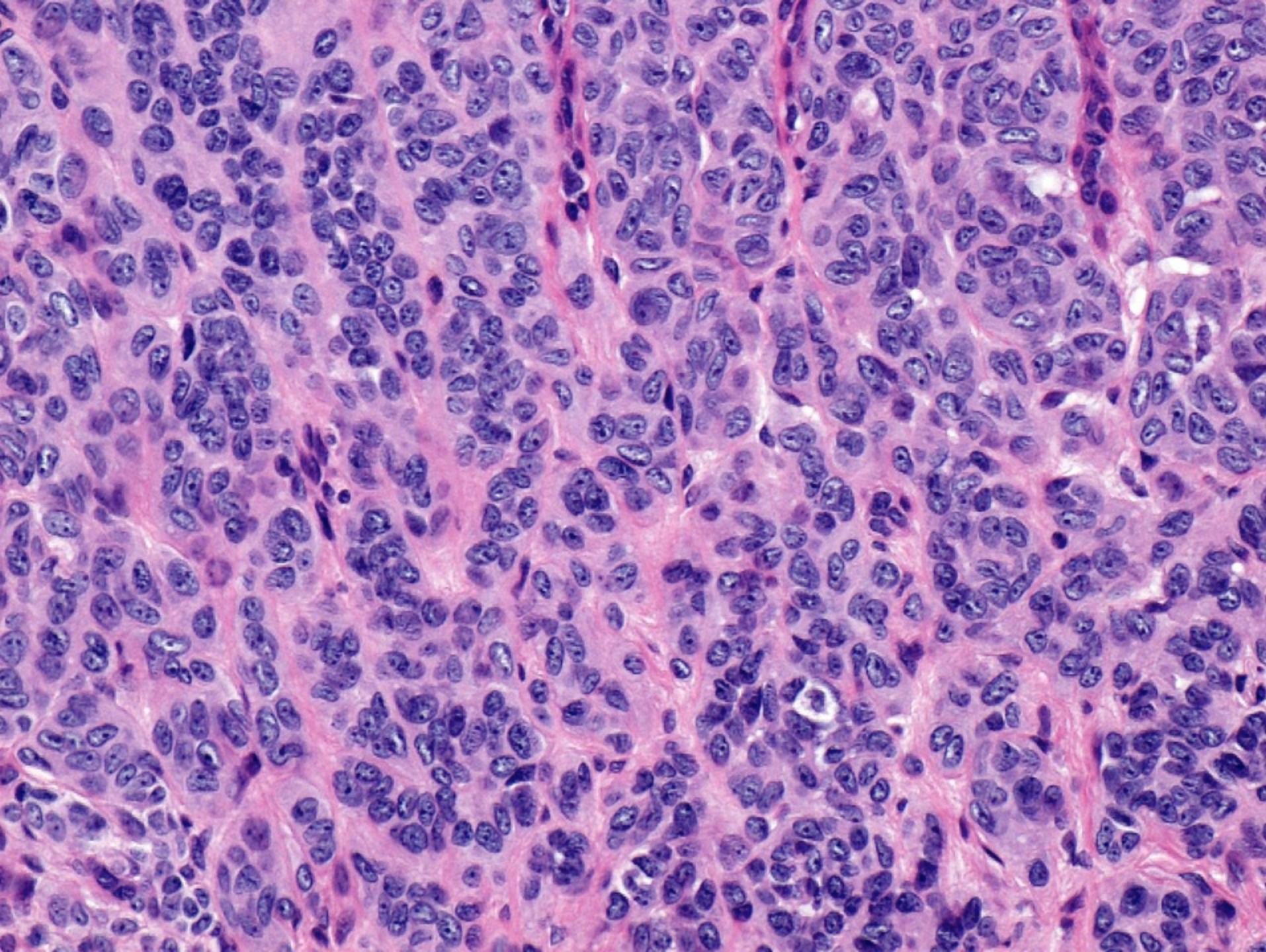


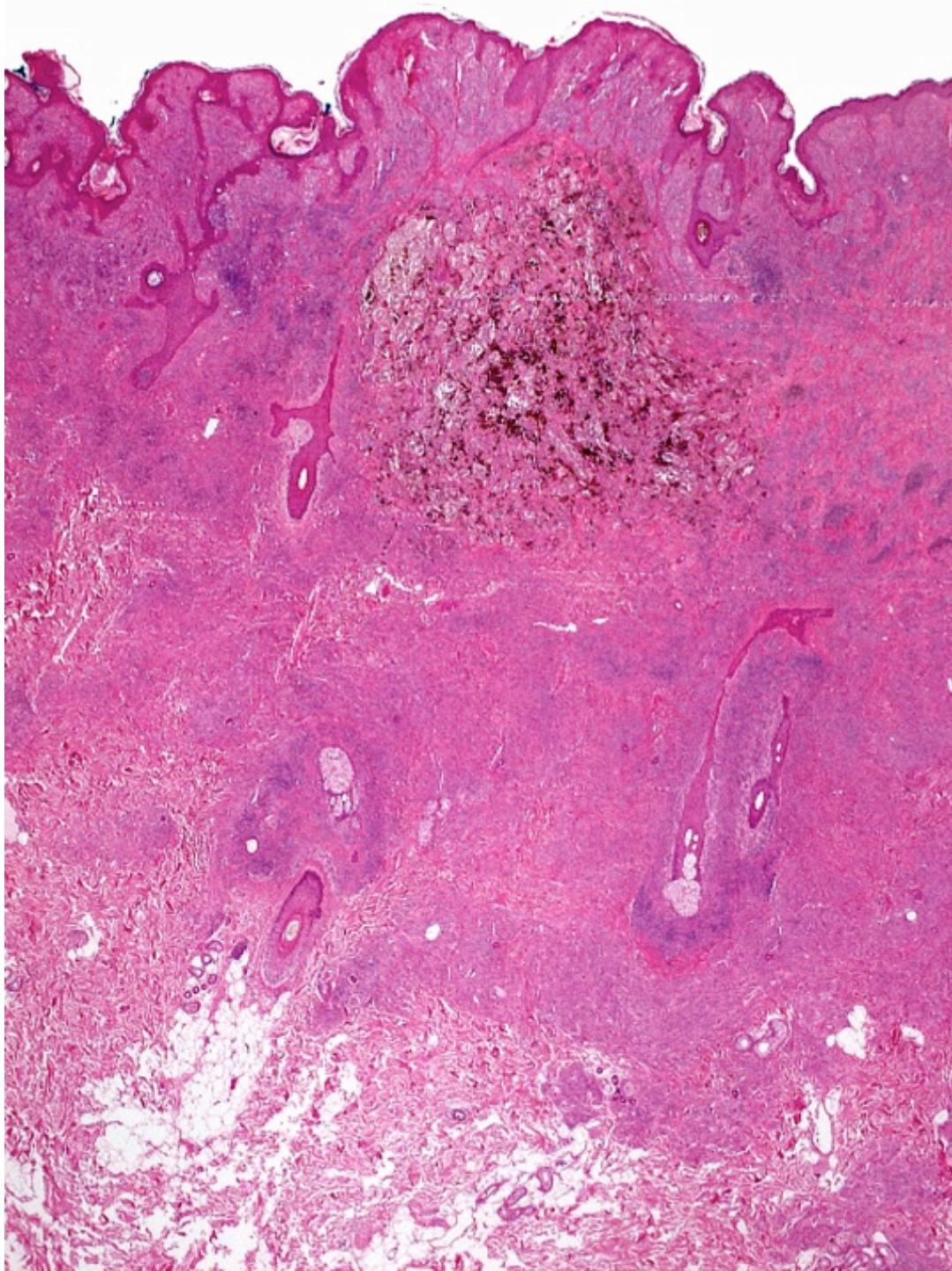


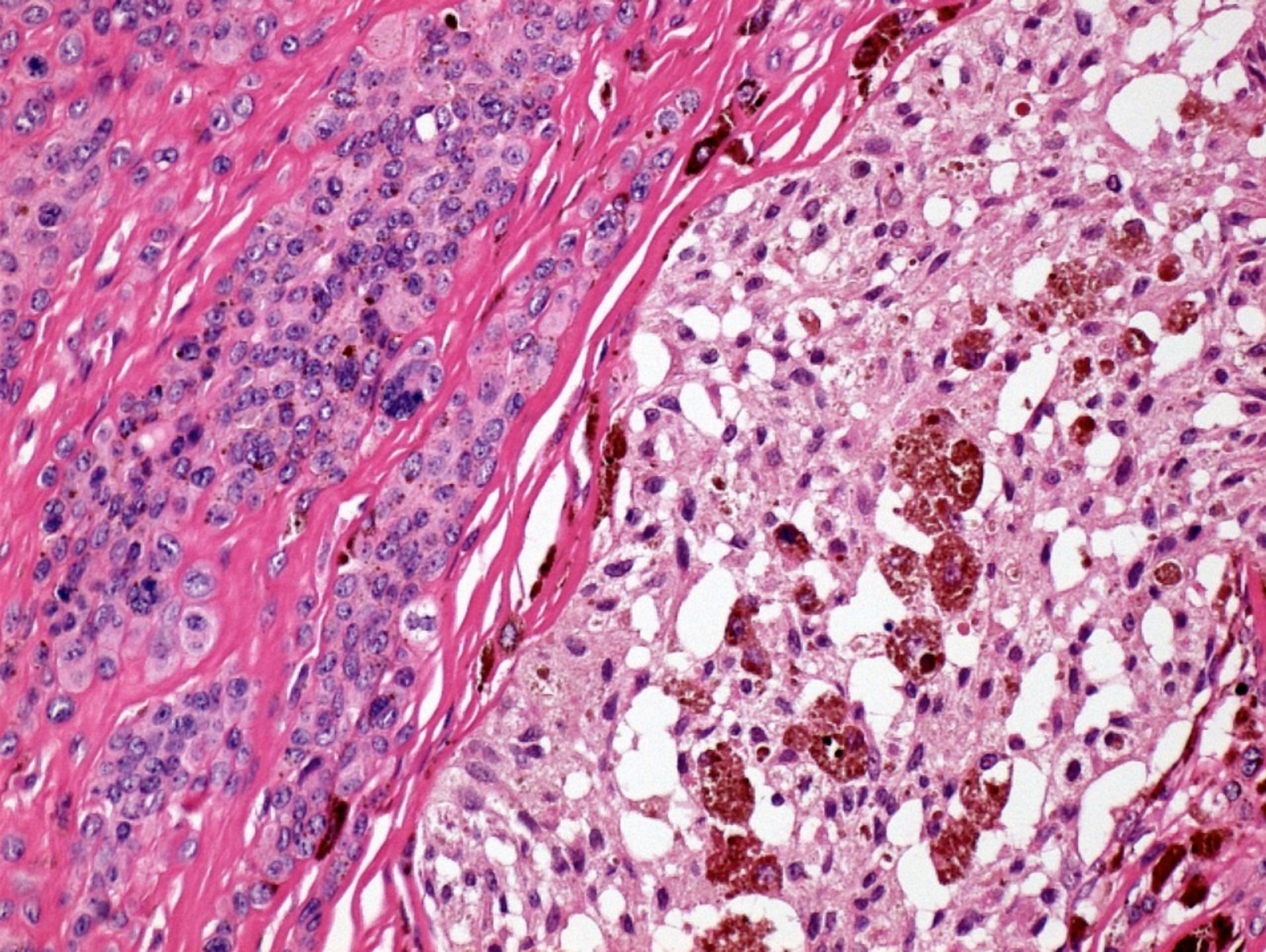


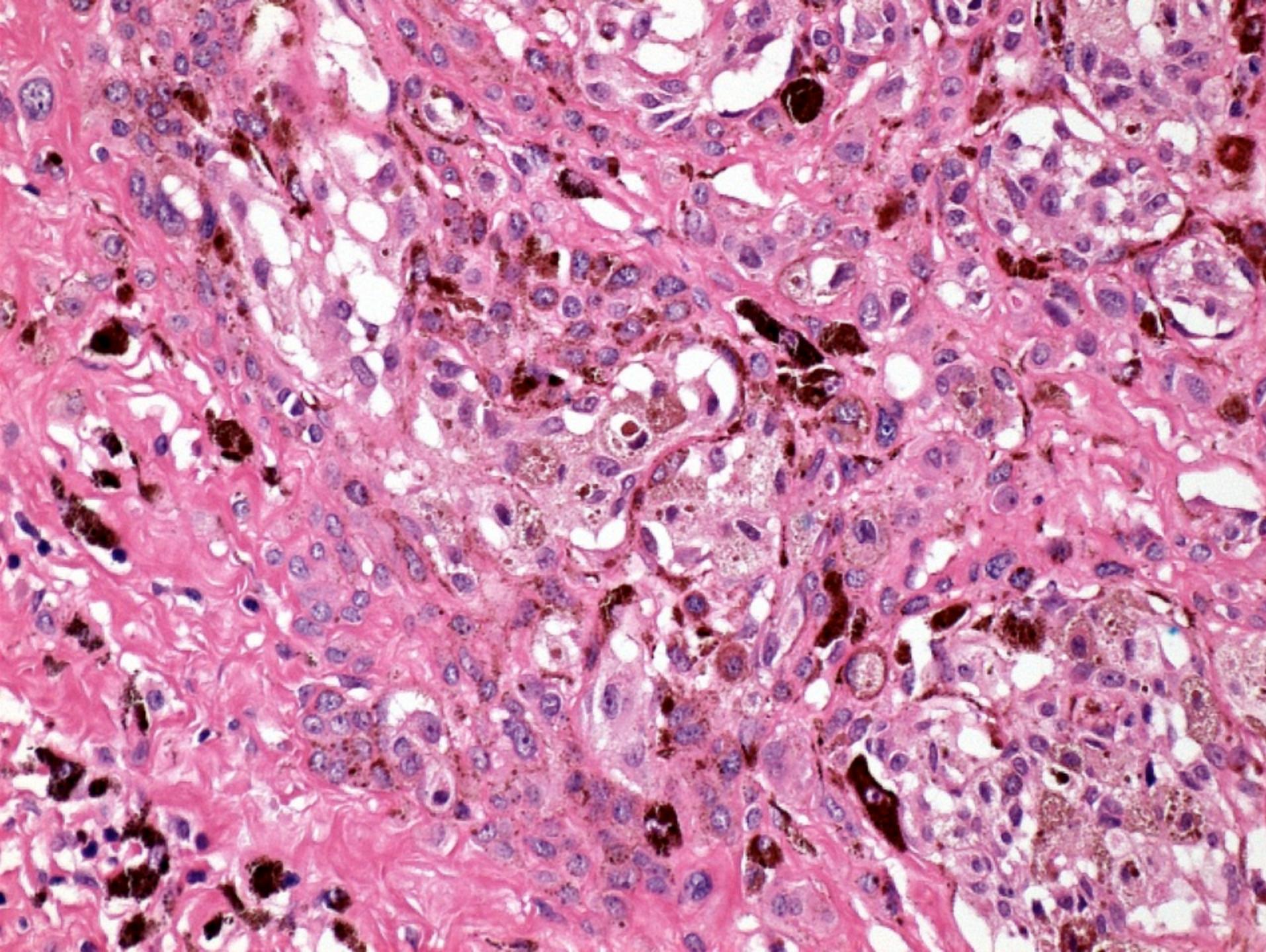


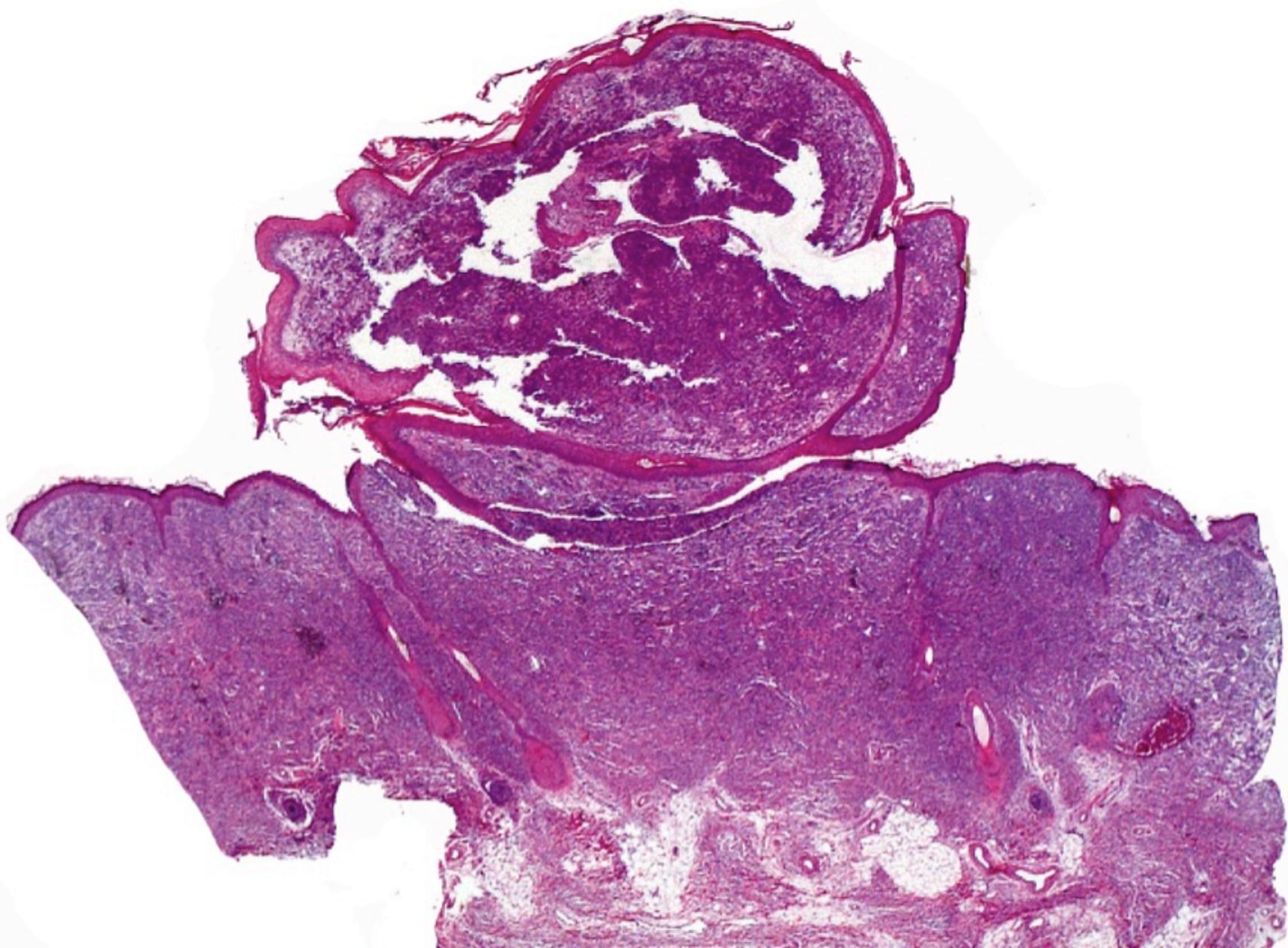


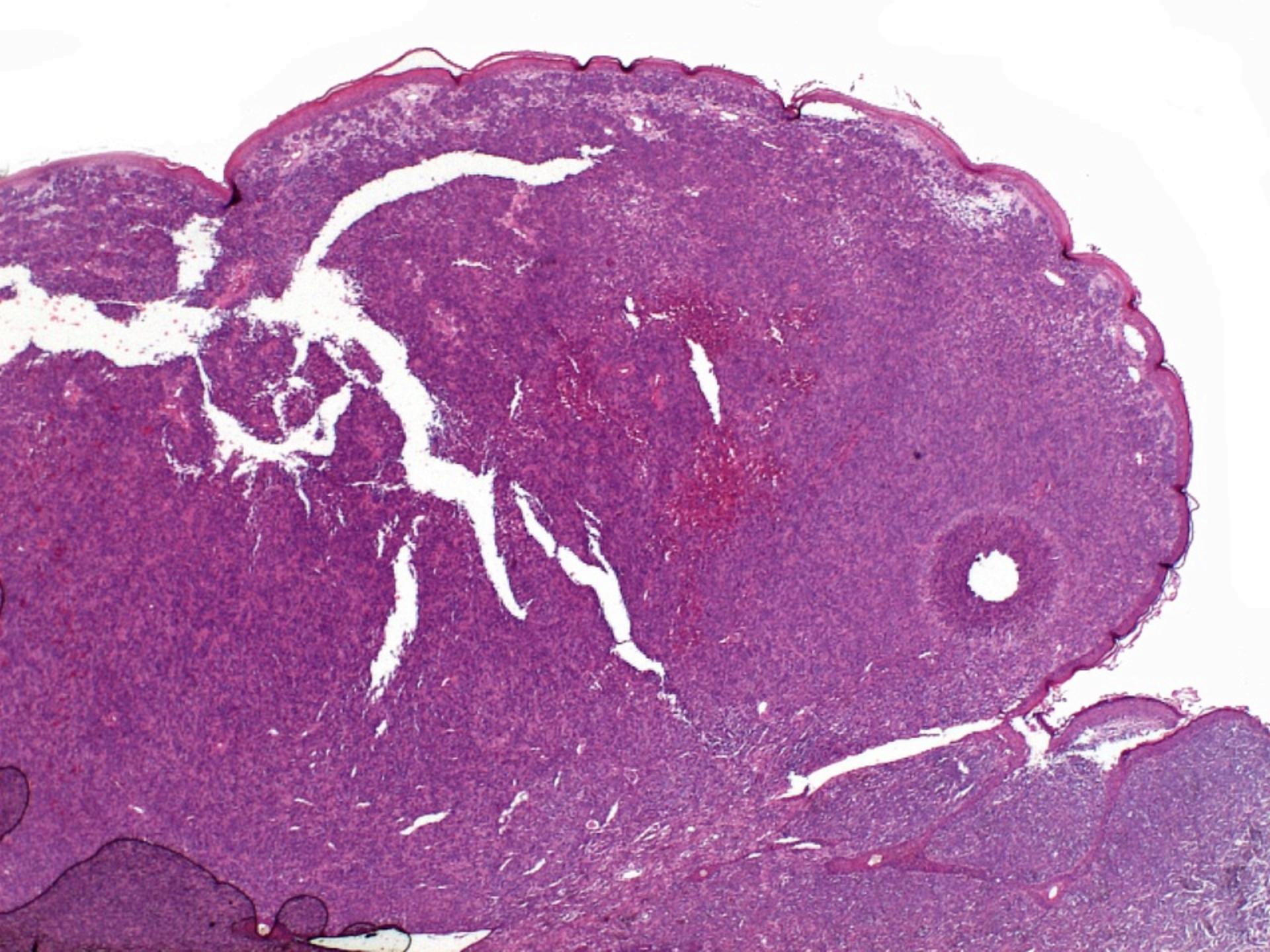


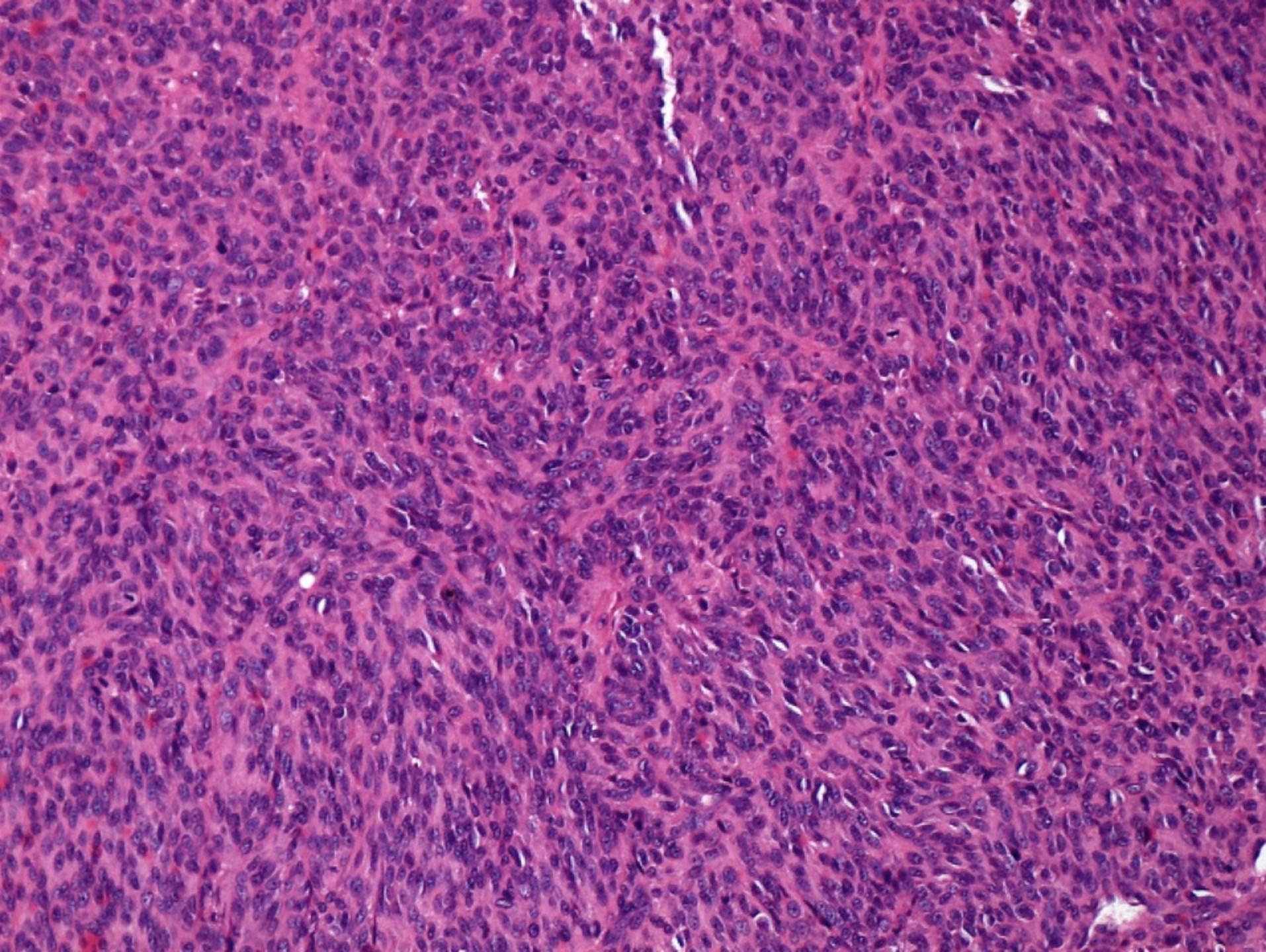


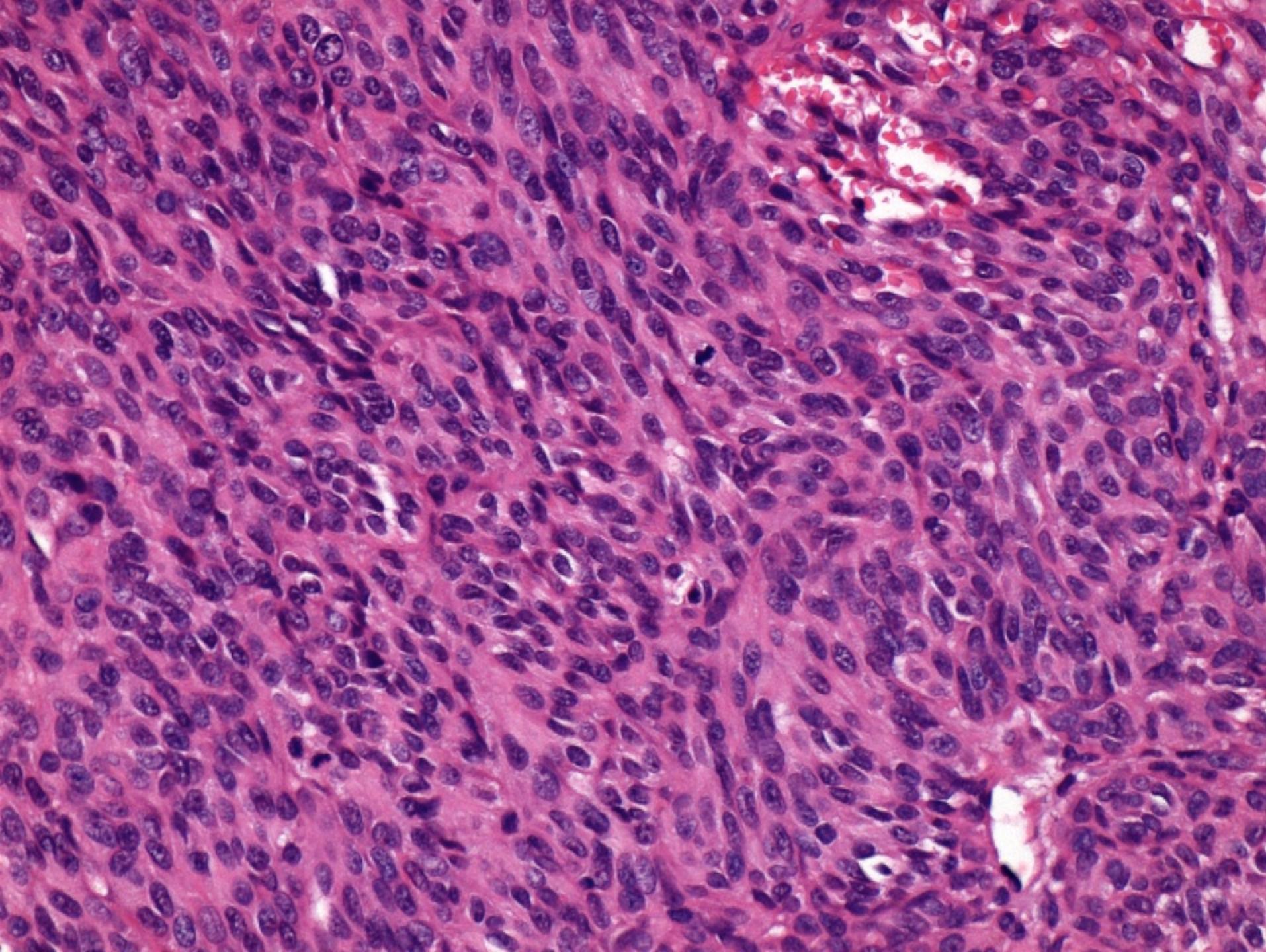


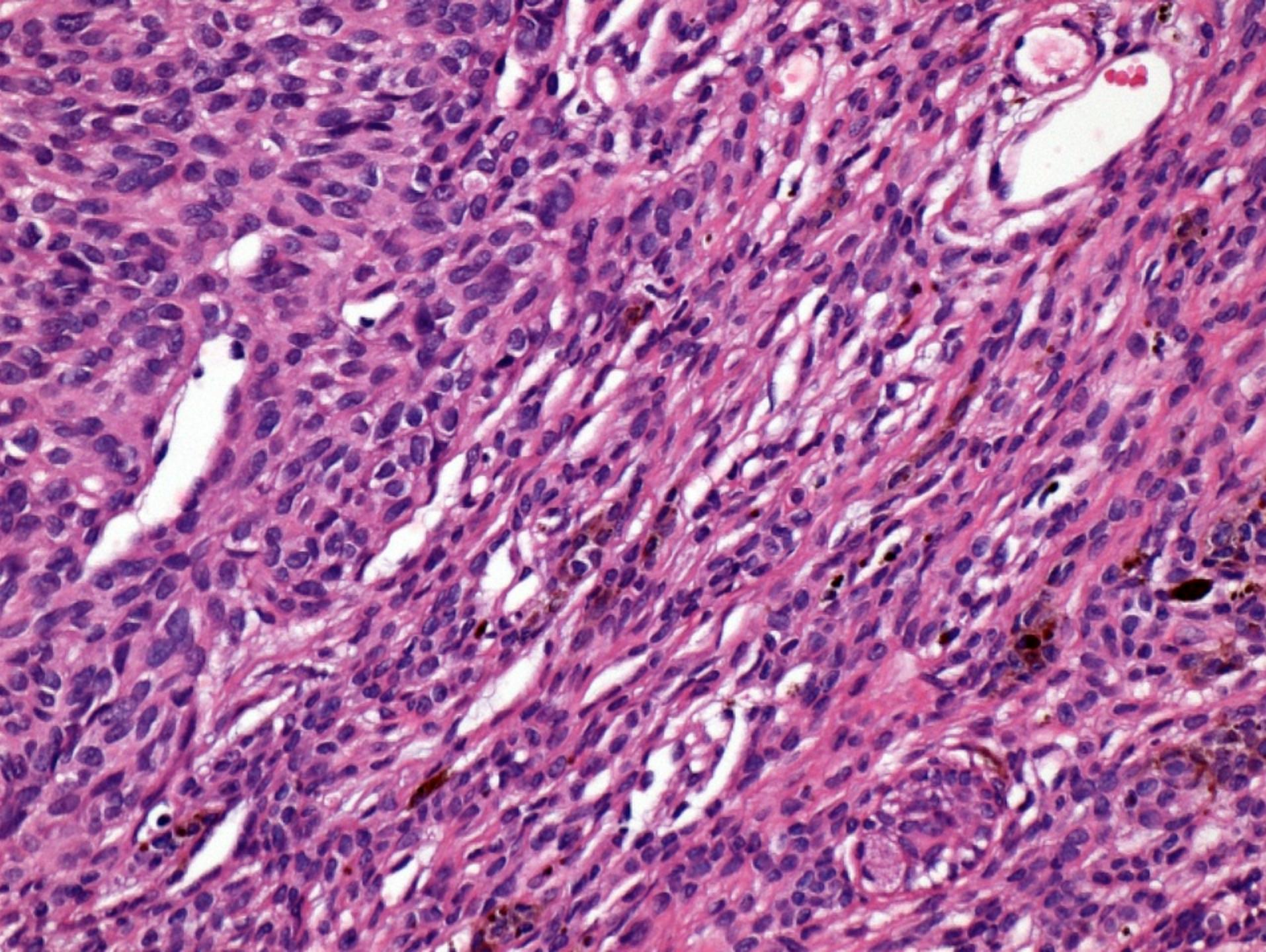












Proliferative Nodule vs Melanoma within Congenital Naevus

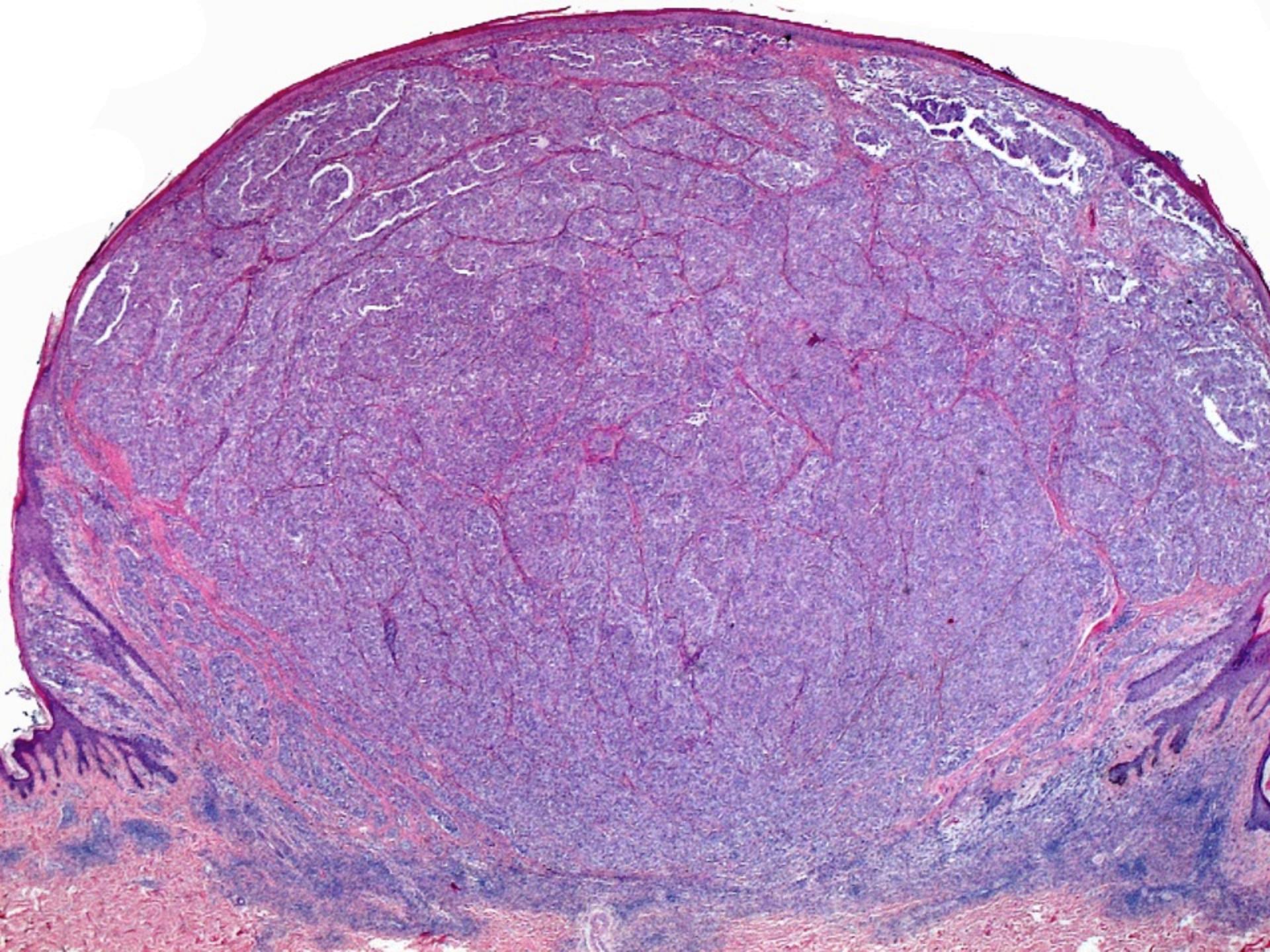
Reliable distinction often difficult but important

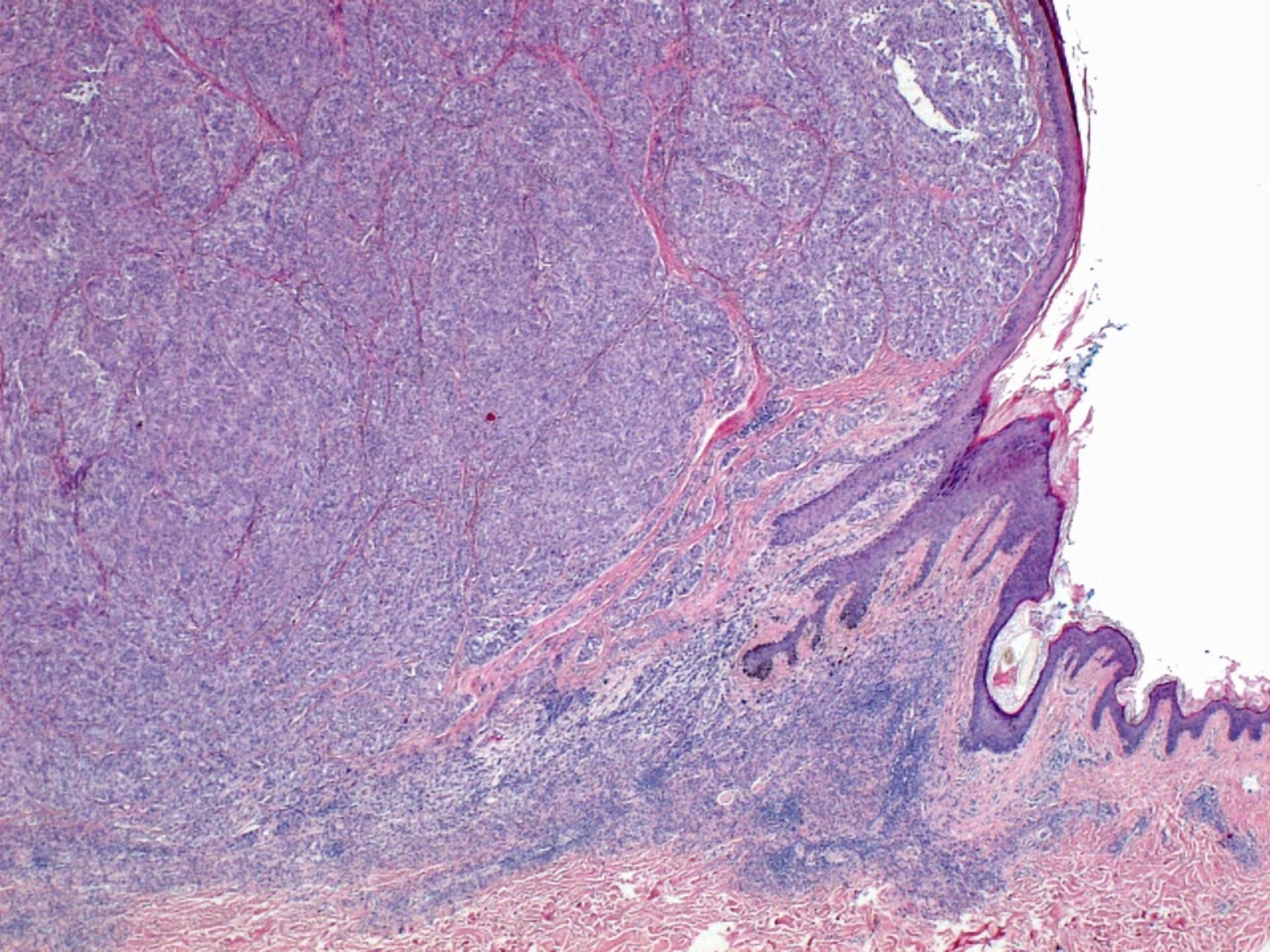
- Proliferative nodule: benign change in CMN
- Melanoma in CMN: aggressive with high risk for disseminated disease and mortality

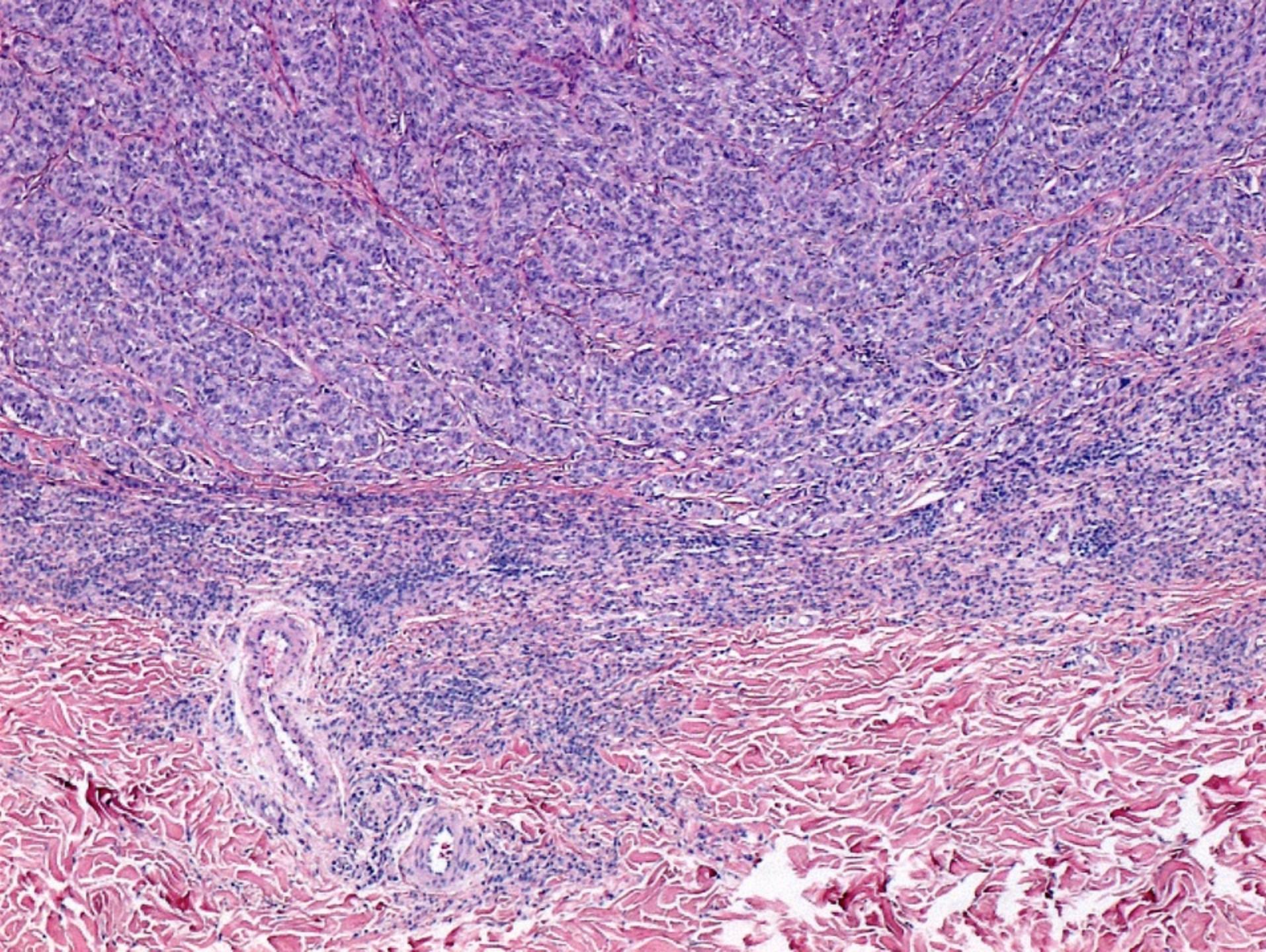
Proliferative Nodule vs Melanoma within Congenital Naevus

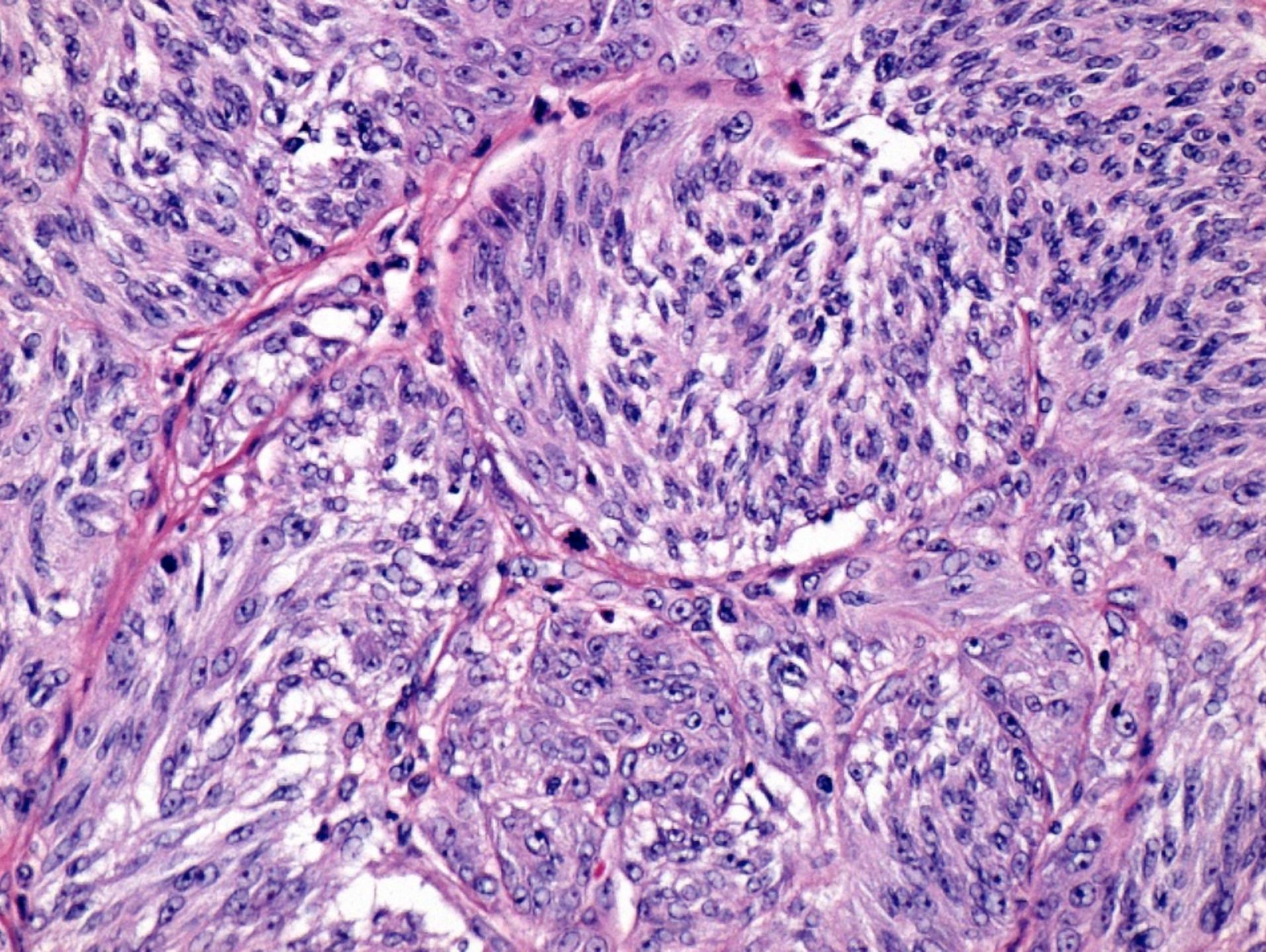
Features in favour of melanoma:

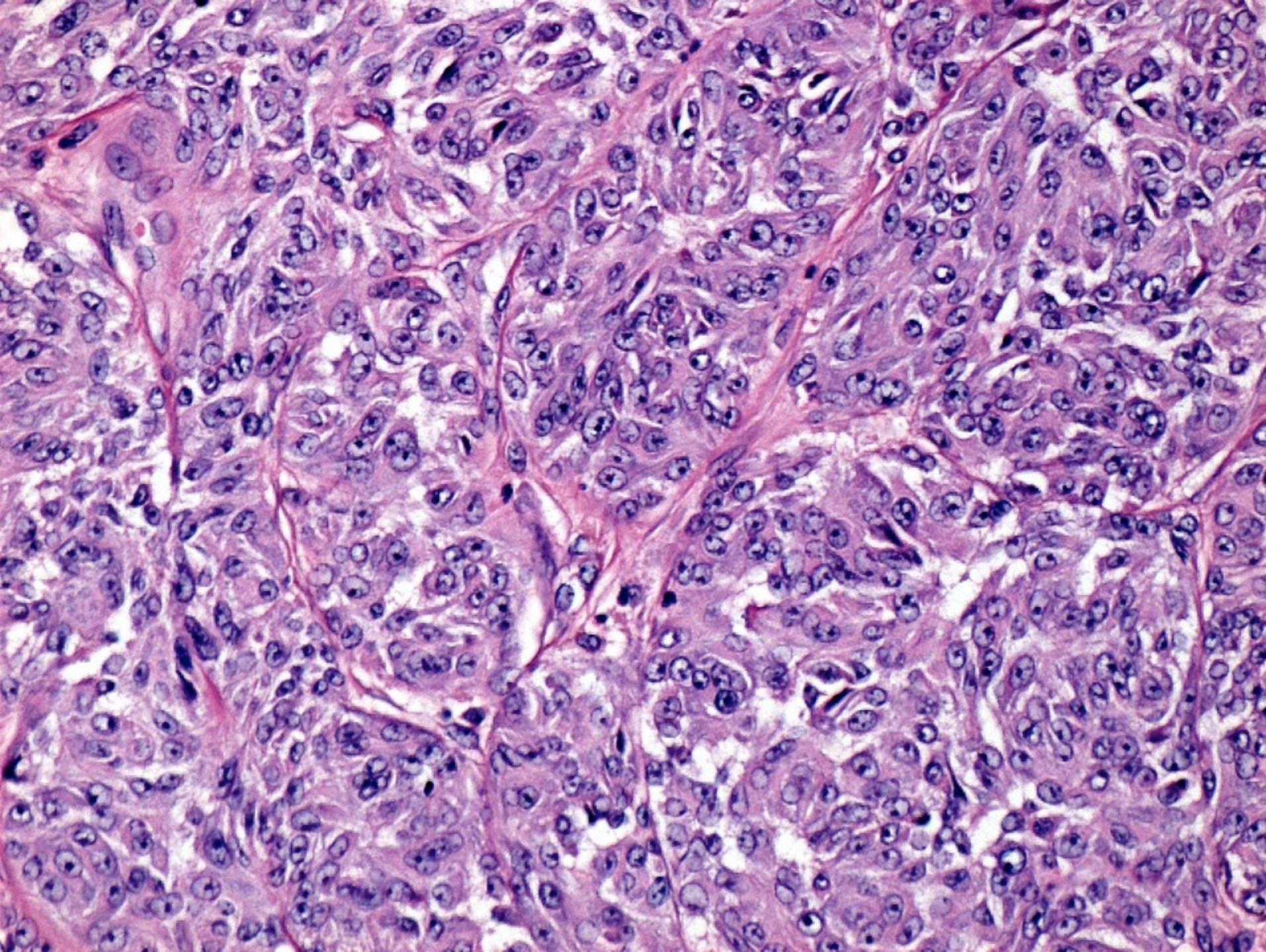
- **High grade and uniform cytological atypia**
- **Necrosis**
- **Frequent and atypical mitoses**
- **Sharp demarcation and expansile growth**
- **In situ component**



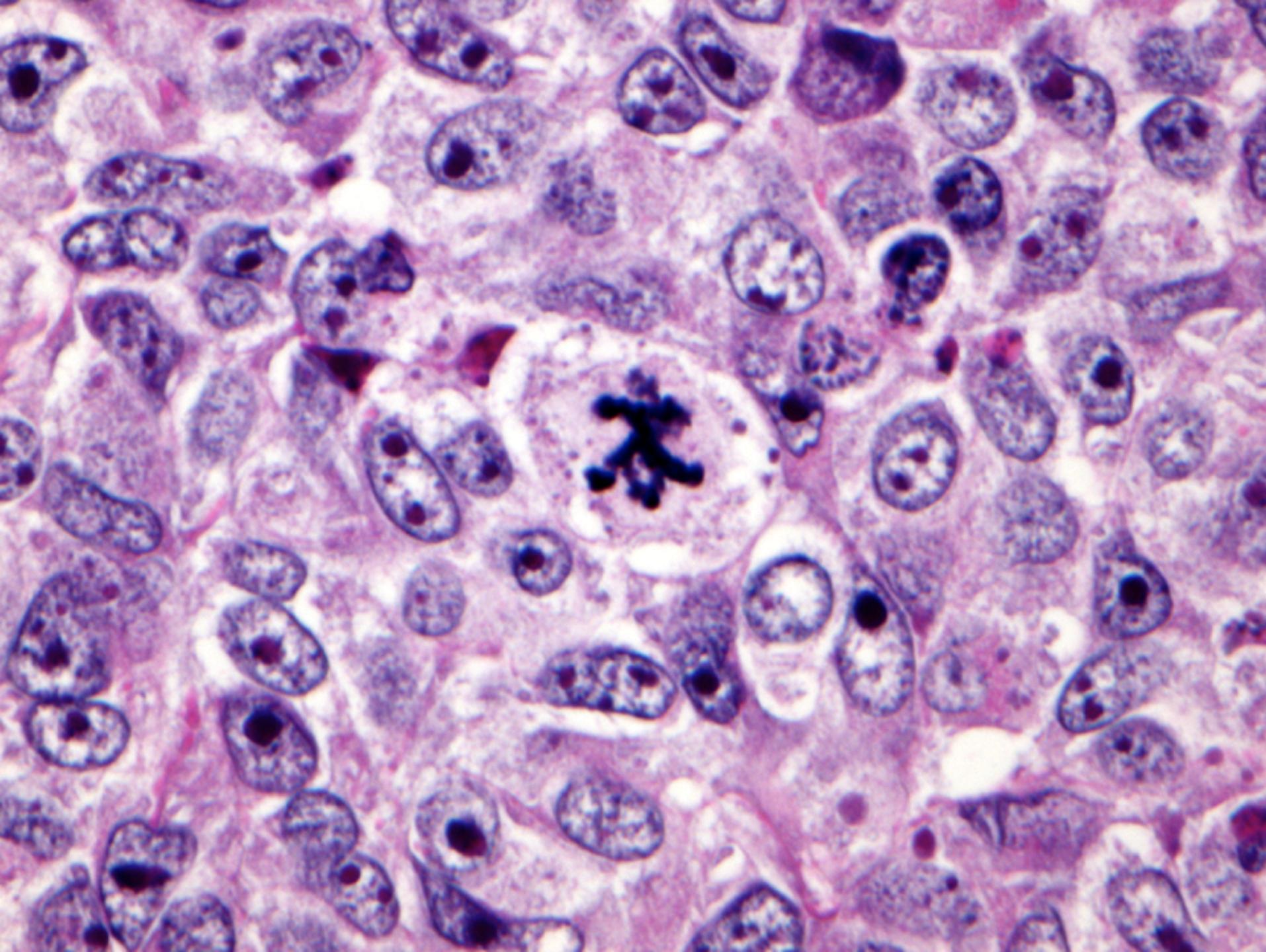


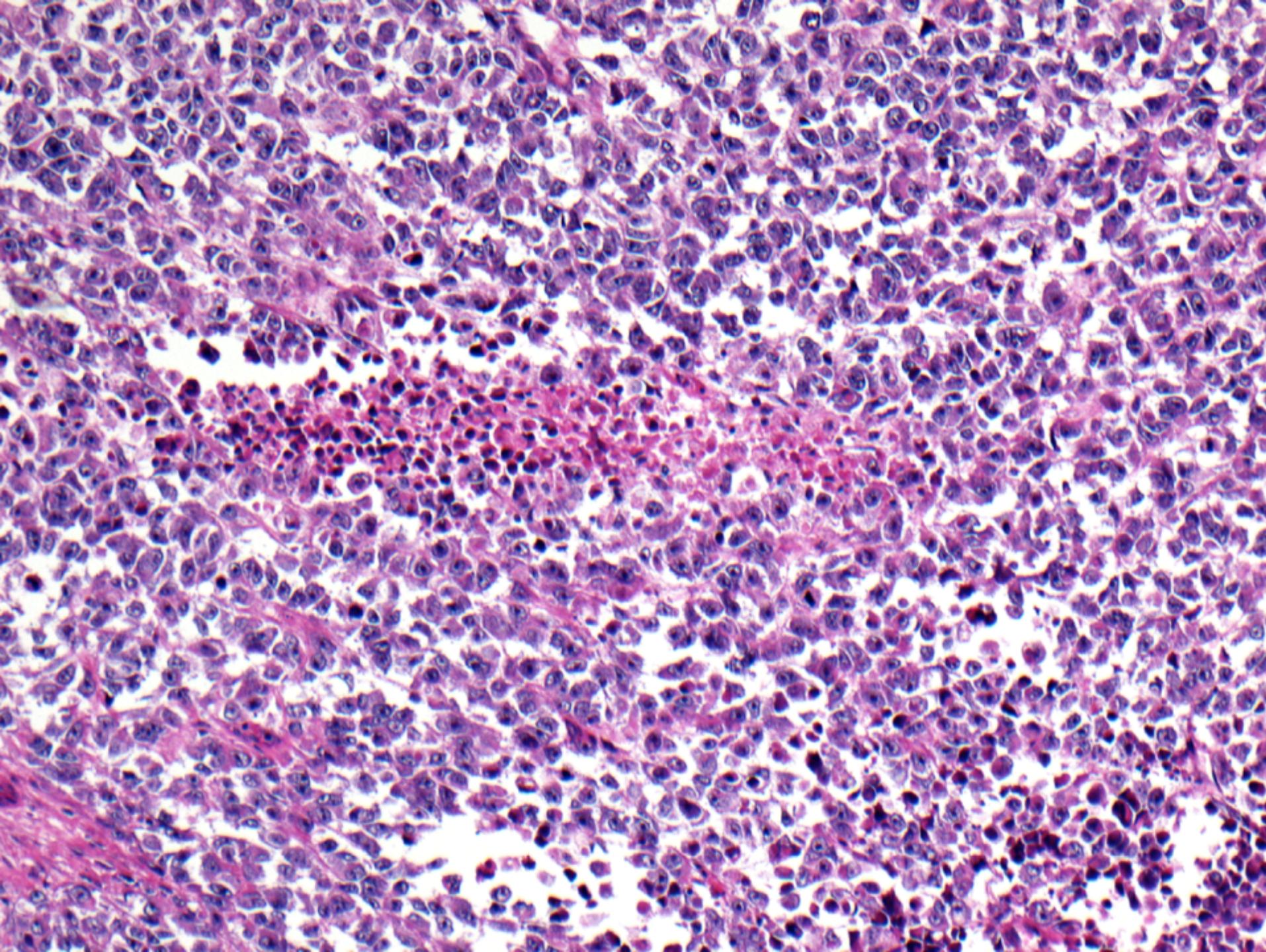


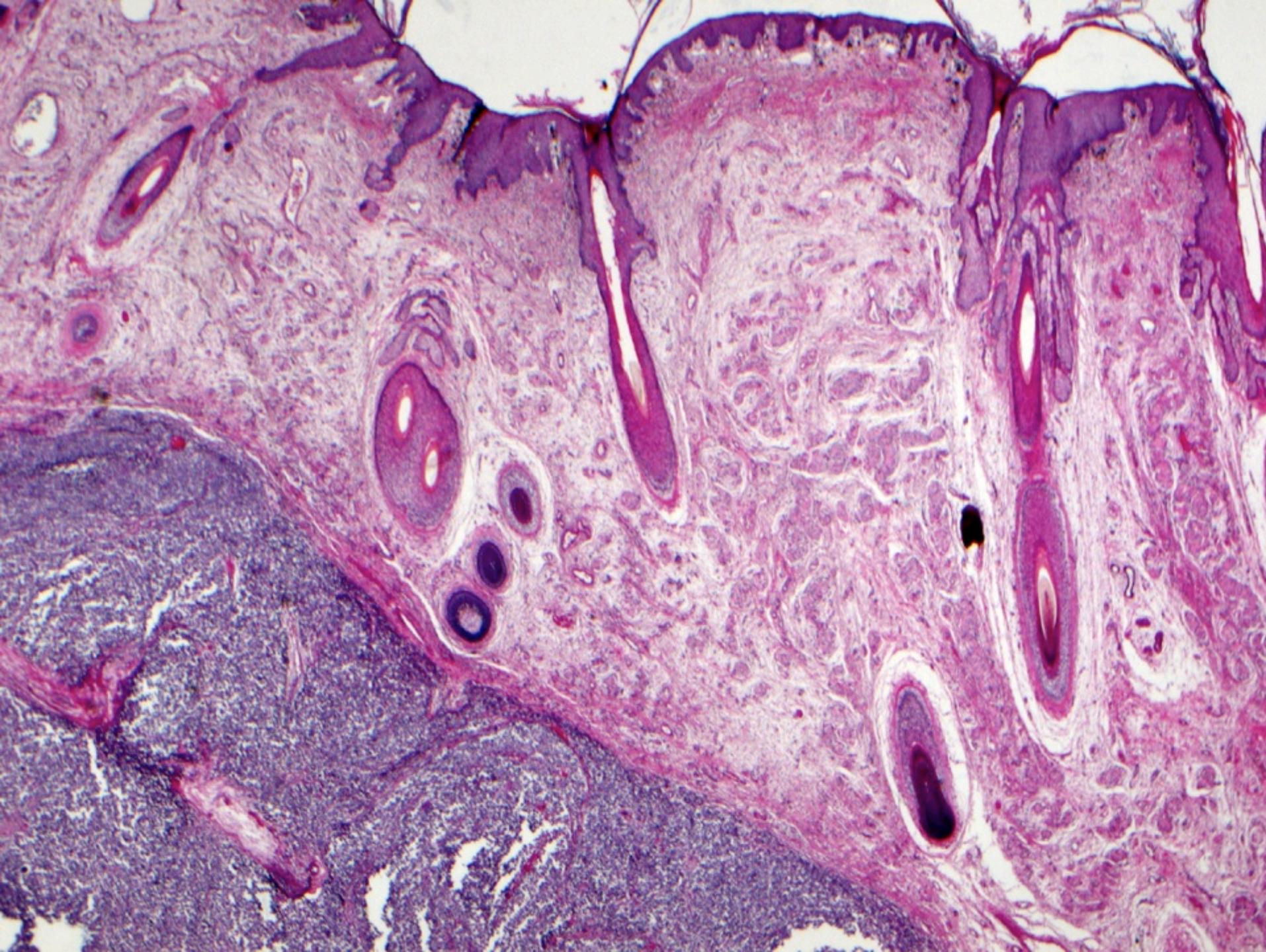


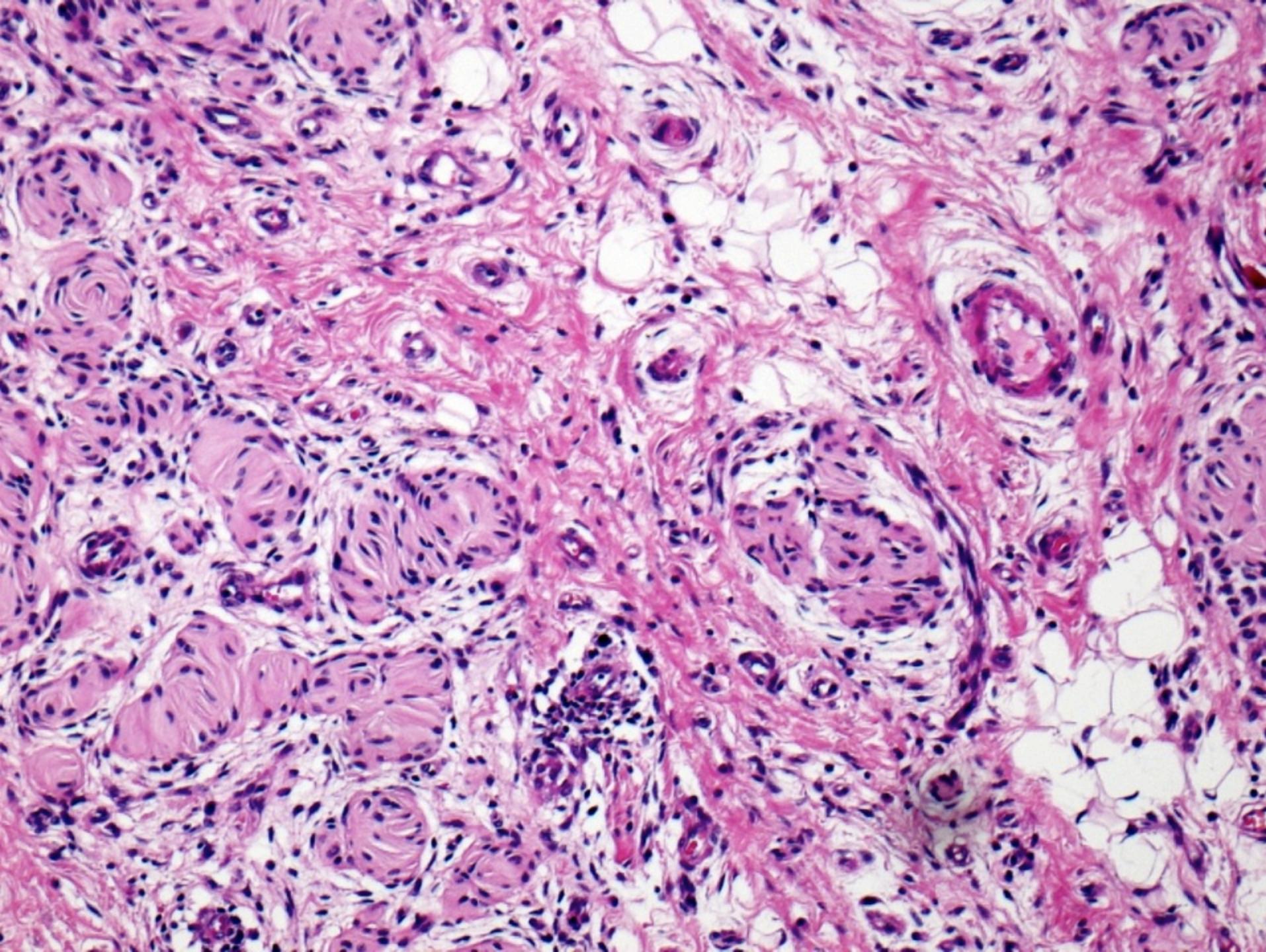












Spitz Naevus

-Introduction-

- **One of the most challenging and controversial aspects of melanocytic tumour pathology to date**
- **Described by Sophie Spitz in 1948 as 'juvenile melanoma'**
- **Favourable outcome despite worrying histological features**
- **Histological features poor predictor of outcome (disease associated mortality in 1/13 patients)**

Spitz Naevus

-Clinical Presentation-

- Wide age spectrum but most common in childhood and adolescence
- Decreasing frequency with age
- Predilection for Caucasians
- Slight female predominance
- Wide anatomic distribution
 - Face and ear in childhood
 - Trunk and extremities in adulthood
- Non-pigmented, red to skin coloured papule <1cm in diameter

Spitz Naevus

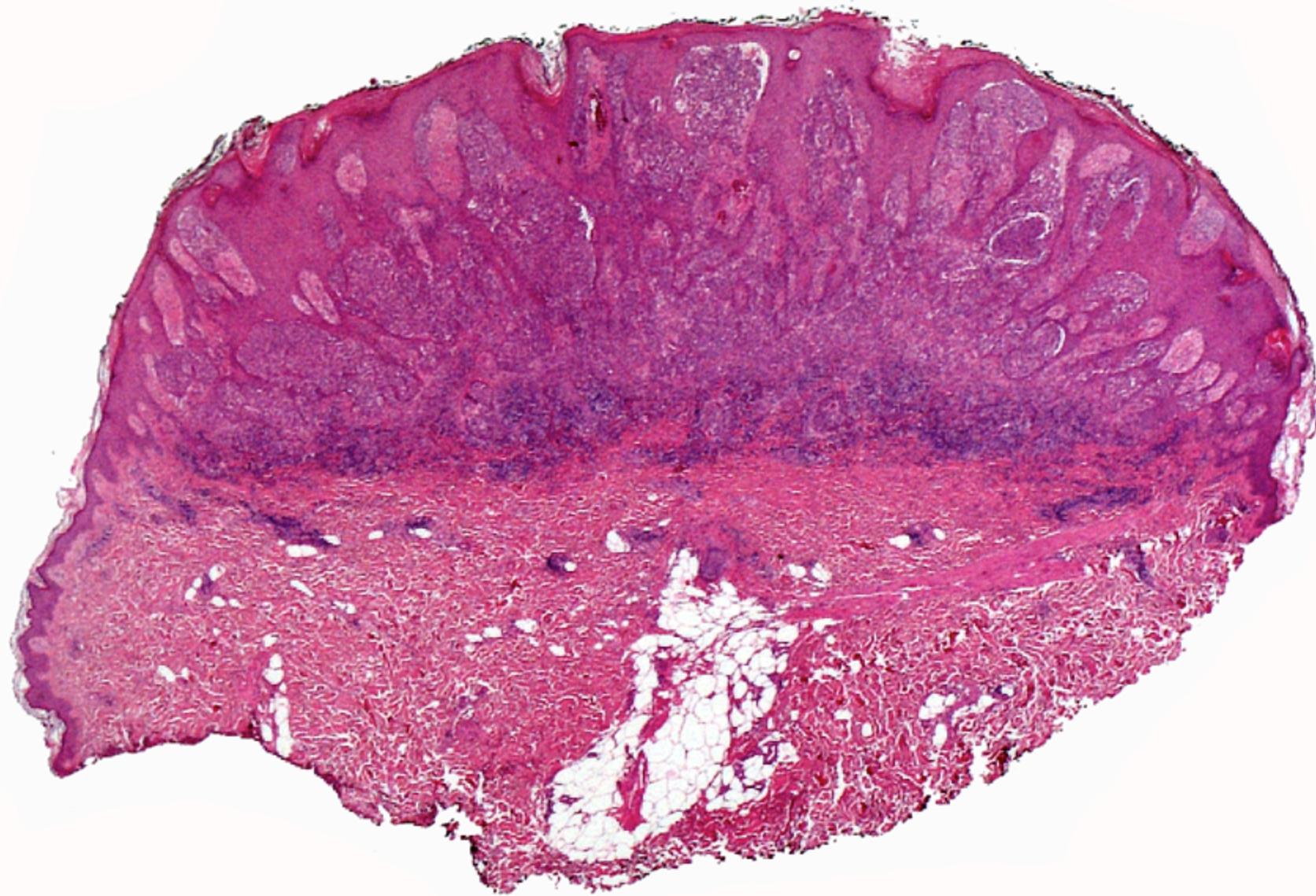
-Problems-

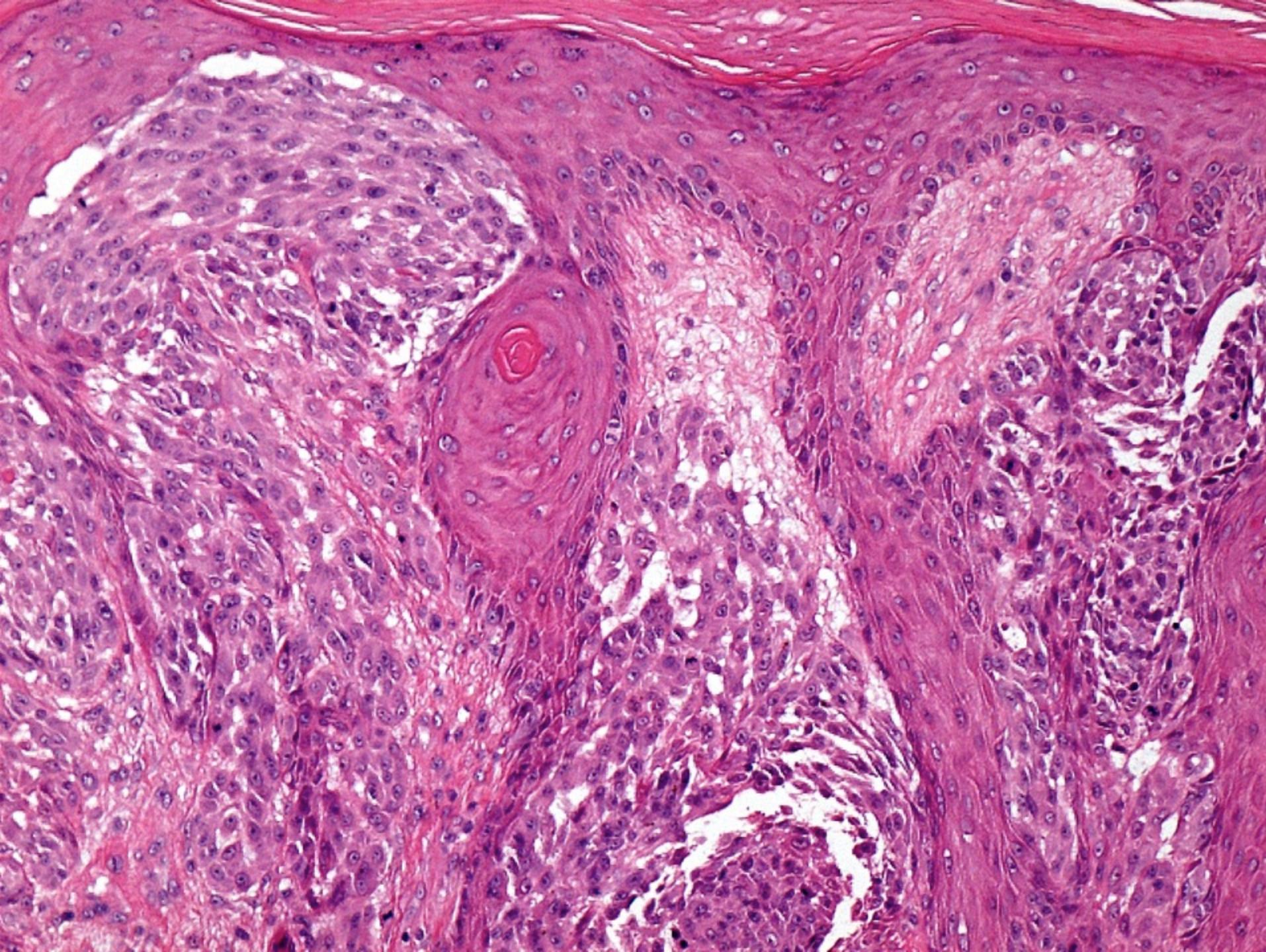
65 years after Sophie Spitz' publication

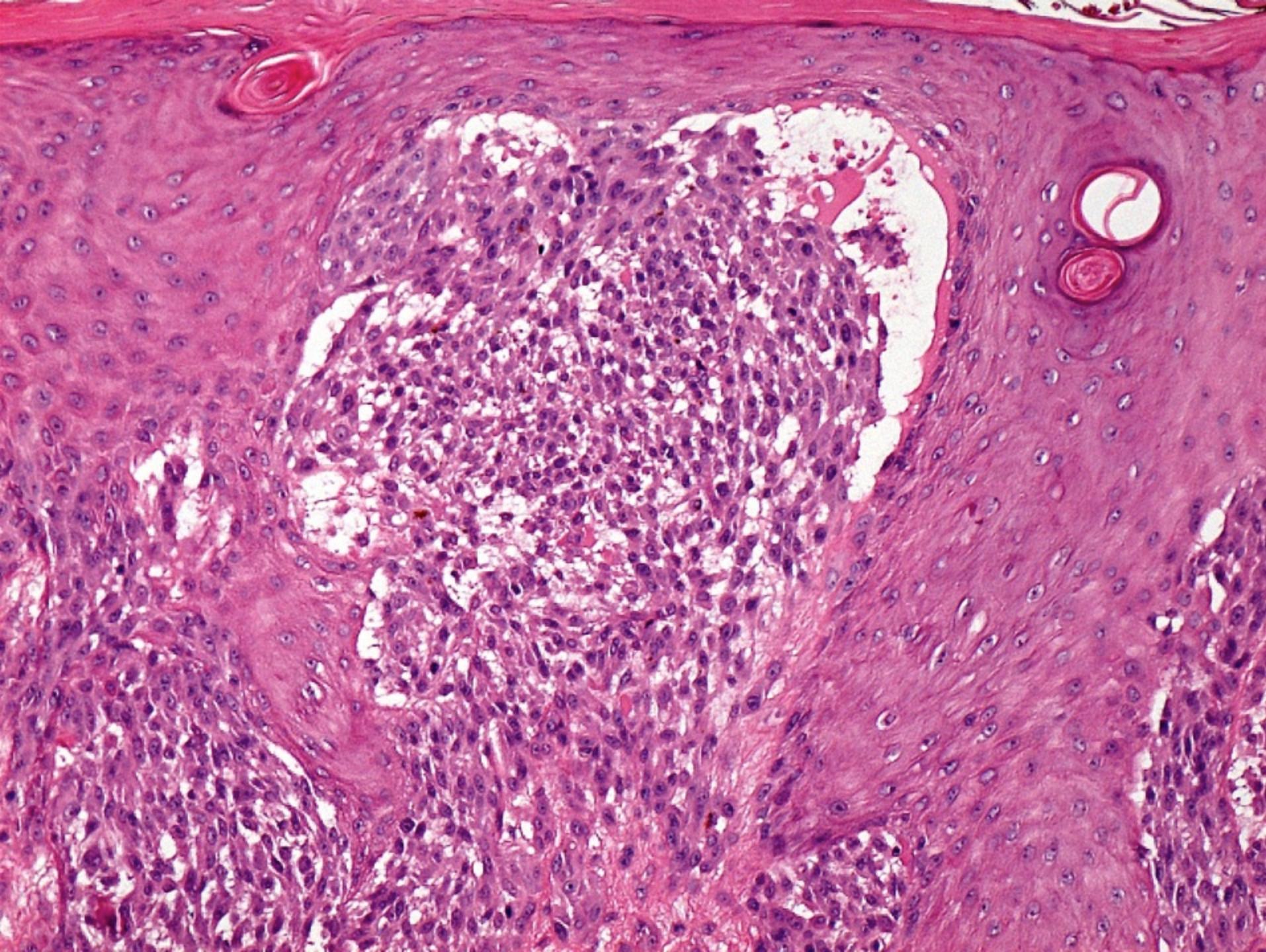
- Poor insight into the biology of Spitz tumours**
- Difficult to predict behaviour**

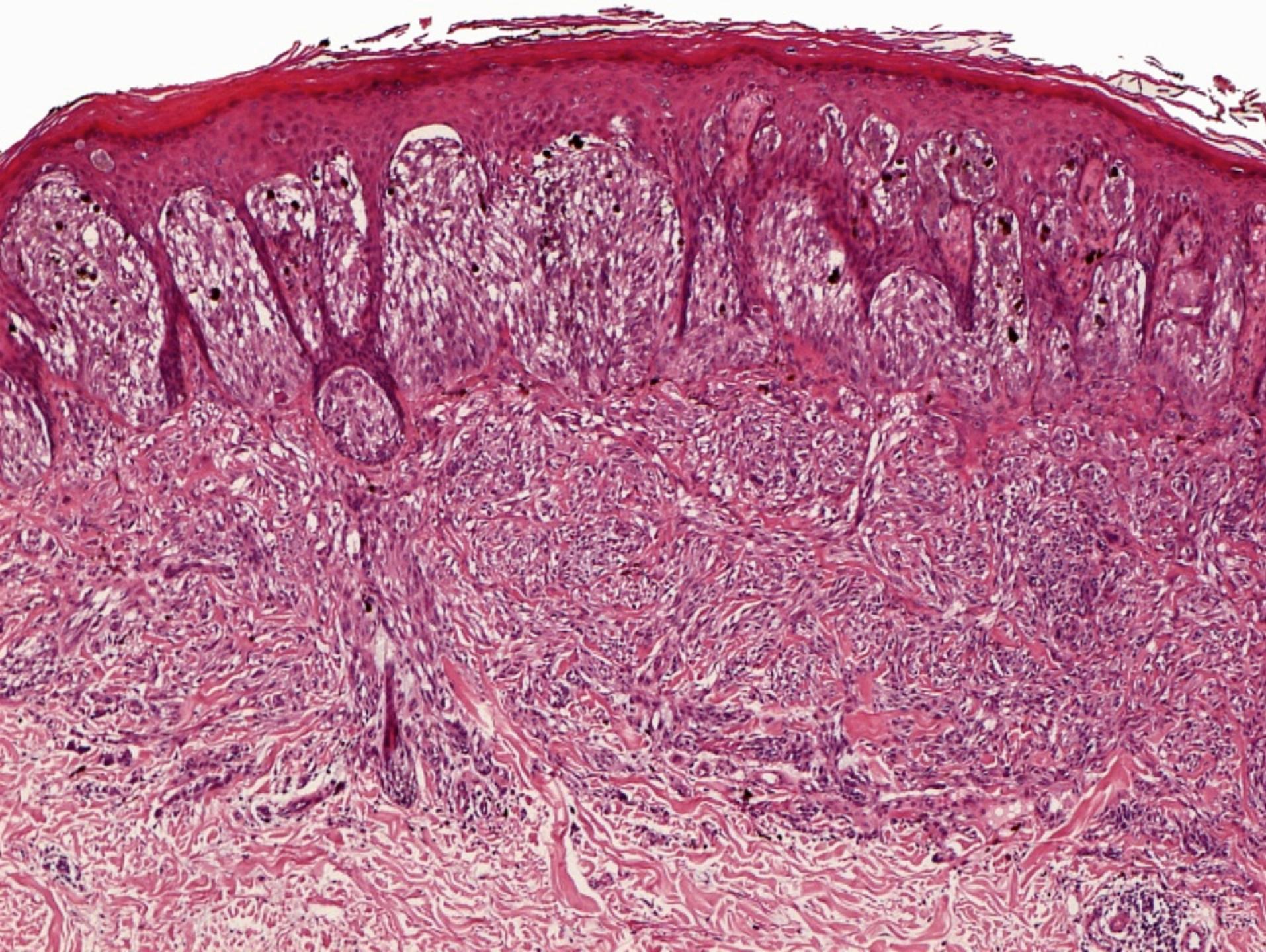
Classification into

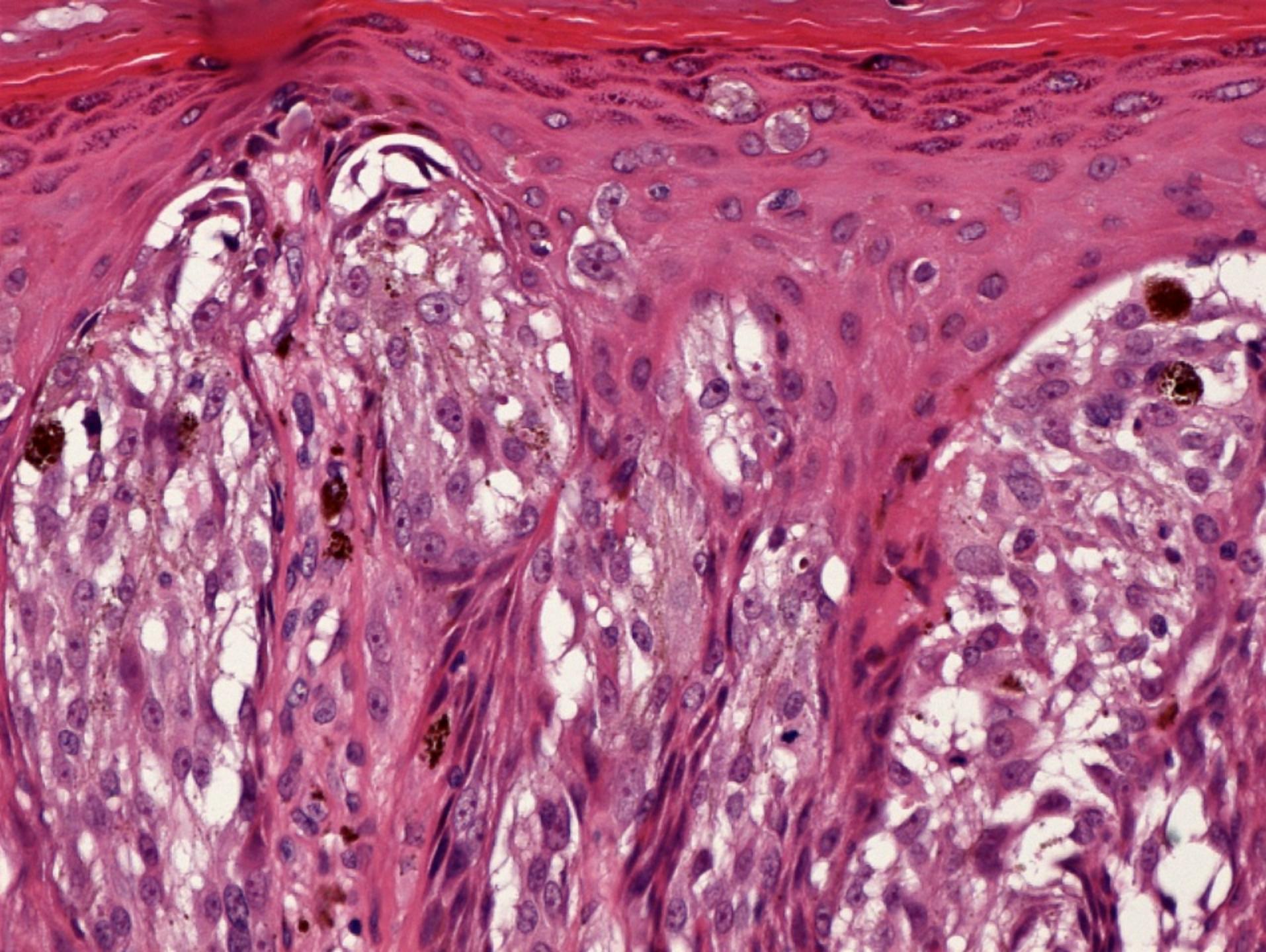
- Spitz Naevus**
- Atypical Spitz Tumour/Spitz Tumour of Uncertain Malignant Potential**
- Spitzoid Melanoma**

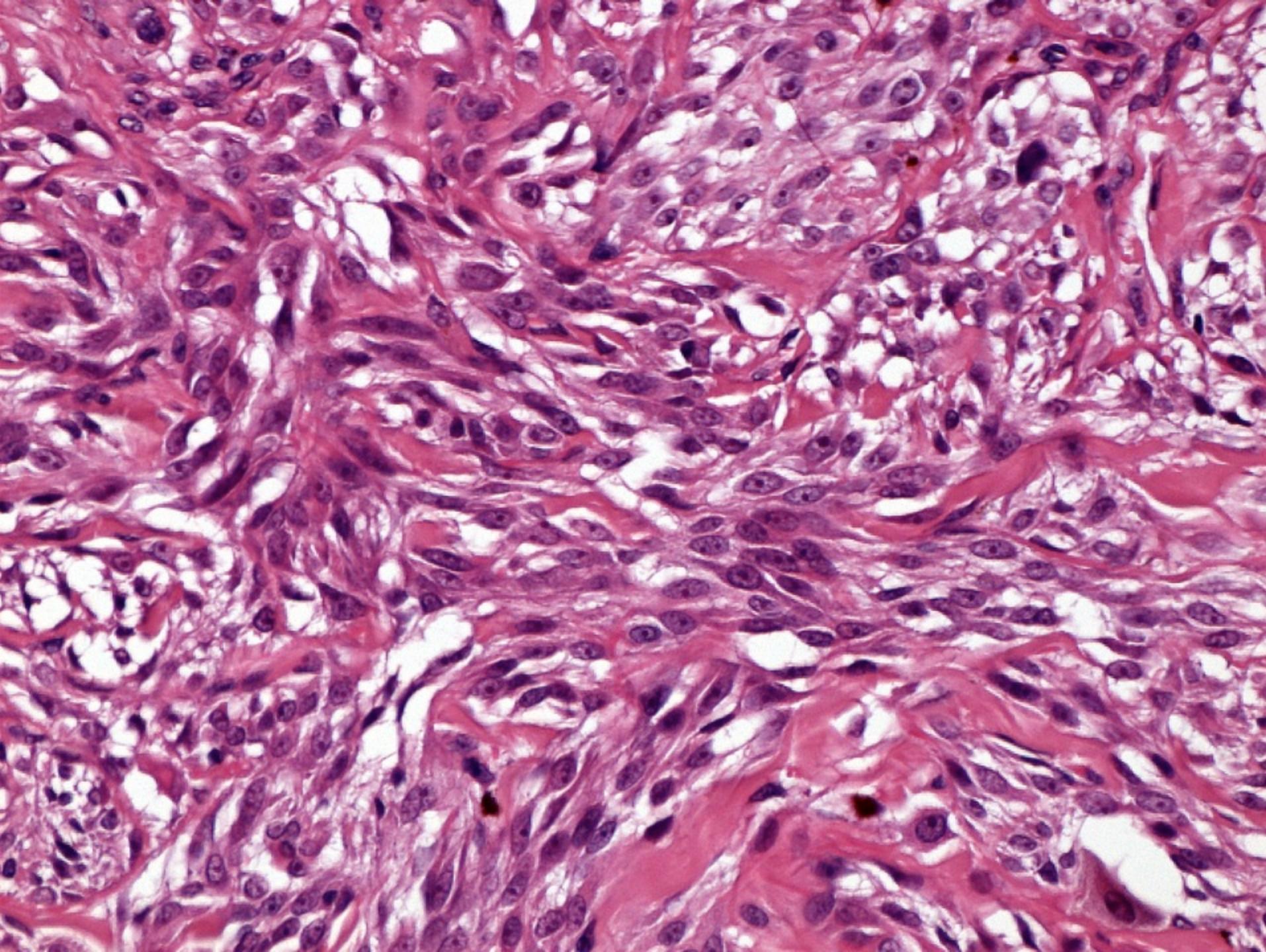


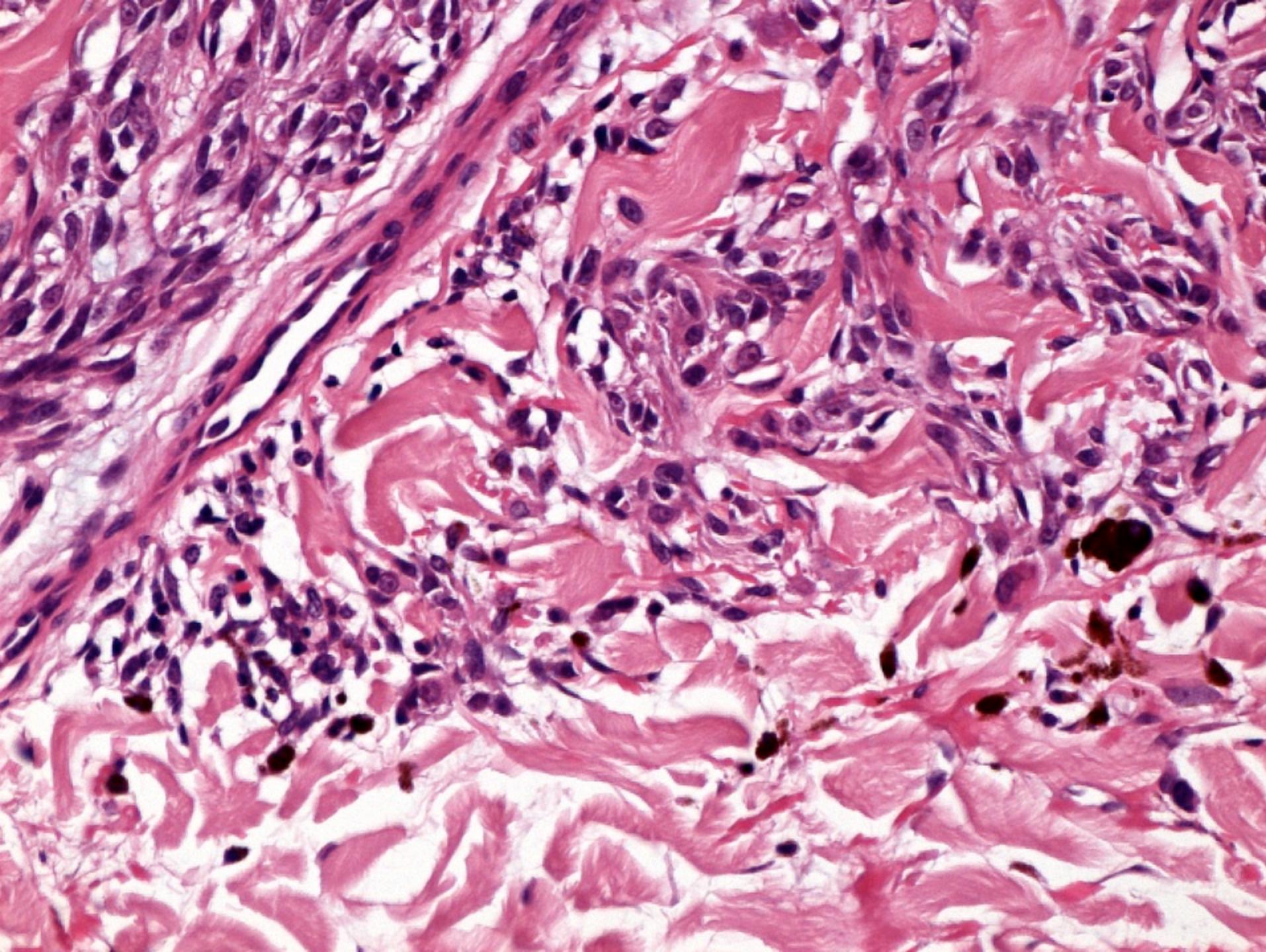


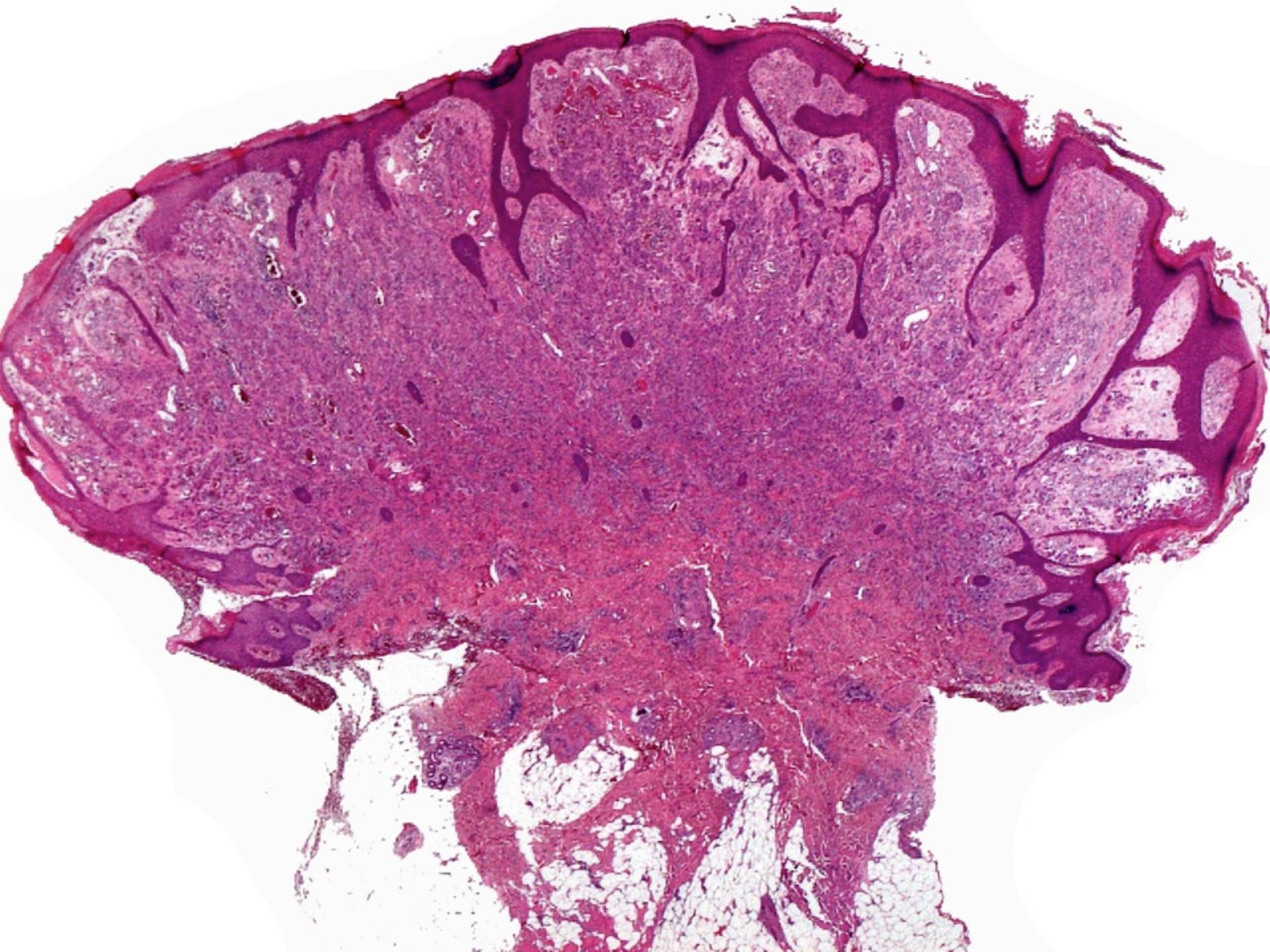


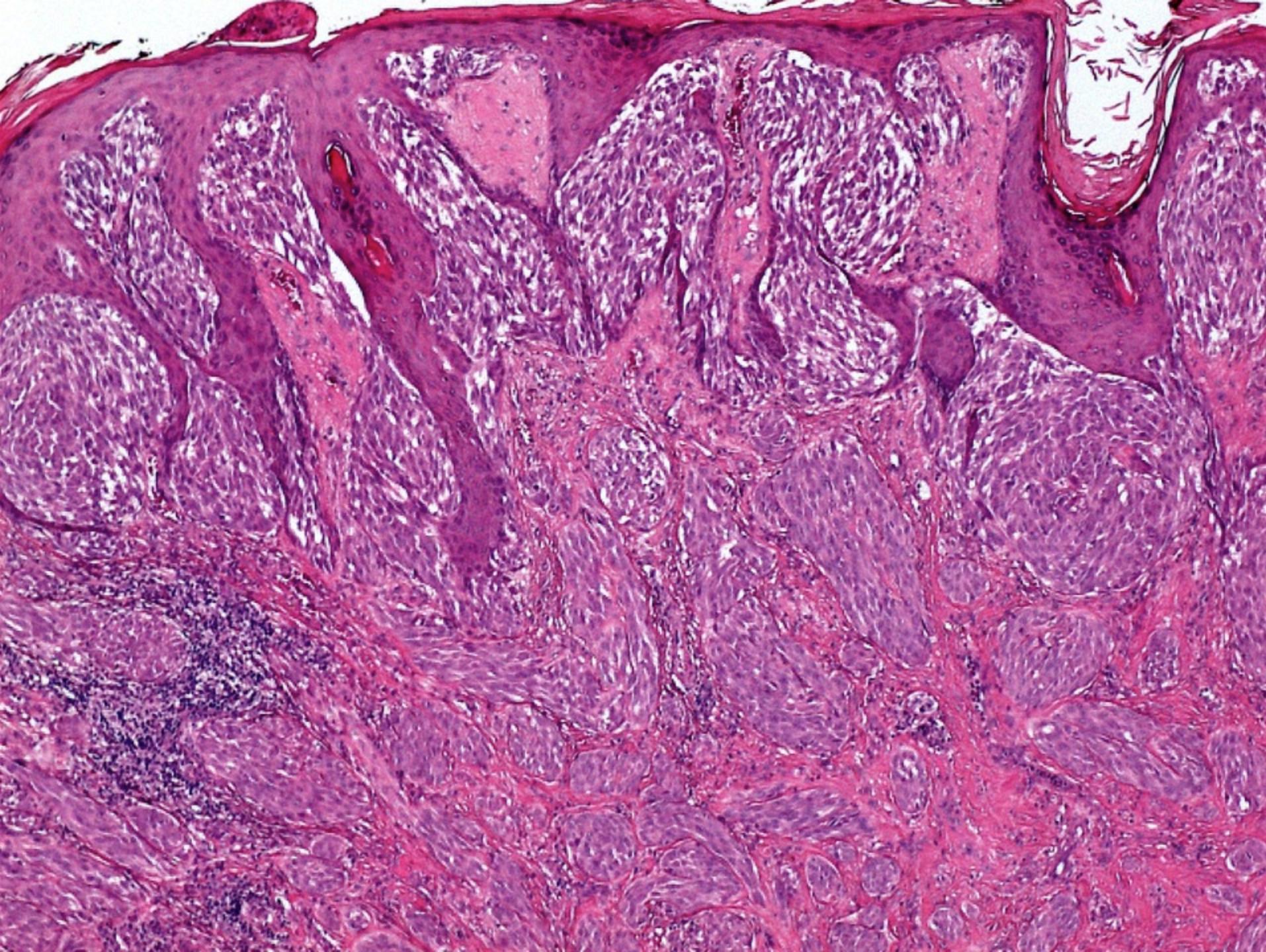


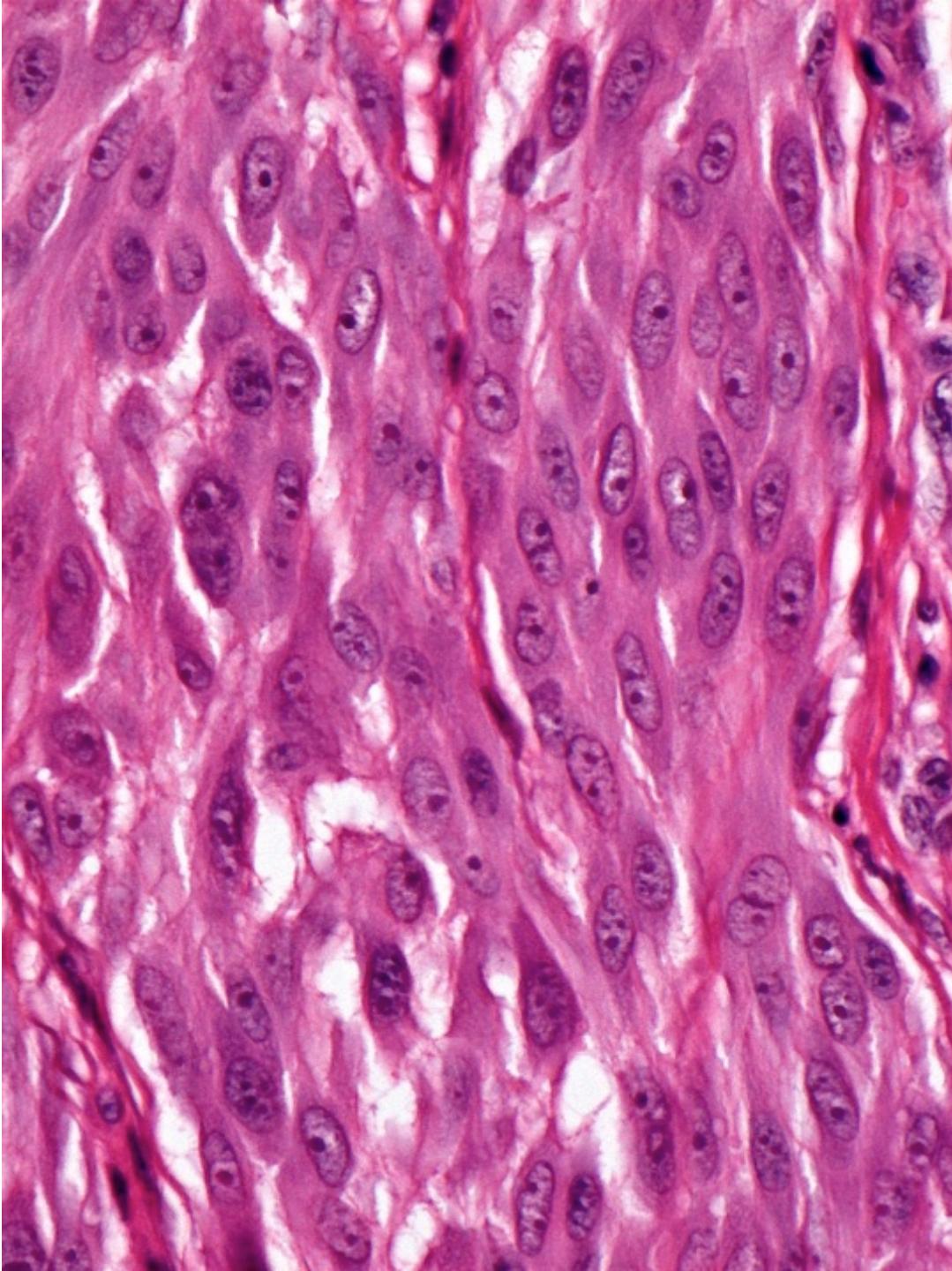


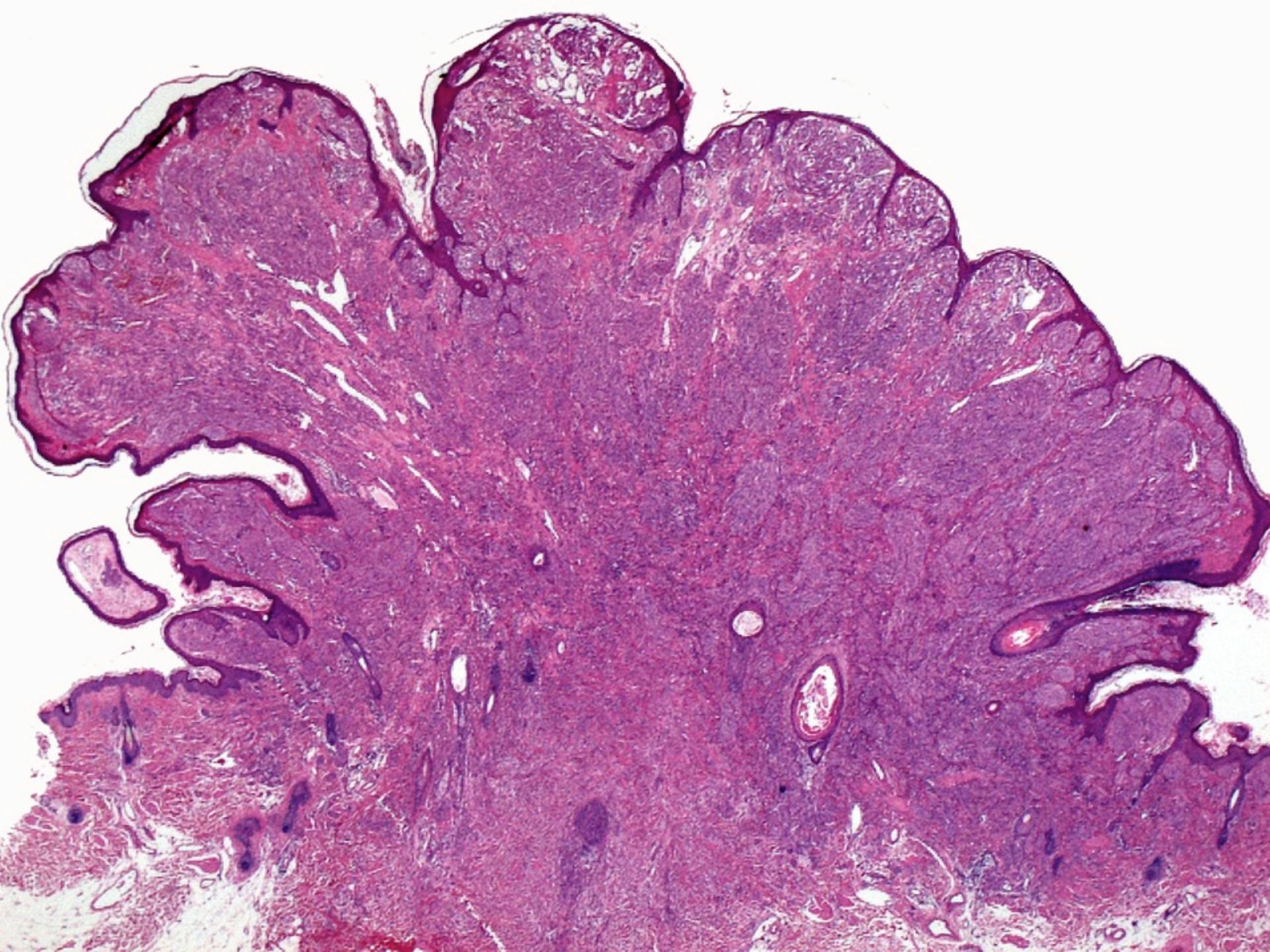


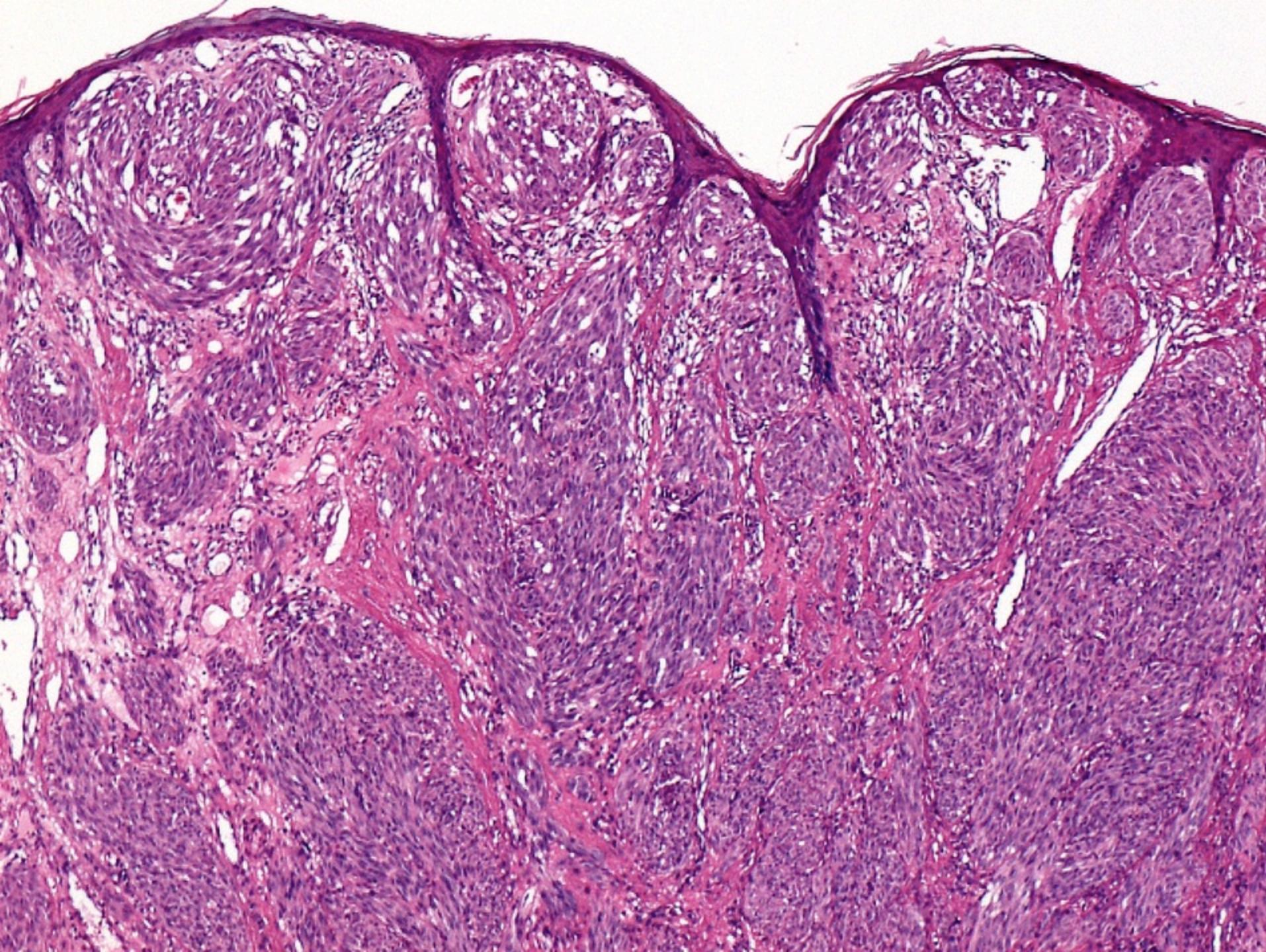


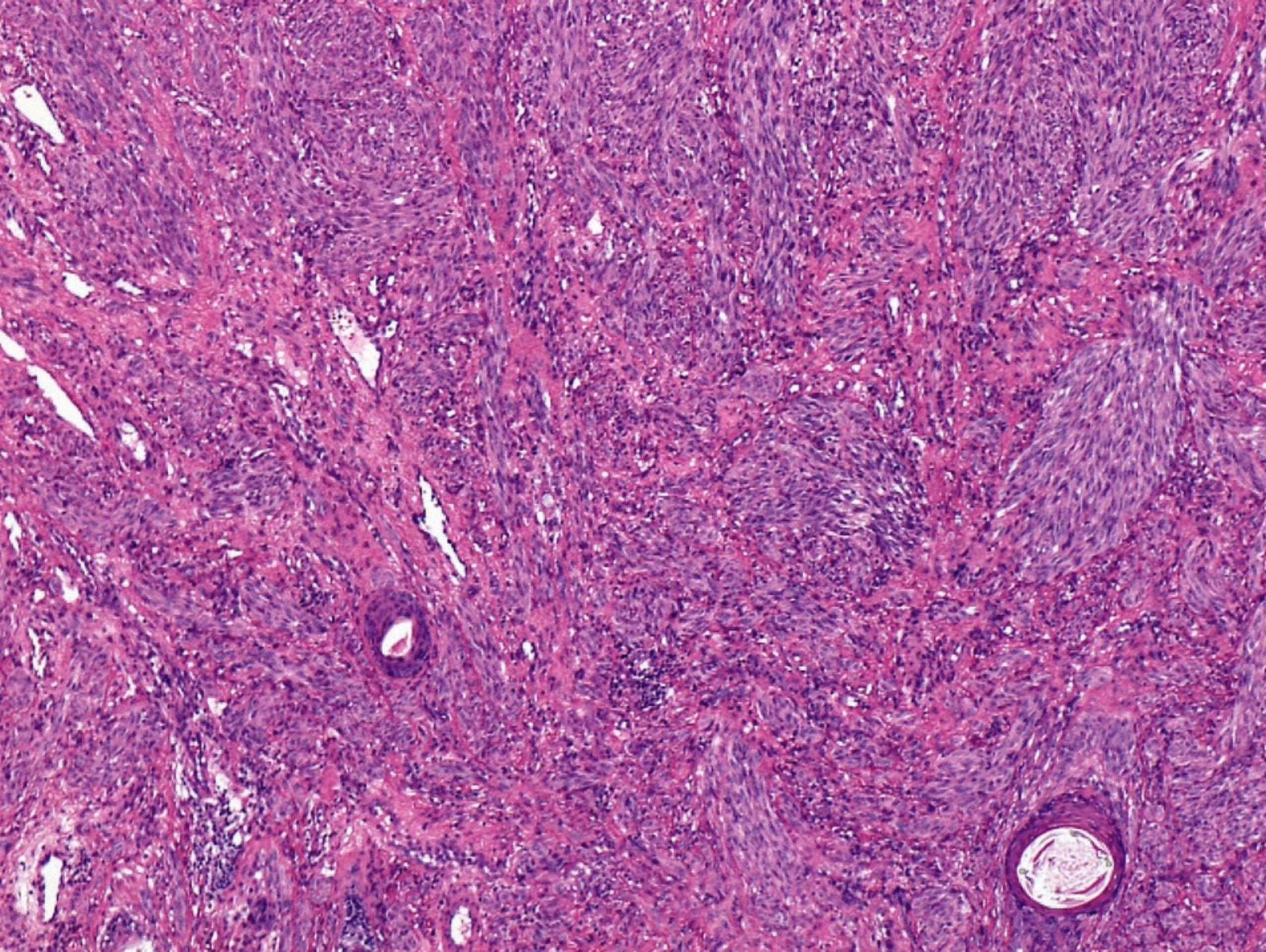


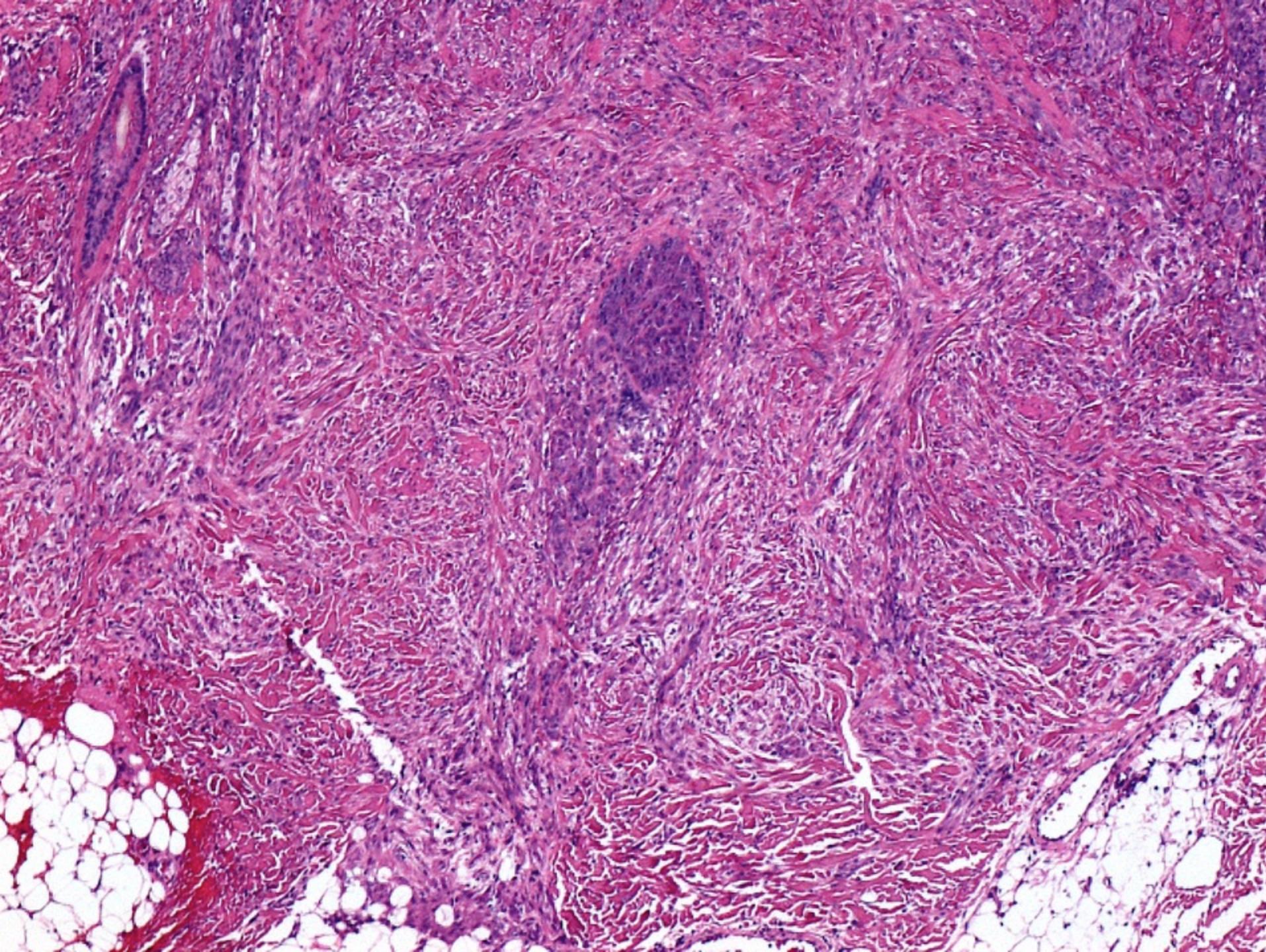


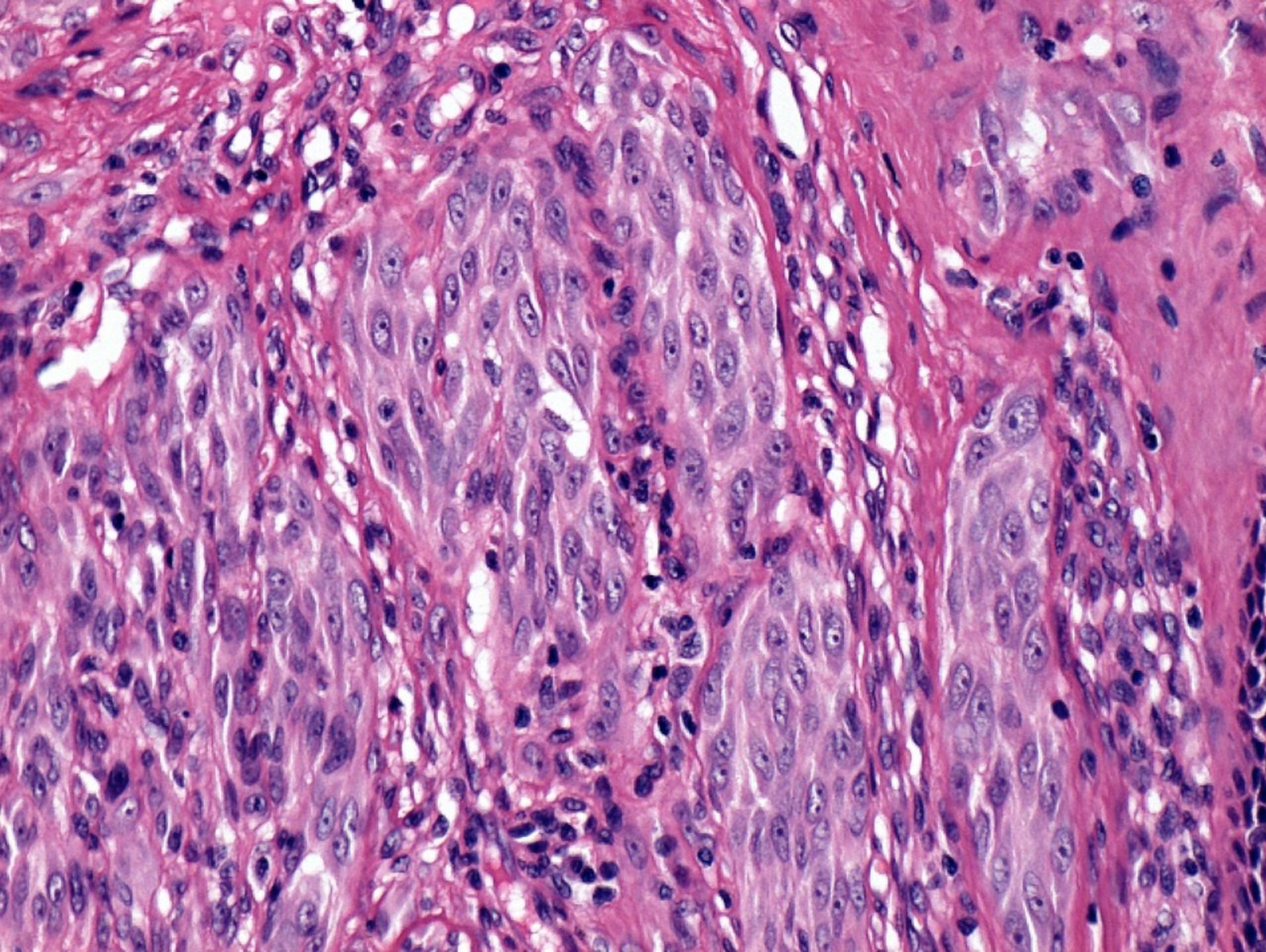


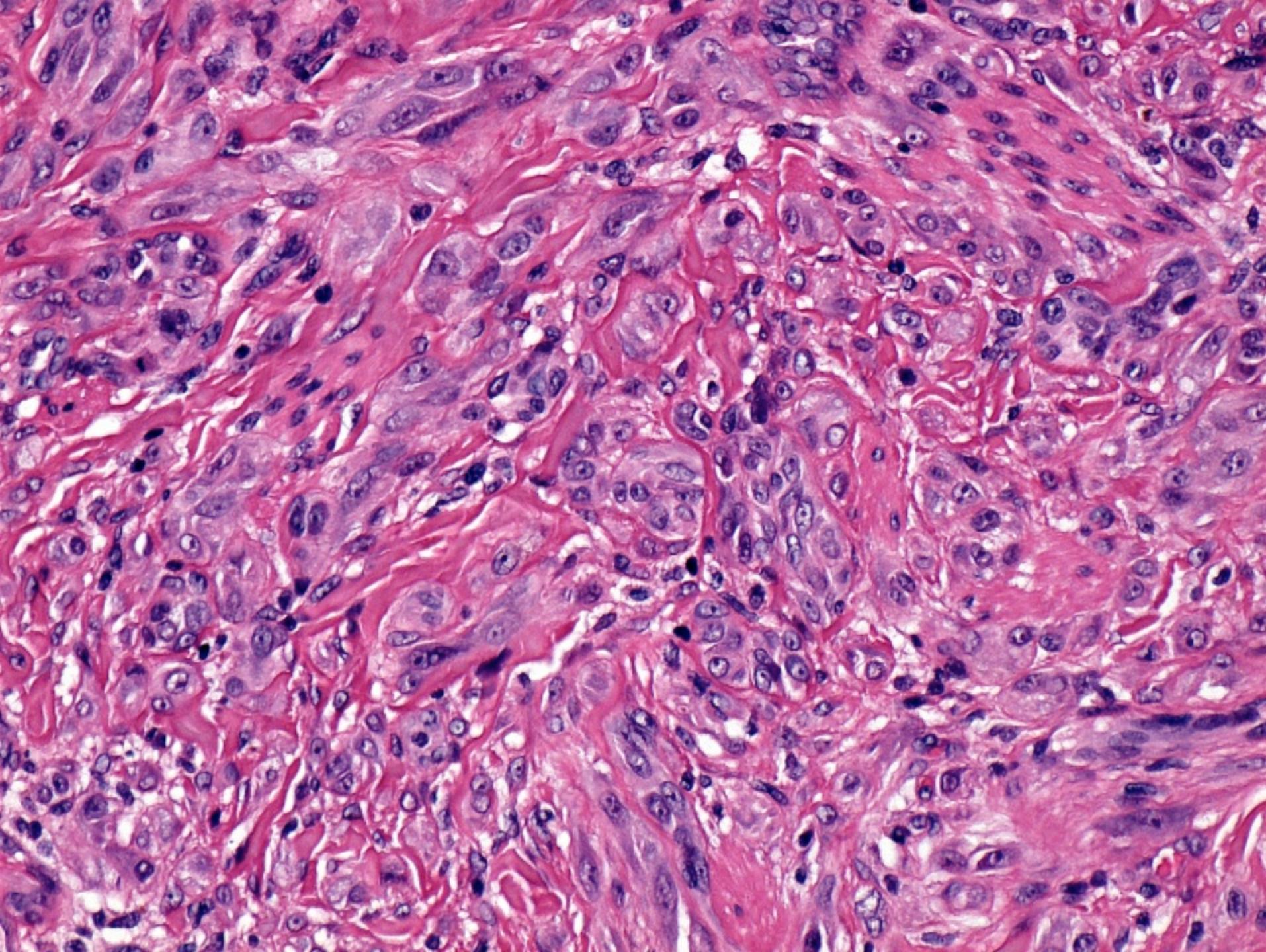


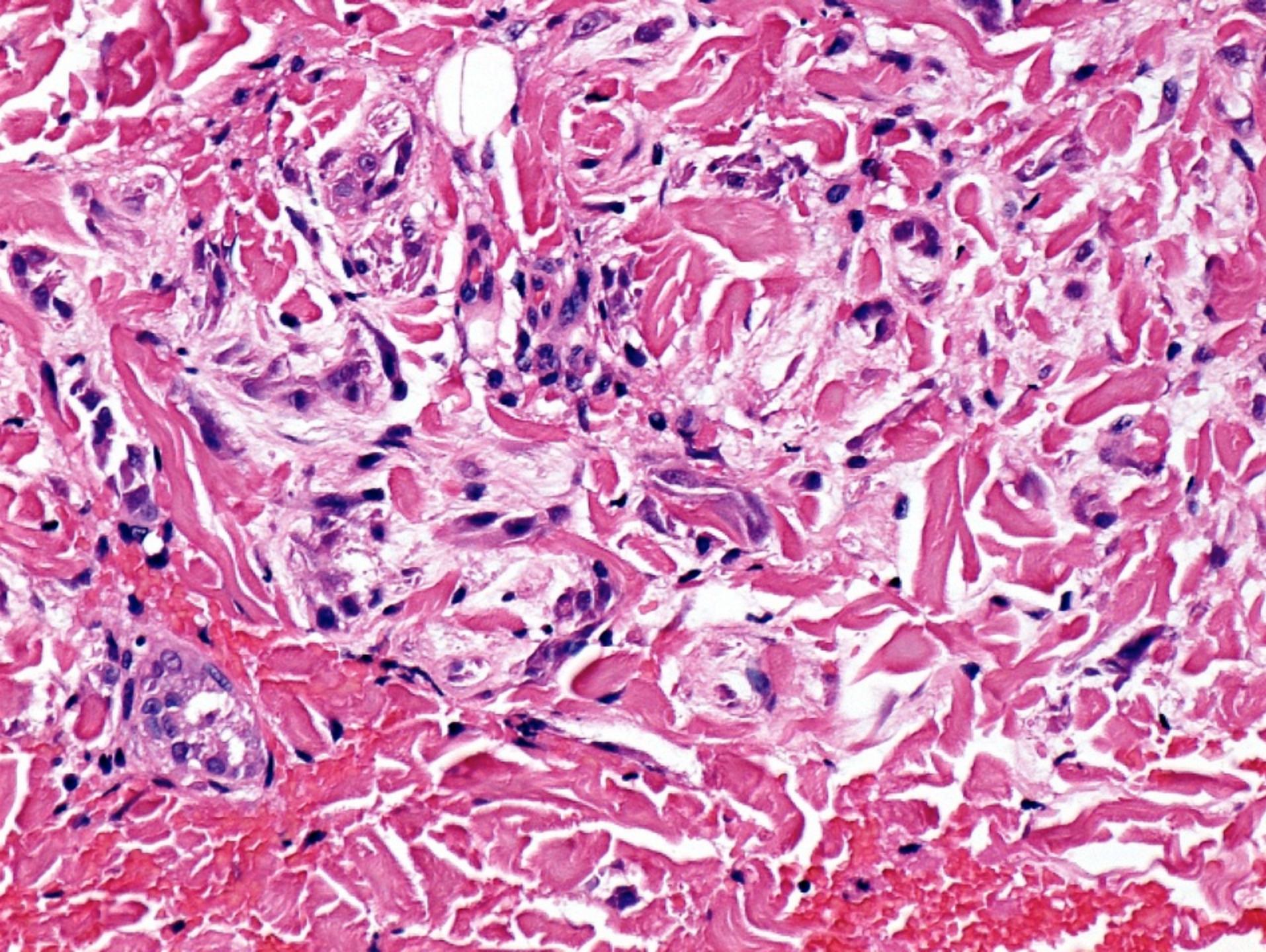


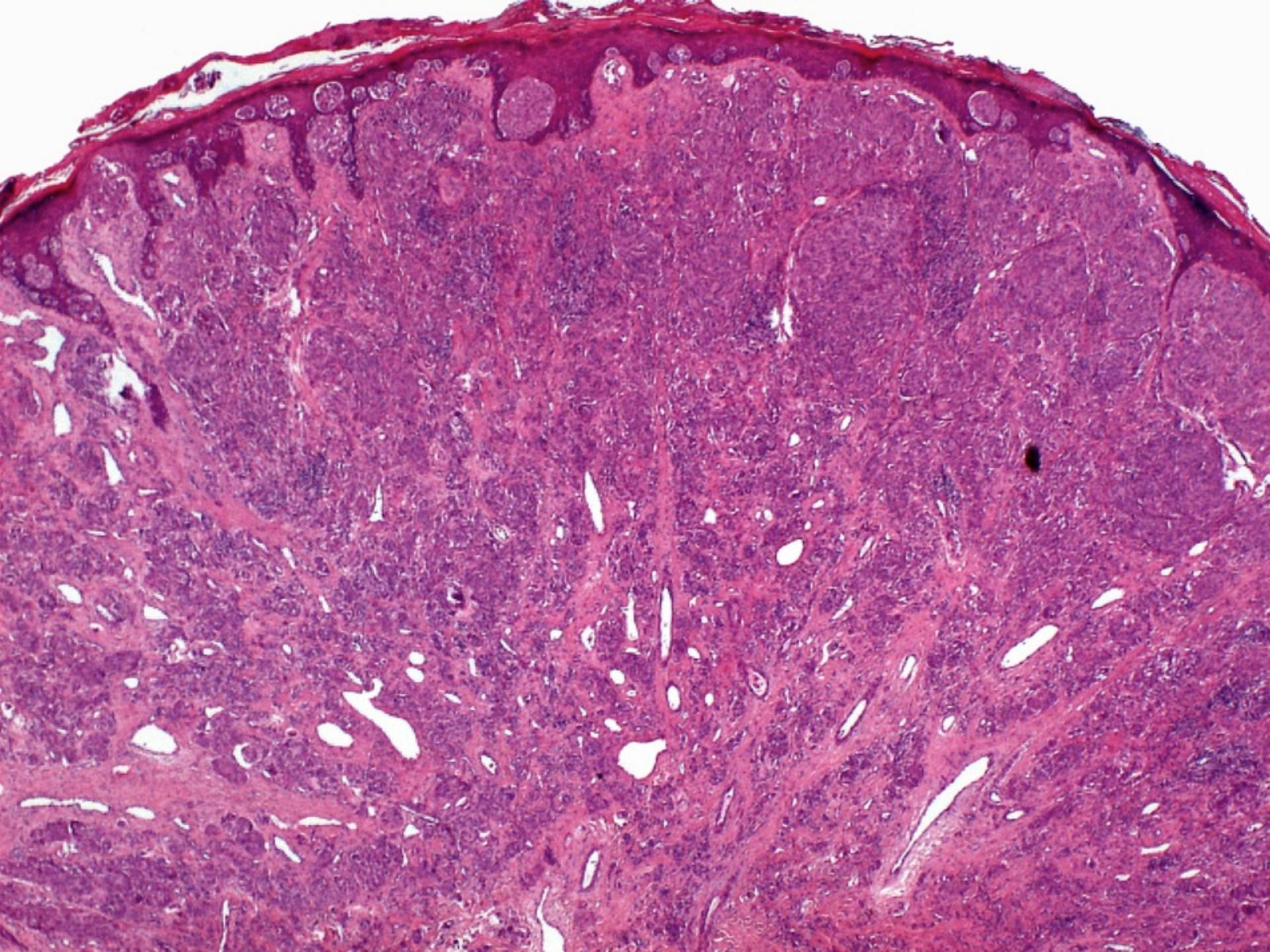


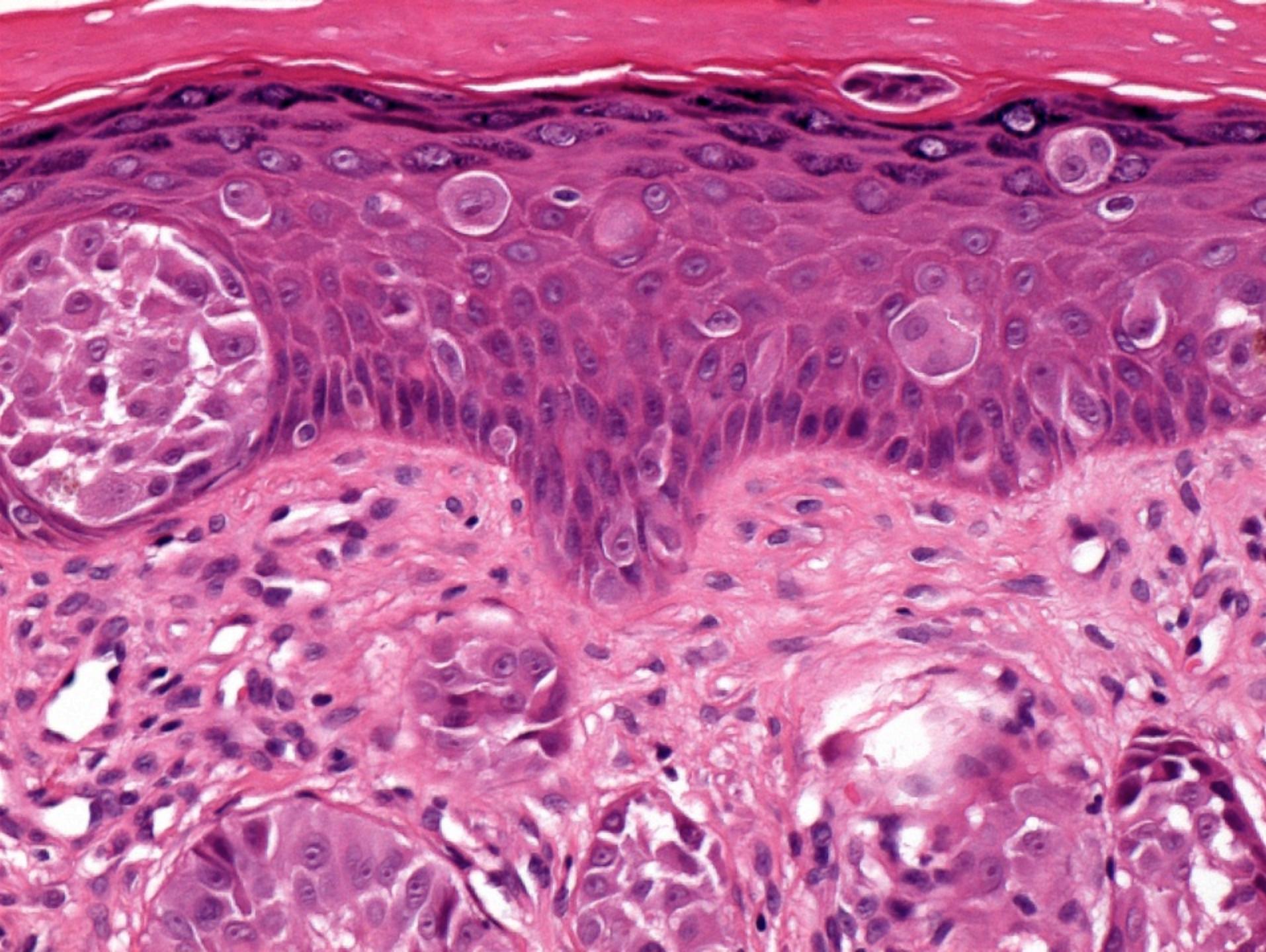


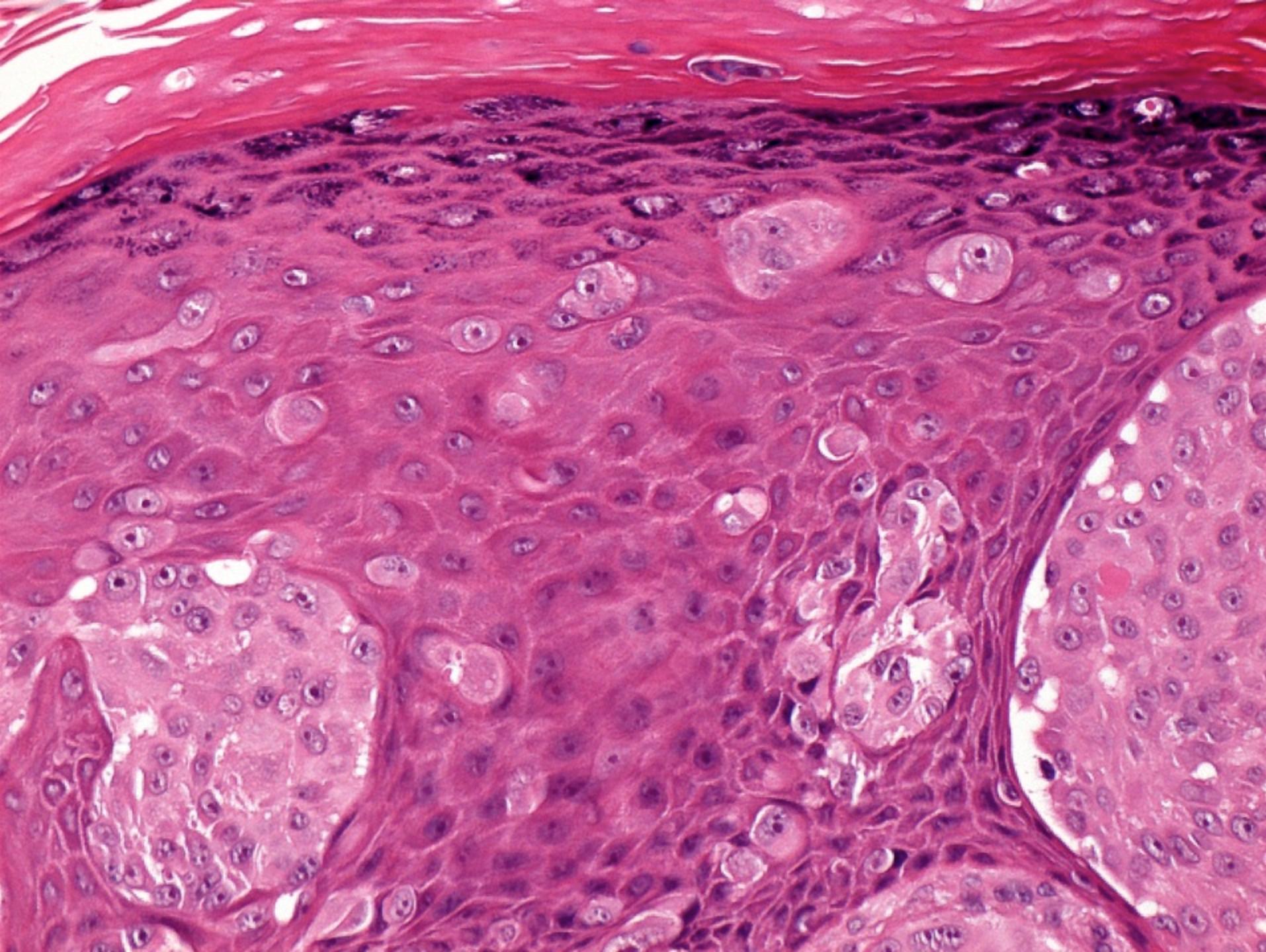


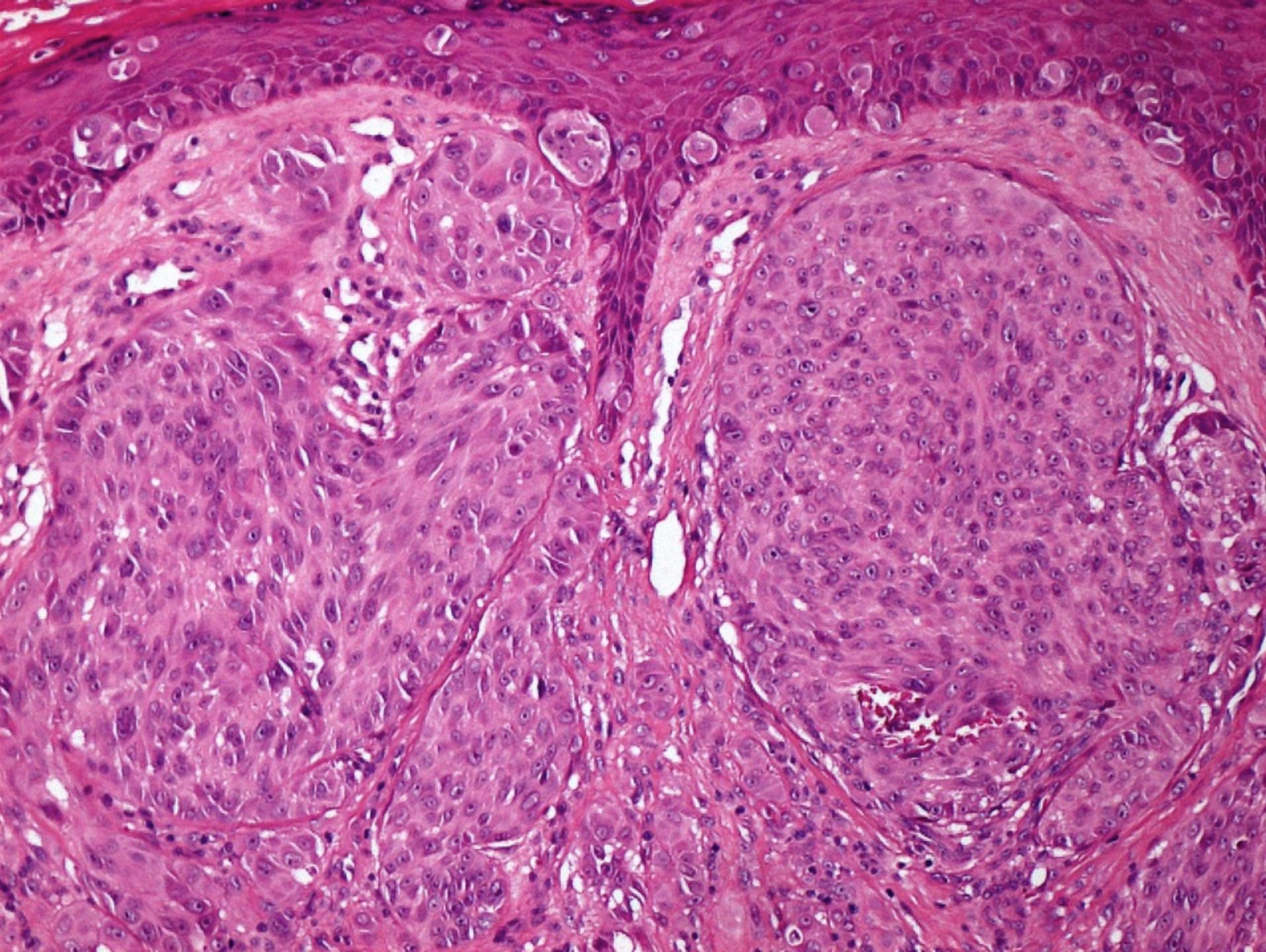


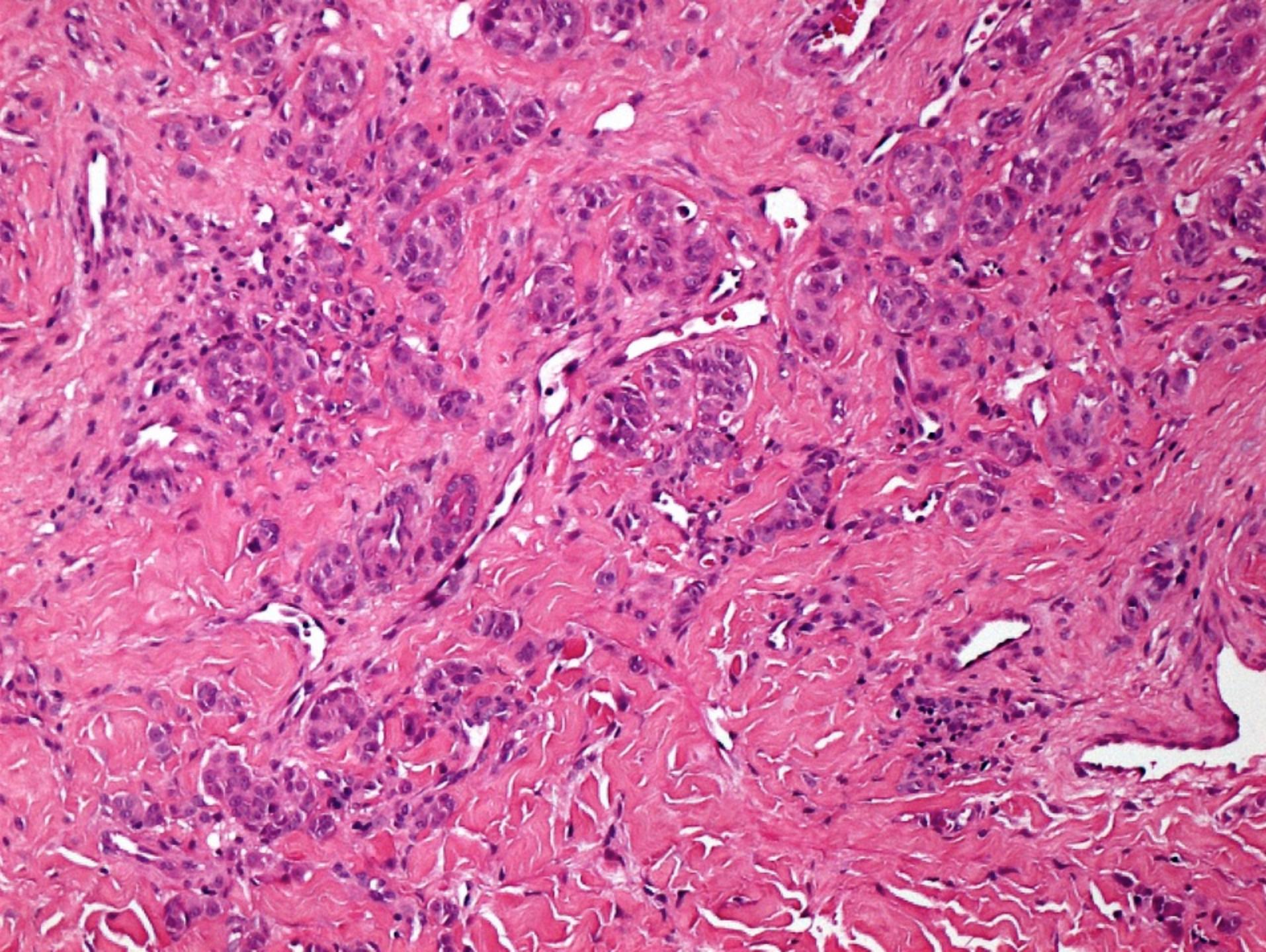


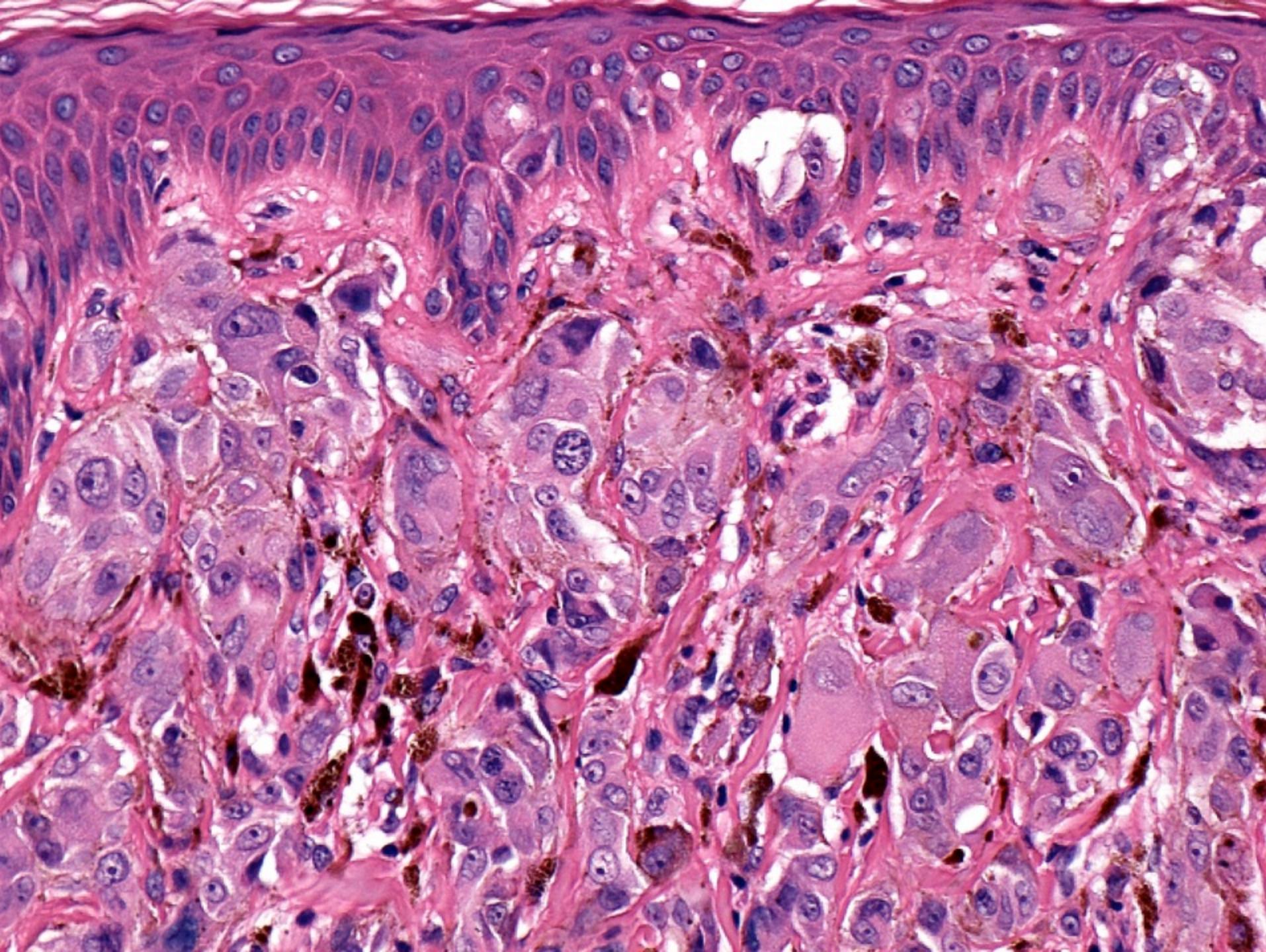


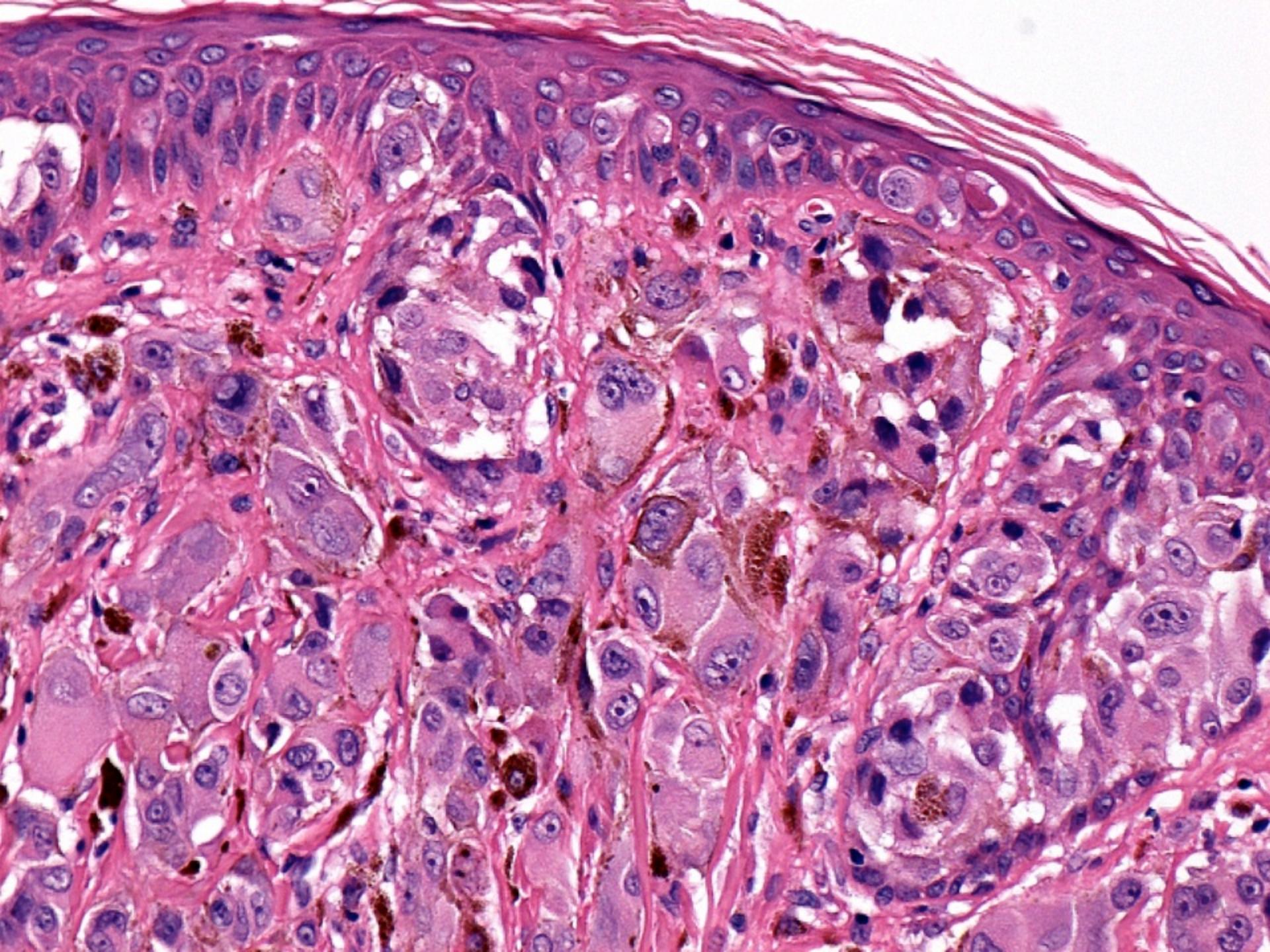


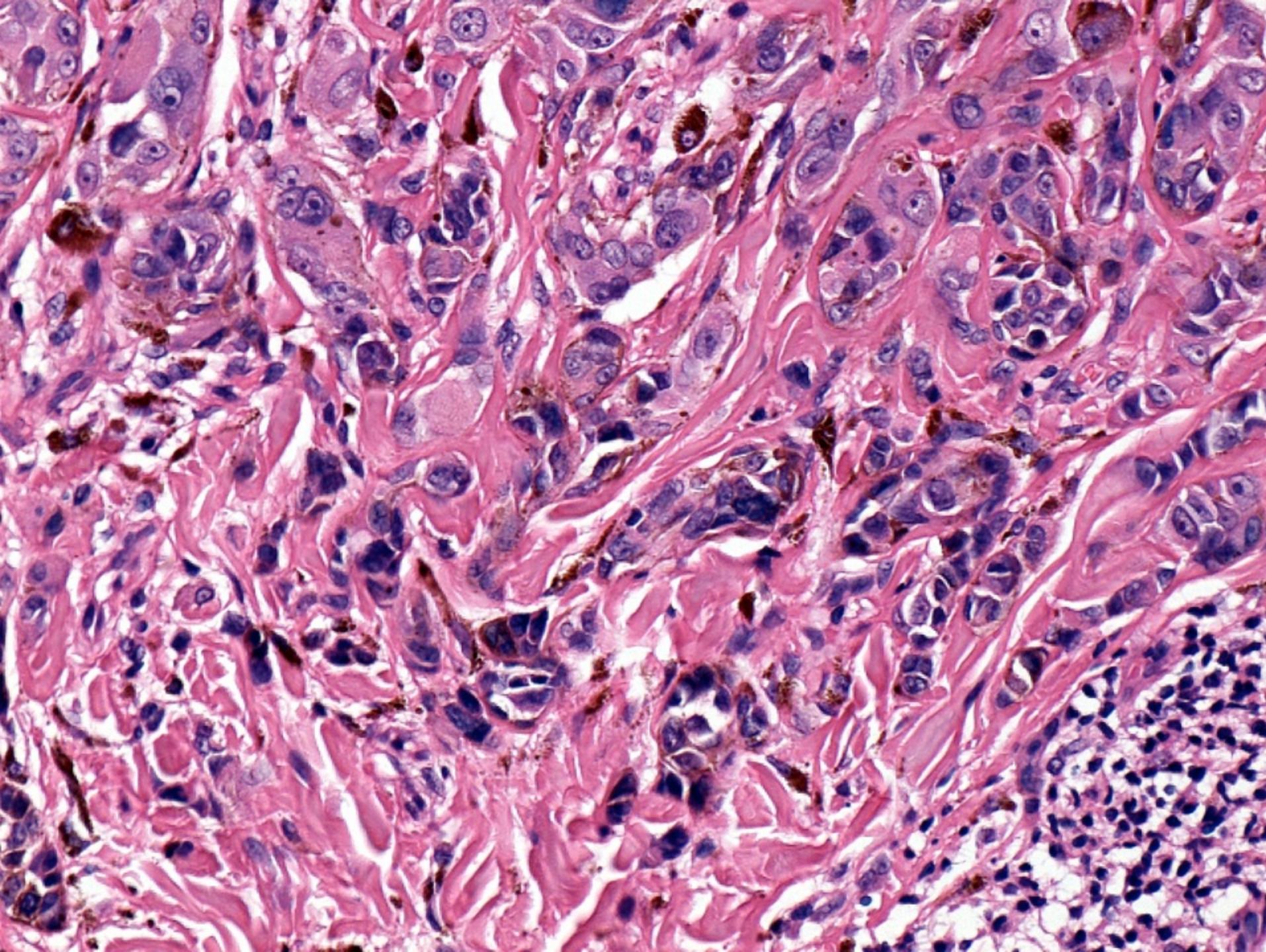


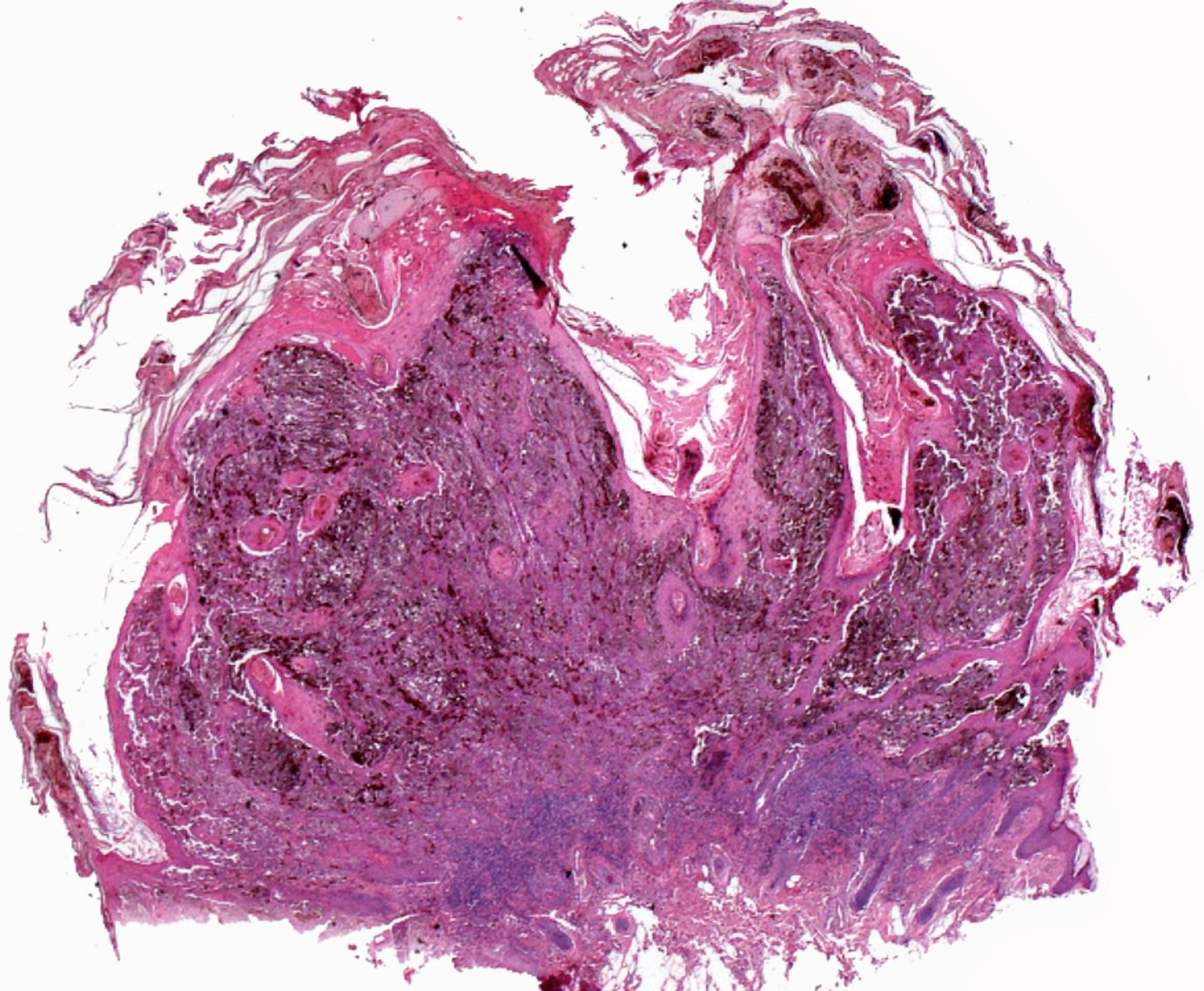


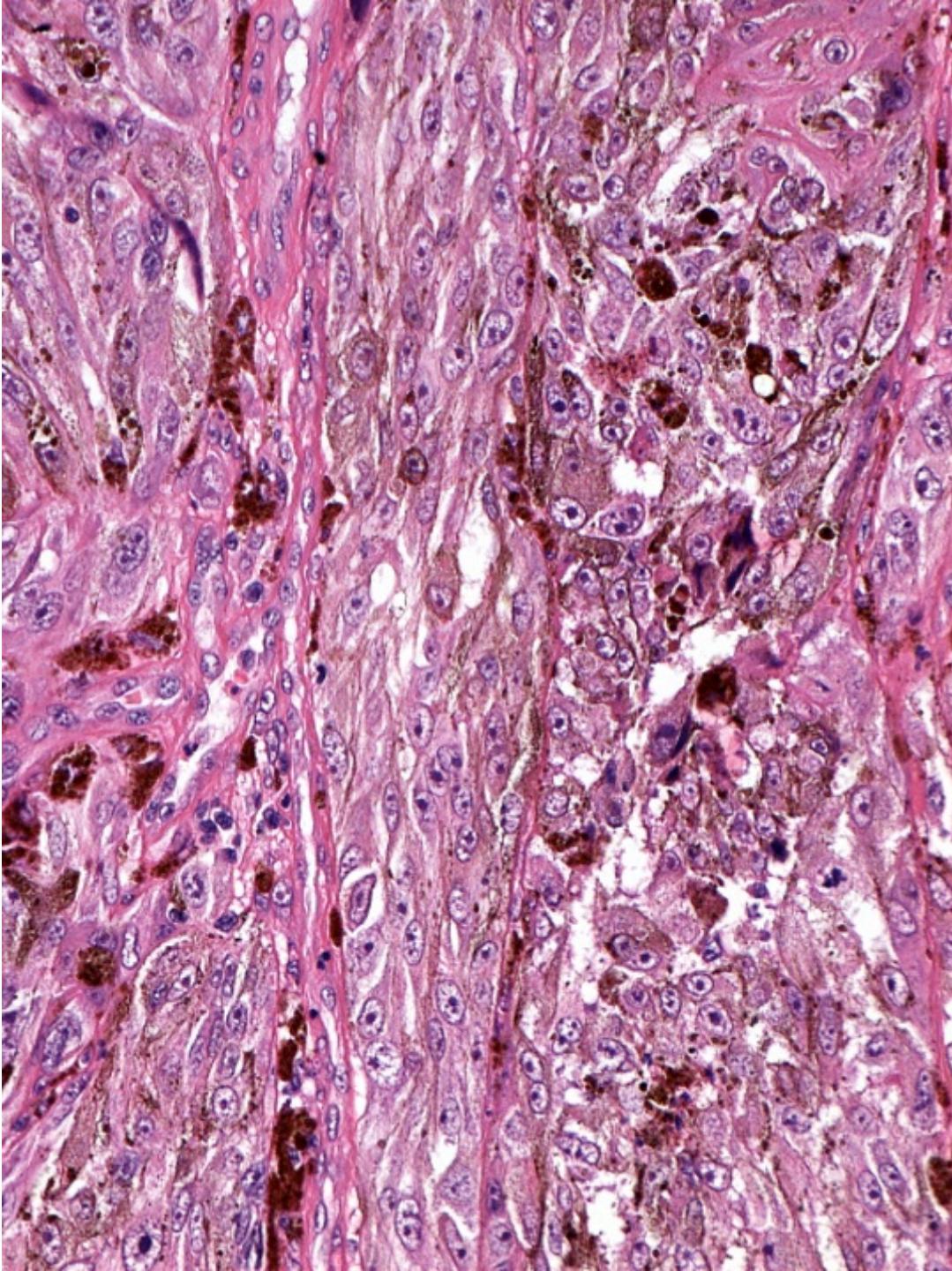


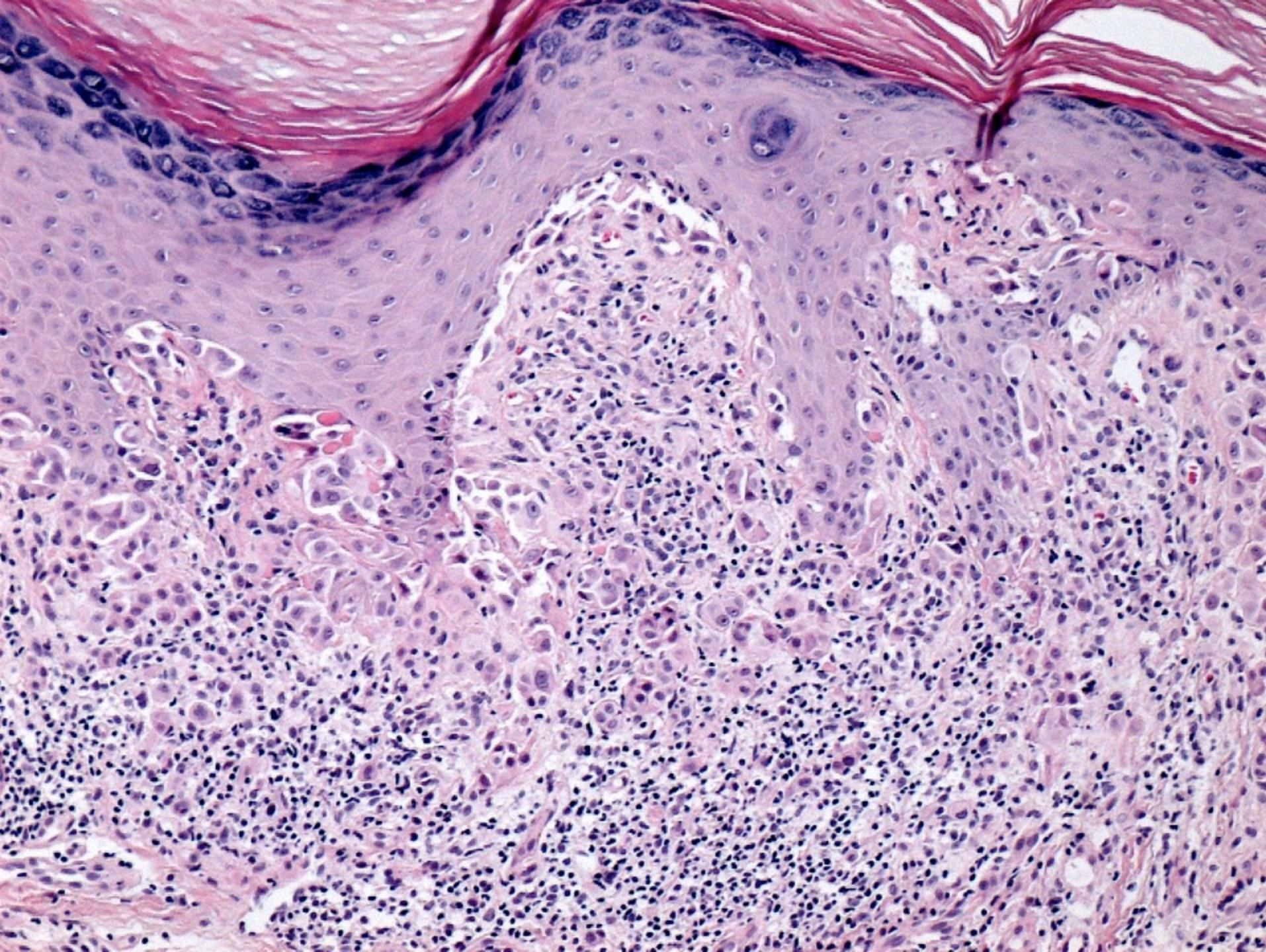


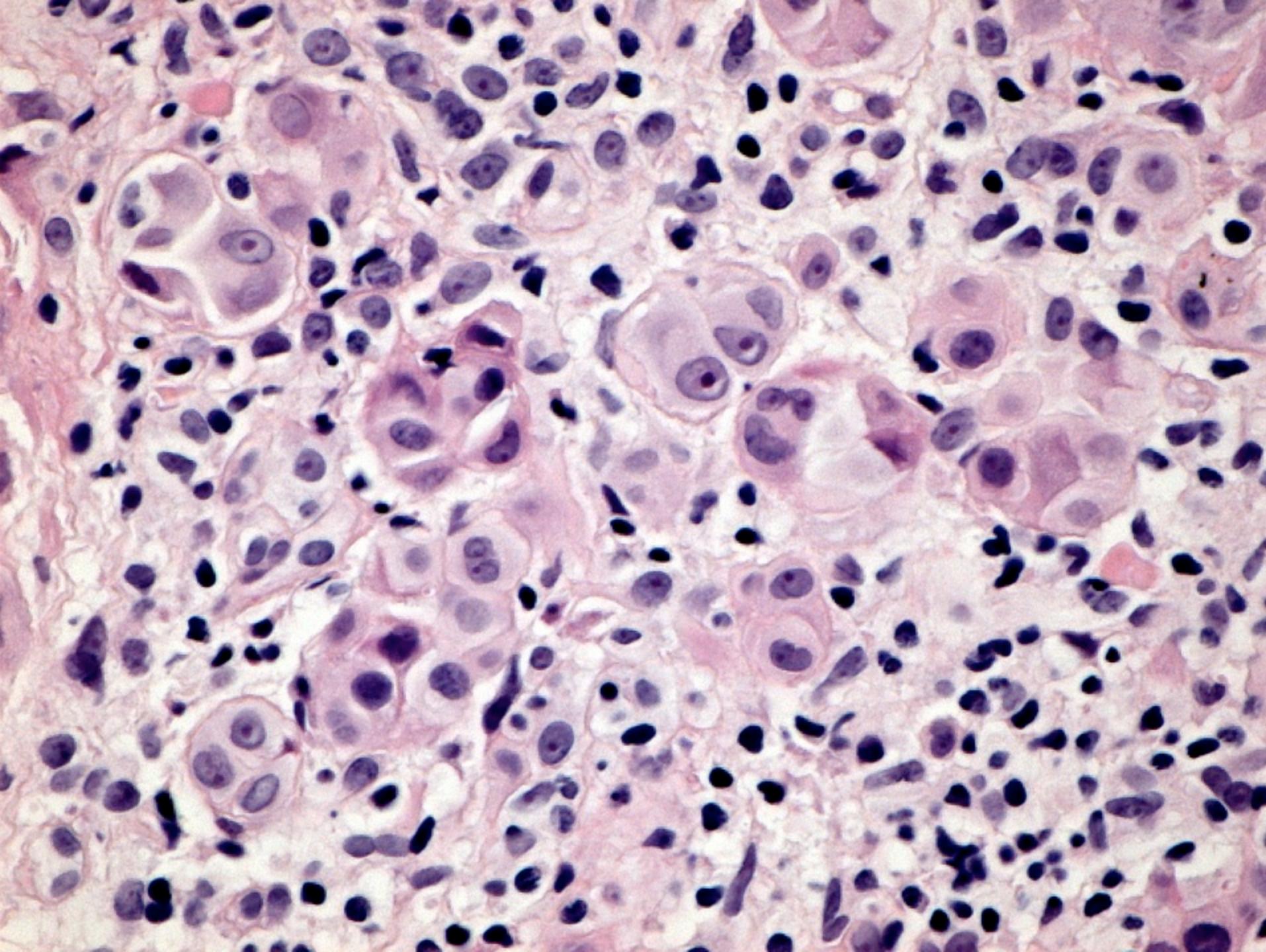




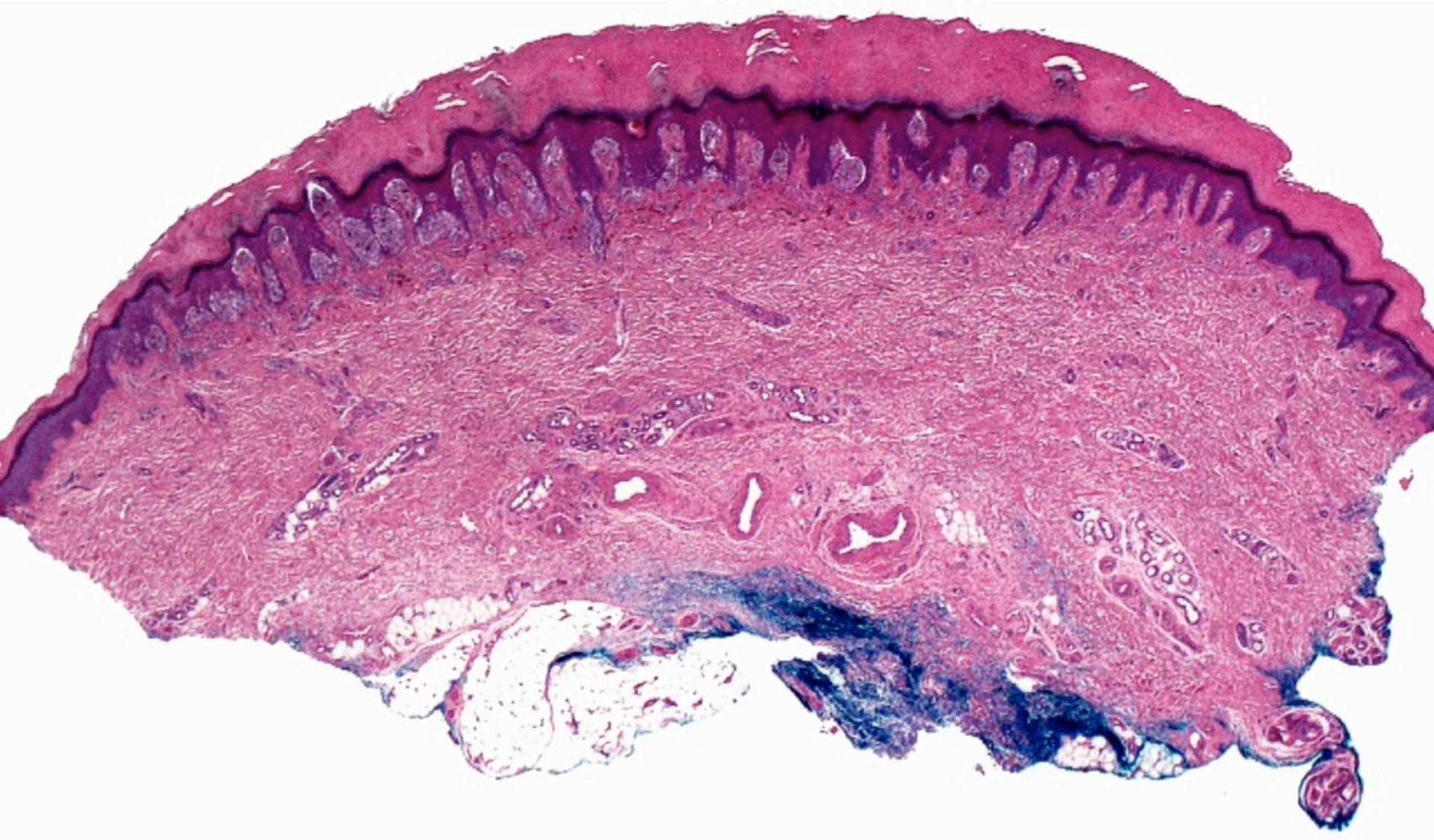


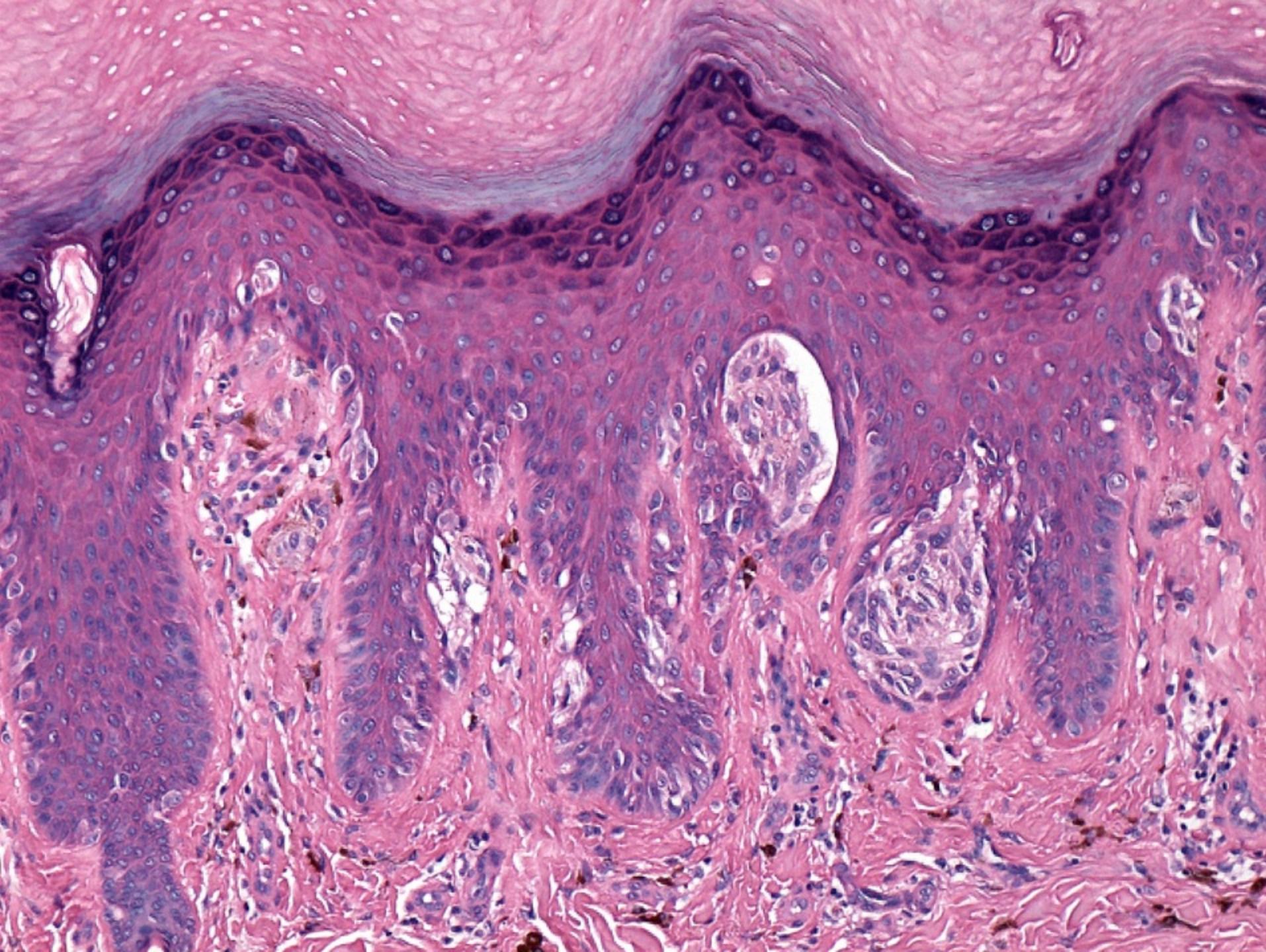


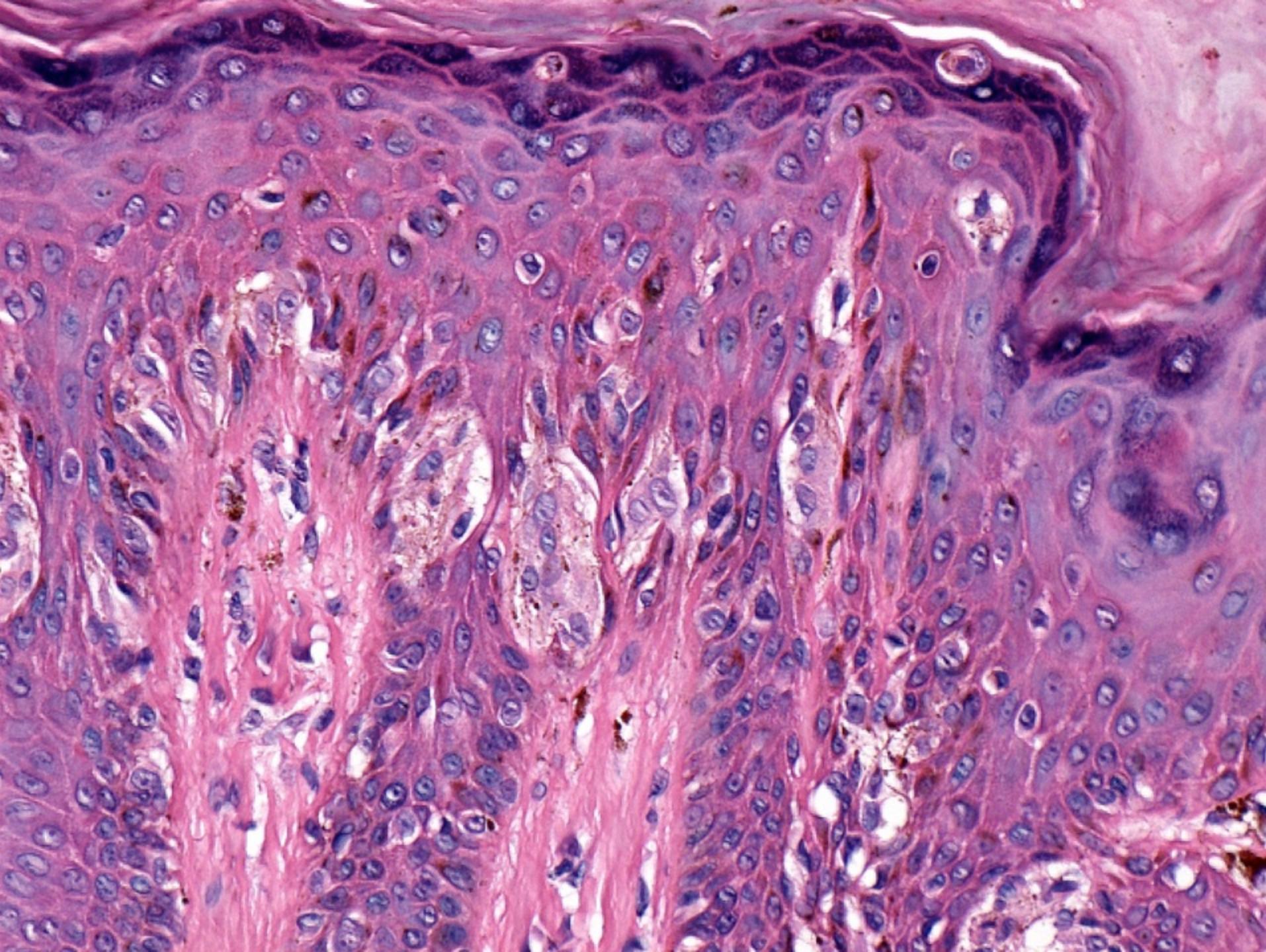


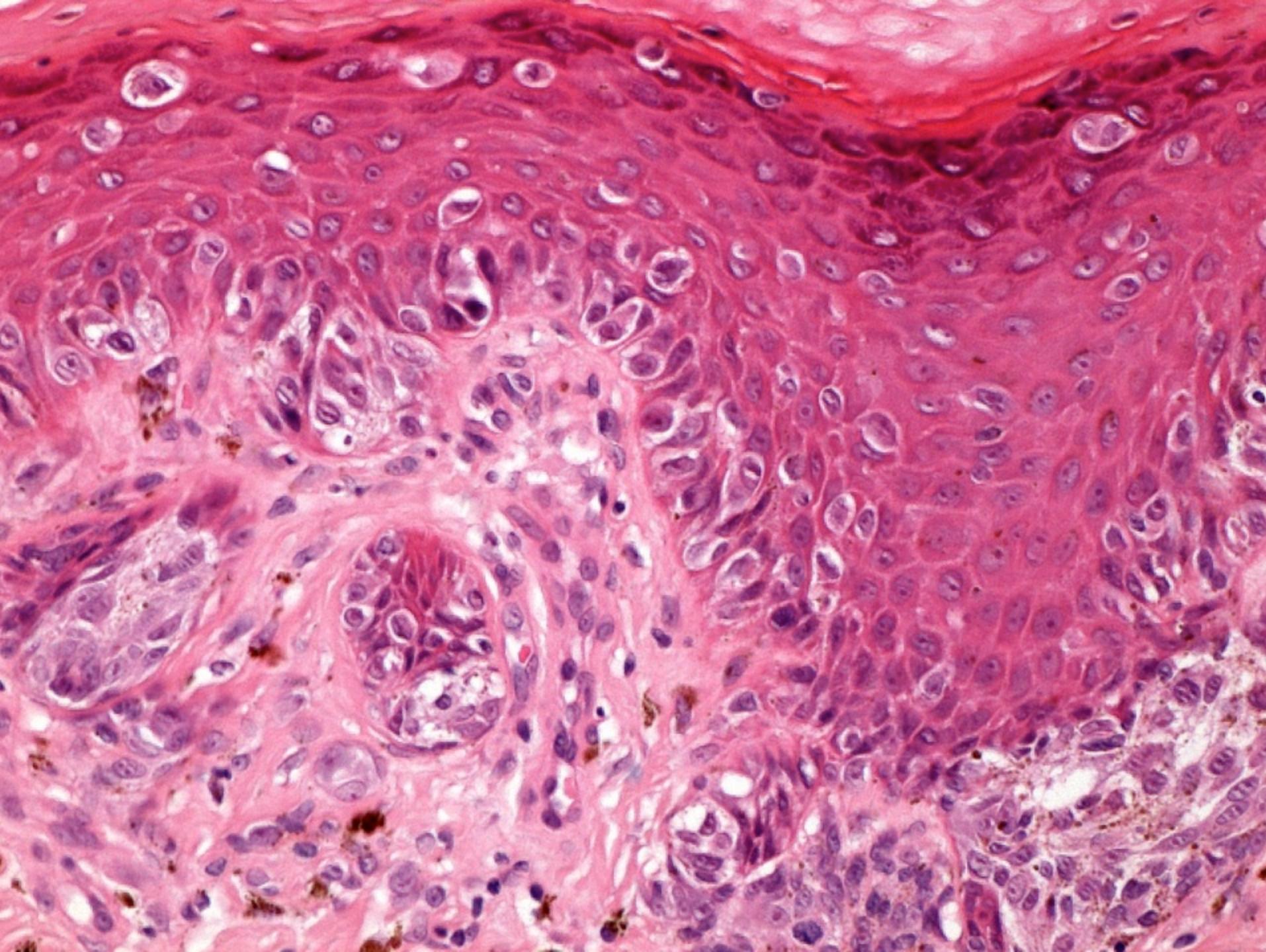


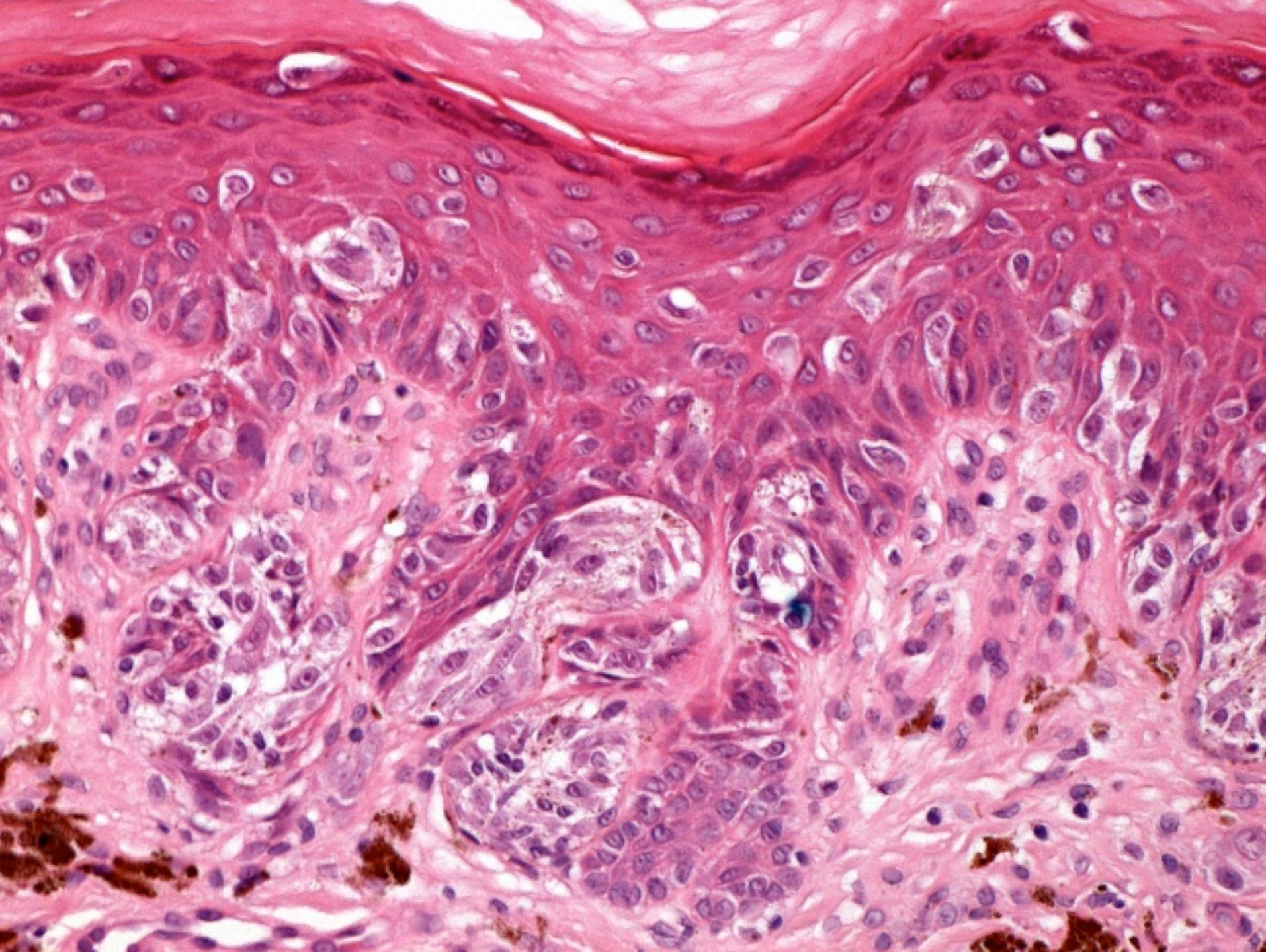
Acral Spitz Naevus

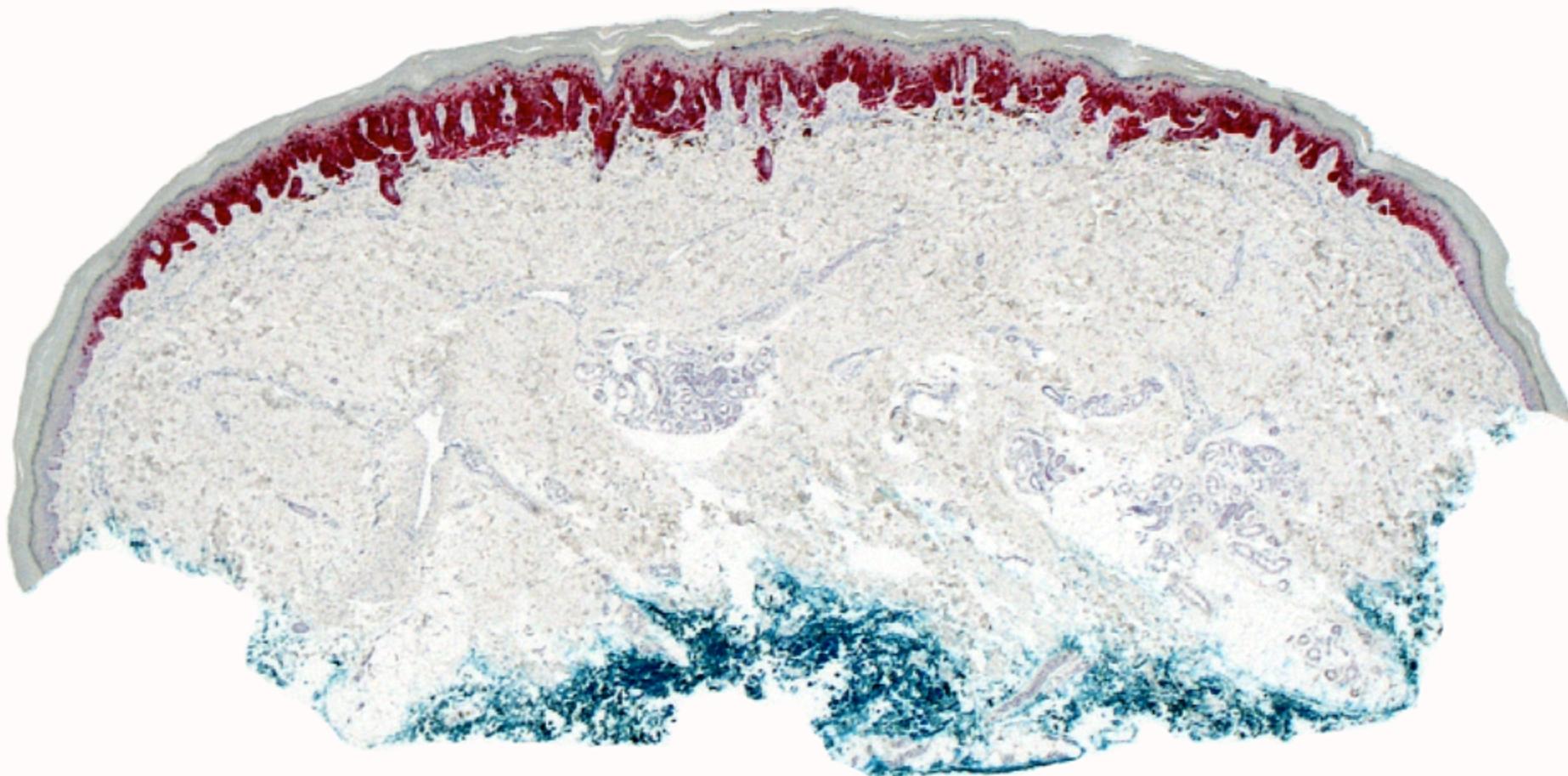












Melan a



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Atypical Spitz Tumour/Spitzoid Melanoma

-Concerning Features-

Architecture:

Diameter in mm (>10 mm)

Depth in mm (involvement of subcutaneous fat)

Ulceration

Poor circumscription

Diffuse Pagetoid spread

High cellular density

Lack of zonation and maturation

Asymmetry

Few or no dull pink (Kamino) bodies

Cytology:

High nuclear to cytoplasmic ratios

Loss of delicate or dispersed chromatin patterns

Thickening of nuclear membranes

Hyperchromatism

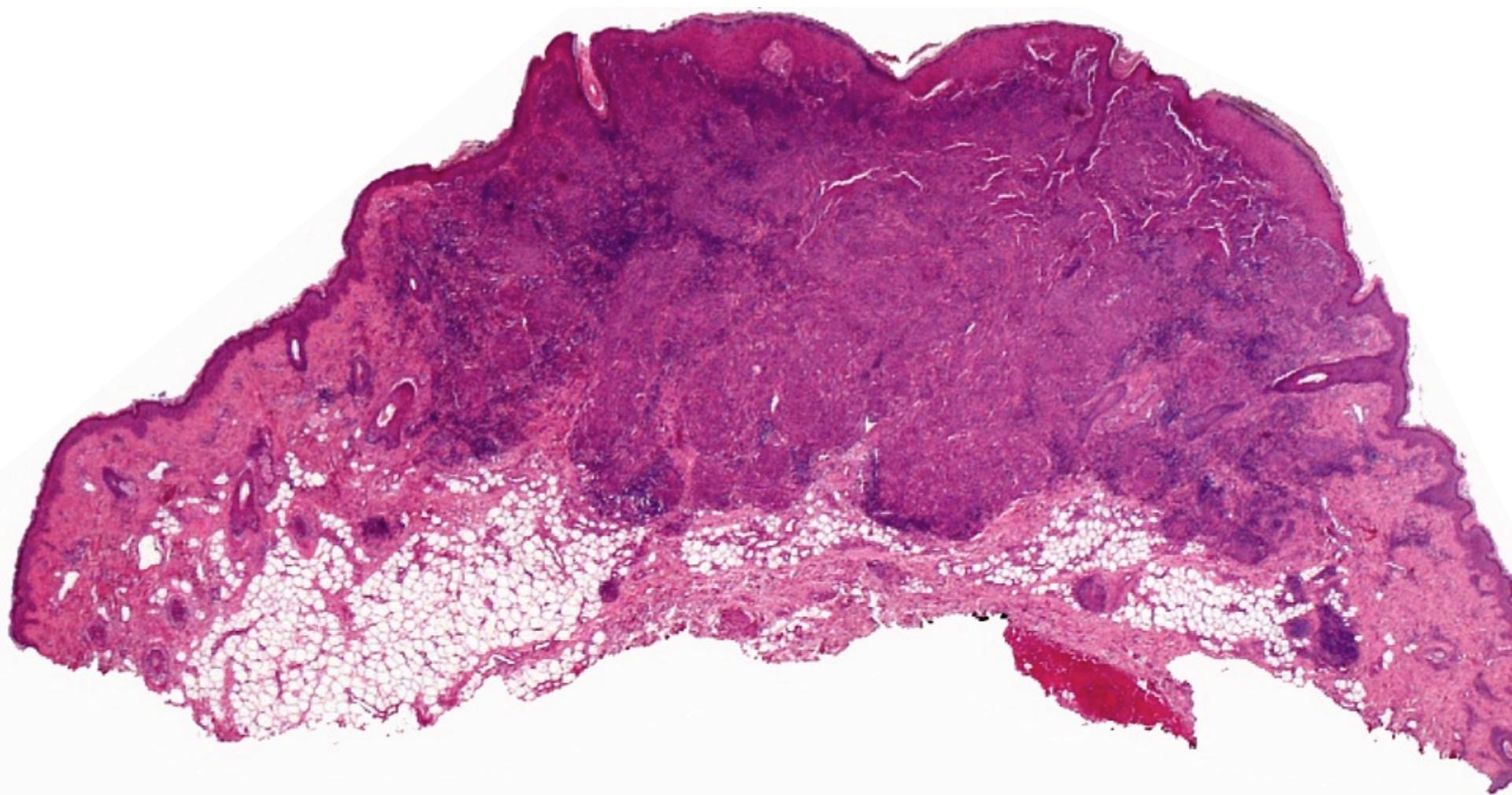
Large nucleoli

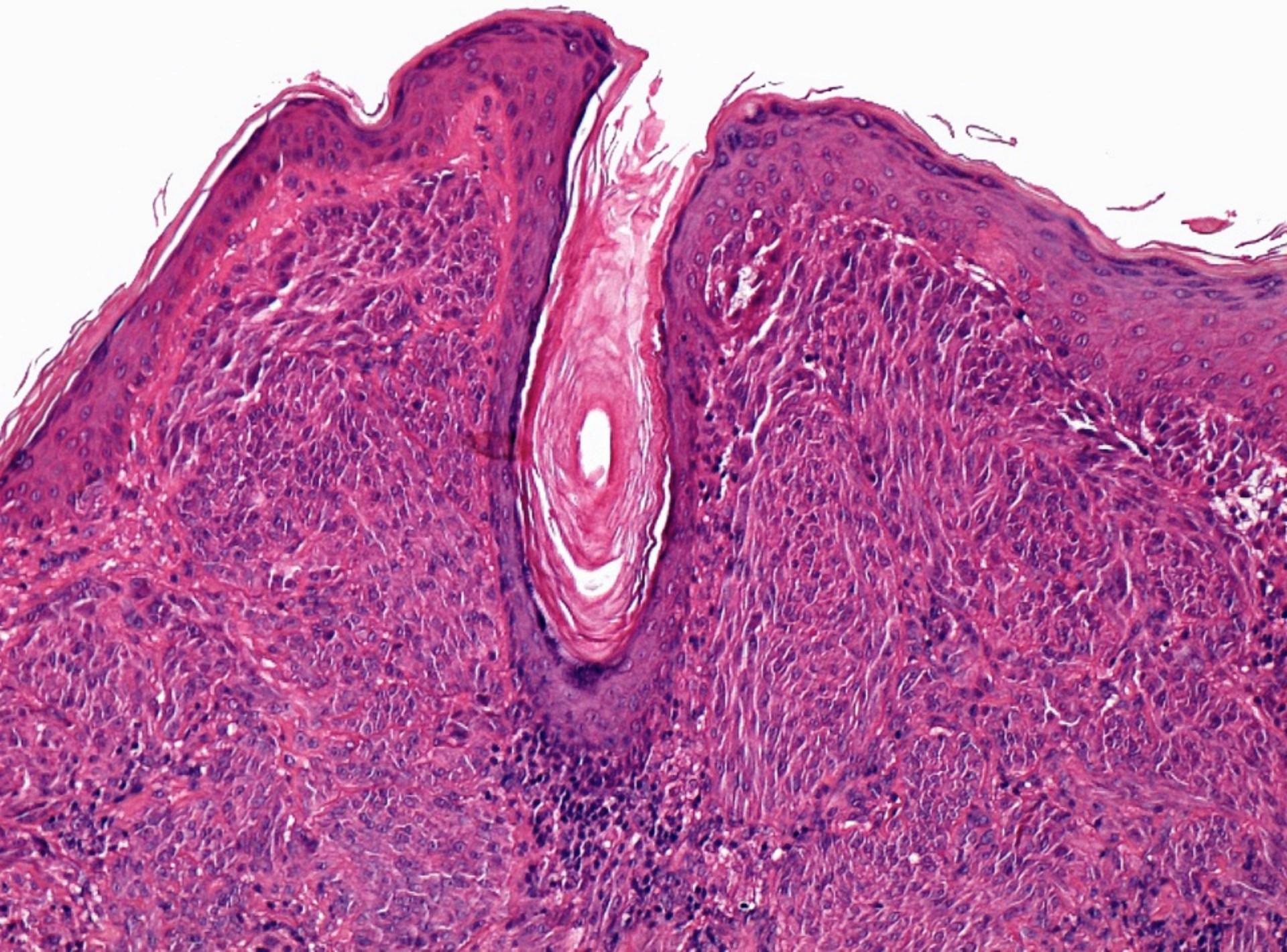
Proliferation:

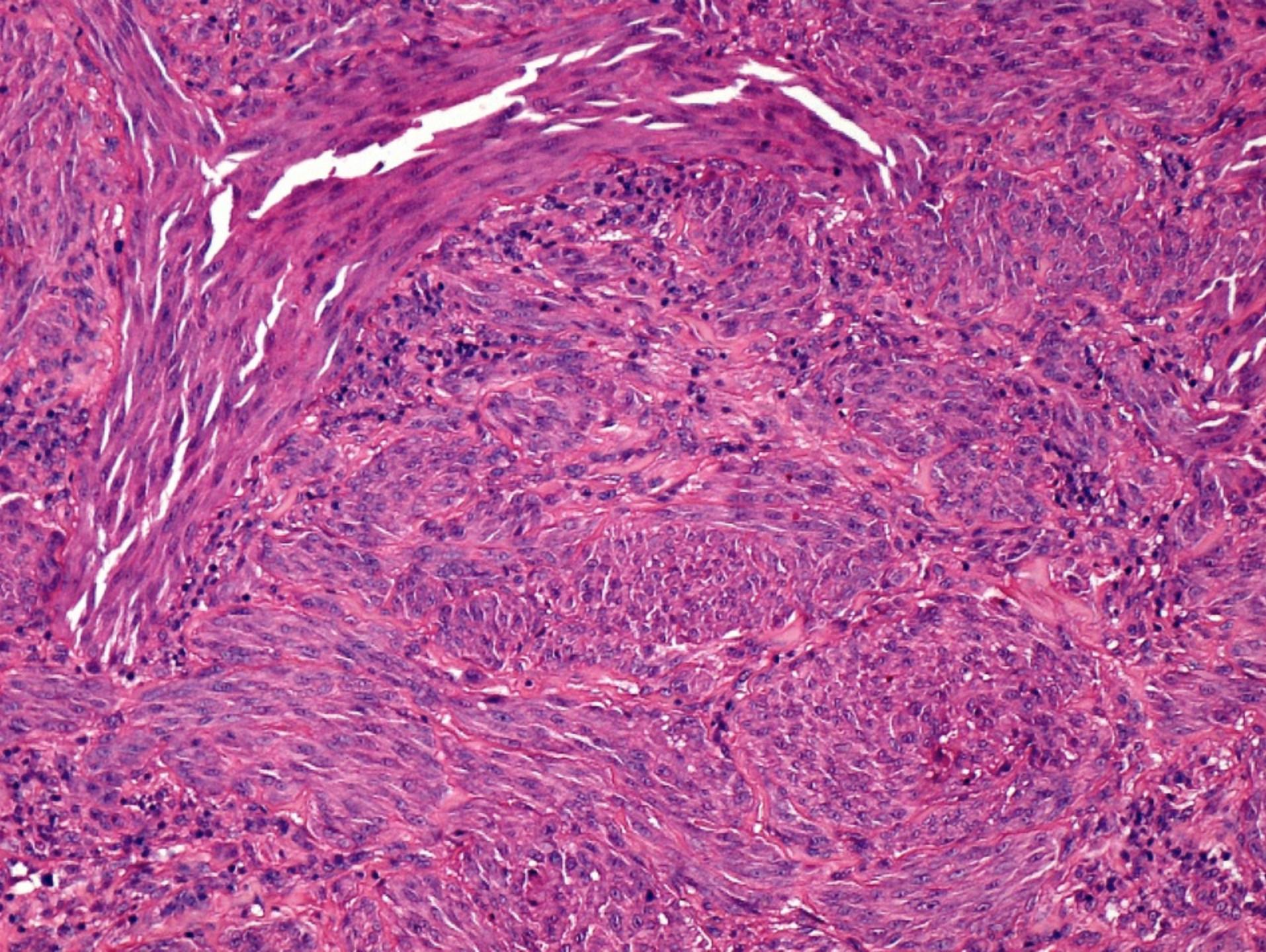
Significant mitotic rate

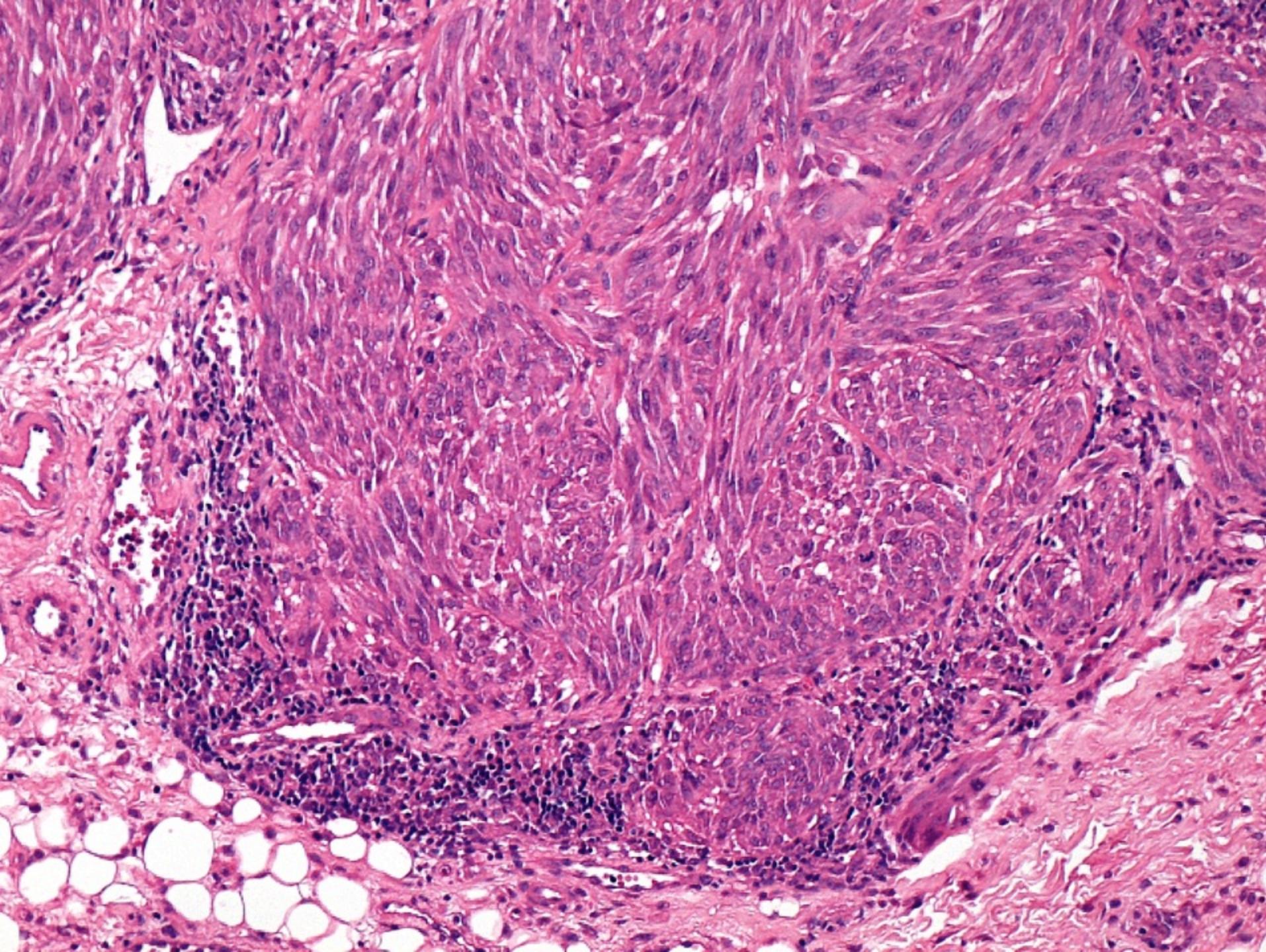
Deep/marginal mitoses

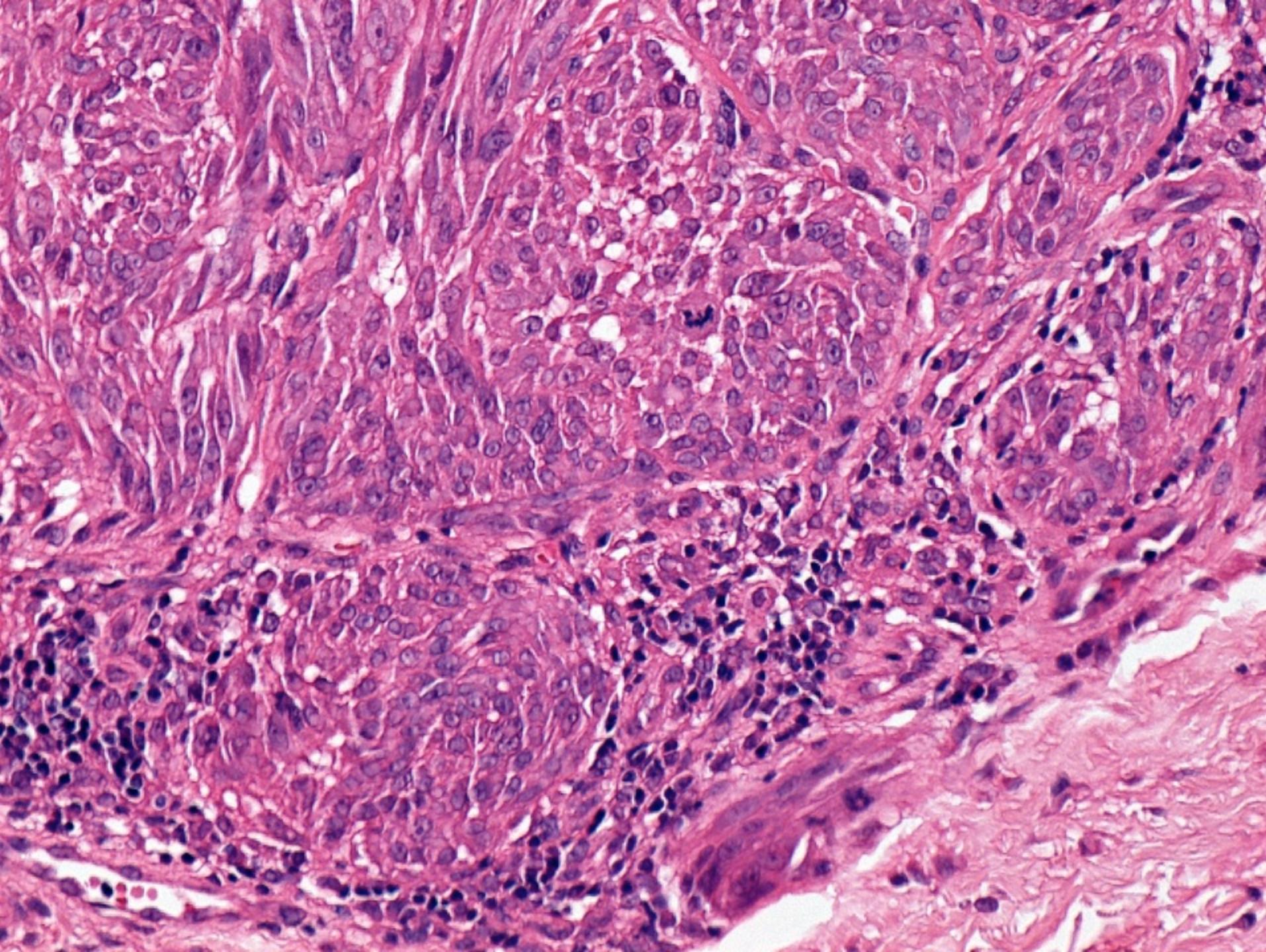
Increased mib-1 proliferation index

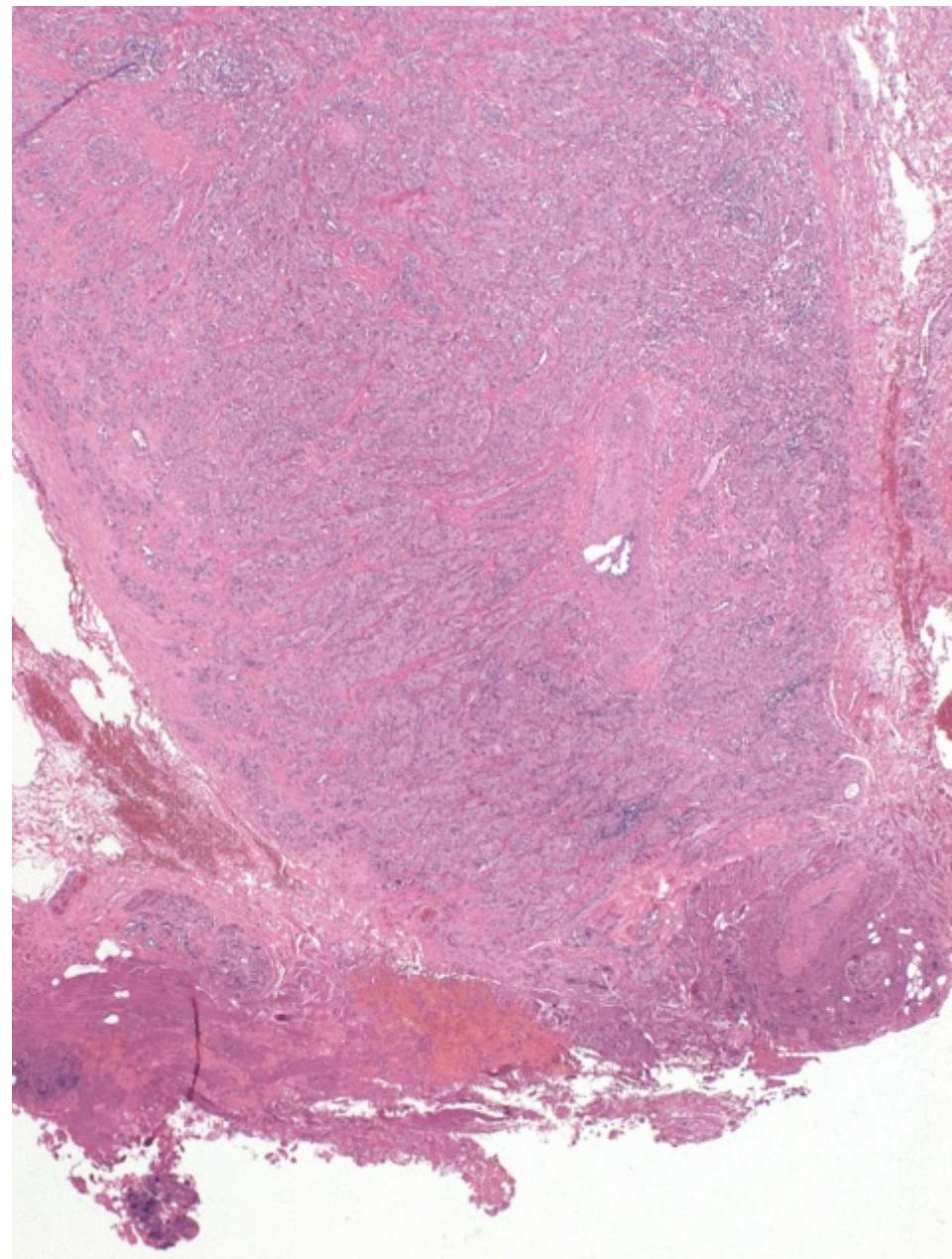
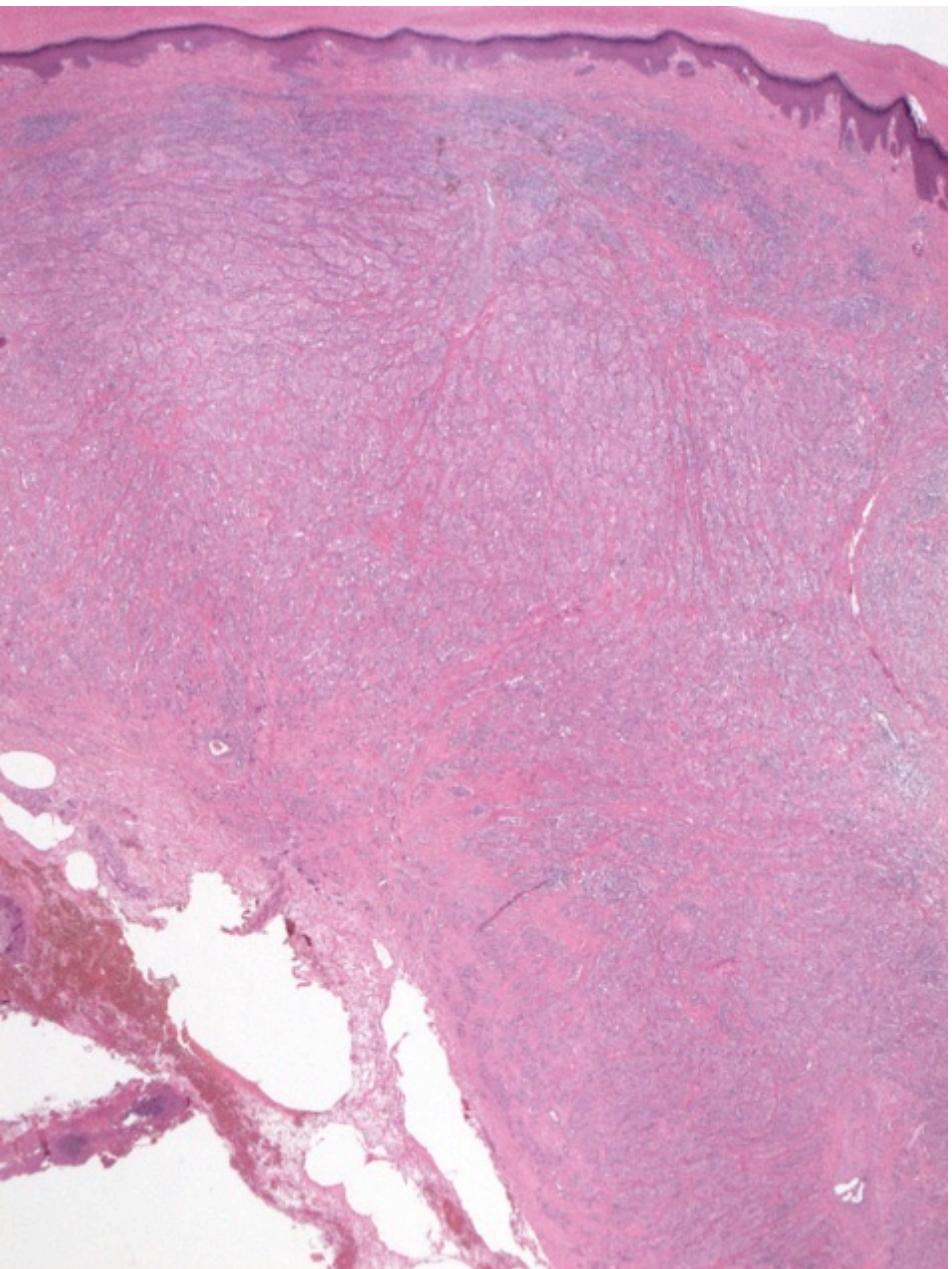


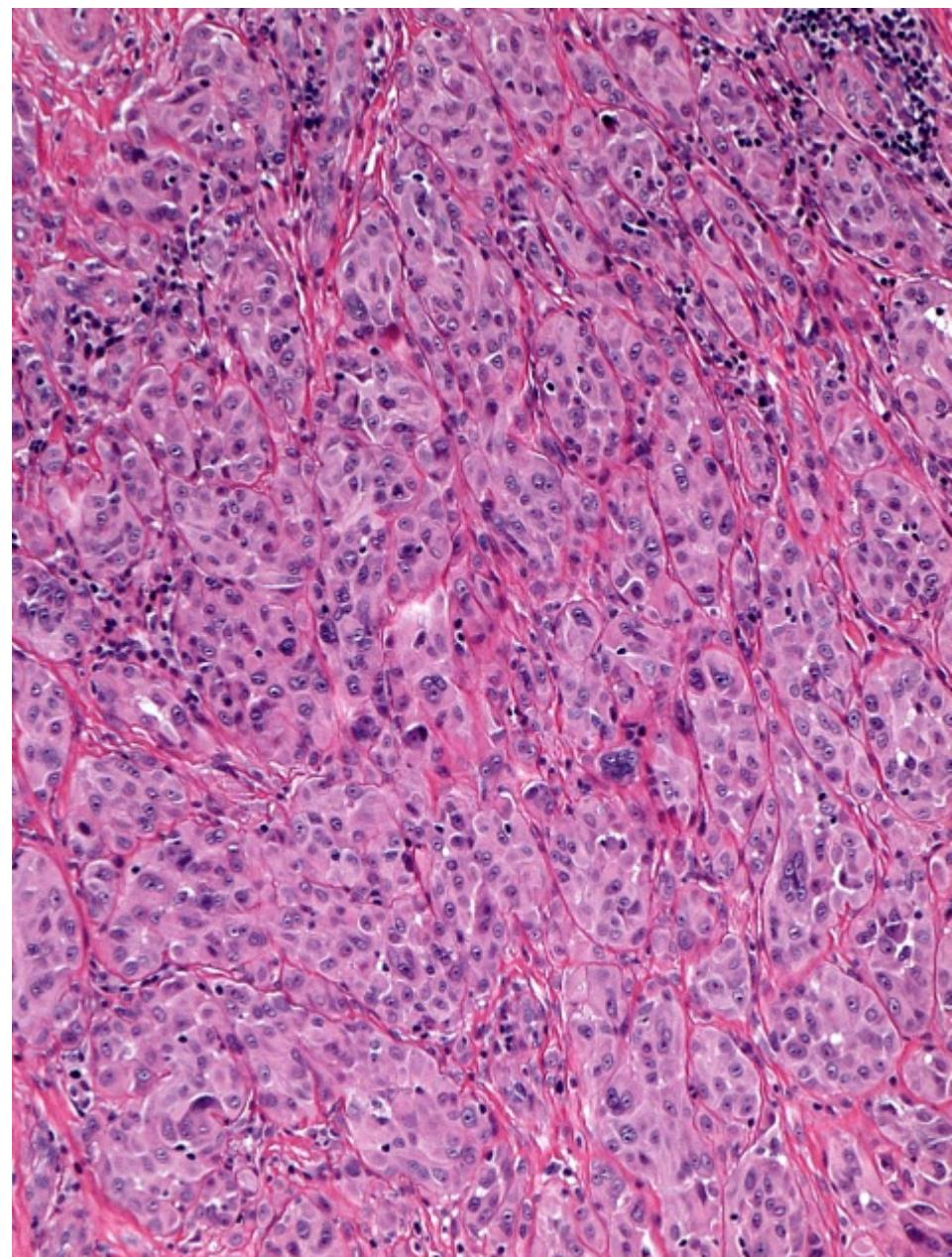
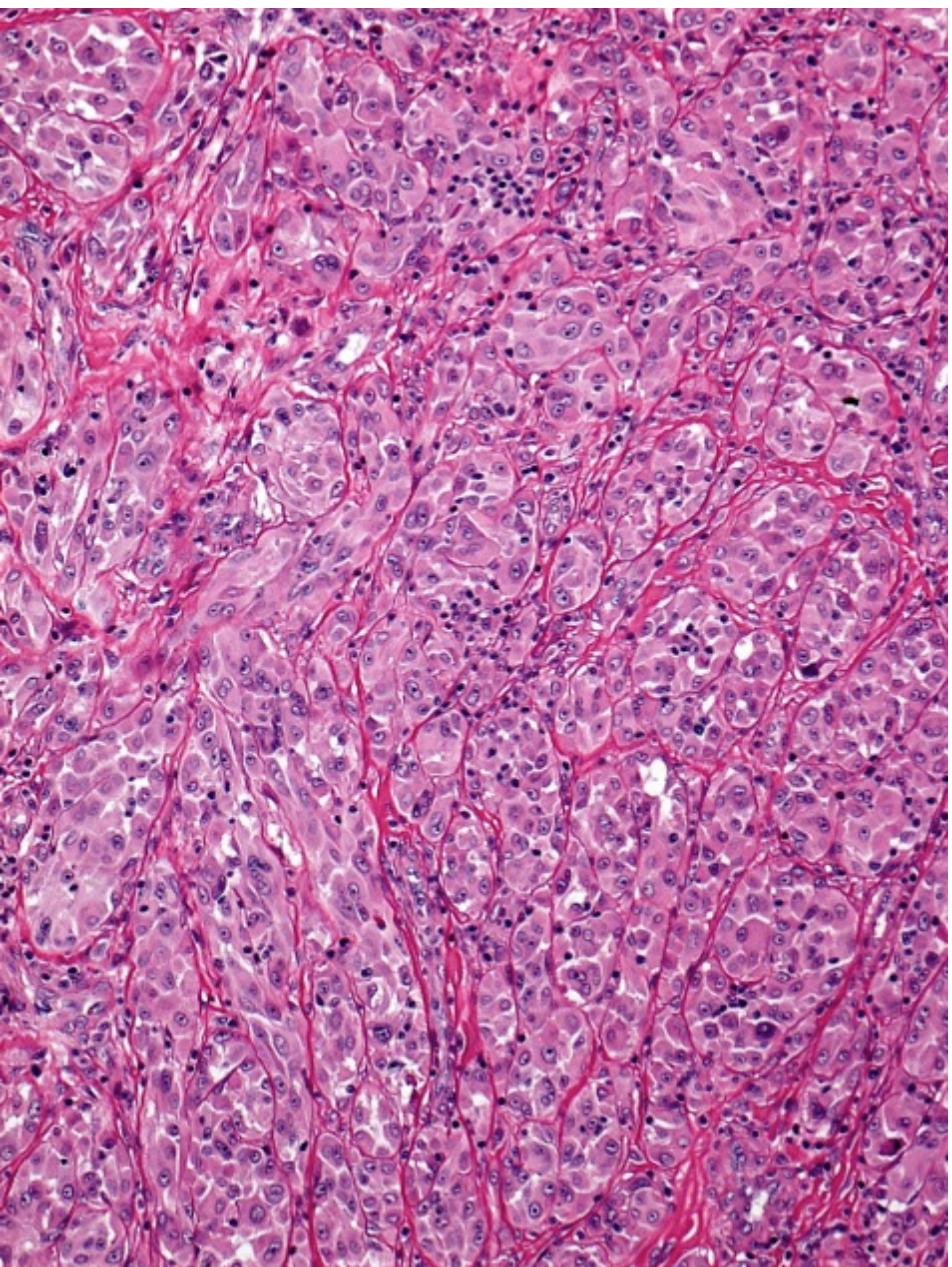


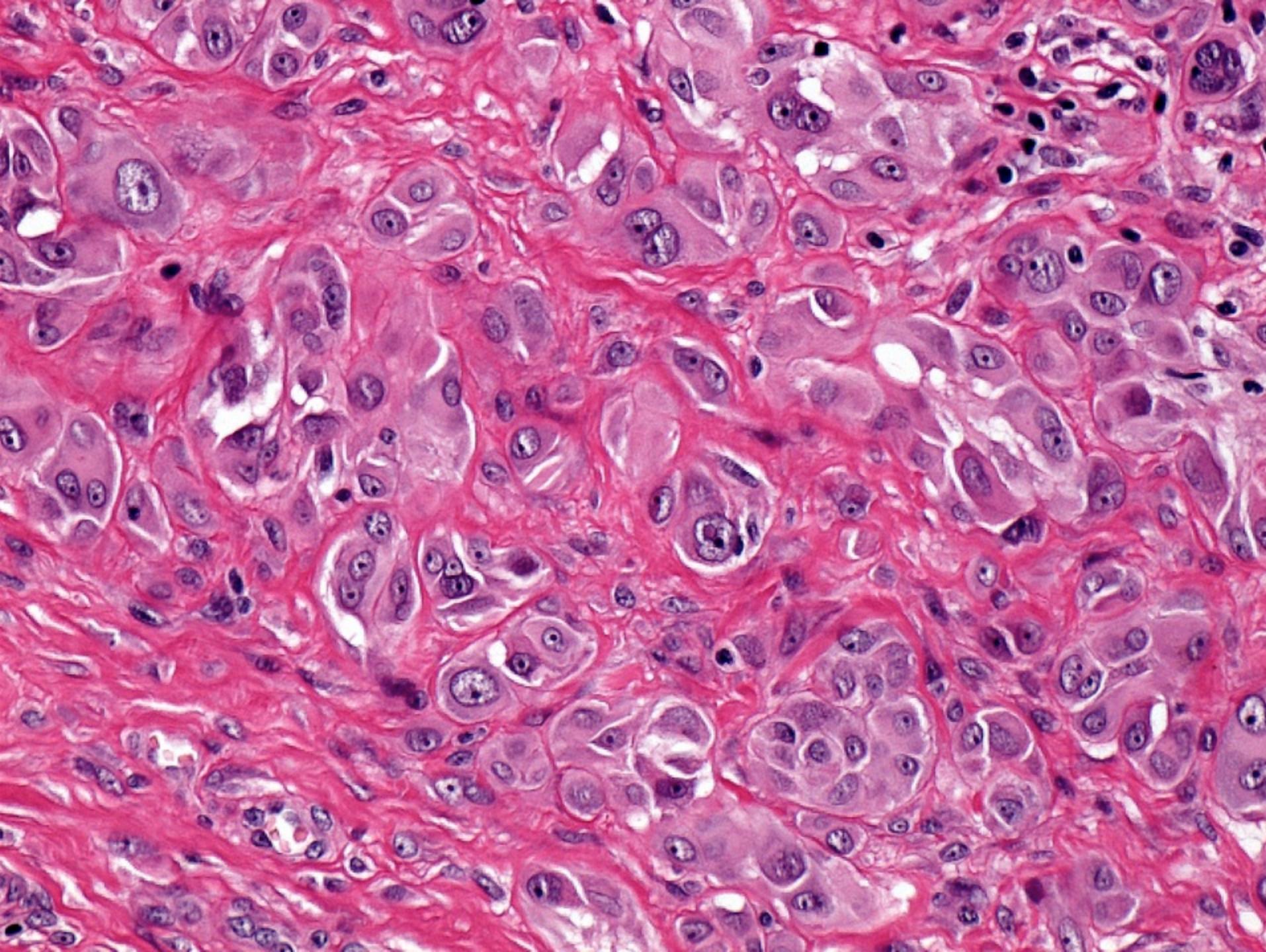


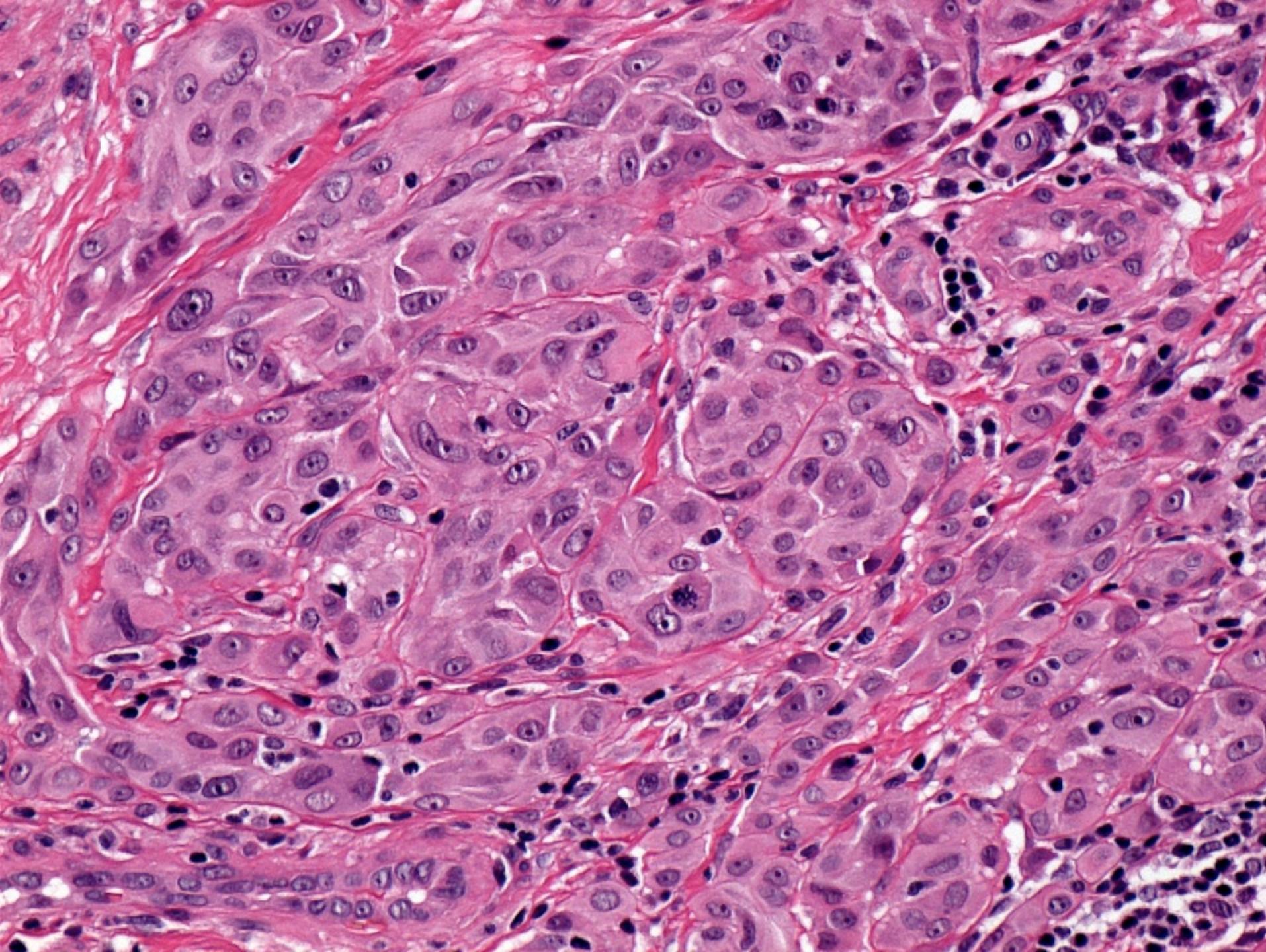


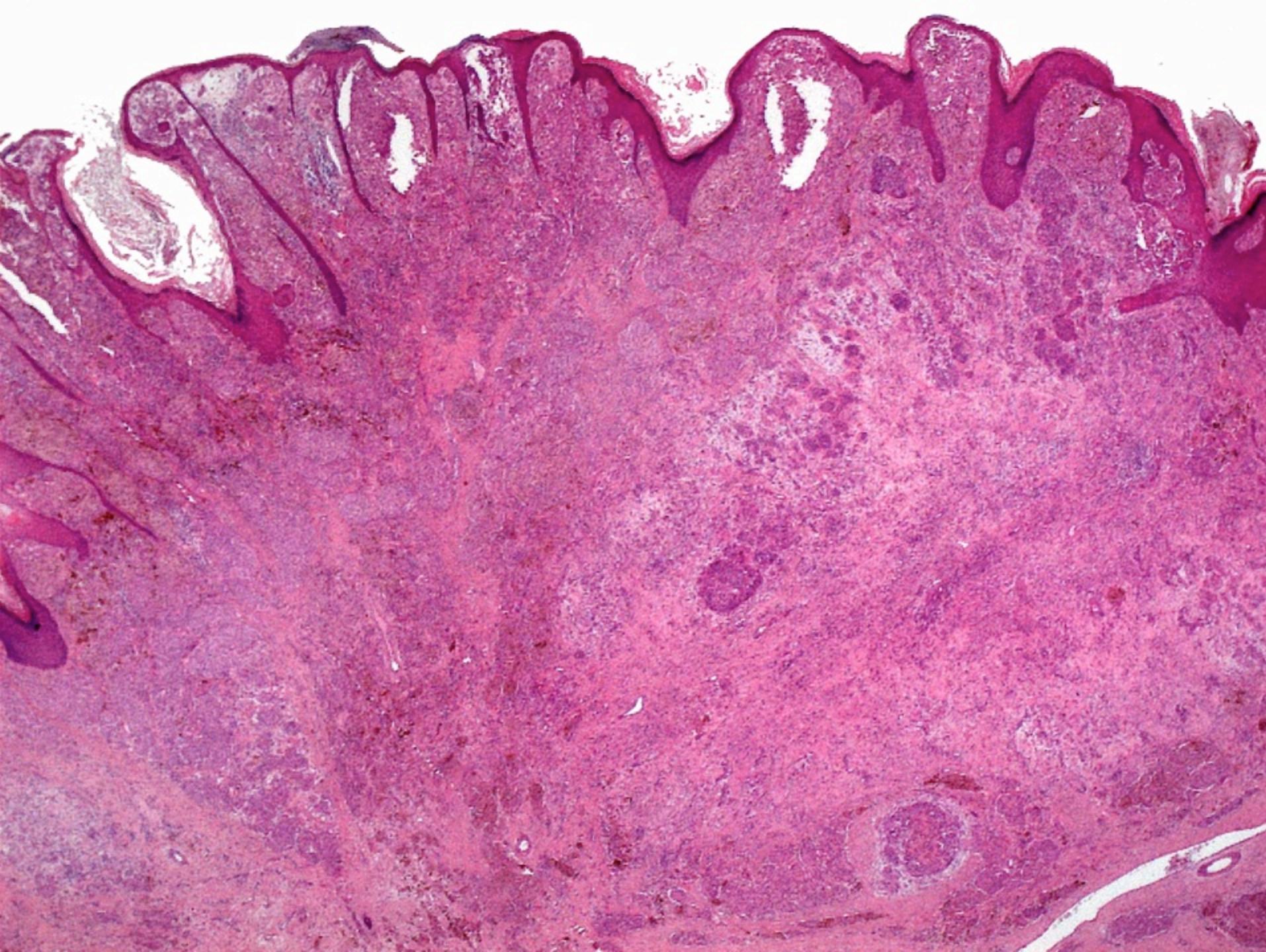


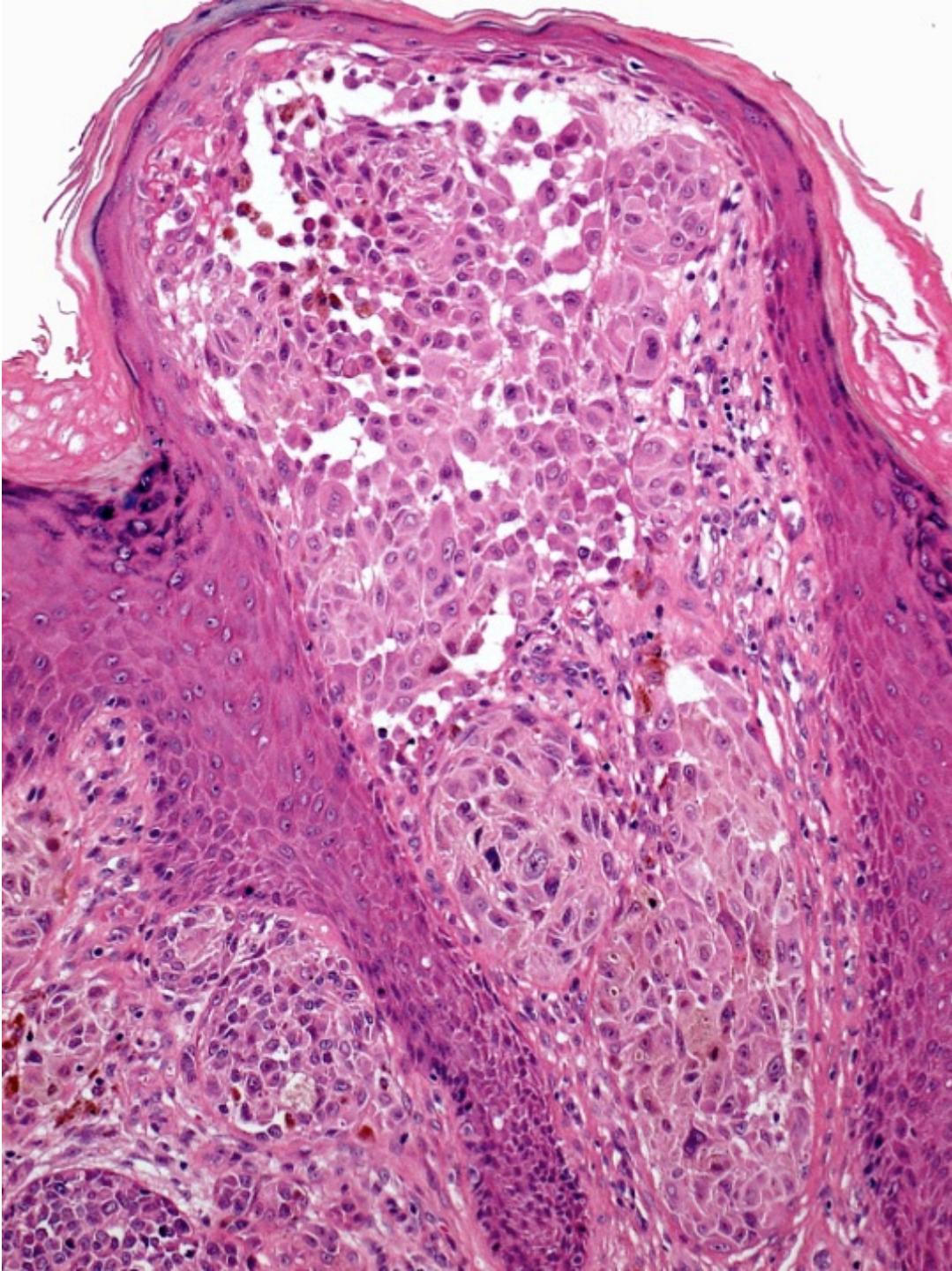


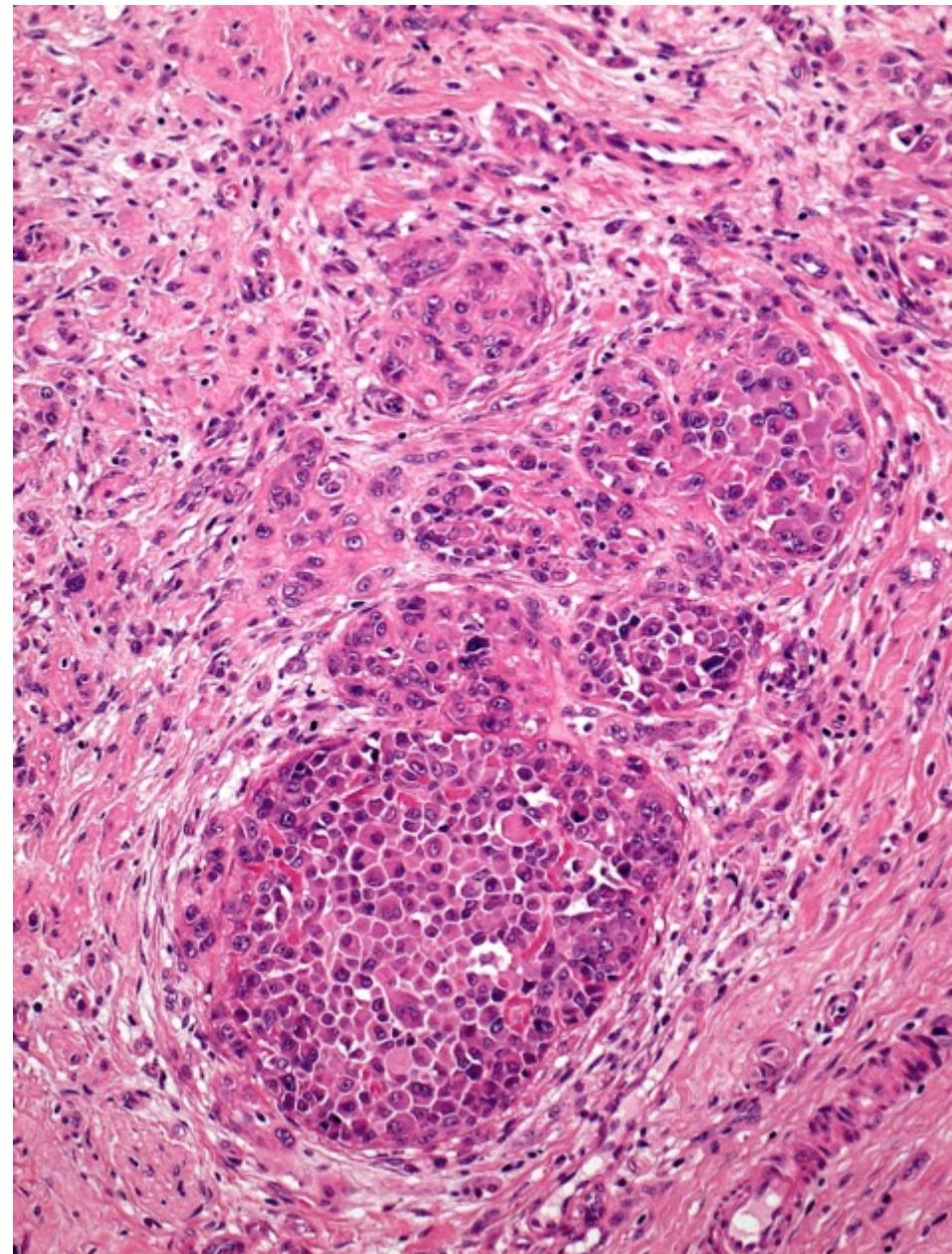
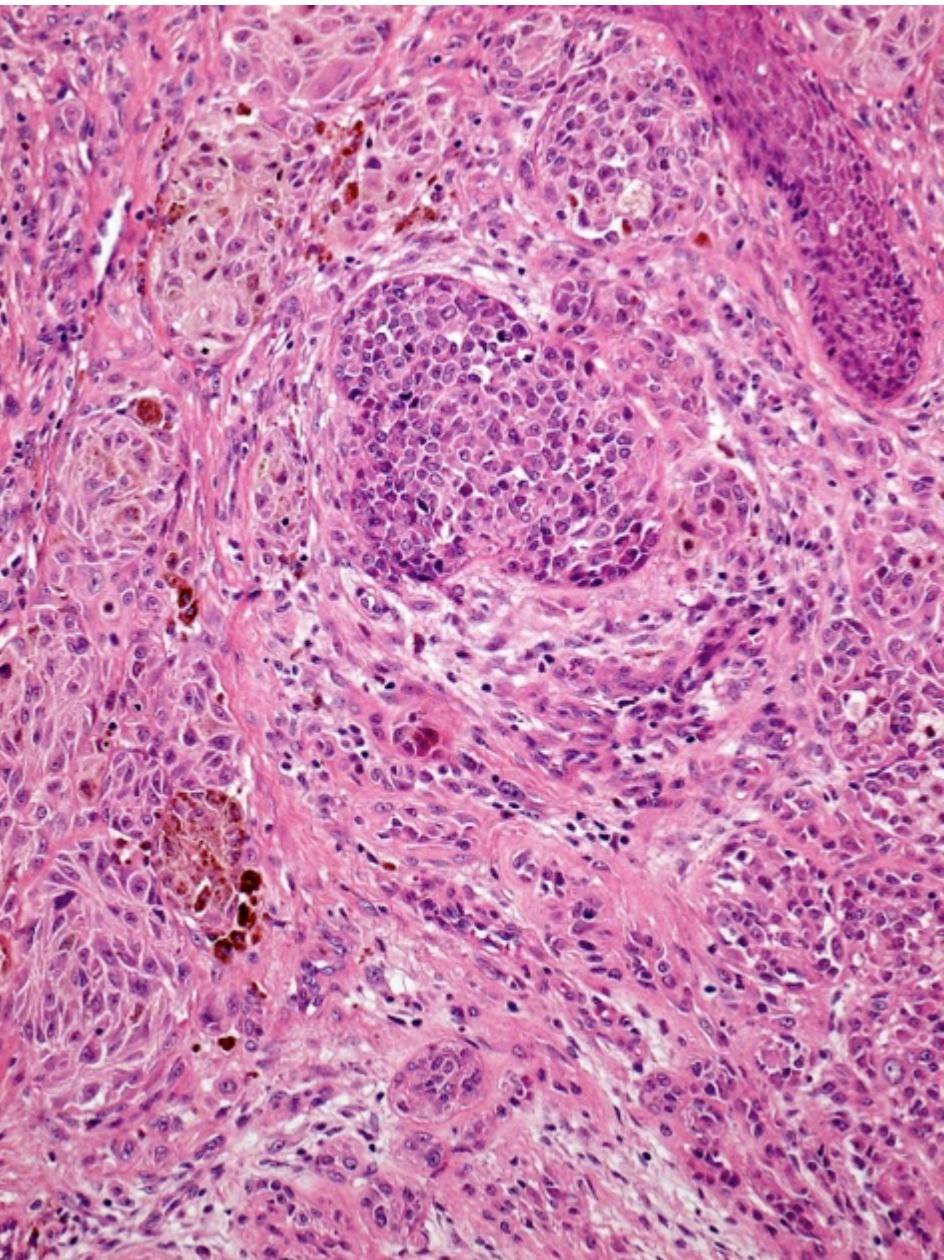


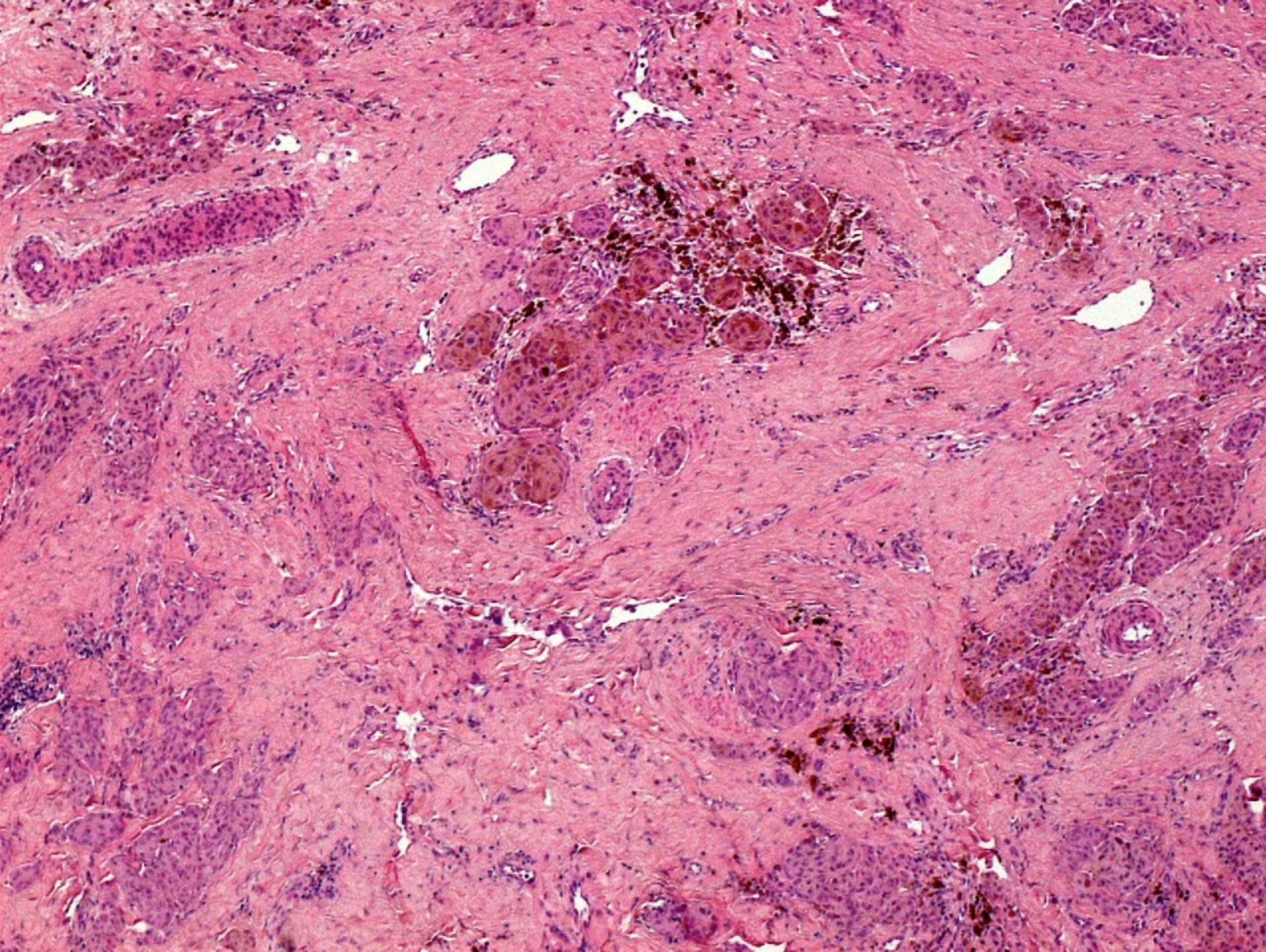


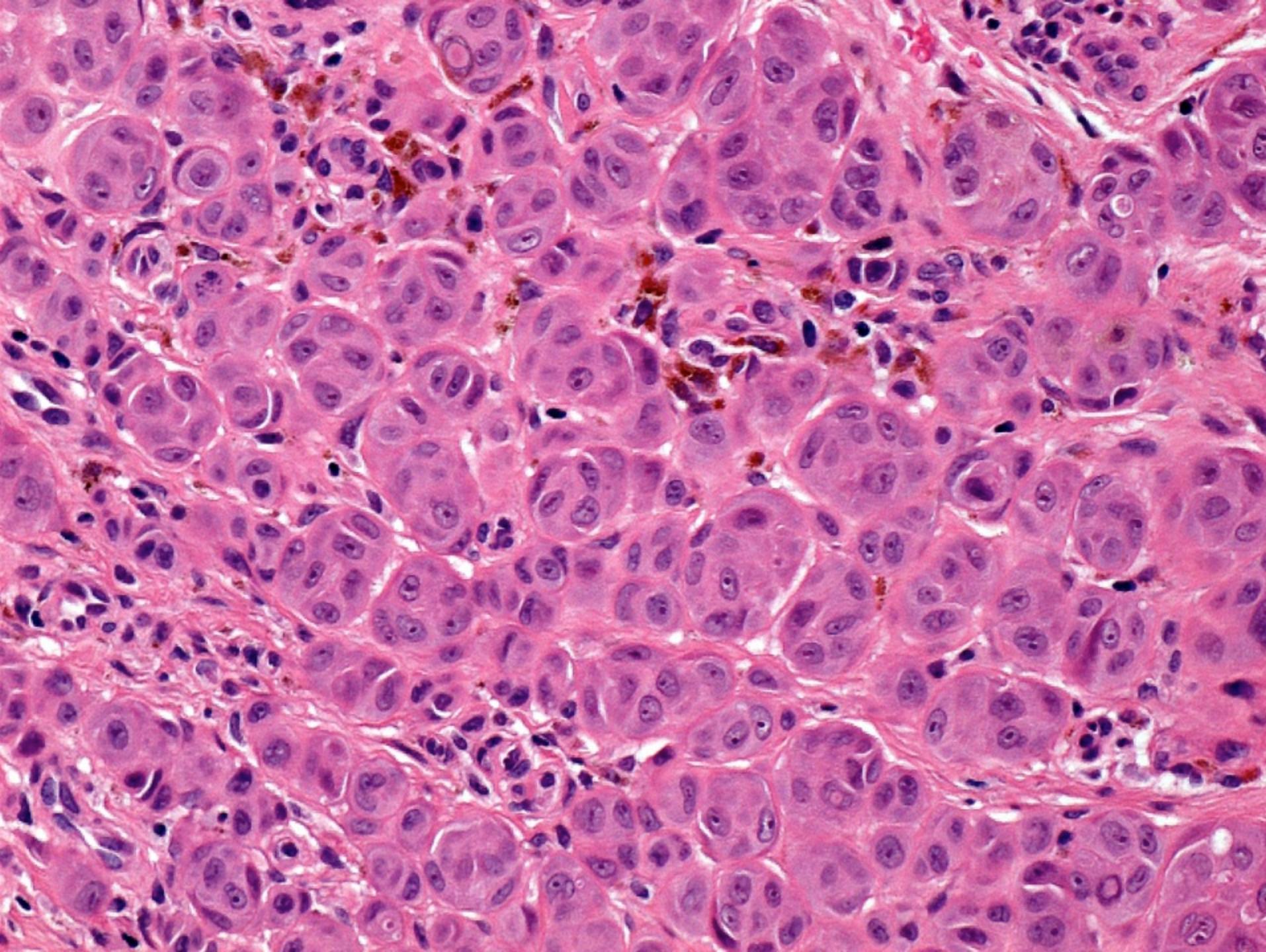


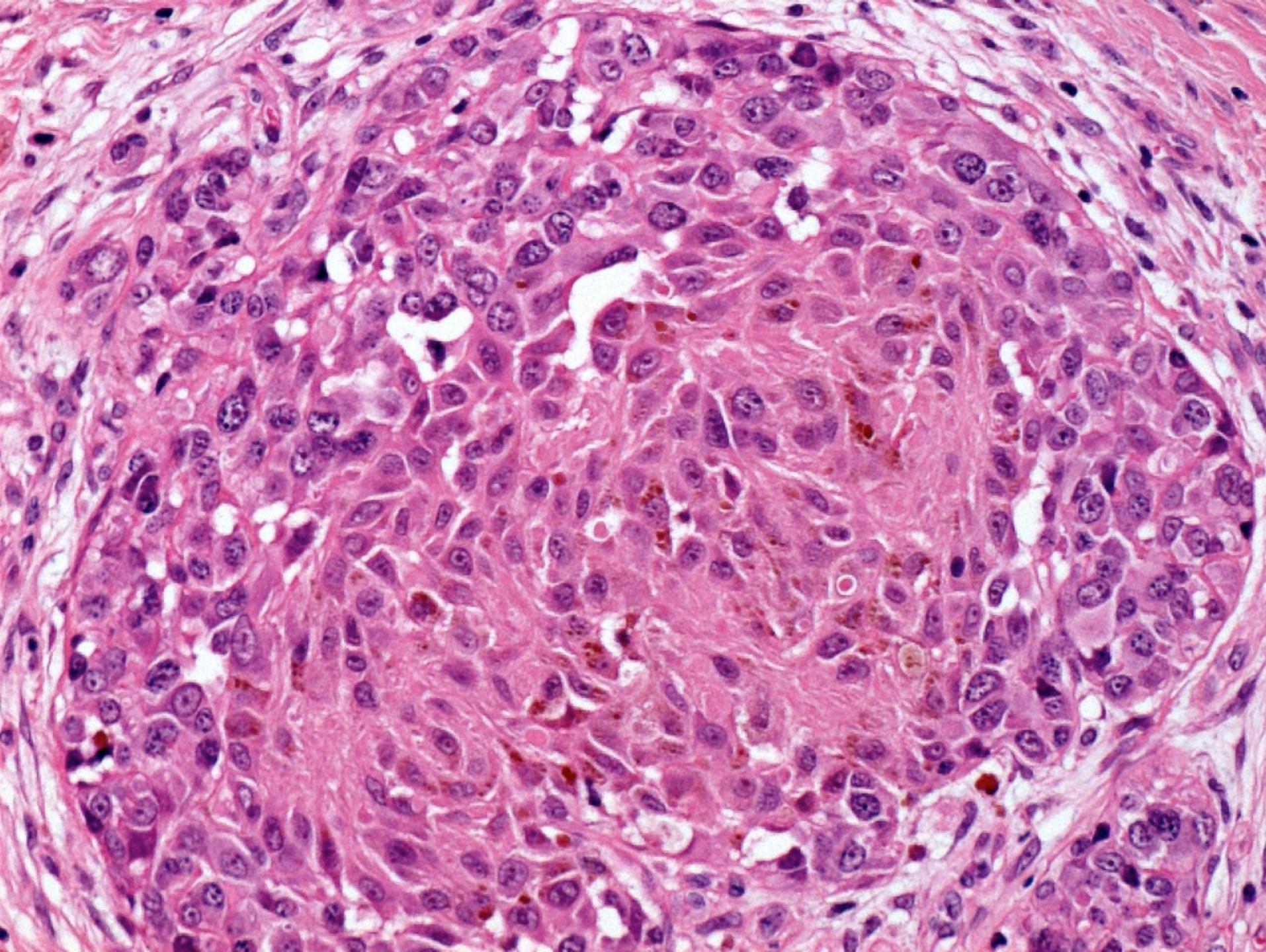


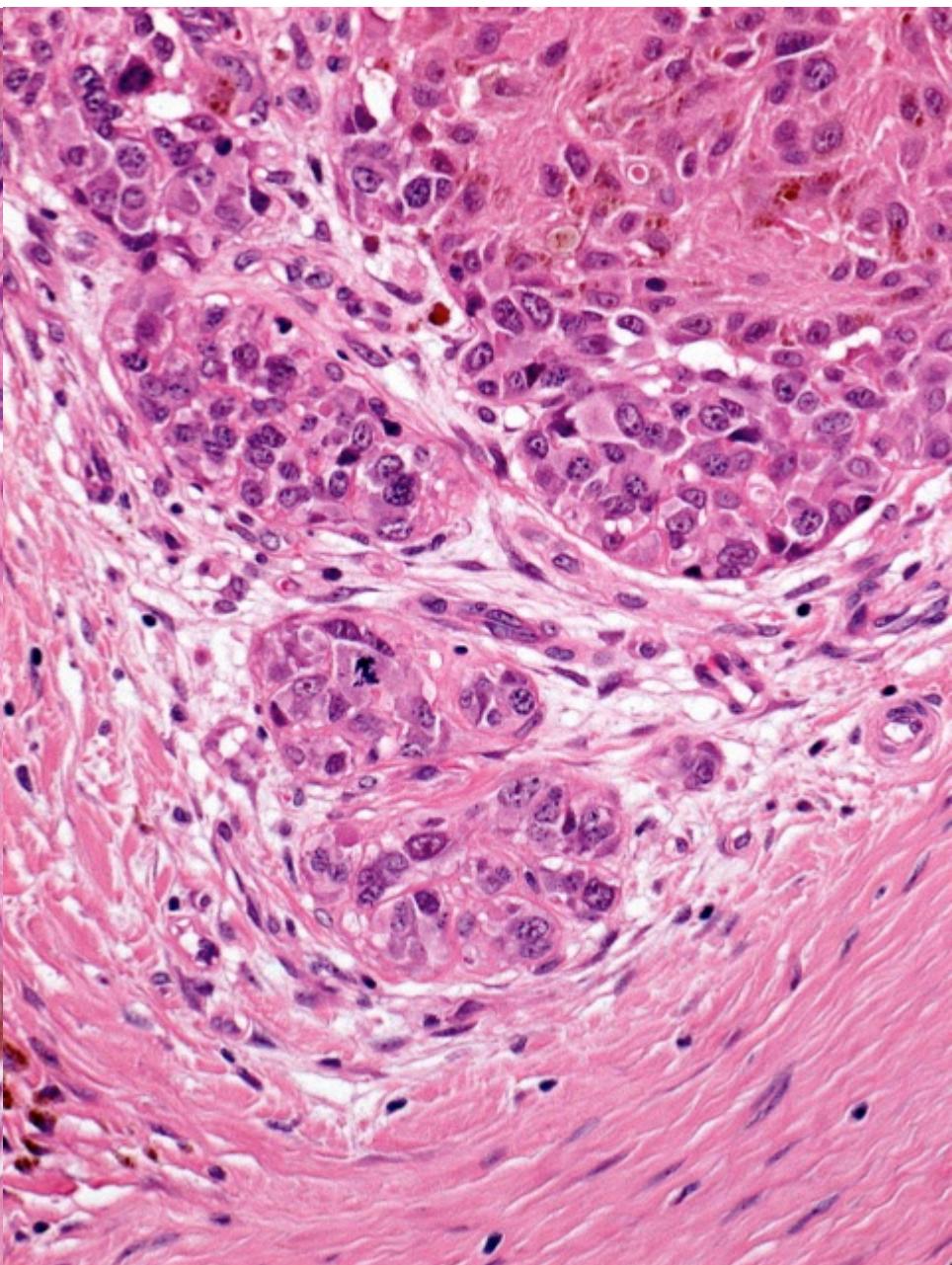
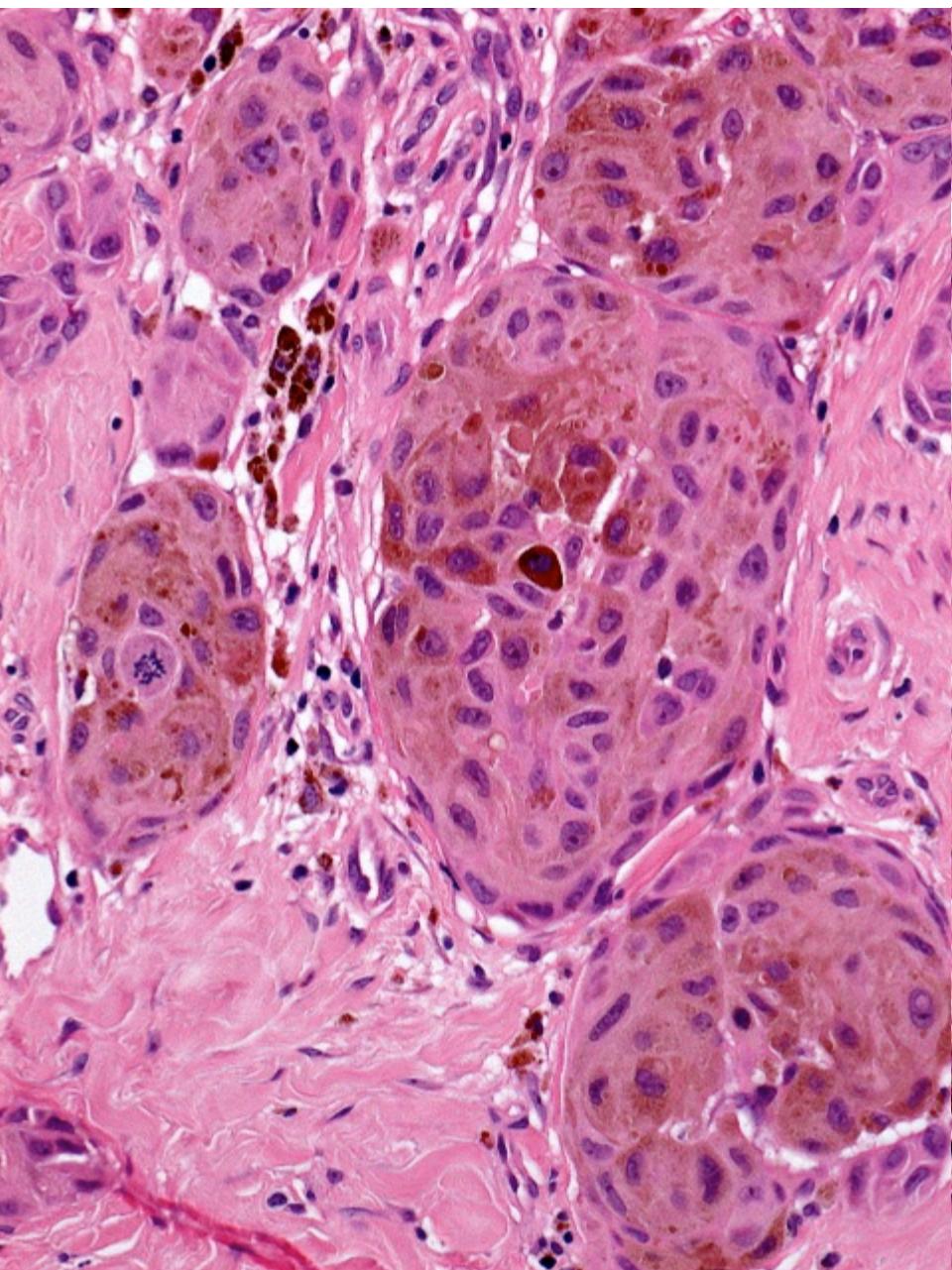


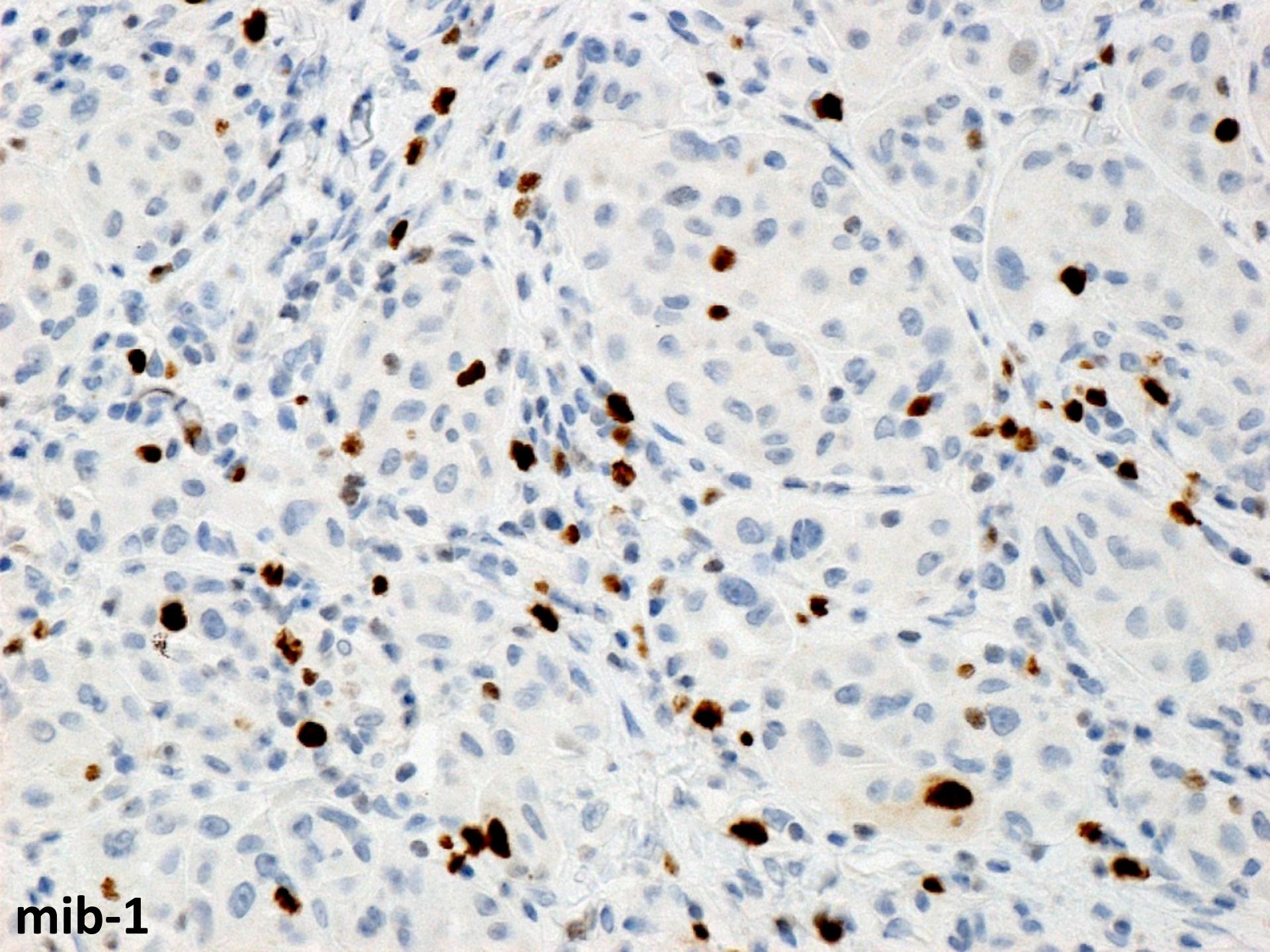




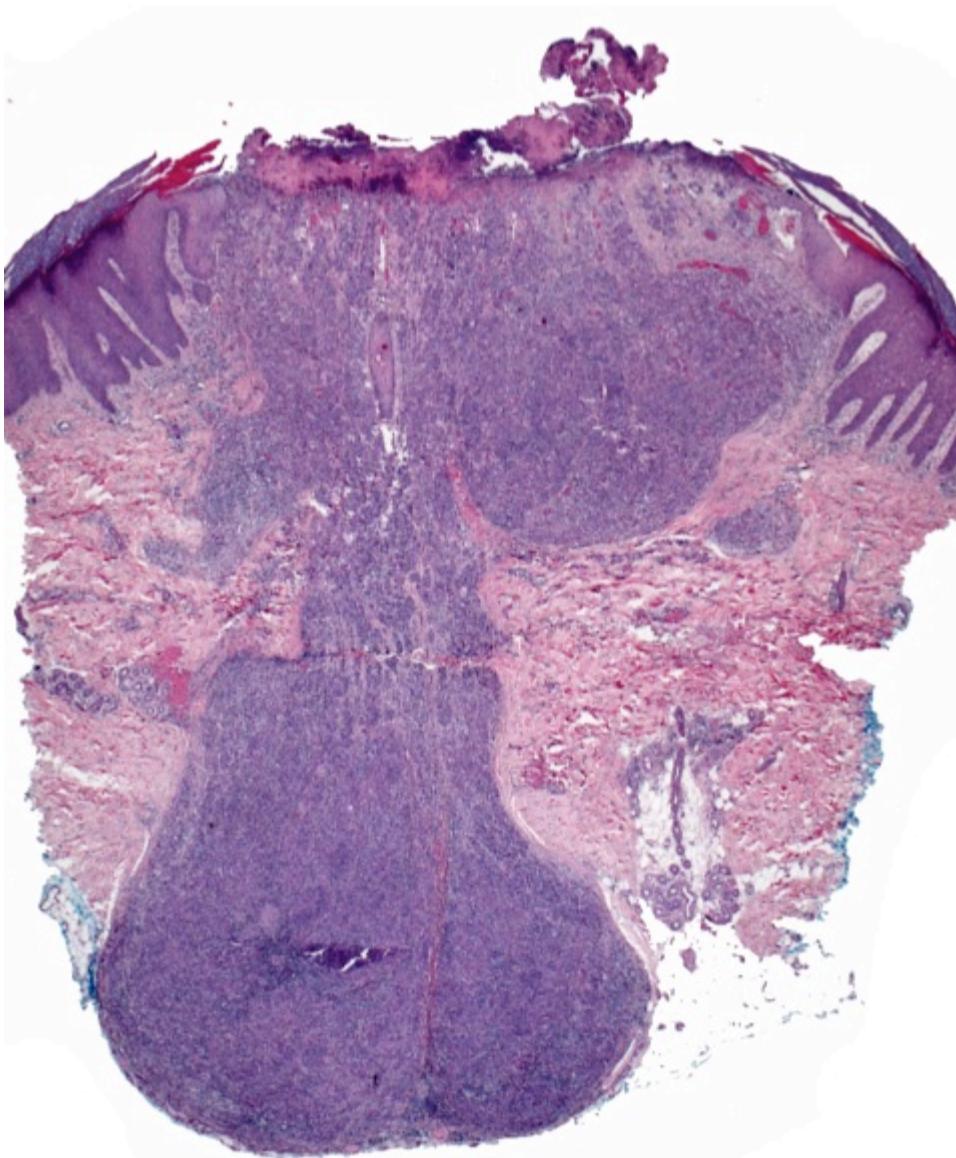


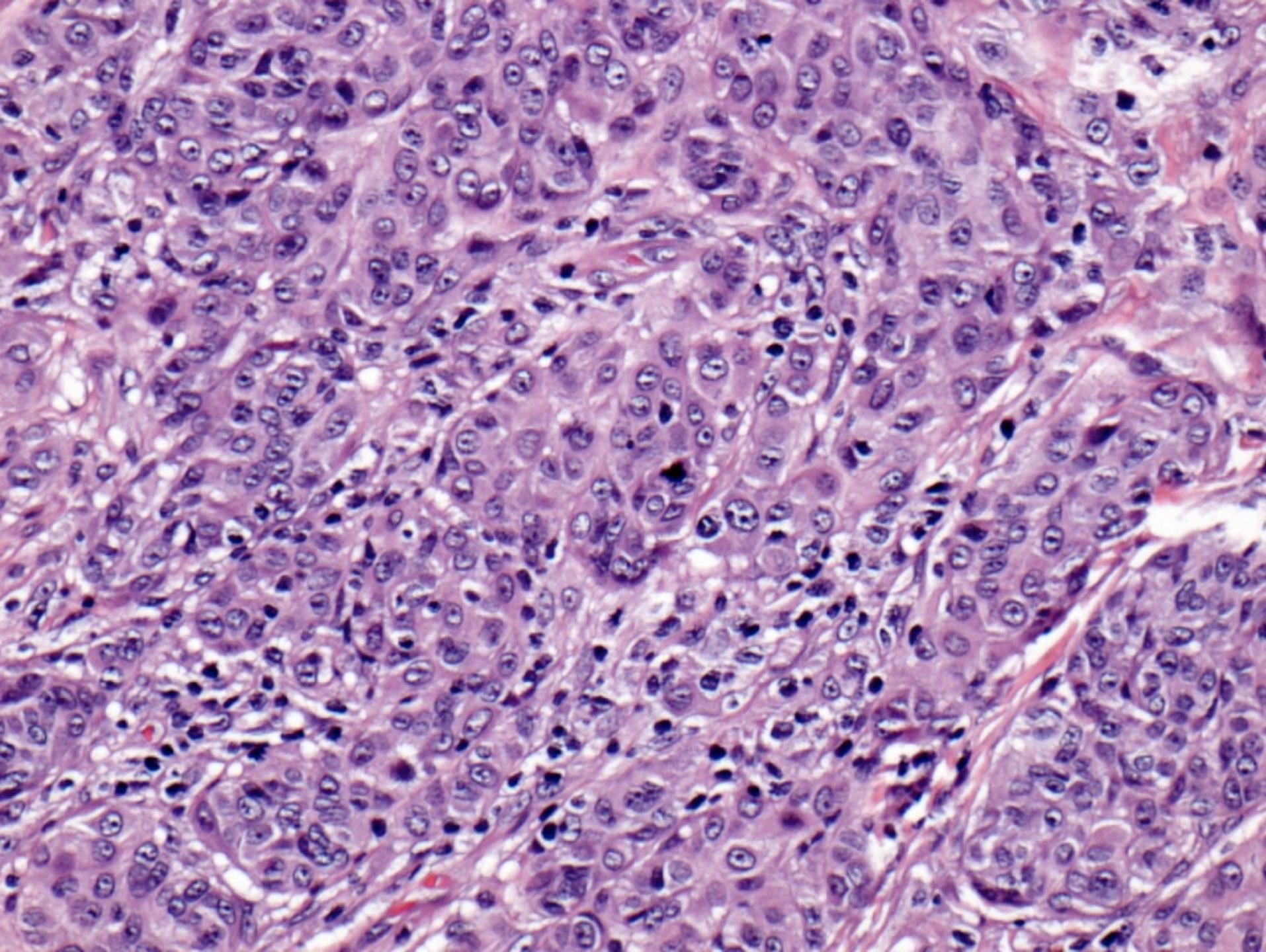


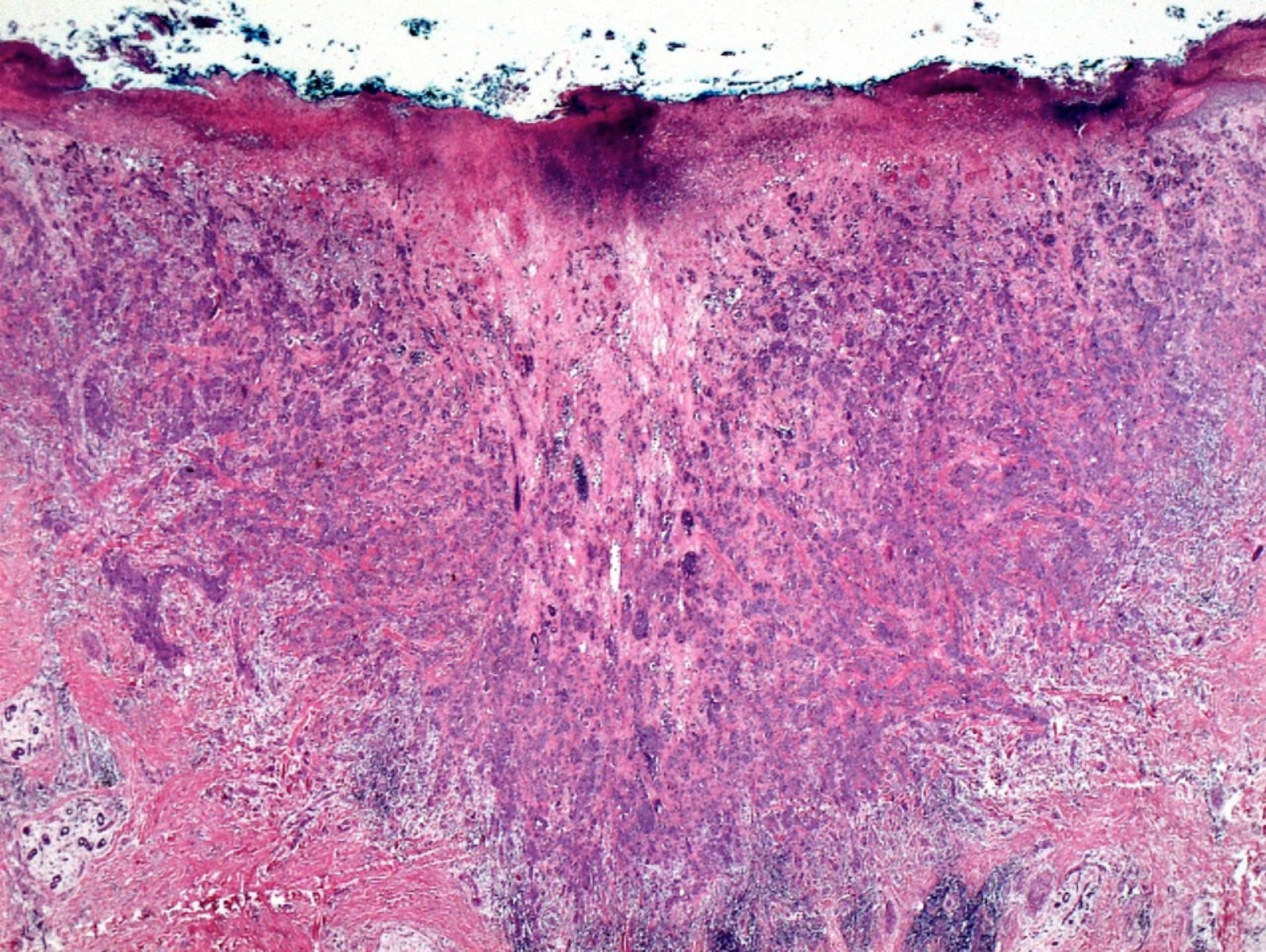


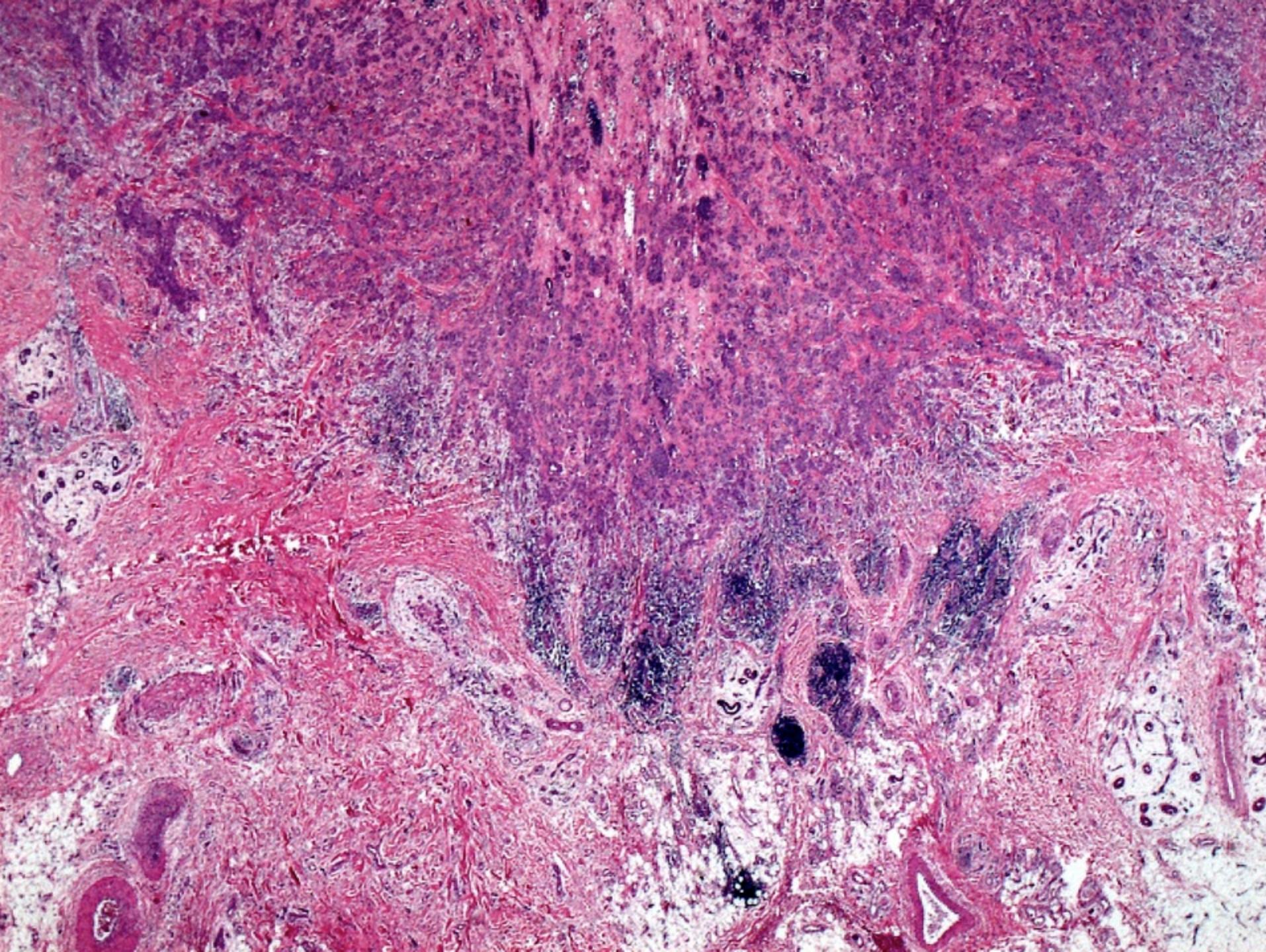


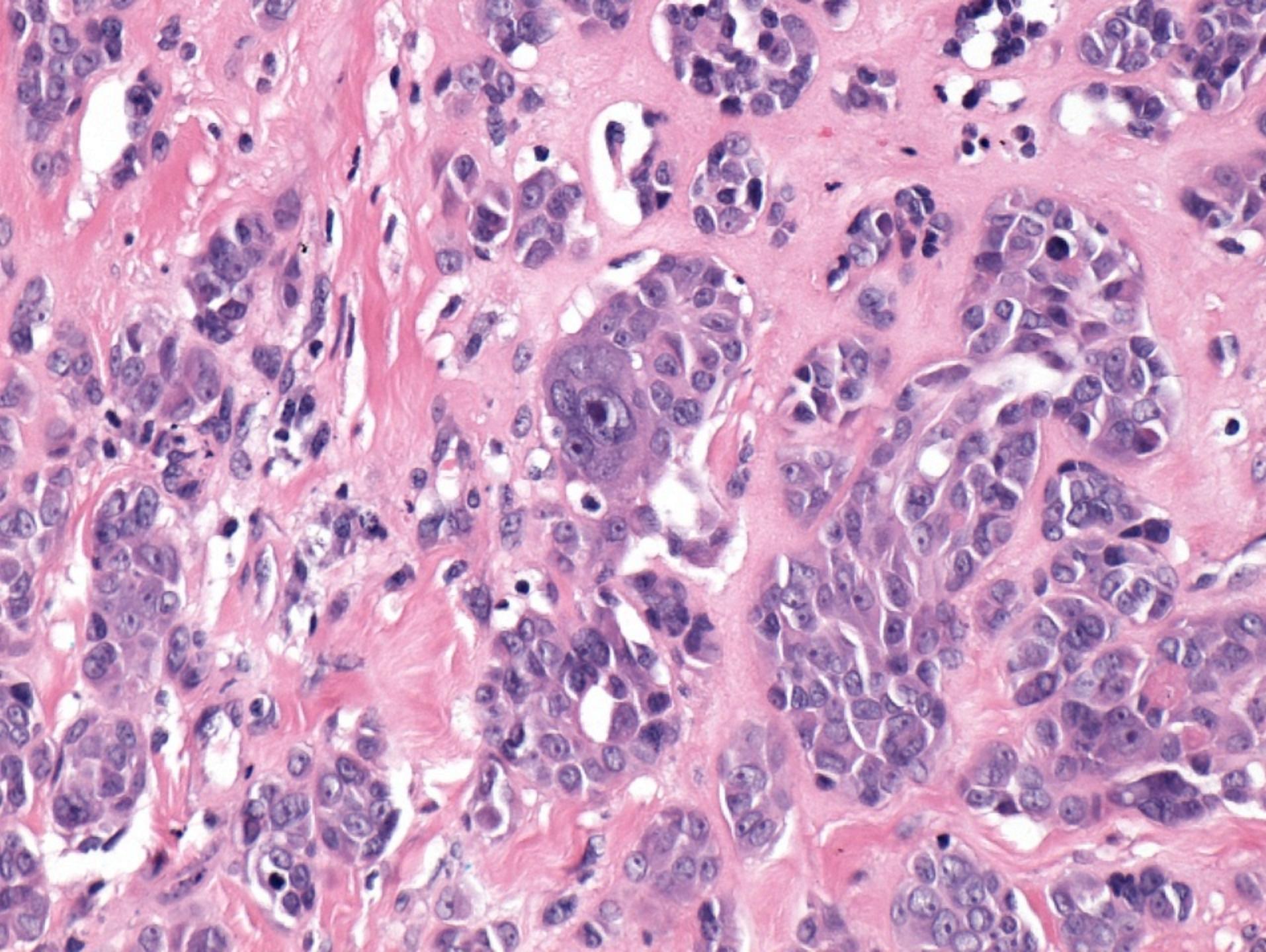
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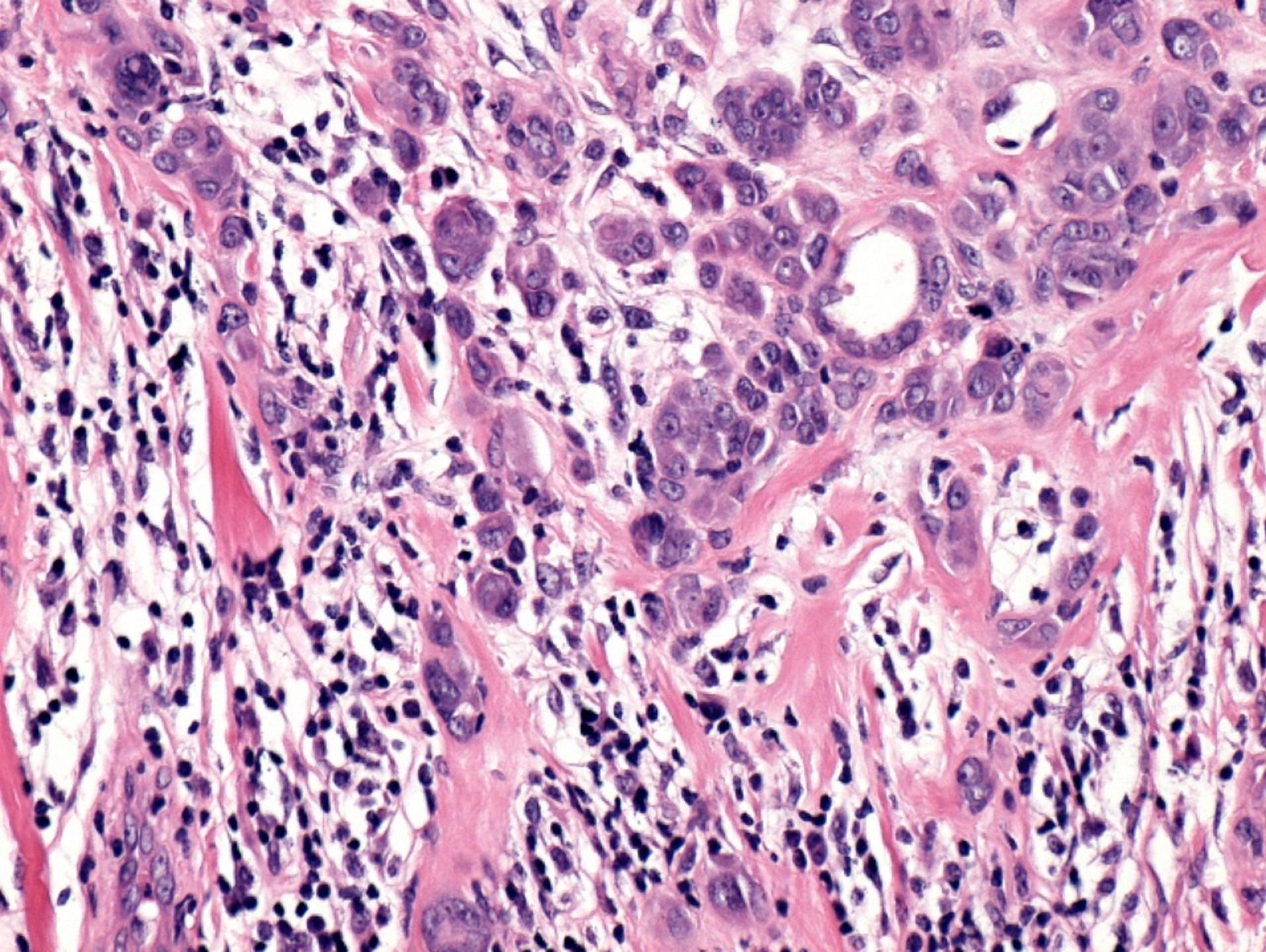


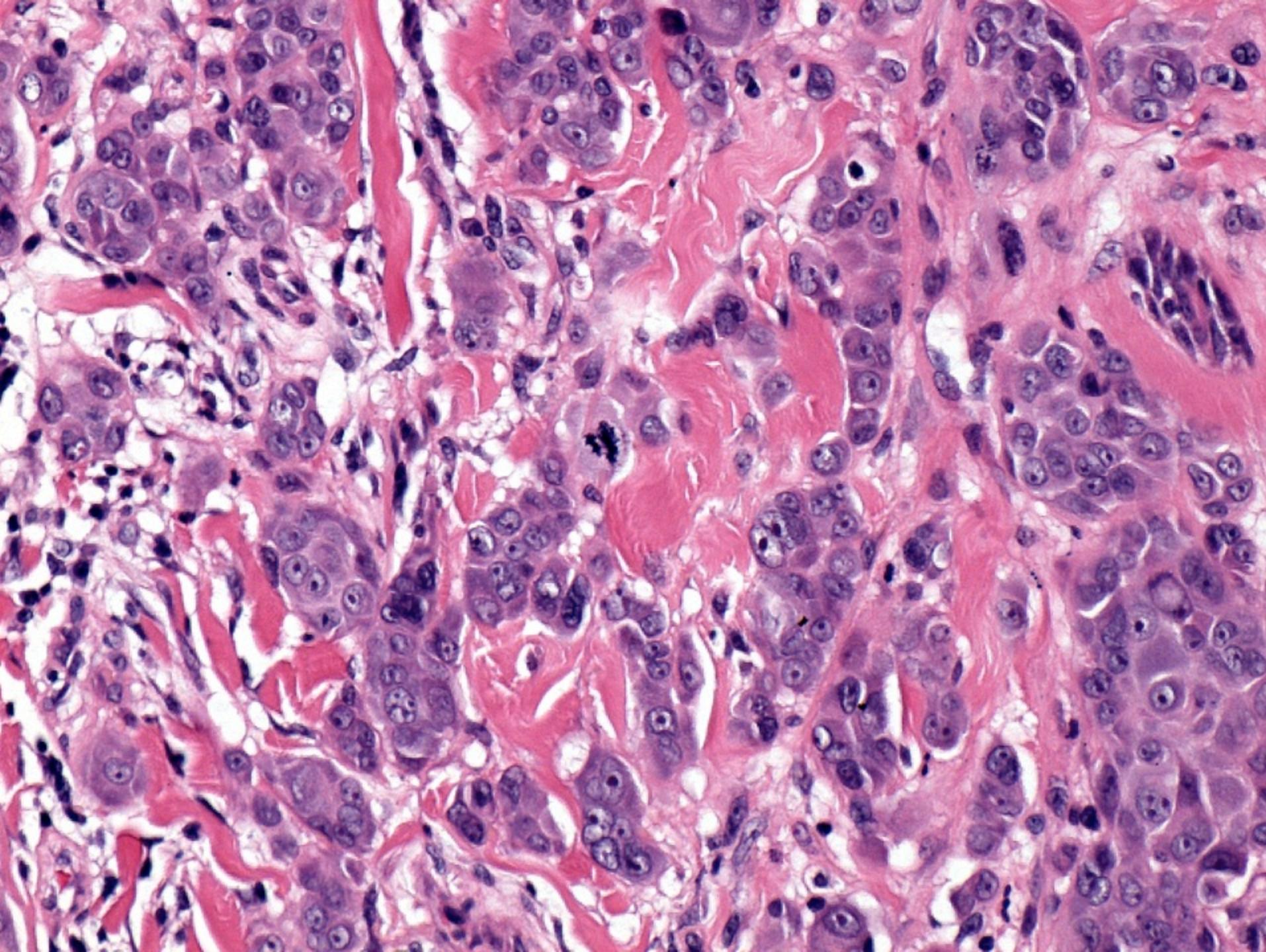


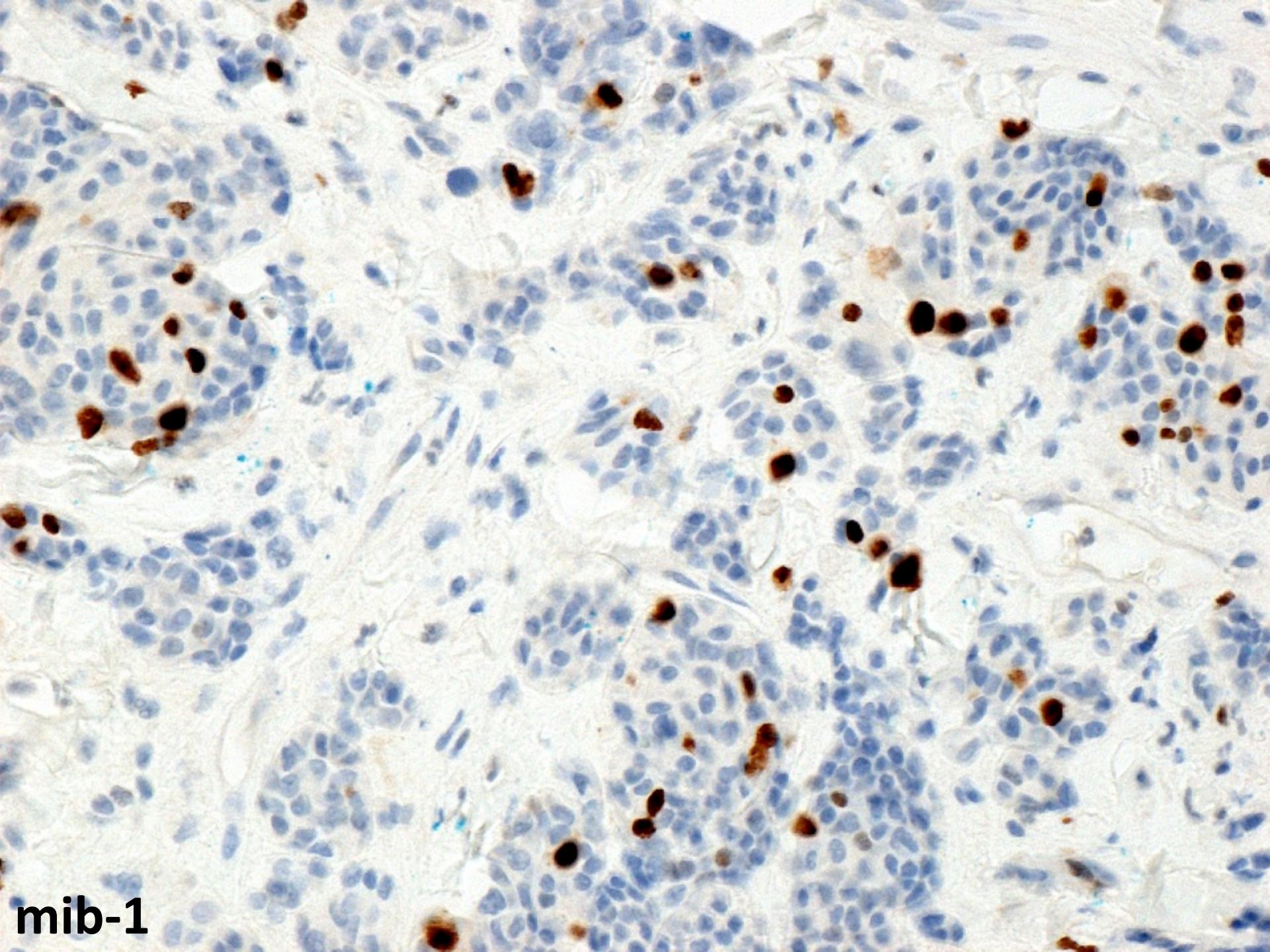




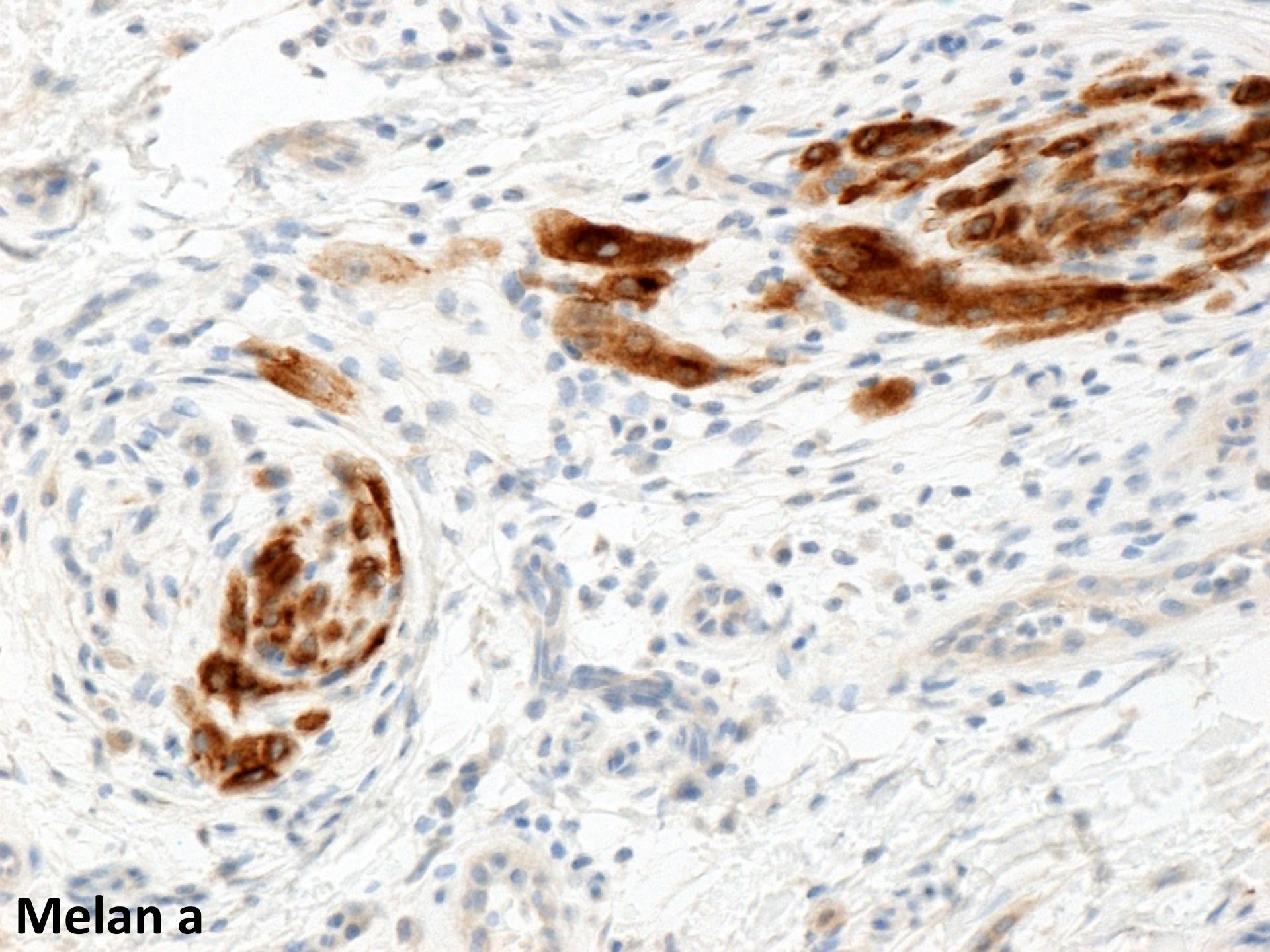




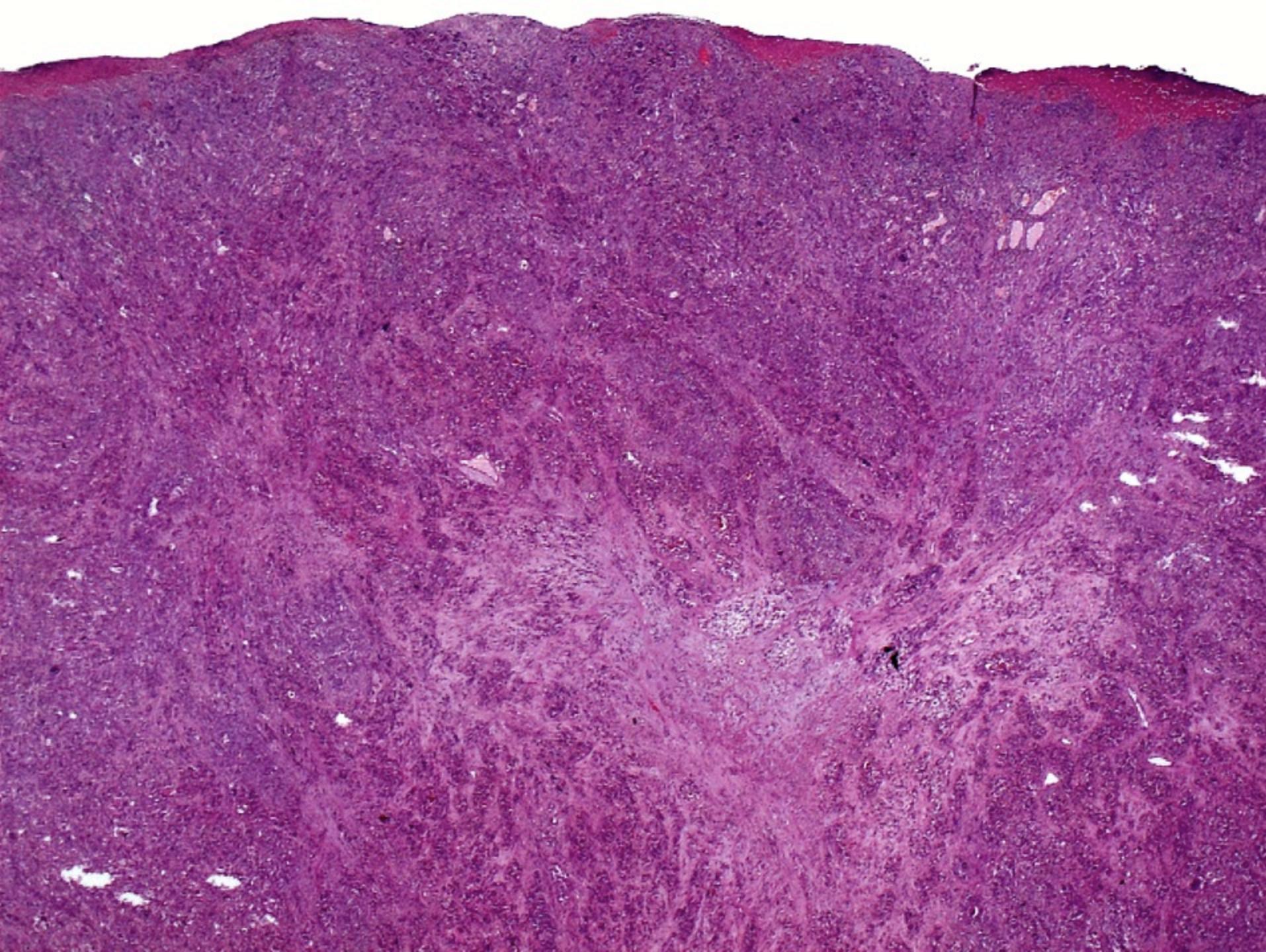


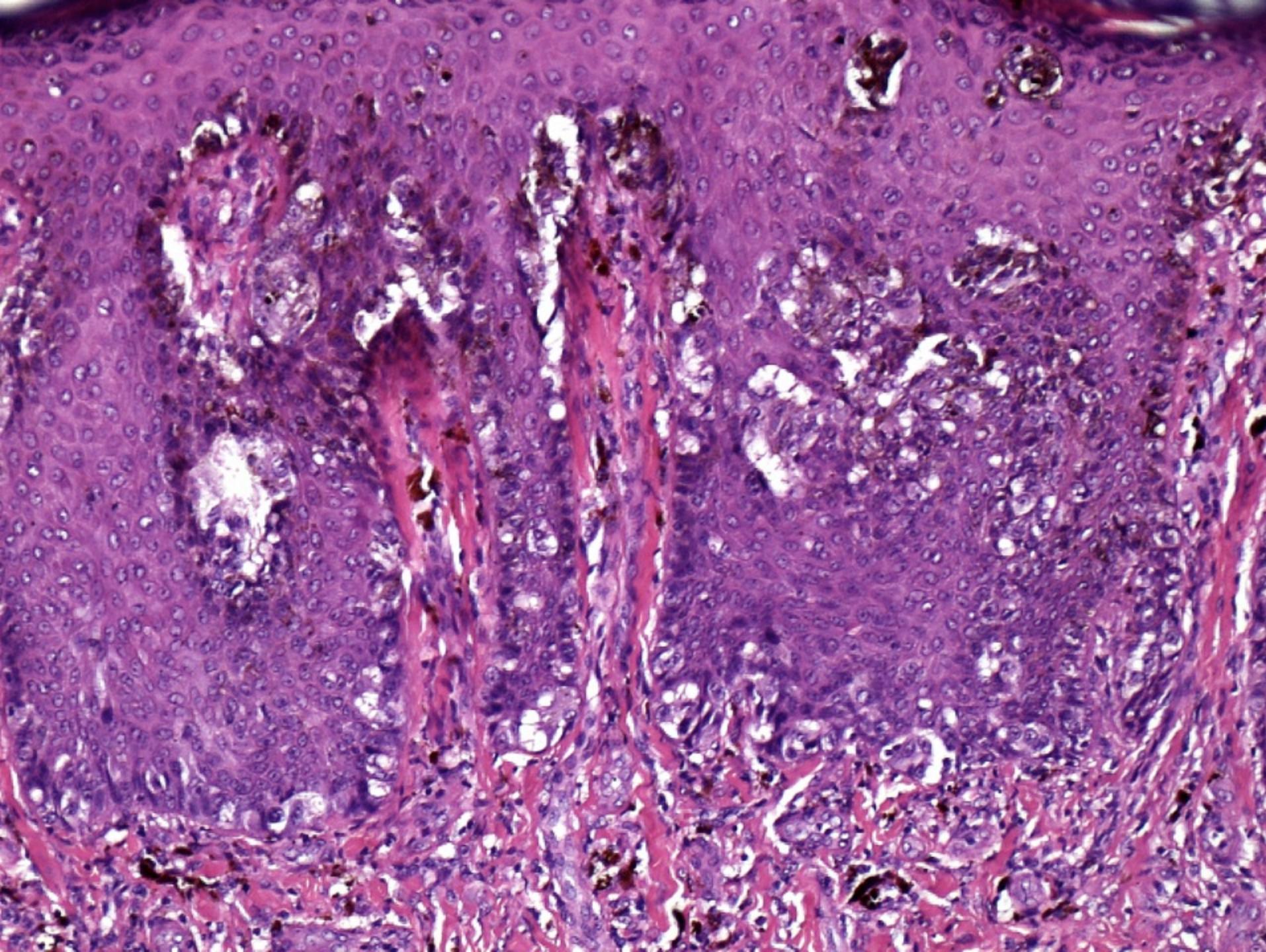


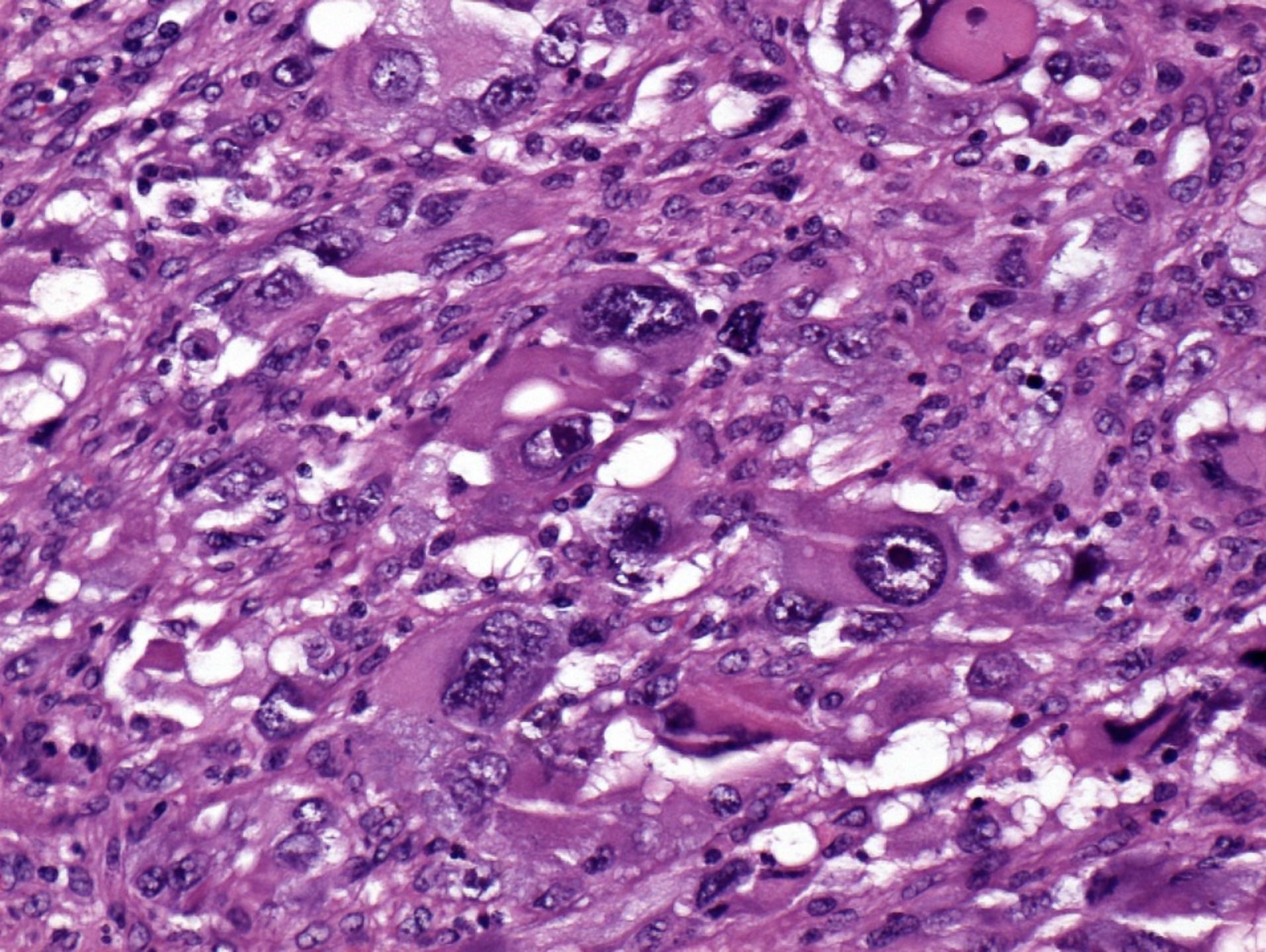
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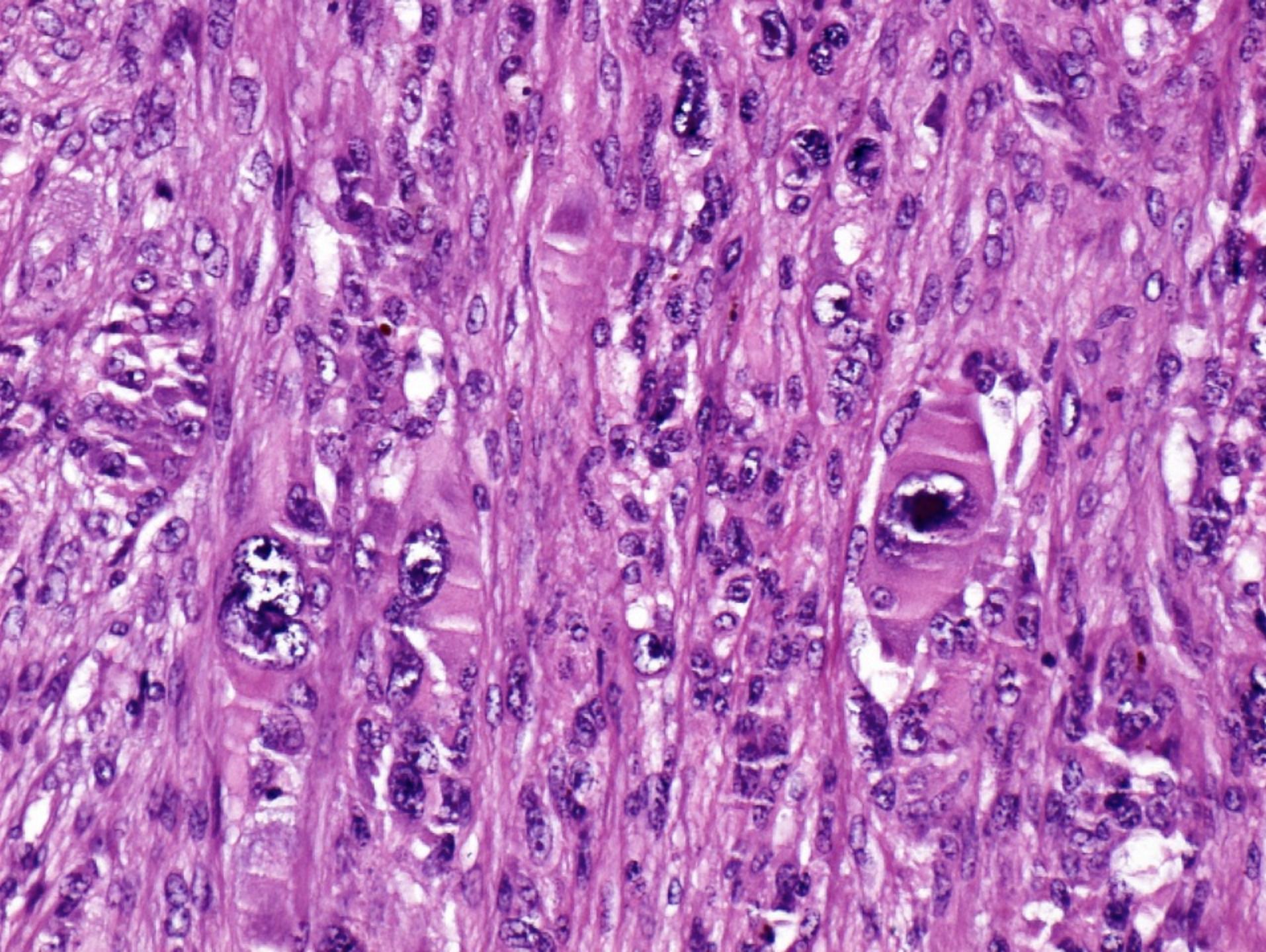


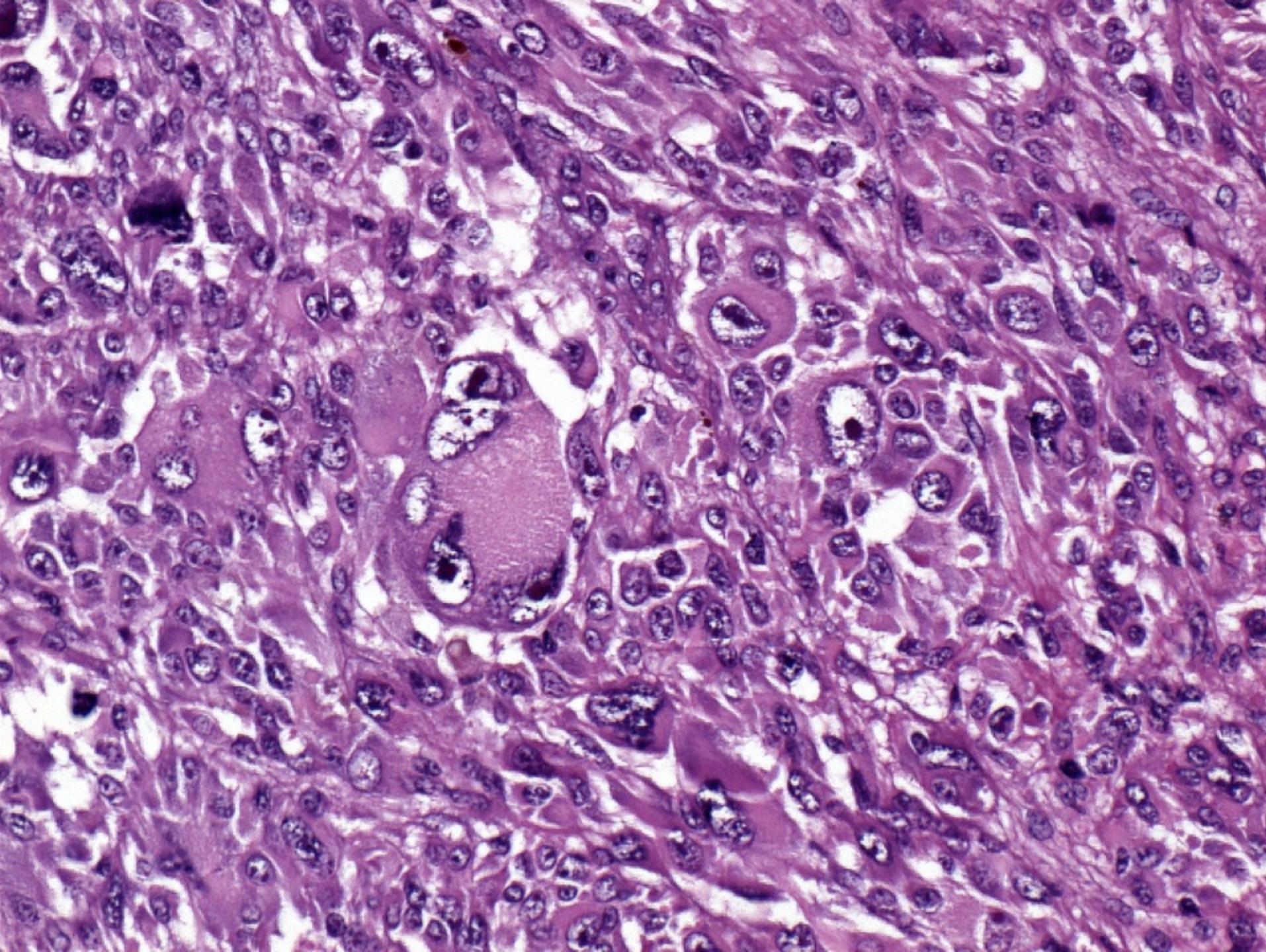
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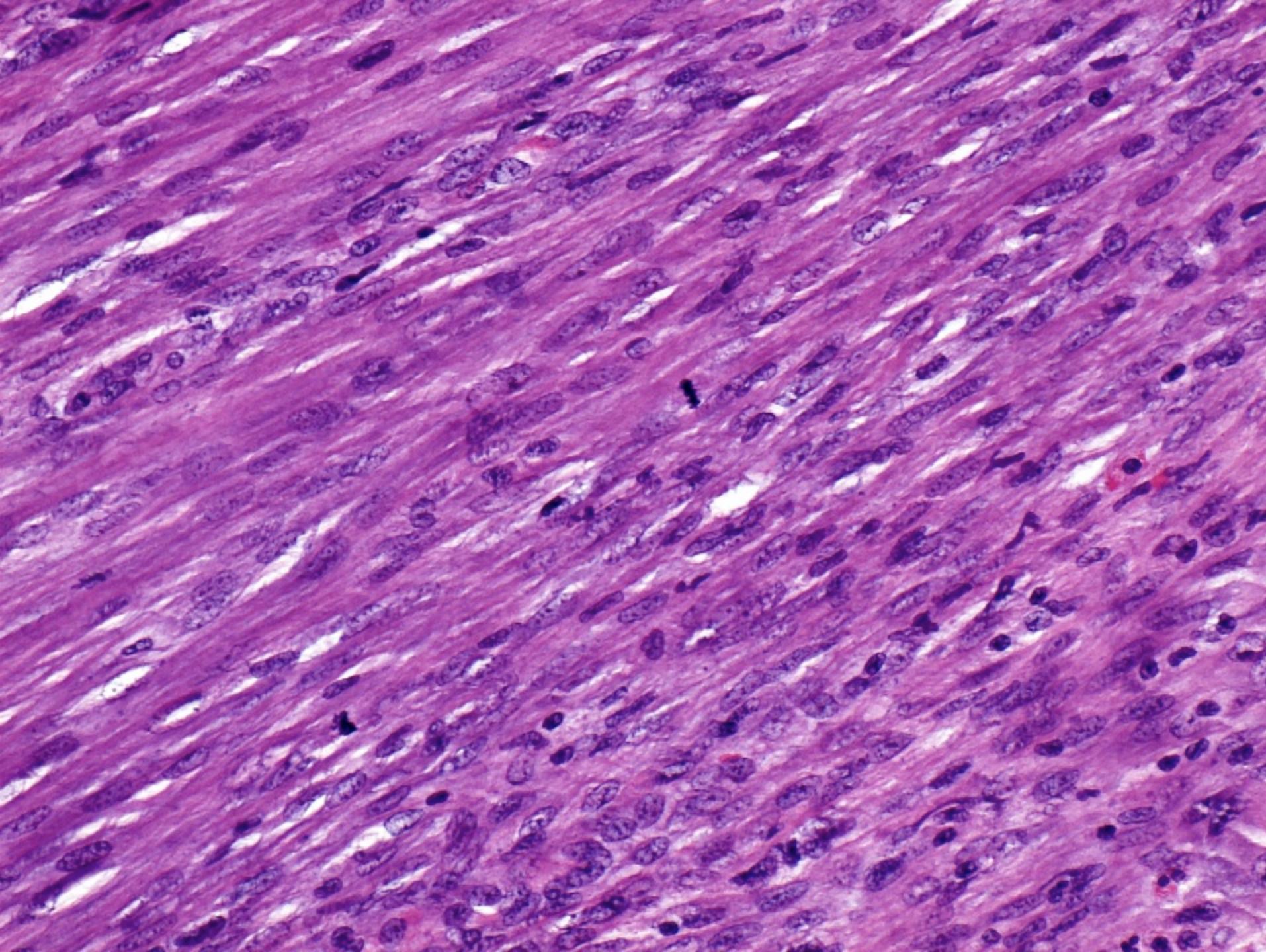


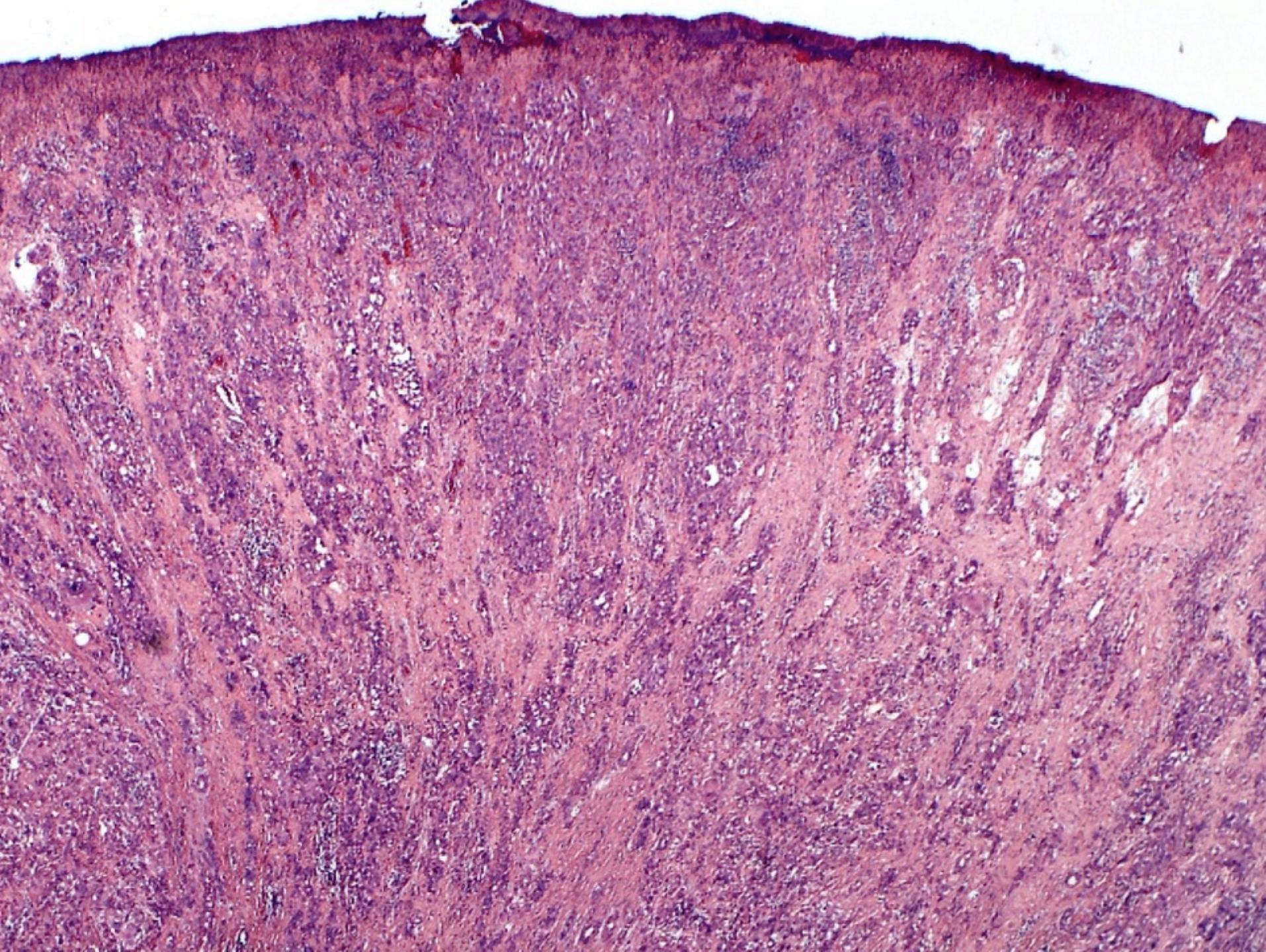


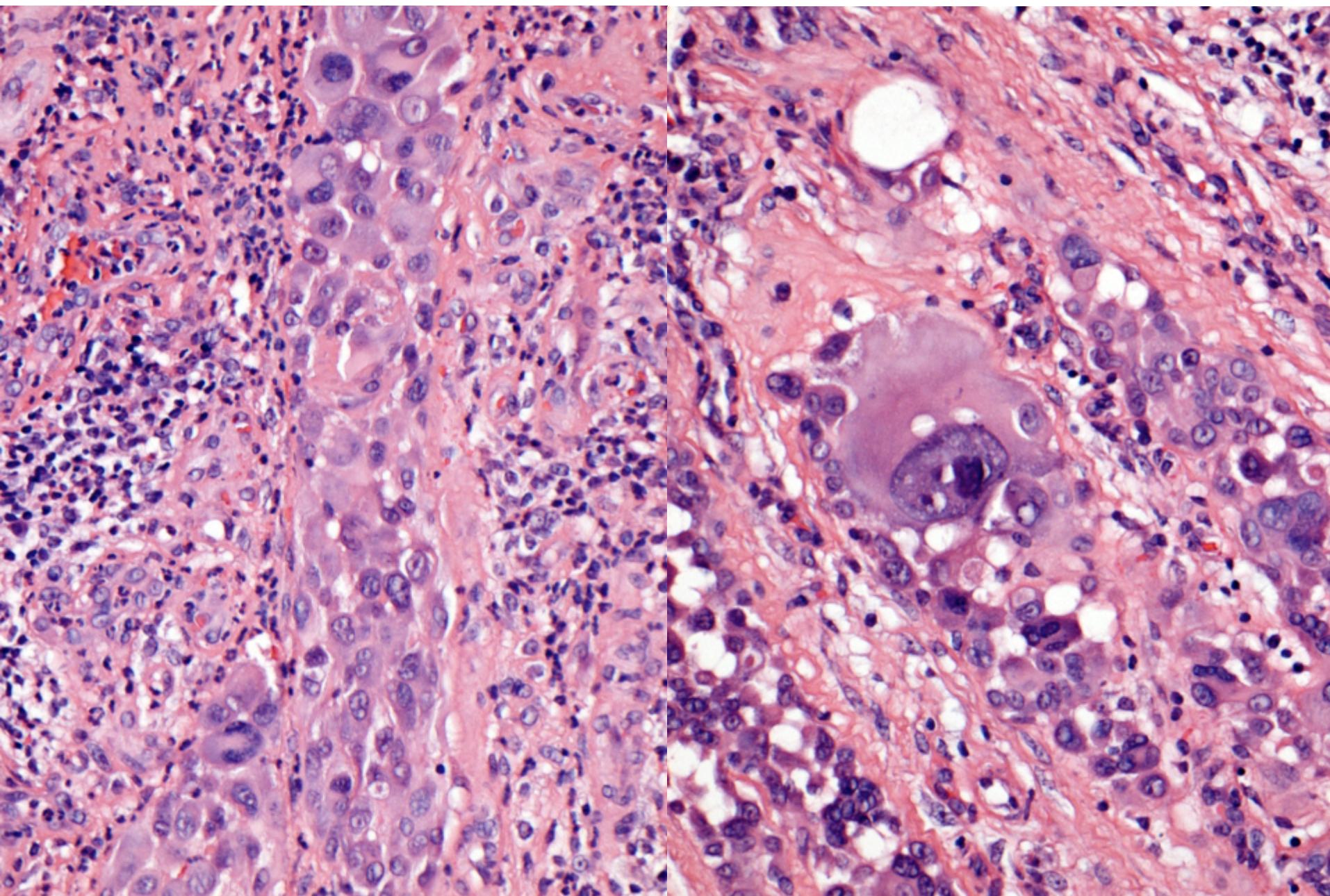












Spitzoid Melanoma

- **Distinction from Atypical Spitz Tumour**
largely arbitrary
- **Criteria quantitative rather qualitative**

Spitzoid Melanoma

-Behaviour-

In young children (<10 years):

- Favourable behaviour
- Risk for involvement of loco-regional lymph nodes
- Rare disseminated disease and mortality

Distinction from Atypical Spitz Tumour and classification as Spitzoid Melanoma flawed in this age group using histological criteria

Histology poor predictor of outcome

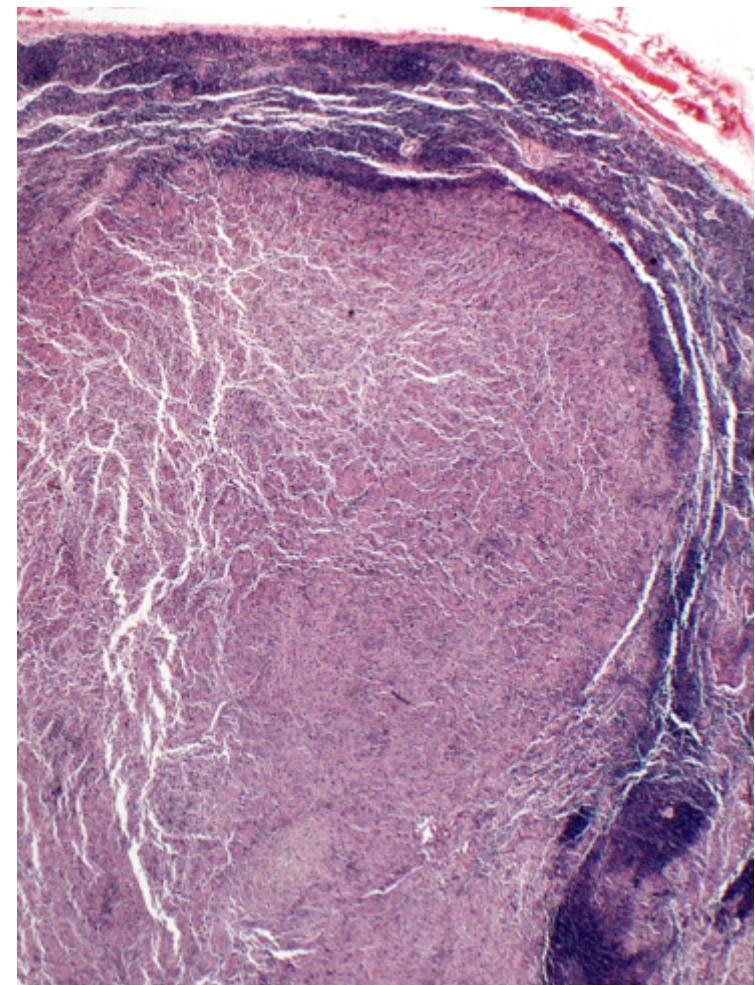
Perhaps best regarded as Atypical Spitz Tumour / Spitzoid Tumour of uncertain malignant potential

Need for independent prognostic parameters

Spitzoid Melanoma

-Treatment-

- **Surgical excision with clear margins**
- **Clinical follow-up**
- **Sentinel lymph node biopsy contraindicated**



Childhood Melanoma

“Childhood Melanoma”

-Introduction-

- **Melanoma in children is rare**
- **Clinically and morphologically heterogeneous disease**
- **Similar melanoma subtypes as in adults but occurring at different frequencies**
- **Majority are of Nodular and Spitzoid subtypes**
- **Behaviour dependent on histological subtype**

Melanoma in Childhood and Adolescence

-Clinical Presentation-

- **Strong predilection for Caucasians**
 - Most evident after age 5-9 years
 - No ethnic bias in congenital/neonatal melanoma
- **Roughly equal gender distribution**
- **Trunk and extremities most frequently affected**
- **Predilection for head and neck area in young children and infants**

Melanoma in Childhood and Adolescence

-Clinical Presentation-

- **Presenting signs:**
 - Pigmented lesion
 - Size >7mm
 - History of change/growth
 - Bleeding, ulceration, pain, regional lymphadenopathy
- **Less specific symptoms in younger patients:**
 - Often non-pigmented and ulcerated
 - ABCD signs do not apply reliably
 - Clinically impression of DF, Spitz, PG
 - Melanoma only rarely suspected

Melanoma in Childhood

-Risk Factors-

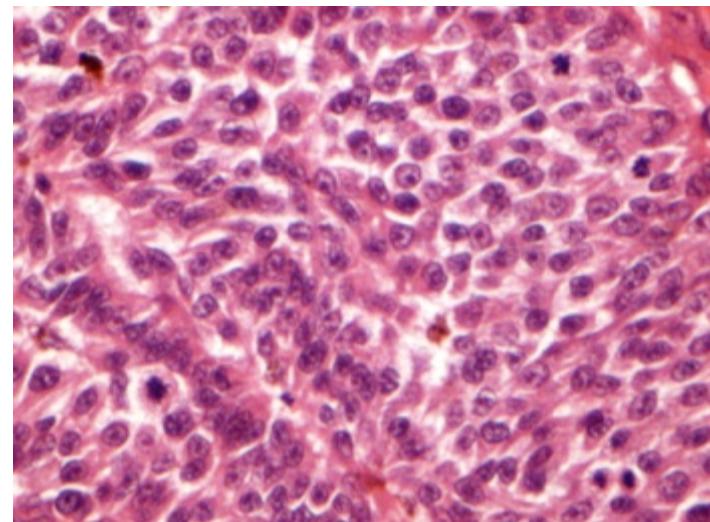
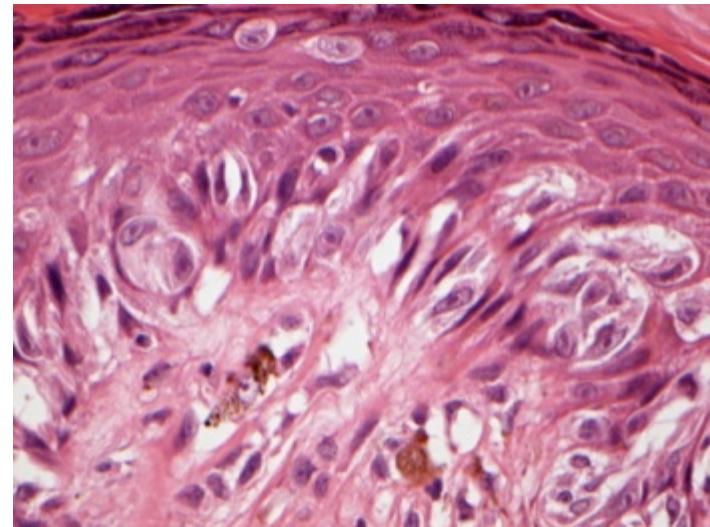
- **Giant Congenital Naevi**
- **Xeroderma Pigmentosum**
- **Sun-sensitivity**
- **Multiple atypical naevi**
- **Positive family history**
- **Immunosuppression**
- **Radiation**
- **Second Malignancy**

Melanoma in Childhood and Adolescence

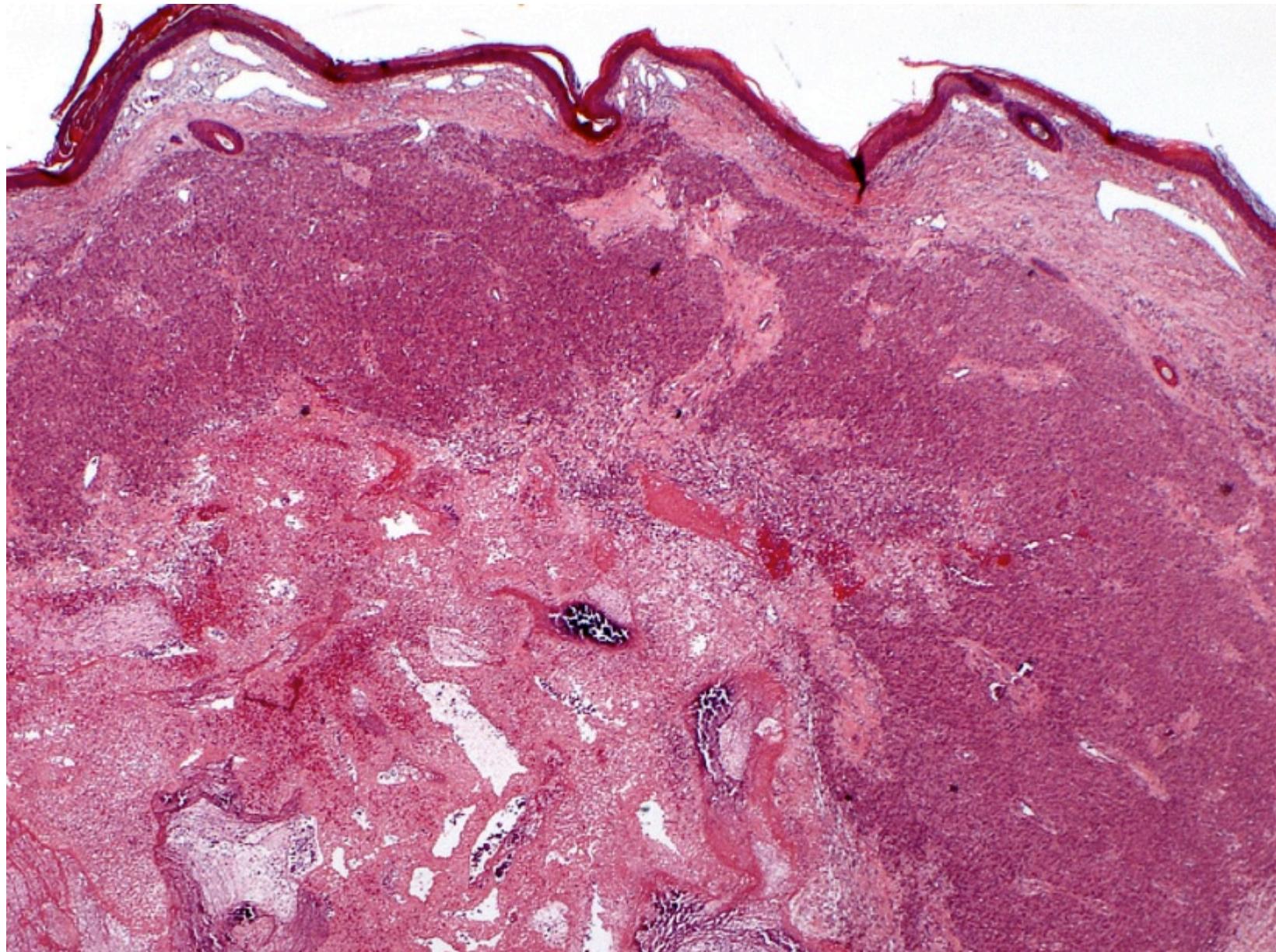
-Histology-

Wide morphological spectrum

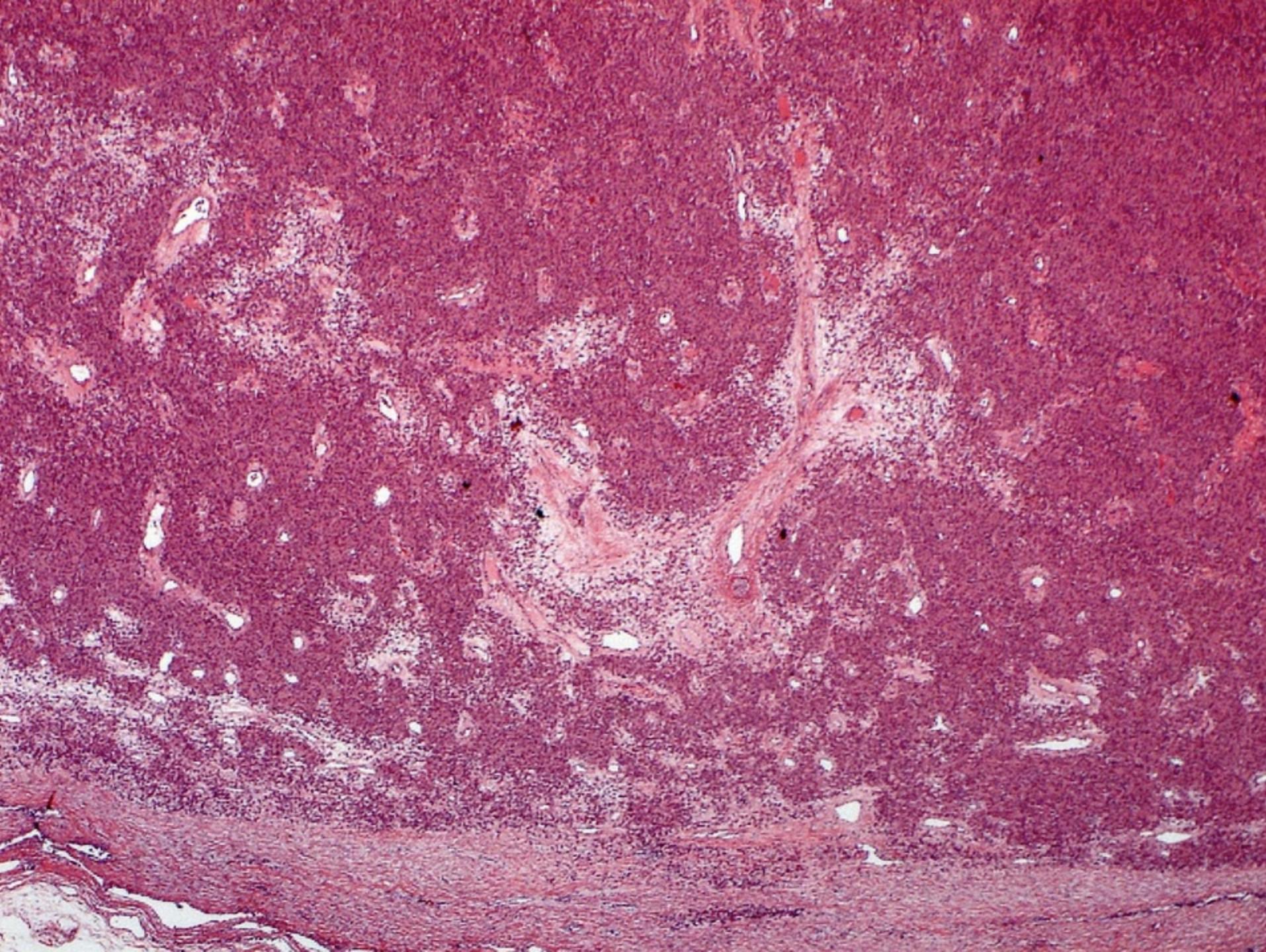
- Nodular
 - Spitzoid
 - Non-Spitzoid
- Superficial Spreading
- Naevoid
- Pigment Synthesizing
- Neurotropic/Desmoplastic

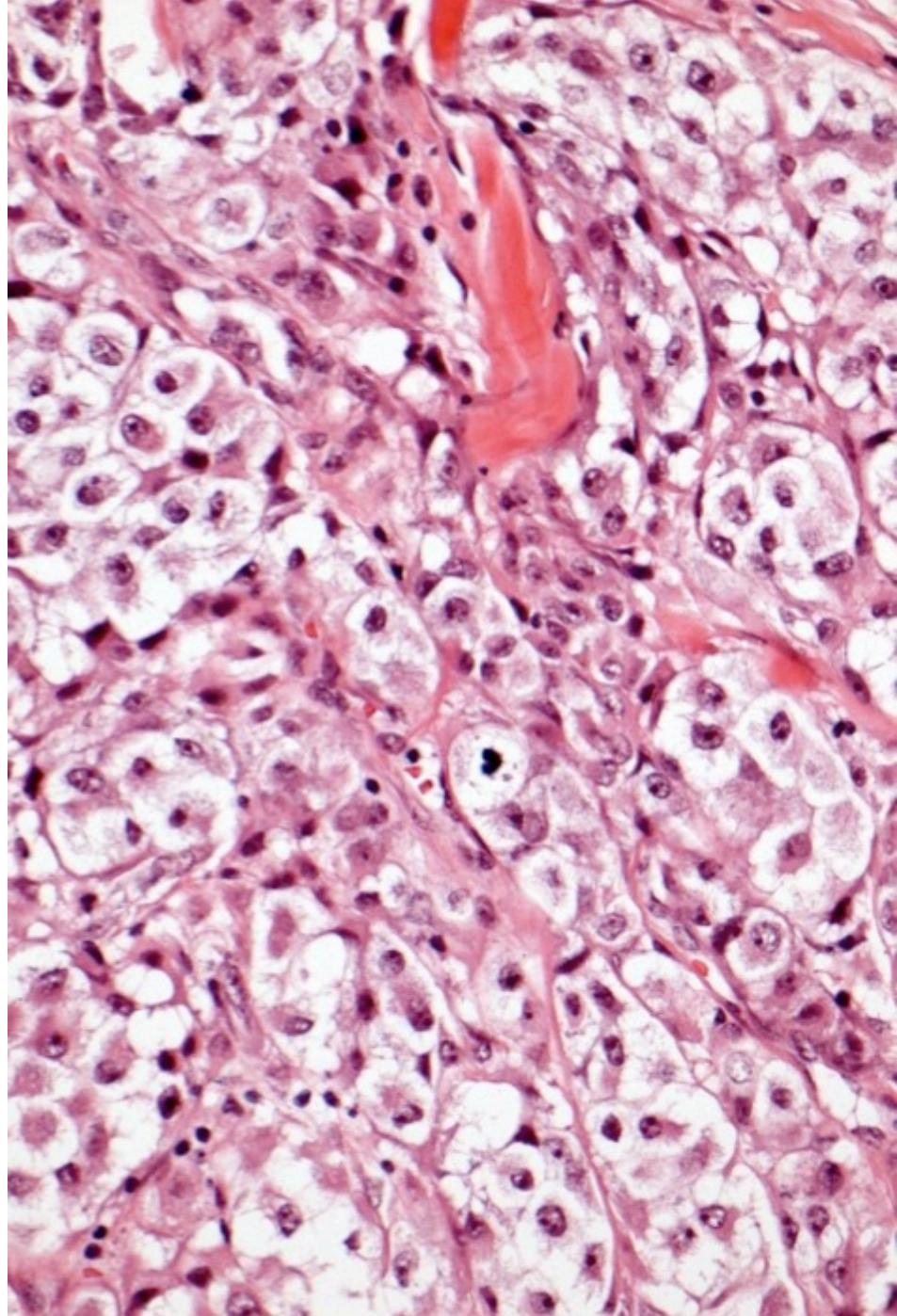
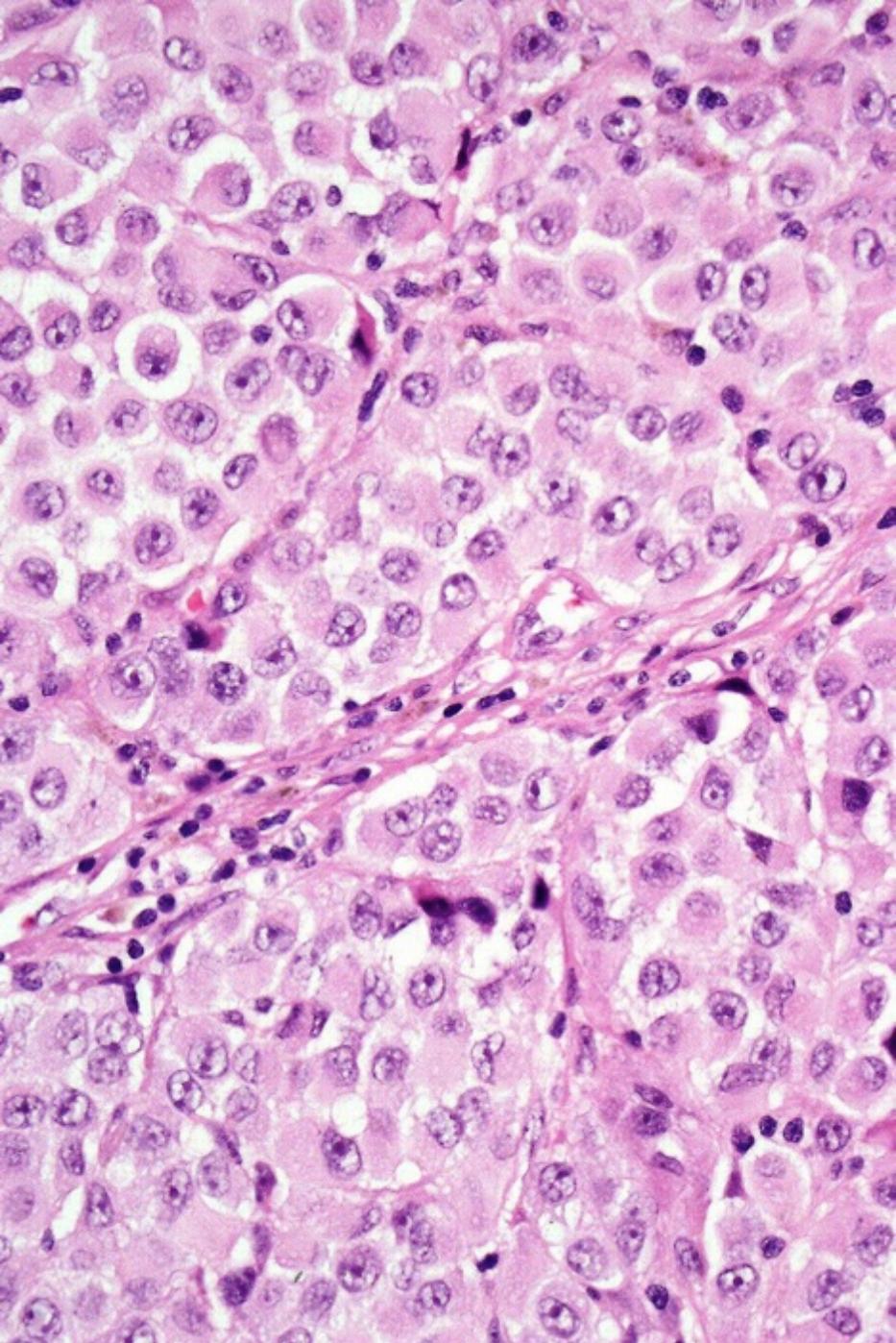


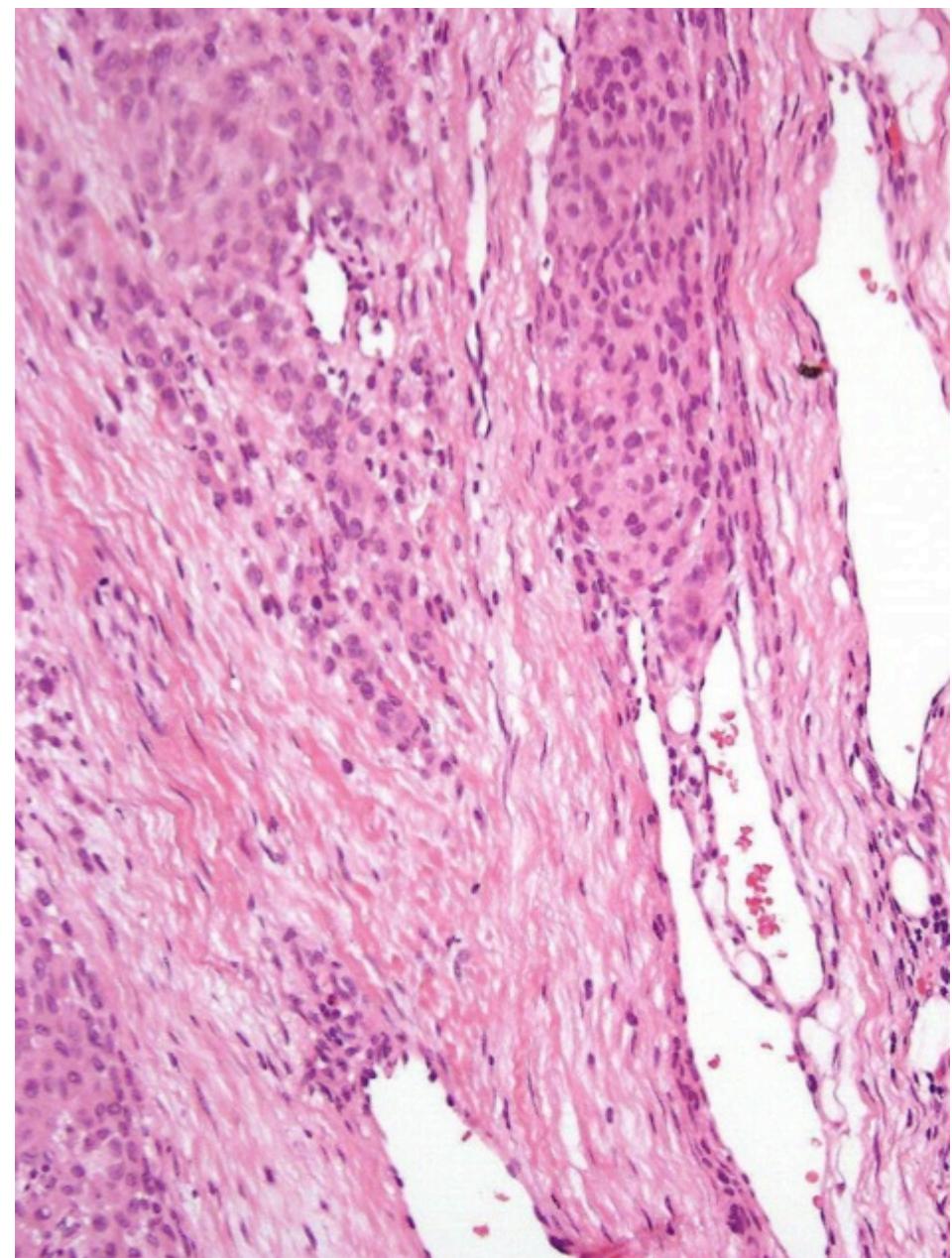
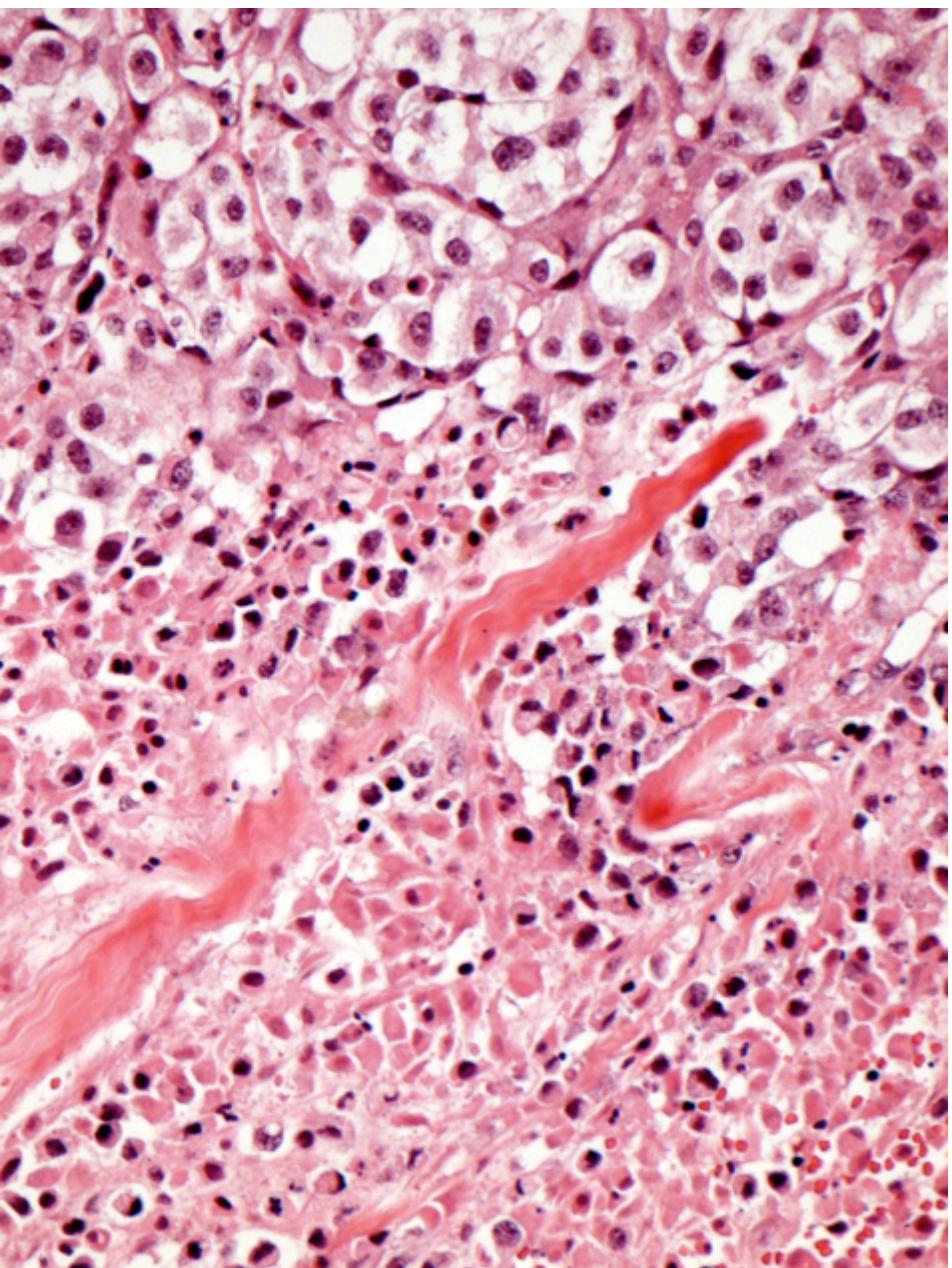
Nodular Non-Spitzoid Melanoma

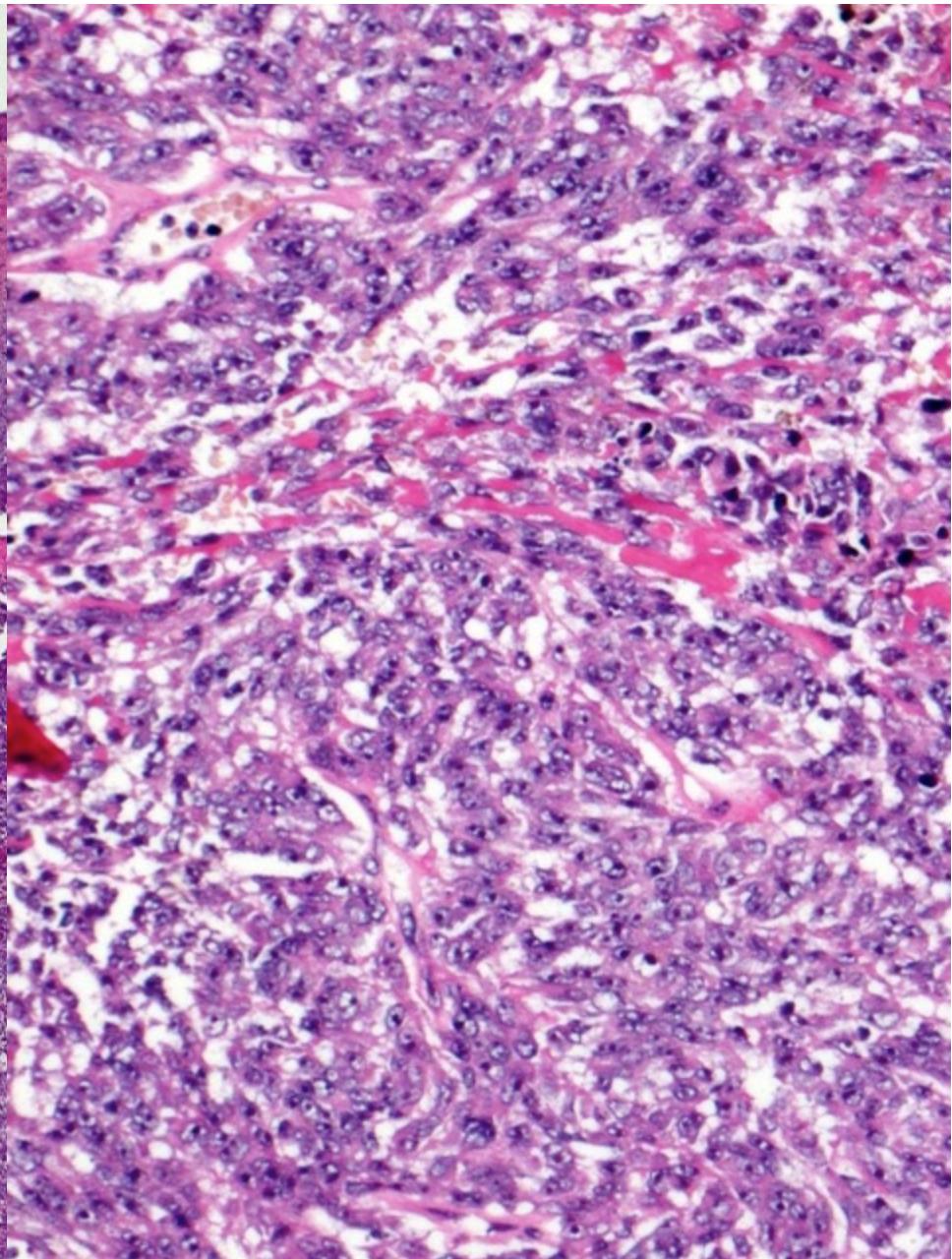
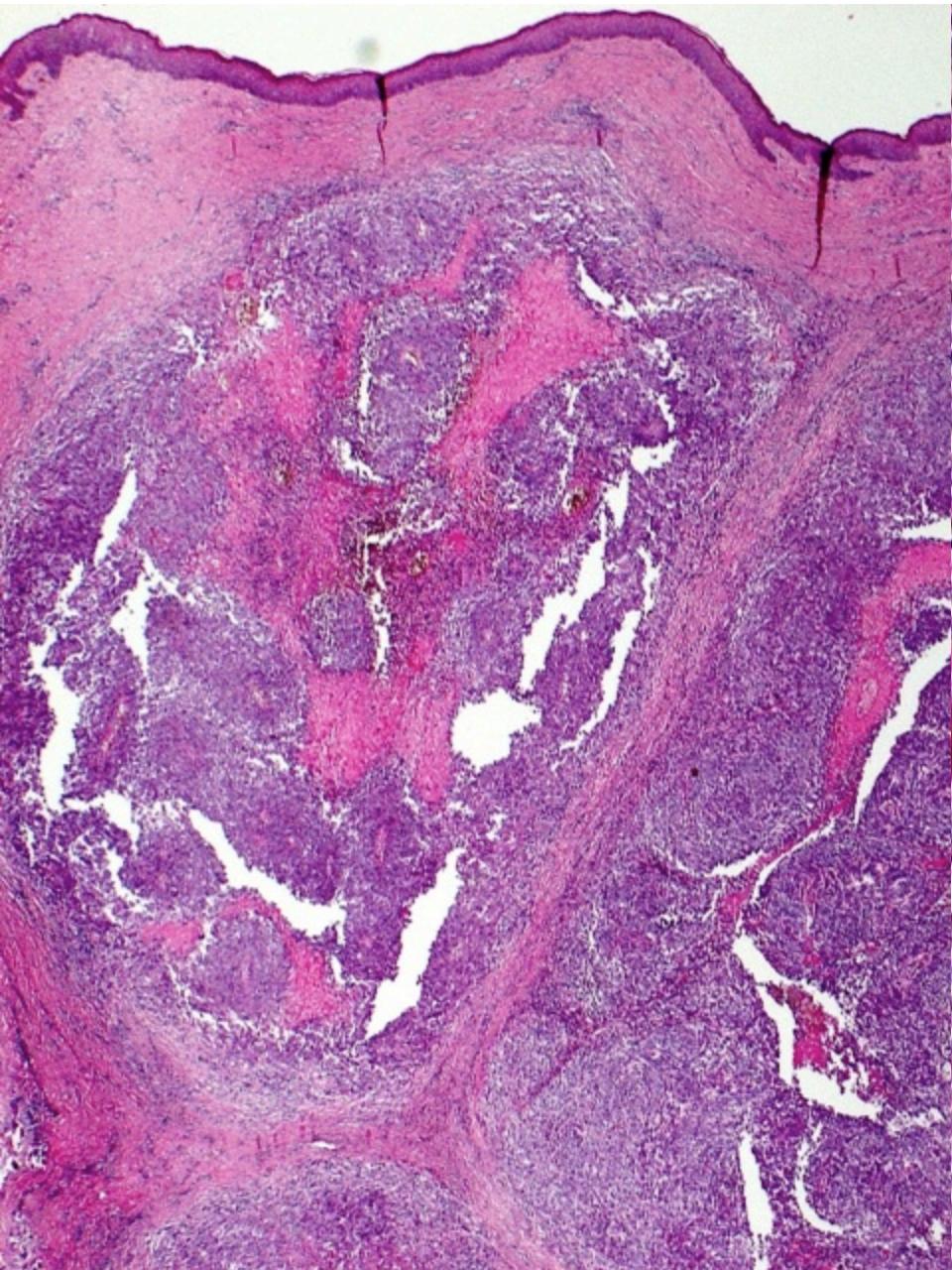


2 months old female with a large pigmented lesion on the back of the neck

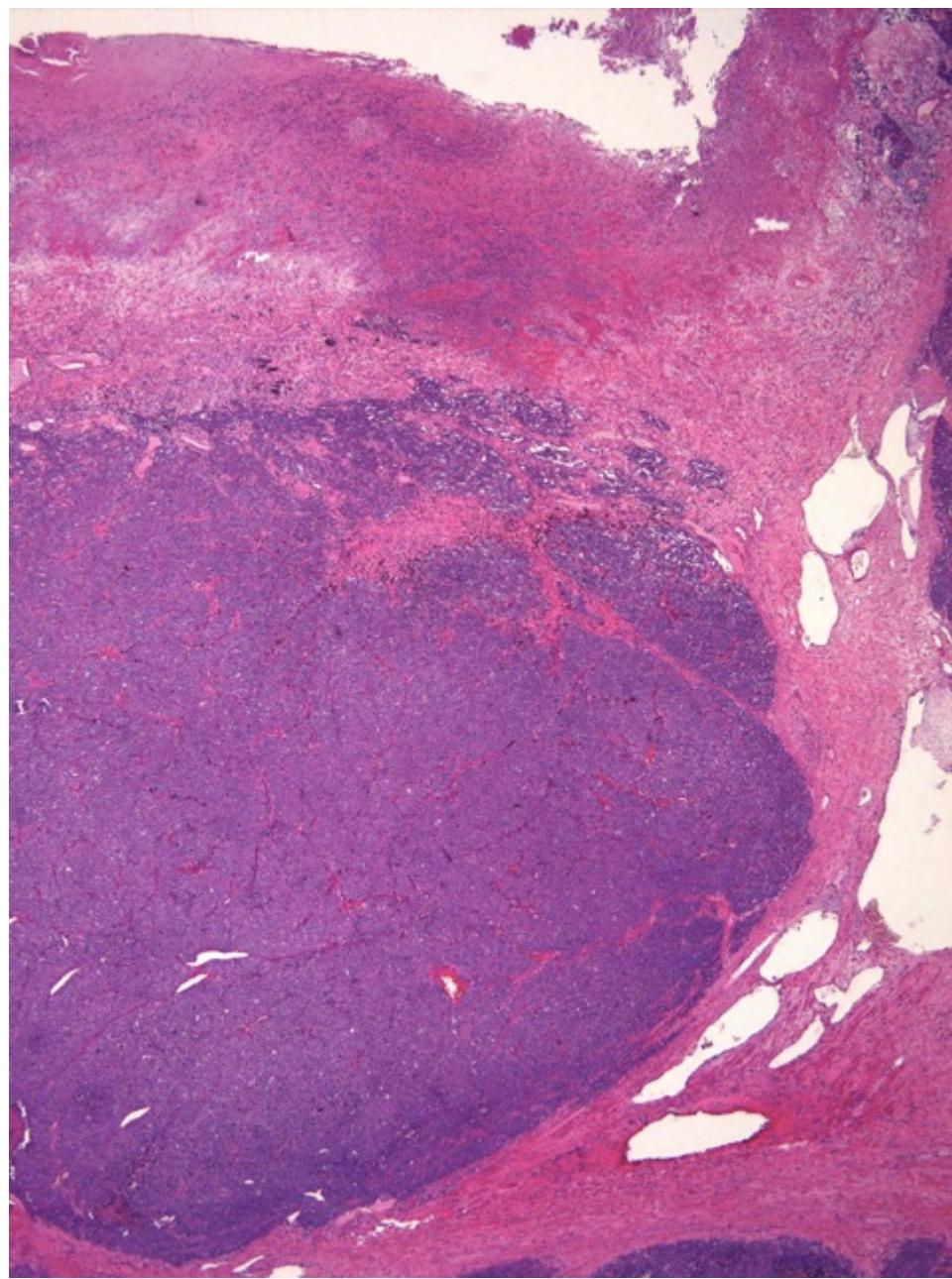


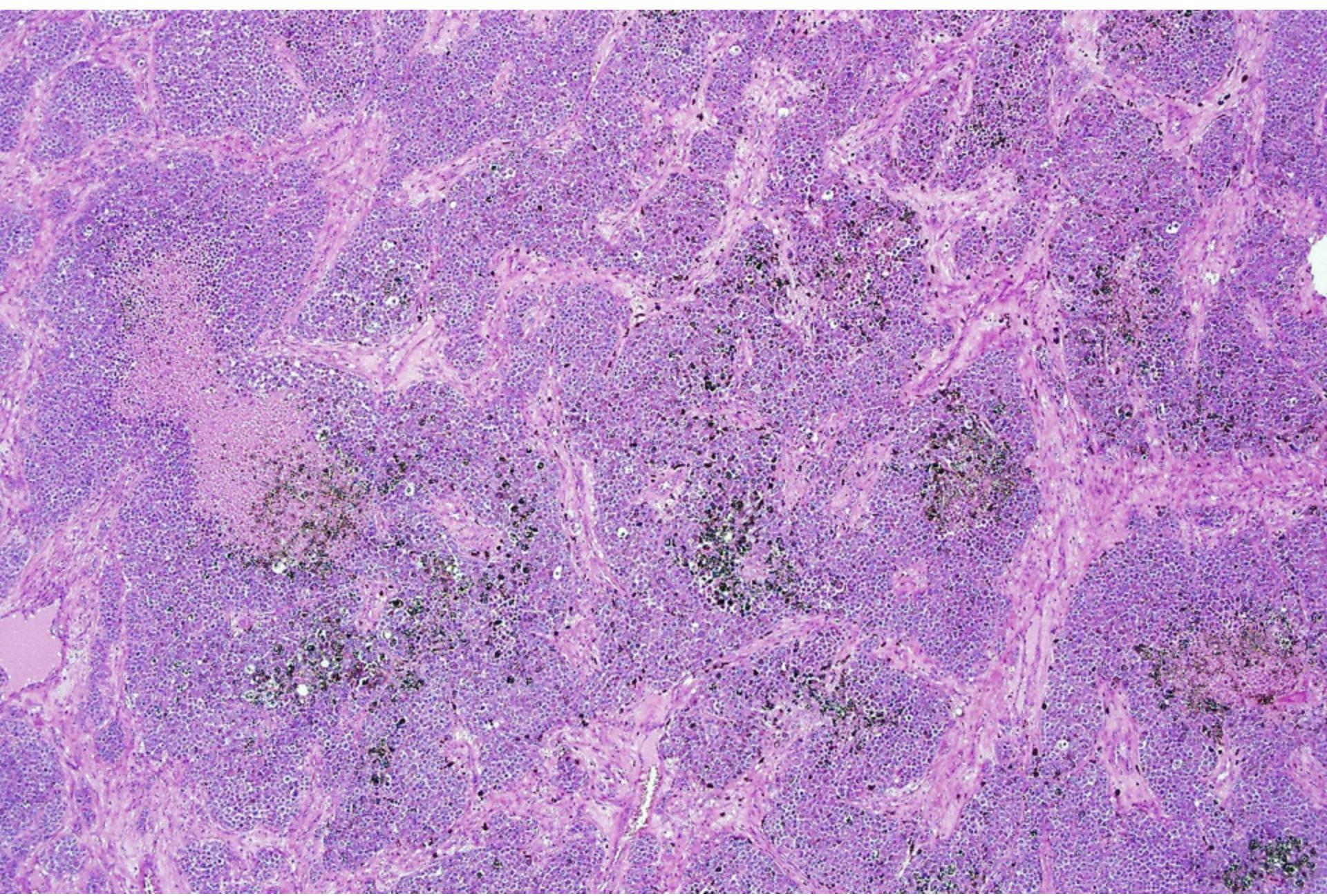


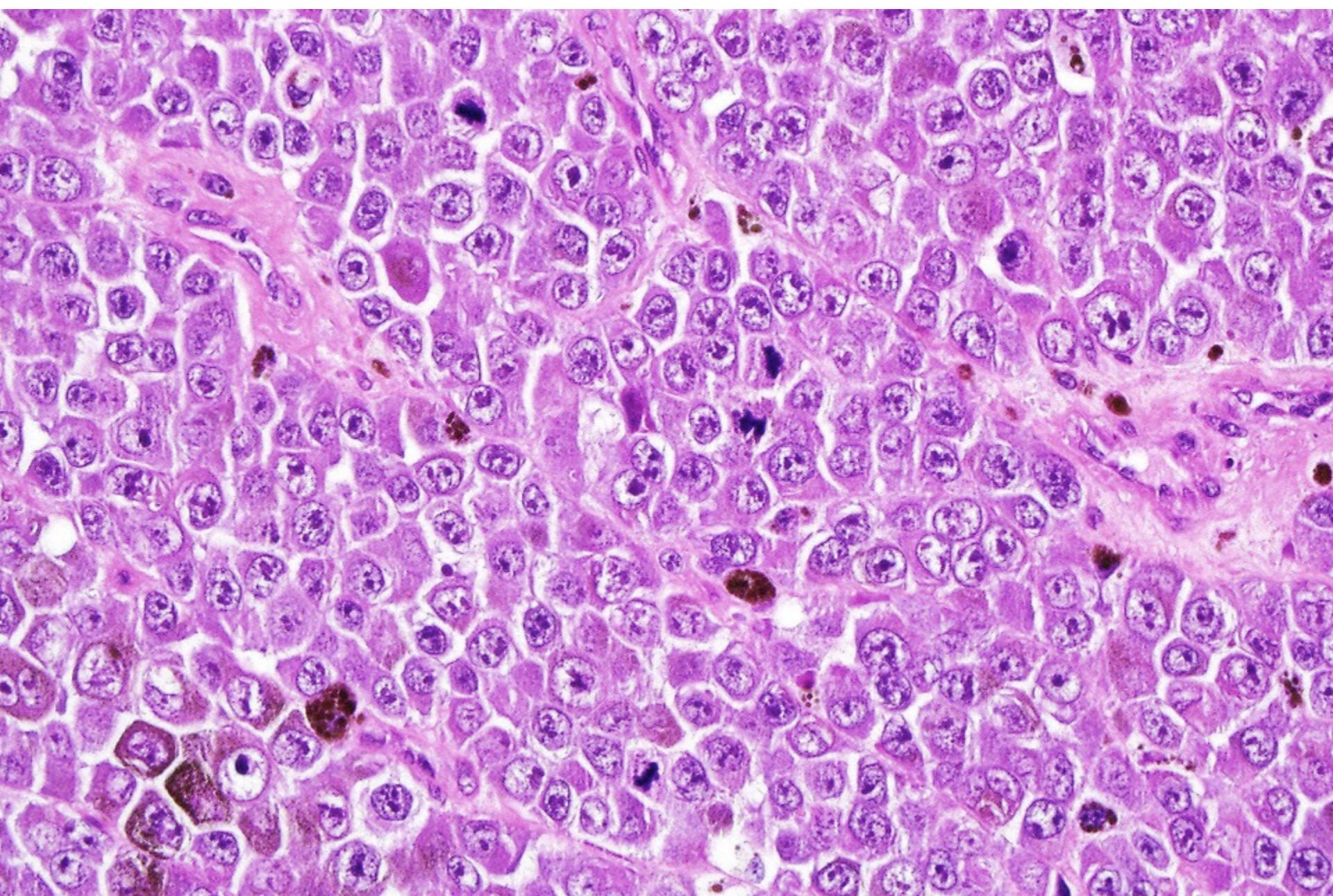


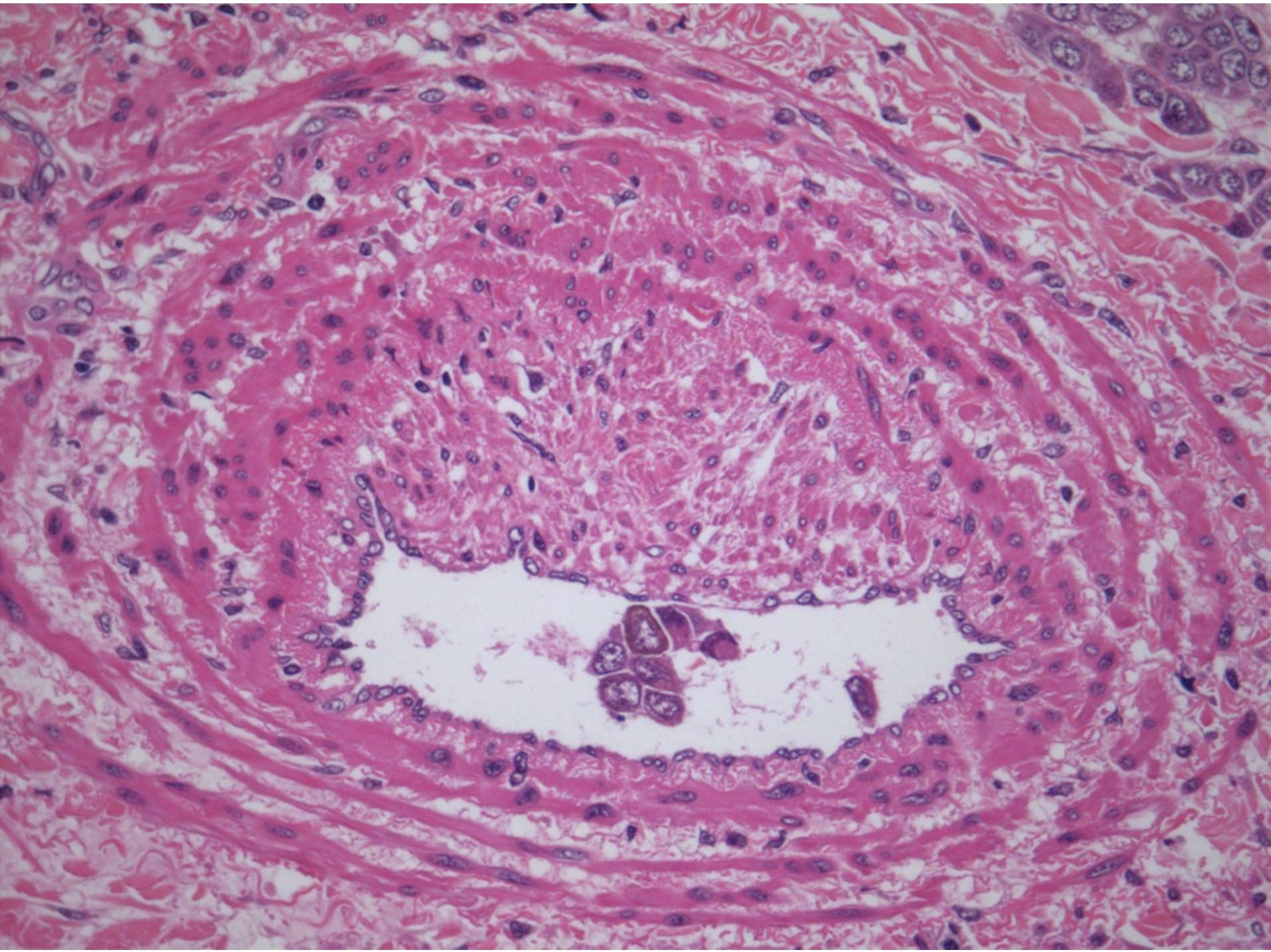


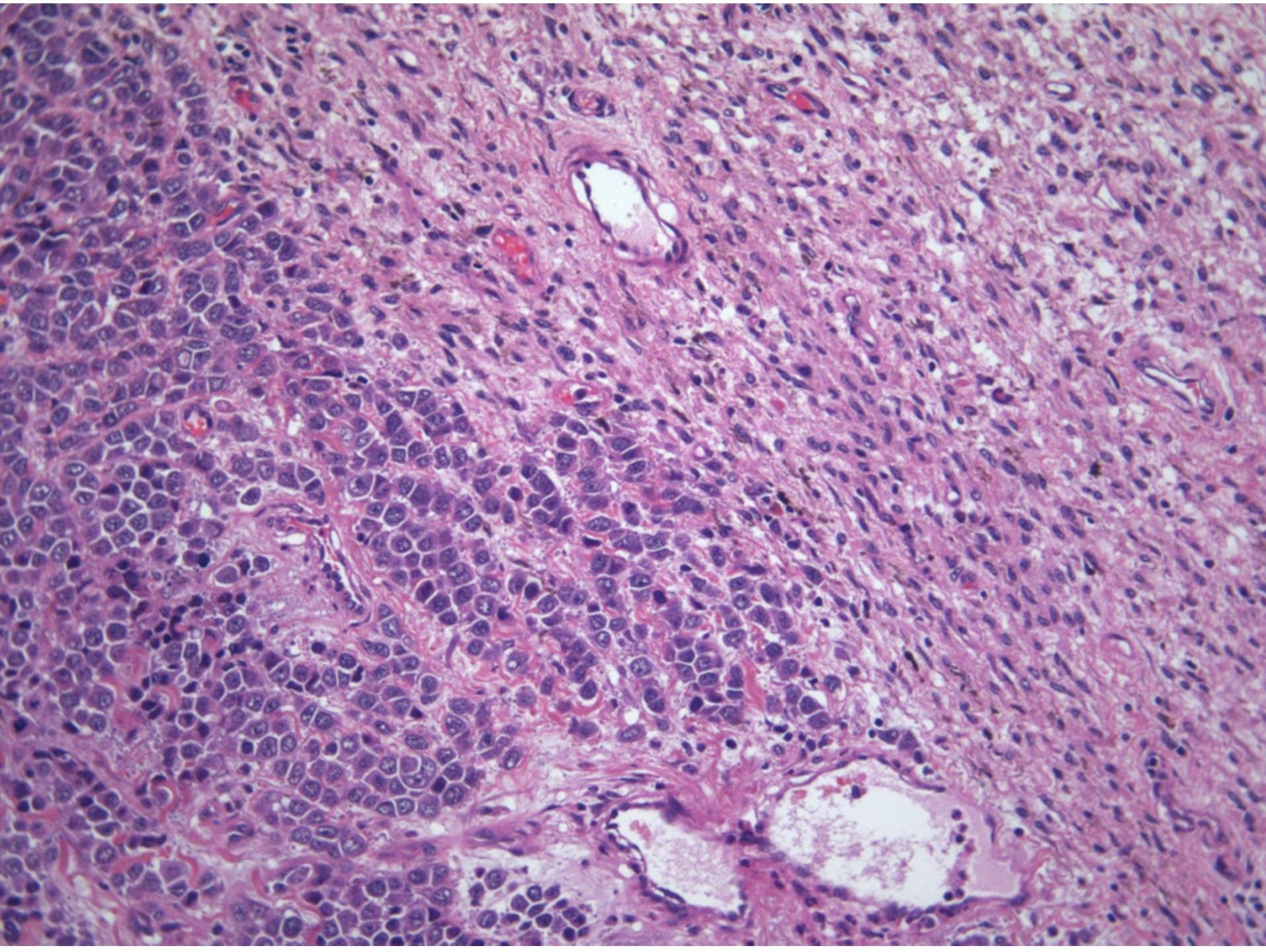
13 year old boy; supraclavicular mas;s Hx of XP and multiple SCC and BCC



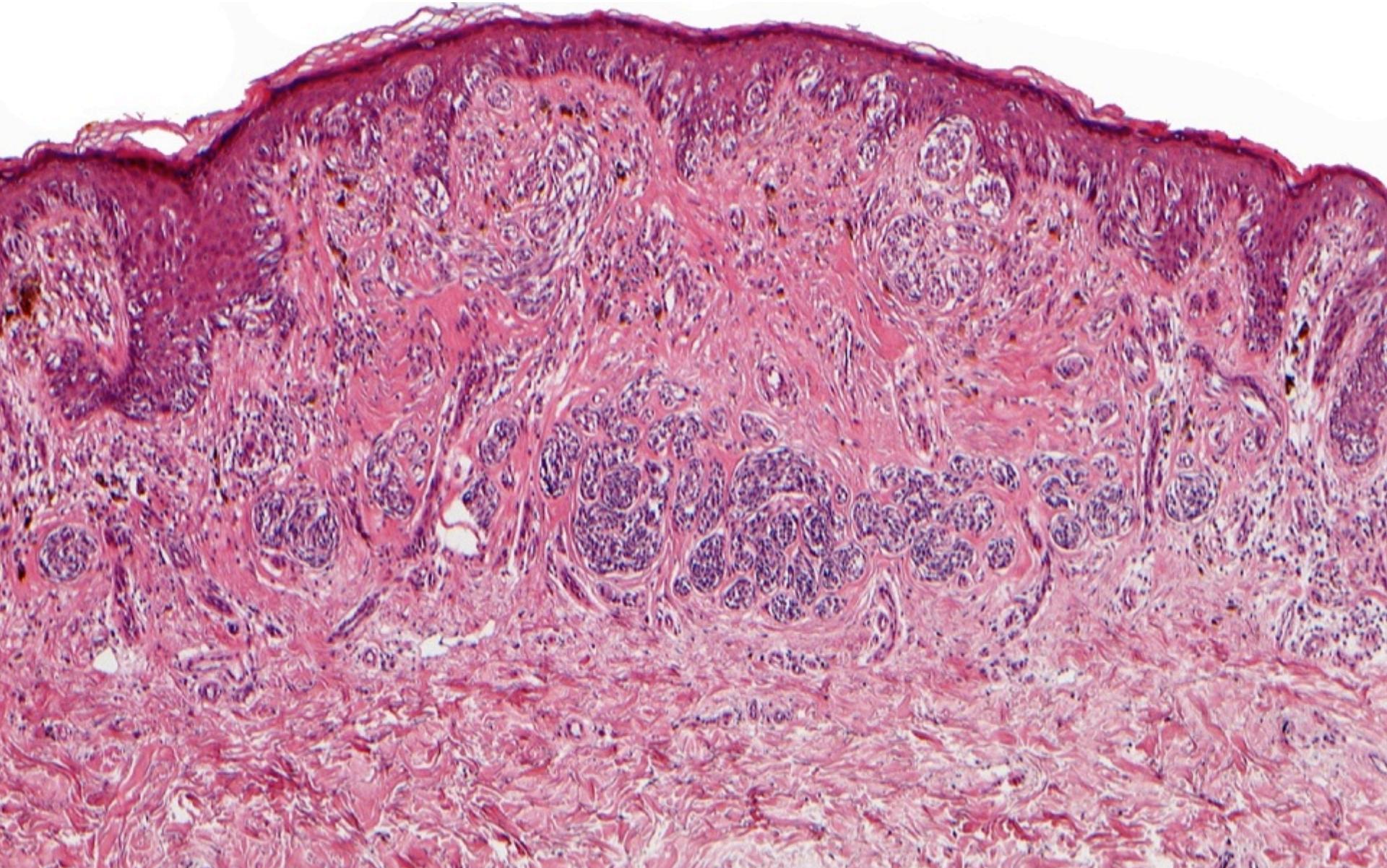




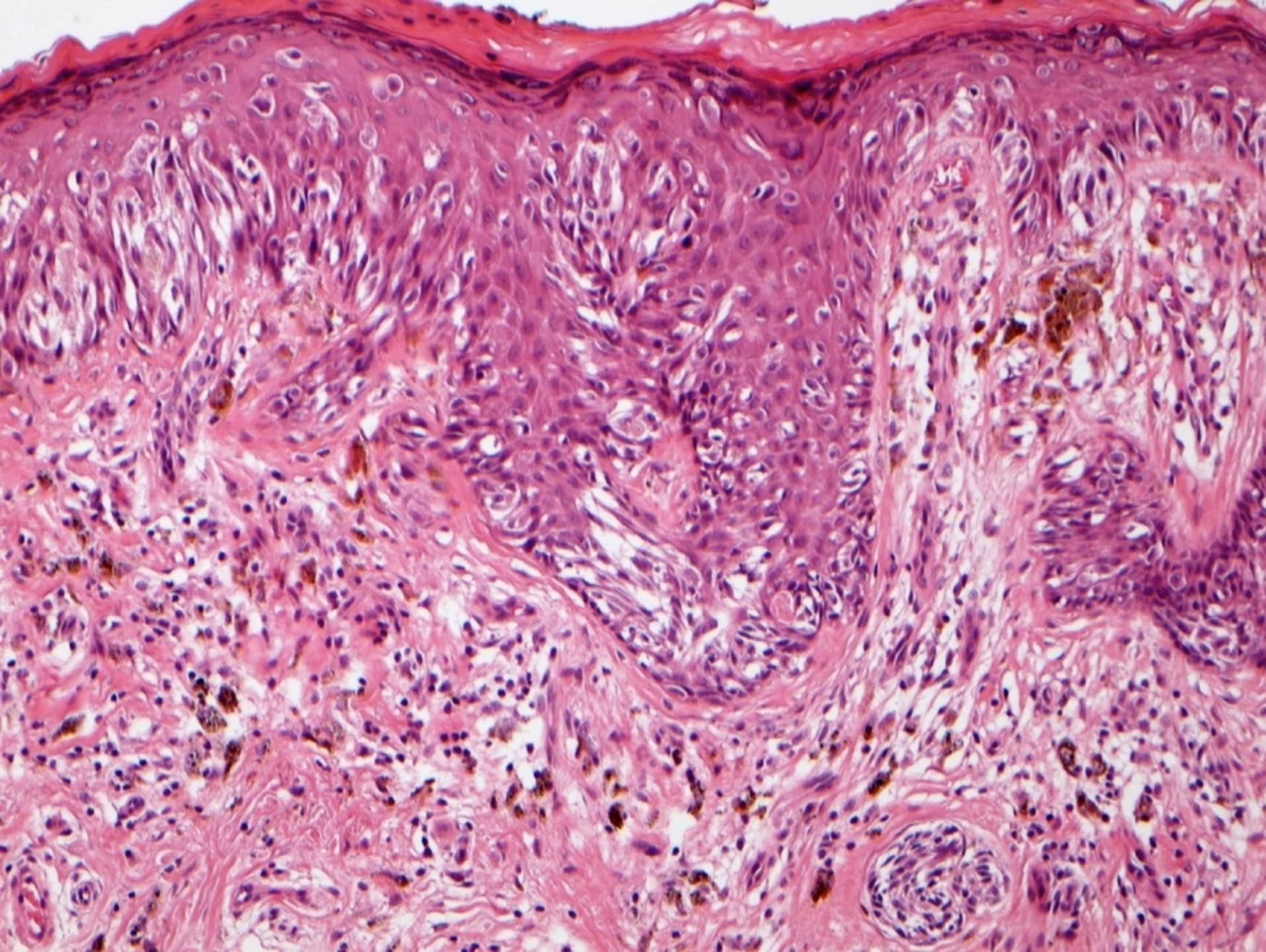


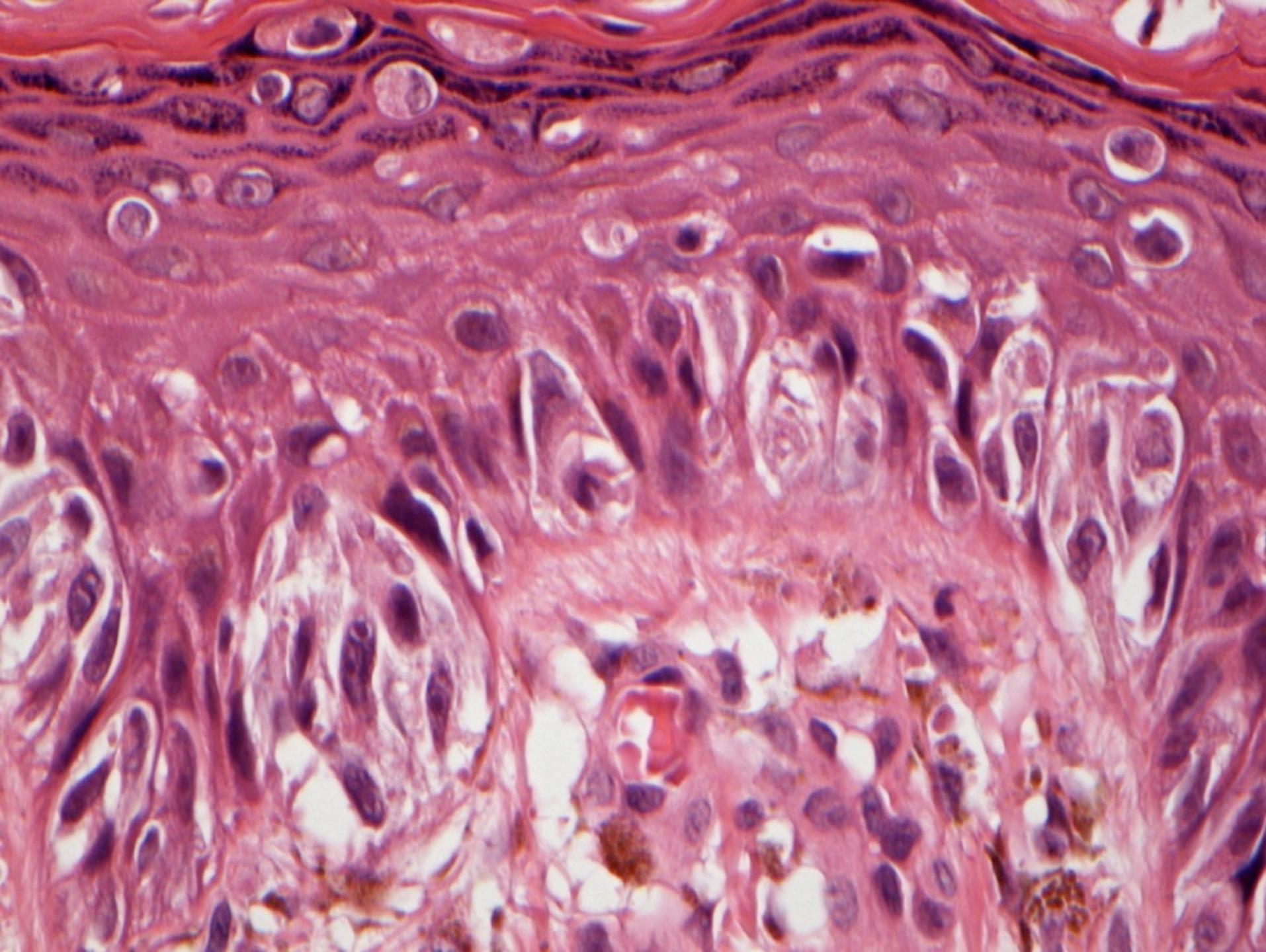


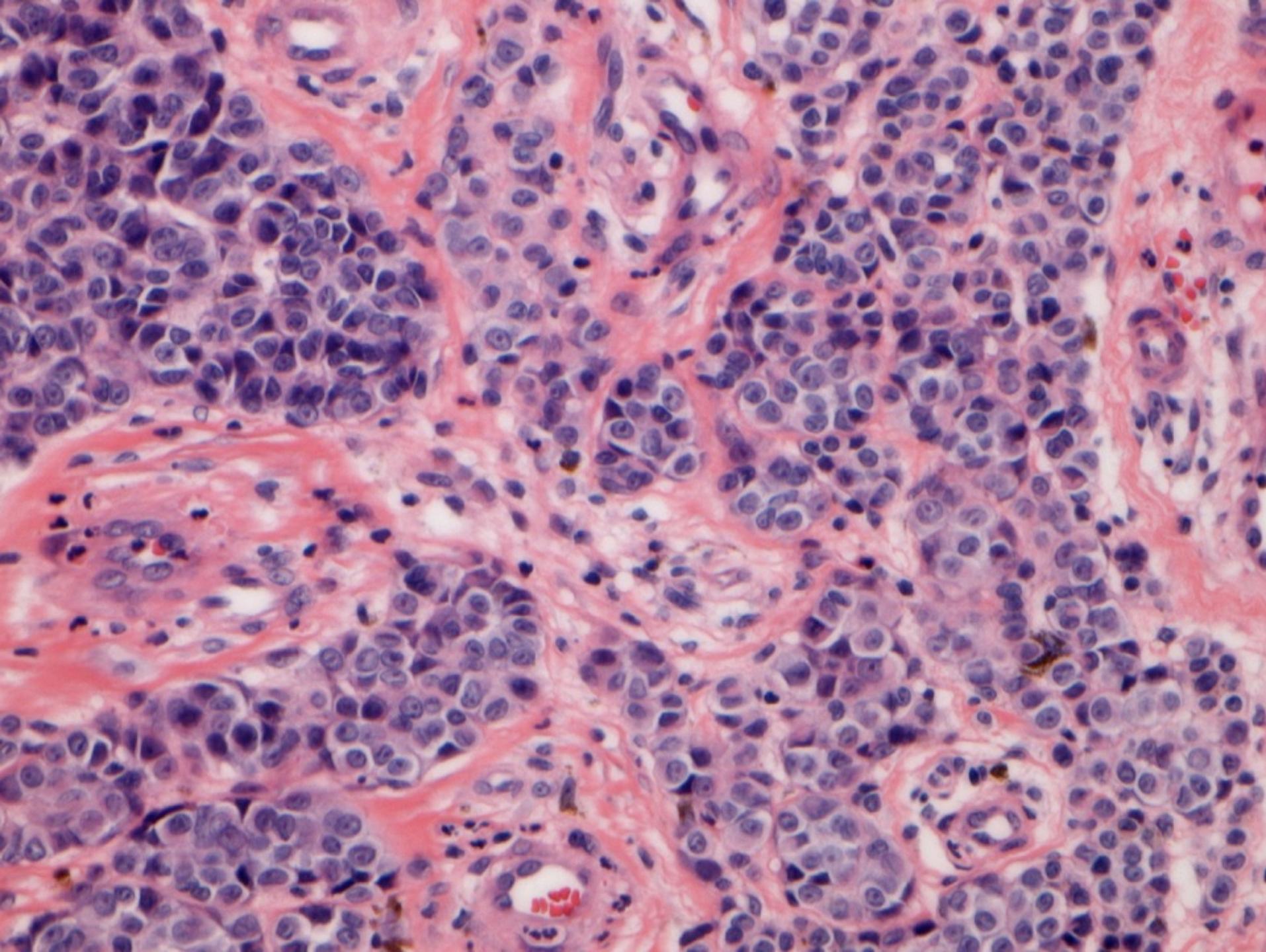
Superficial Spreading Melanoma

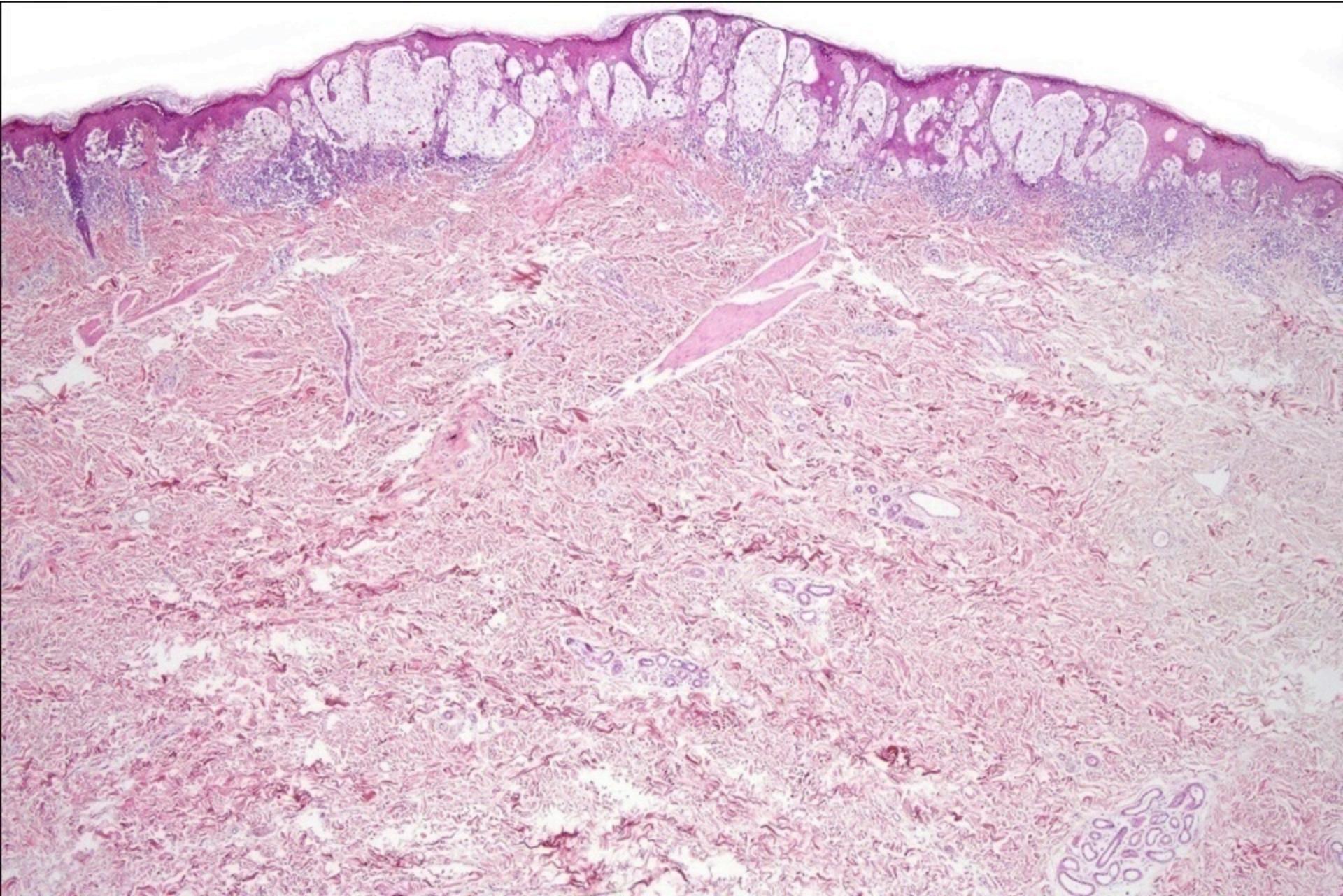


17 year old female, enlarging and changing 7 mm plaque on lower abdomen

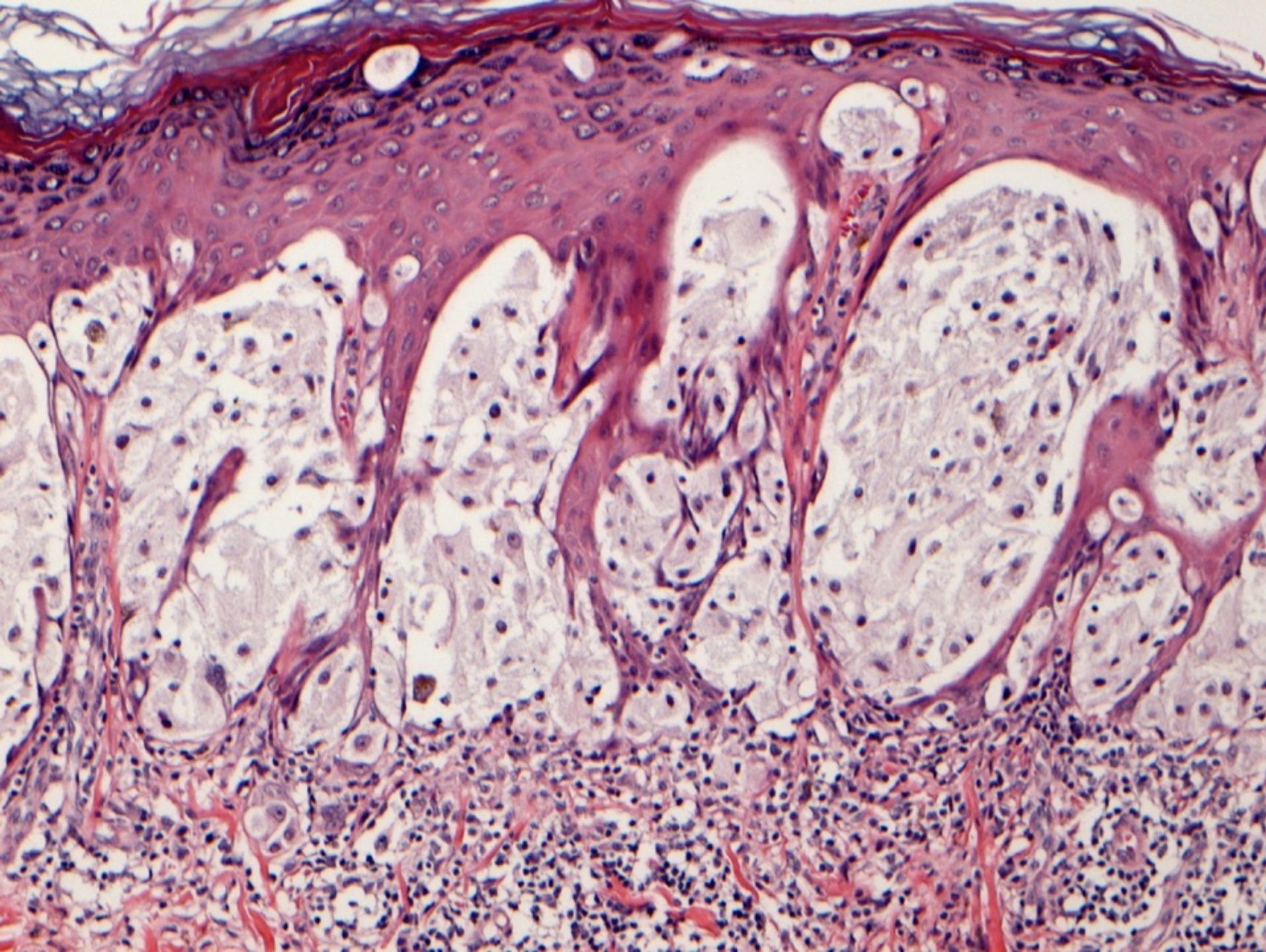


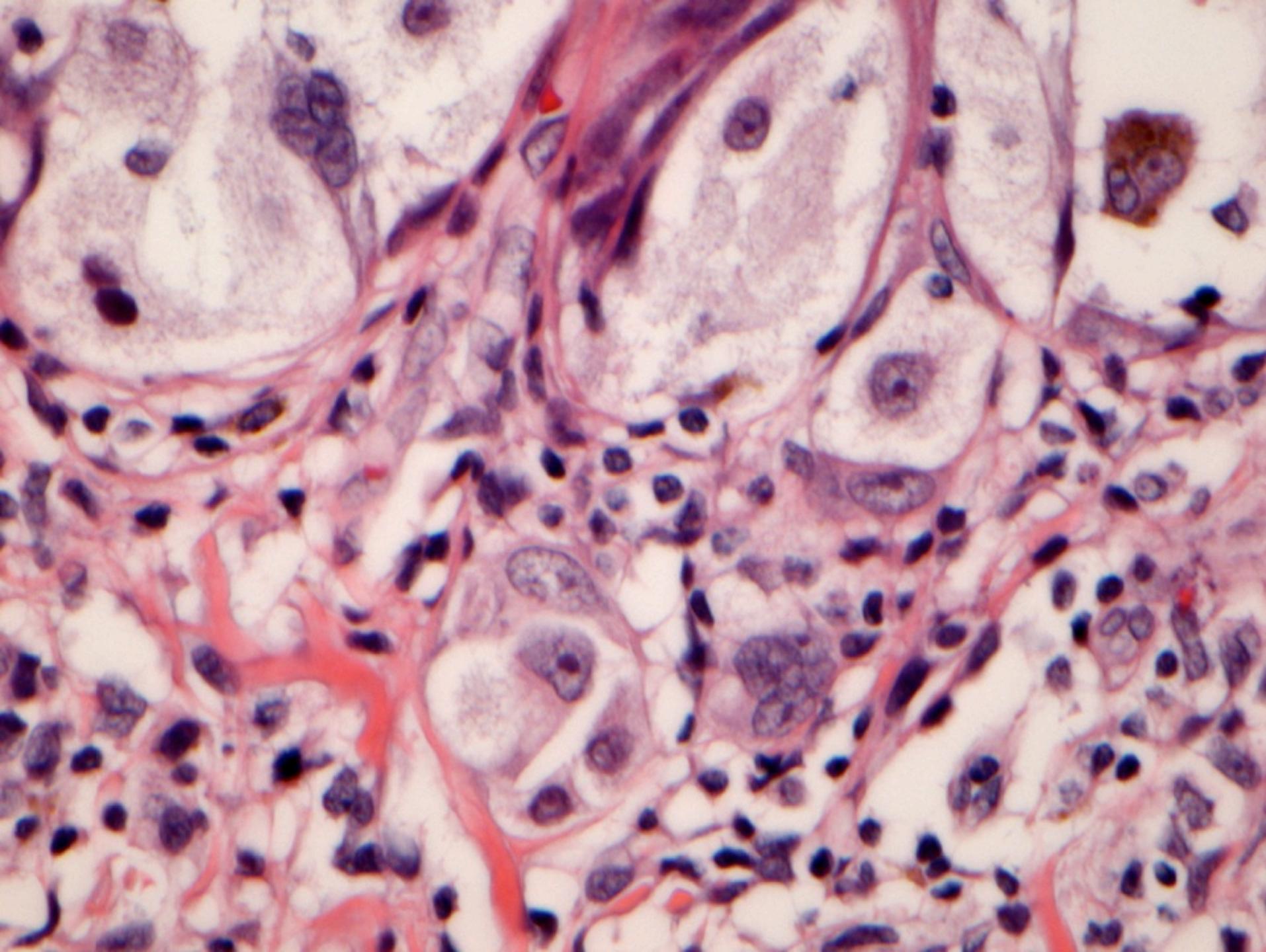




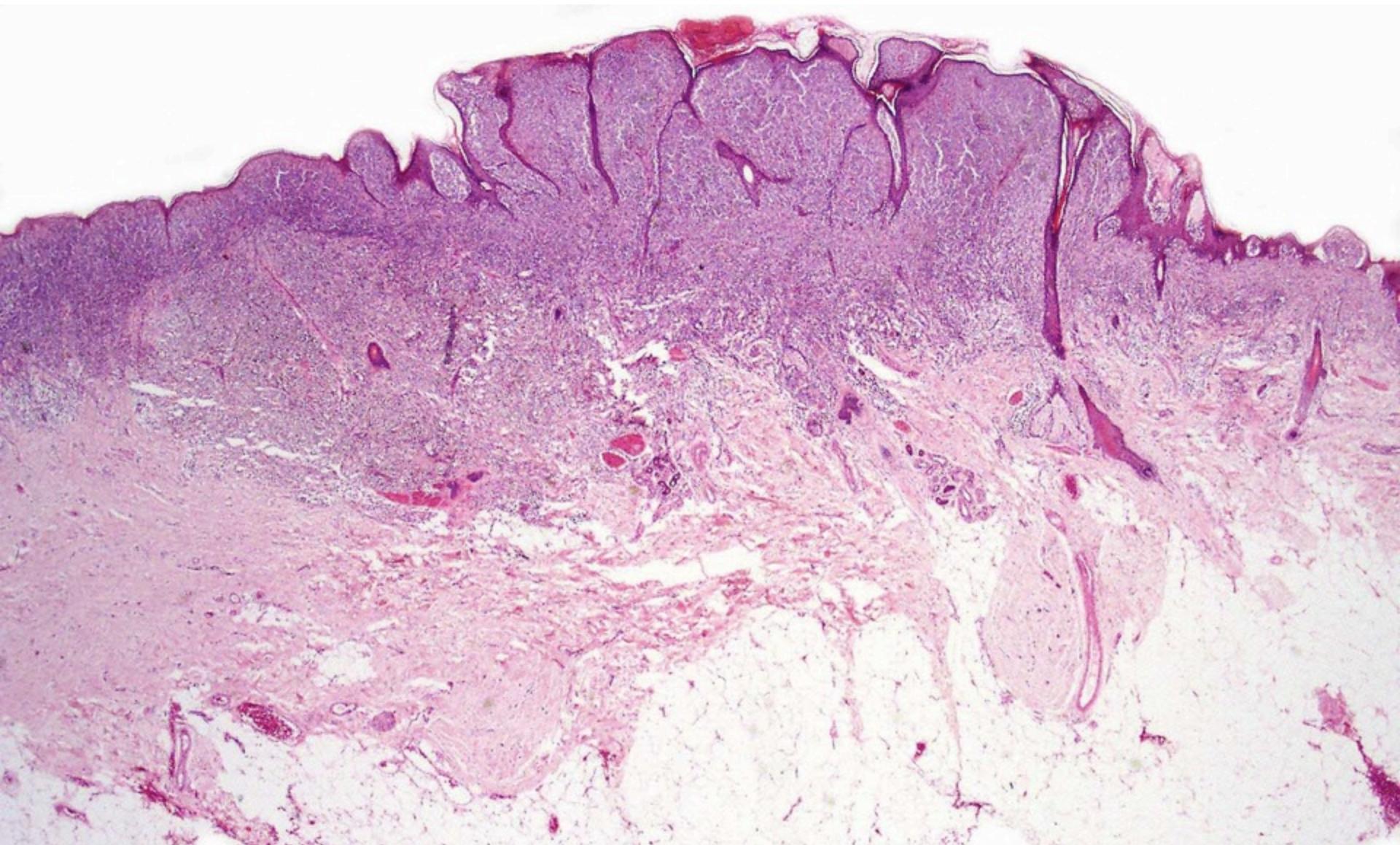


17 year old male with an enlarging warty, brown right leg lesion

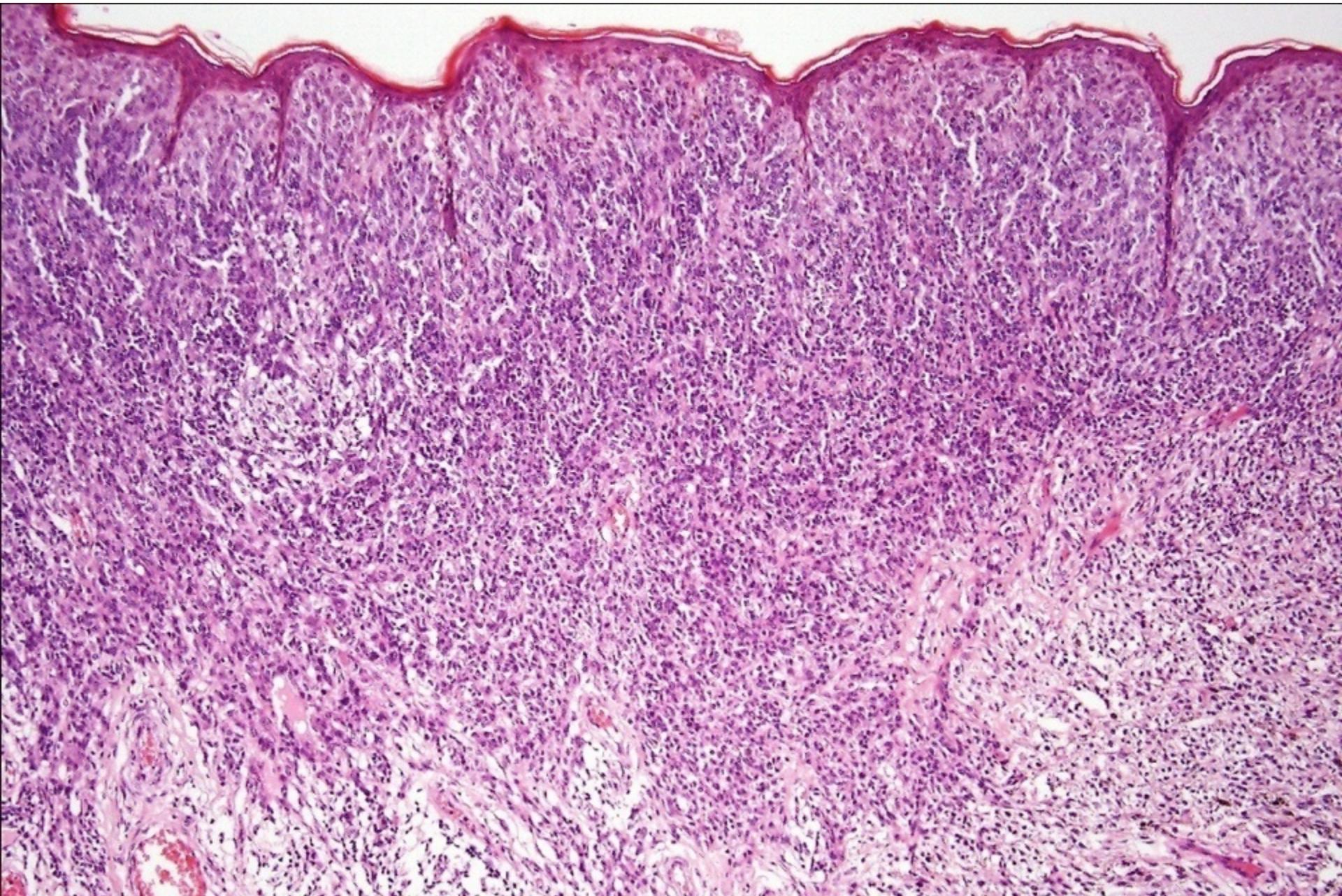


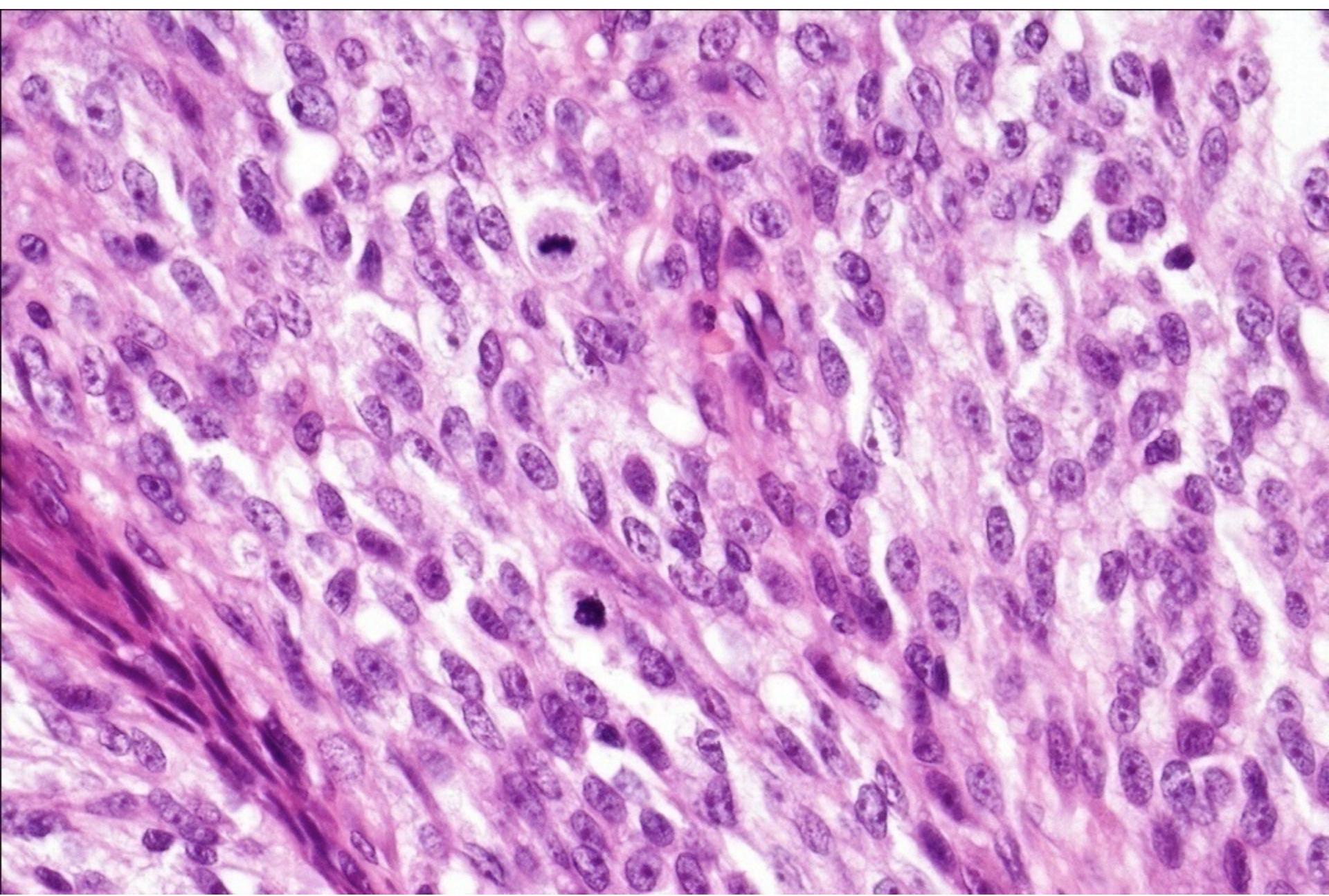


Naevoid Melanoma

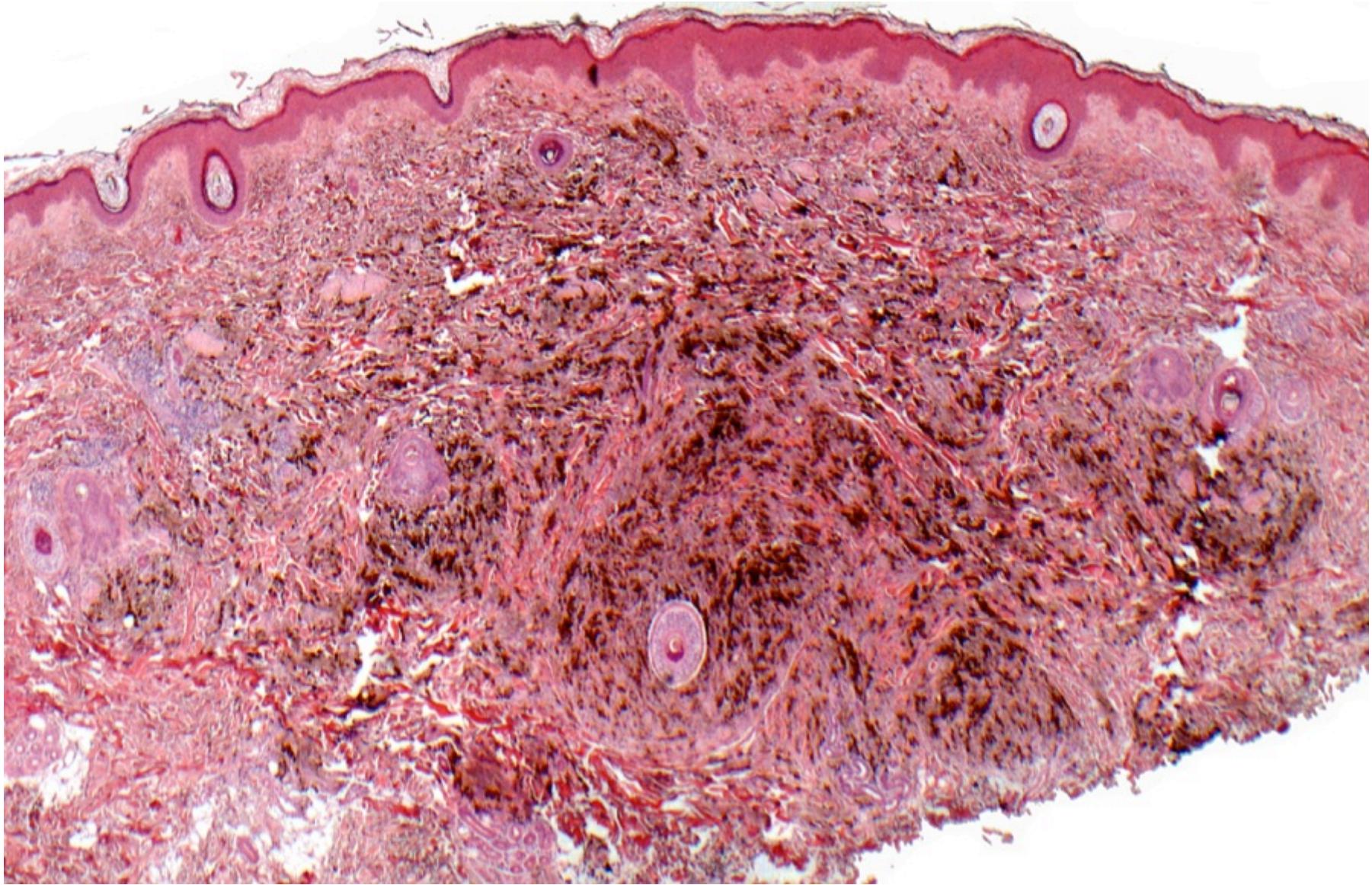


8 year old male with a long standing and recently changing mole on the right cheek

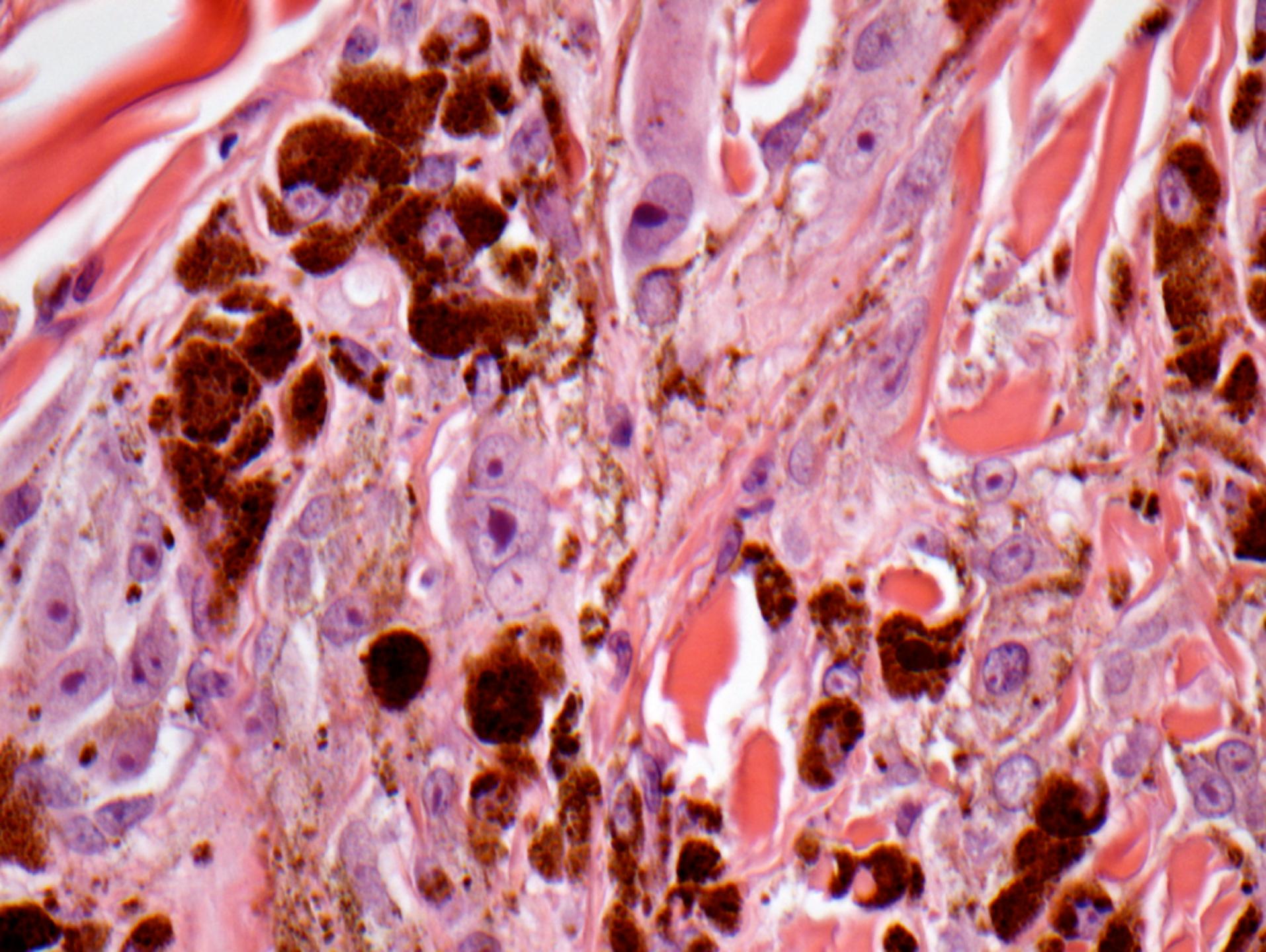




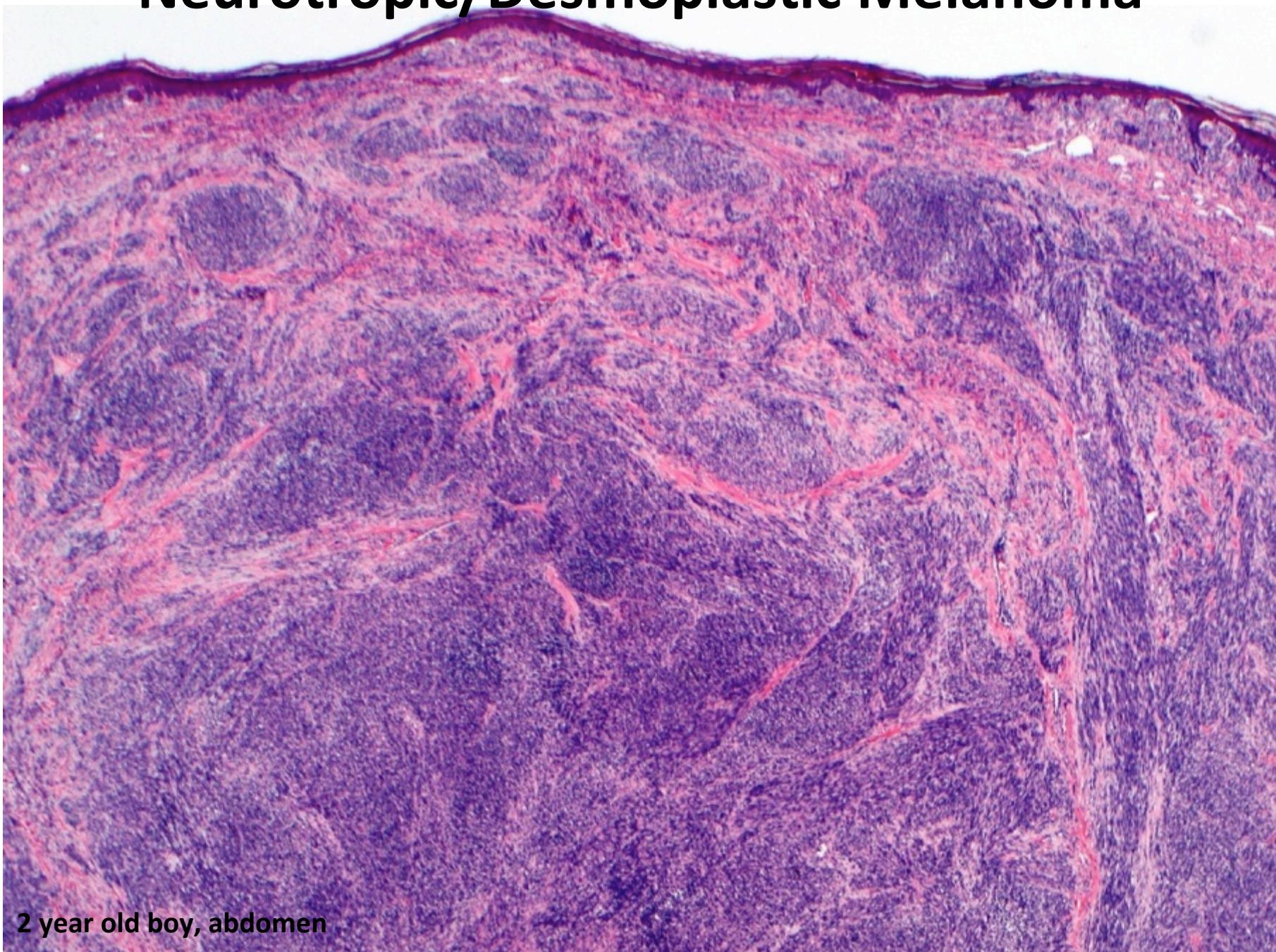
Pigment Synthesizing Melanoma



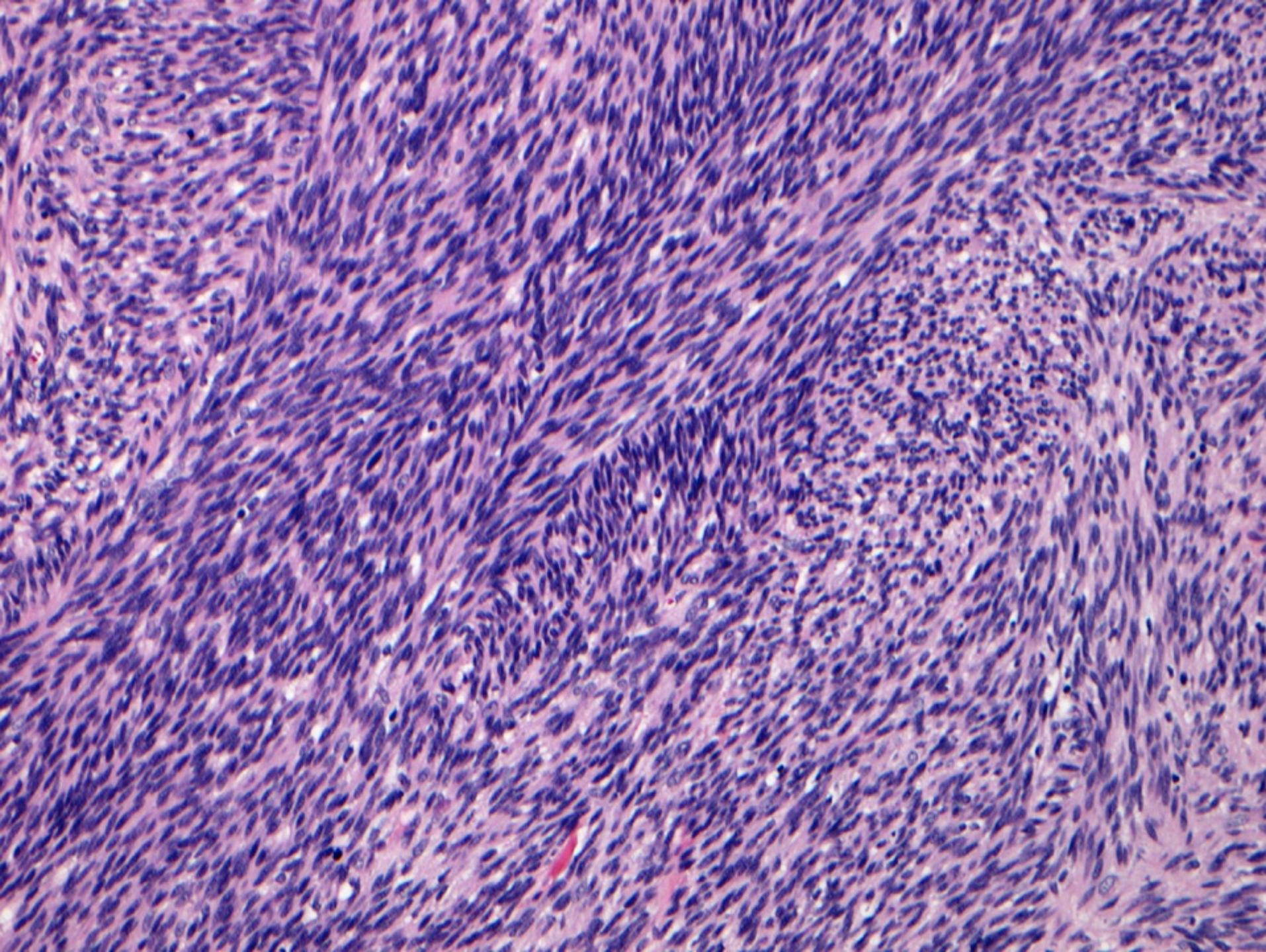
9 year old boy with a pigmented lesion on the left superior deltoid area

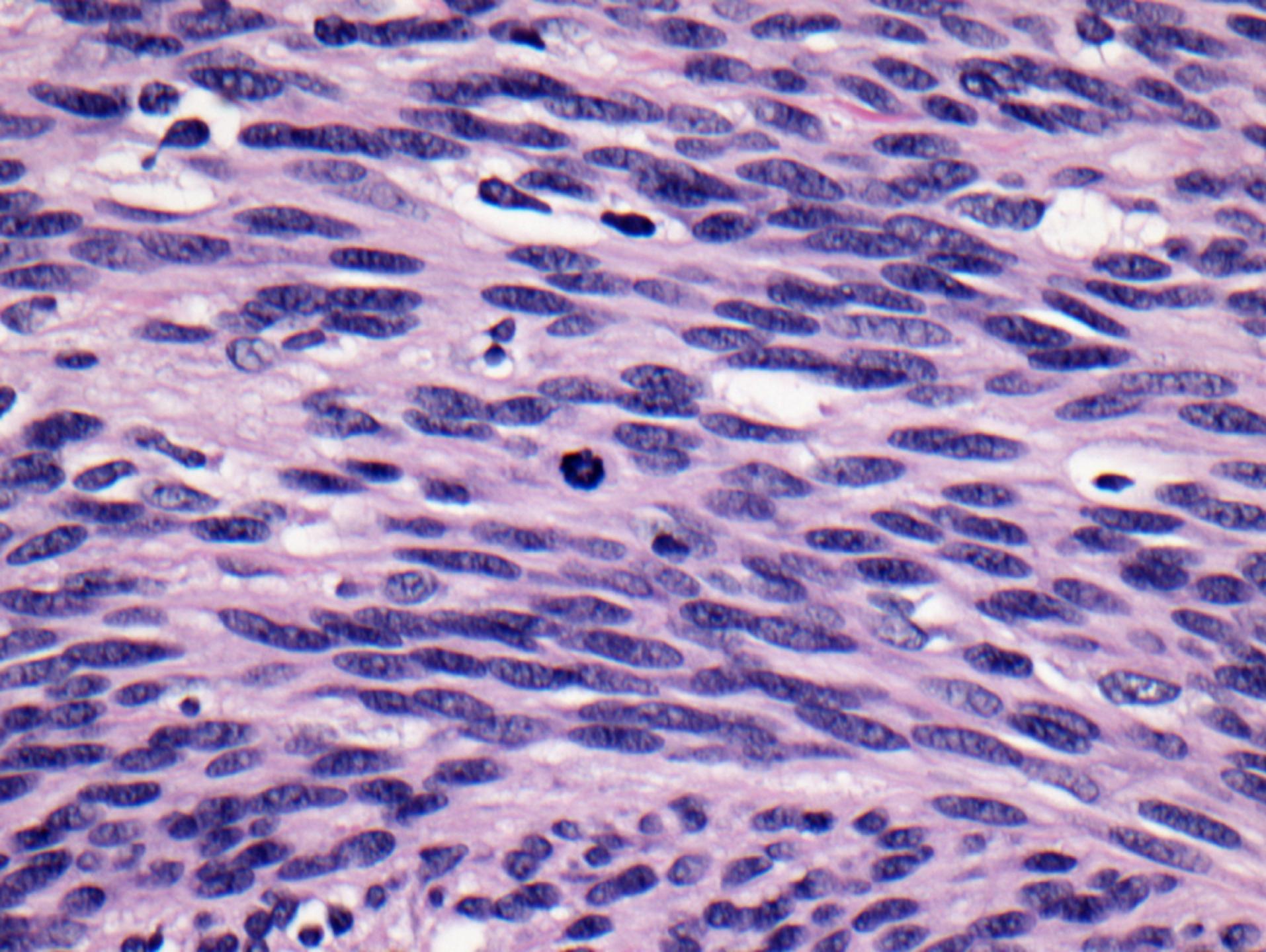


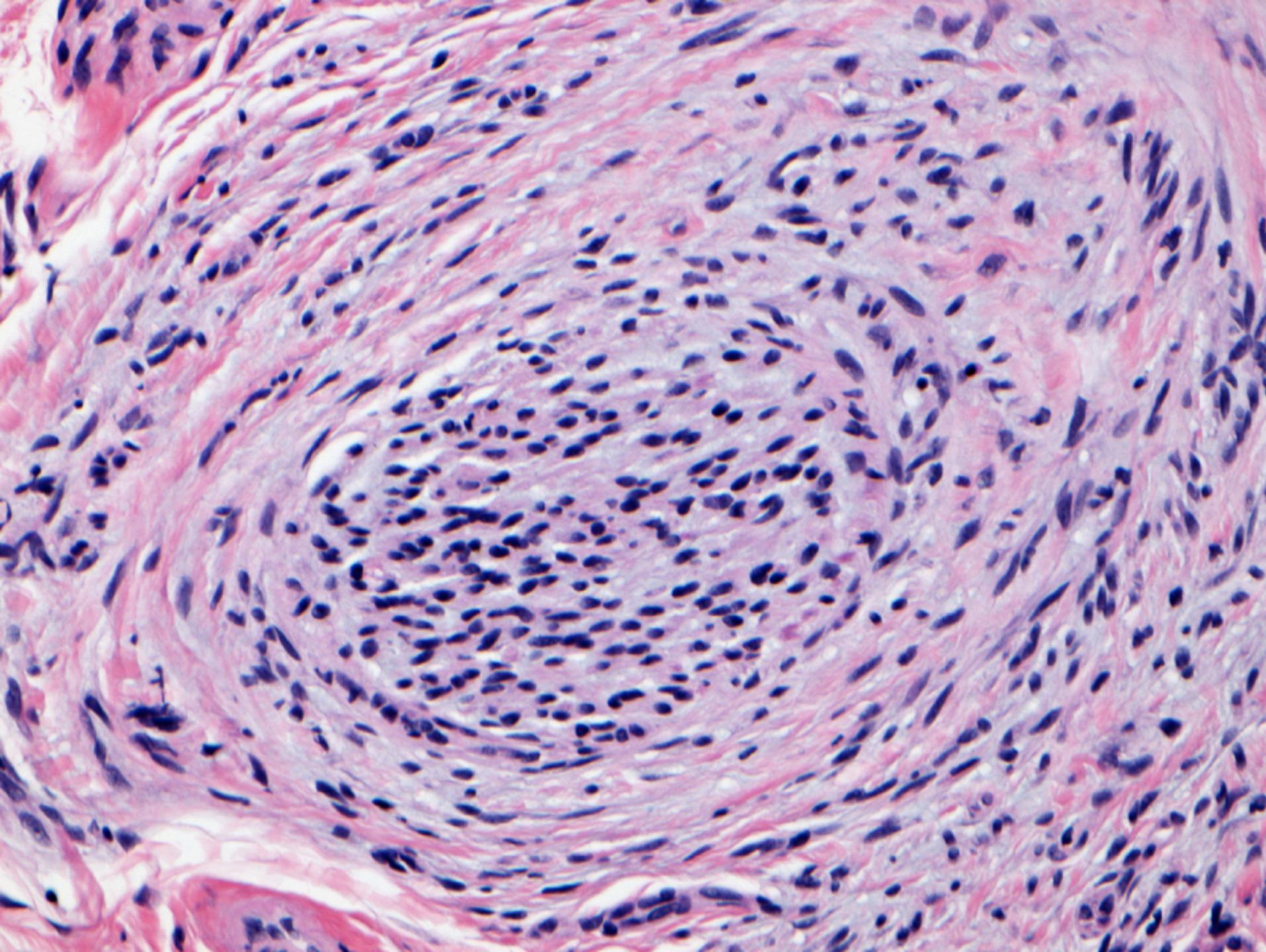
Neurotropic/Desmoplastic Melanoma



2 year old boy, abdomen







Melanoma in Childhood and Adolescence

-Prognostic Factors and Outcome-

- Behaviour of childhood melanoma is controversial and topic of ongoing debate
- Problems:
 - Lack of firm diagnostic criteria
 - Age cut-off
 - Small series
 - Lack of histological review

Behaviour

-Clinical Follow-up

46/64 patients (72%)

Interval: 2-139 months; median: 24 months

- Metastasis: 18 patients (39%)
- LN metastasis: 15 patients (33%)
- SLN metastasis: 8/18 patients (44%)
- Distant metastasis: 7 patients (15%)
- Mortality: 6 patients (13%)

Results

	Disease-related Mortality
n	6
age (yrs)	7mo – 17yrs; median: 12 yrs
gender	M:F = 2:1
site	H&N>E>T
type	Nodular
association	Large CN (n=2)
thickness	2.8-12mm; median: 6 mm
ulceration	4/6
necrosis	2/6
mitoses	18/mm ²
metastasis	6/6
visceral met	5/6

Results

	Nodular M	Sp M	PSM	SSM	Nevoid M
n	21	21	3	12	4
age (yrs)	11	10	9	16	16
site	H&N>E>T	E>H&N>T	H&N	E>T	E>T
thick (mm)	4.0	3.7	3.4	1.0	1.1
ulceration	50%	24%	nil	0.8%	nil
necrosis	25%	nil	nil	nil	nil
mitoses	6.5/mm ²	5/mm ²	1/mm ²	1/mm ²	2.5/mm ²
LN met	57%	24%	100%	nil	30%
Dist met	50%	nil	nil	nil	nil
mortality	40%	nil	nil	nil	nil

Melanoma in Childhood and Adolescence

-Prognostic Factors and Outcome-

Biologically heterogeneous disease

Wide histological spectrum

- **SSM and naevoid melanoma**
 - Presentation in adolescence
 - Extremities and trunk
 - Thin melanomas with favourable outcome

Melanoma in Childhood and Adolescence

-Prognostic Factors and Outcome-

- Nodular Melanoma, Spitzoid Melanoma and Pigment Synthesizing Melanoma
 - Younger age at presentation
 - Head and neck location

But

- Tumours with Spitzoid morphology and pigment synthesis
 - Favourable outcome despite LN metastasis
- Nodular melanoma and melanoma in large CN
 - High risk for disseminated disease and mortality

Melanoma in Childhood and Adolescence

-Staging and Treatment-

- Staging and treatment analogous to adulthood melanoma
- Surgery is mainstay of treatment
- Value of sentinel lymph node biopsy and adjuvant therapy questionable especially in Spitzoid/pigment synthesizing tumours

Melanocytic Lesions in Children

-Conclusion-

- Wide morphological spectrum
- Vast majority benign despite concerning histological features
- Pitfalls:
 - neonatal naevi
 - proliferative nodules
 - Spitzoid tumours
- True melanoma exists even in young children
- It is rare but shows an aggressive clinical course



MANY THANKS!!!!
ANY ??????