

# Atlas Peripheral Neuroblastic Tumors

International Neuroblastoma  
Pathology Committee

Definition  
of  
Peripheral Neuroblastic Tumors

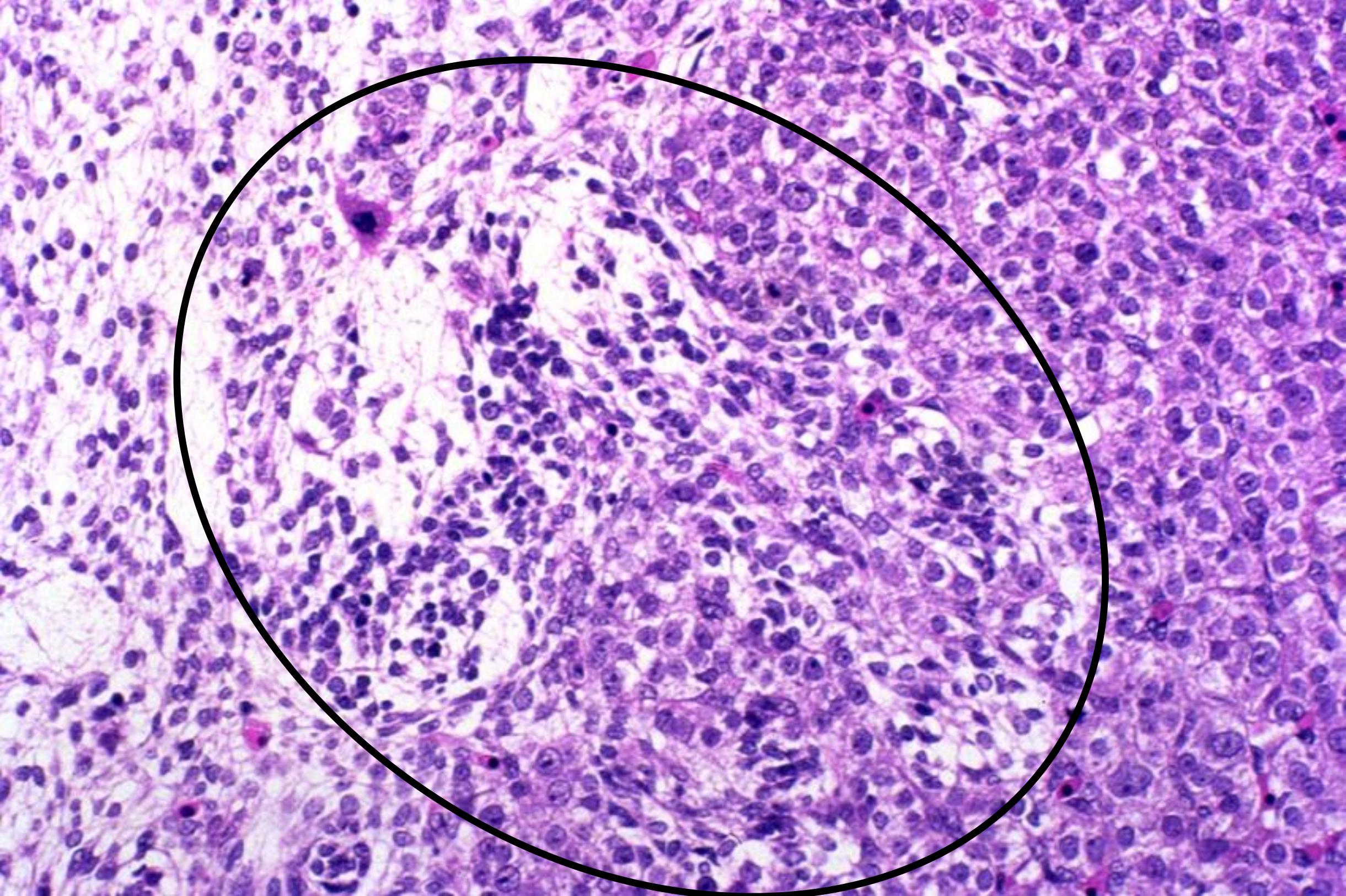
# Embryology

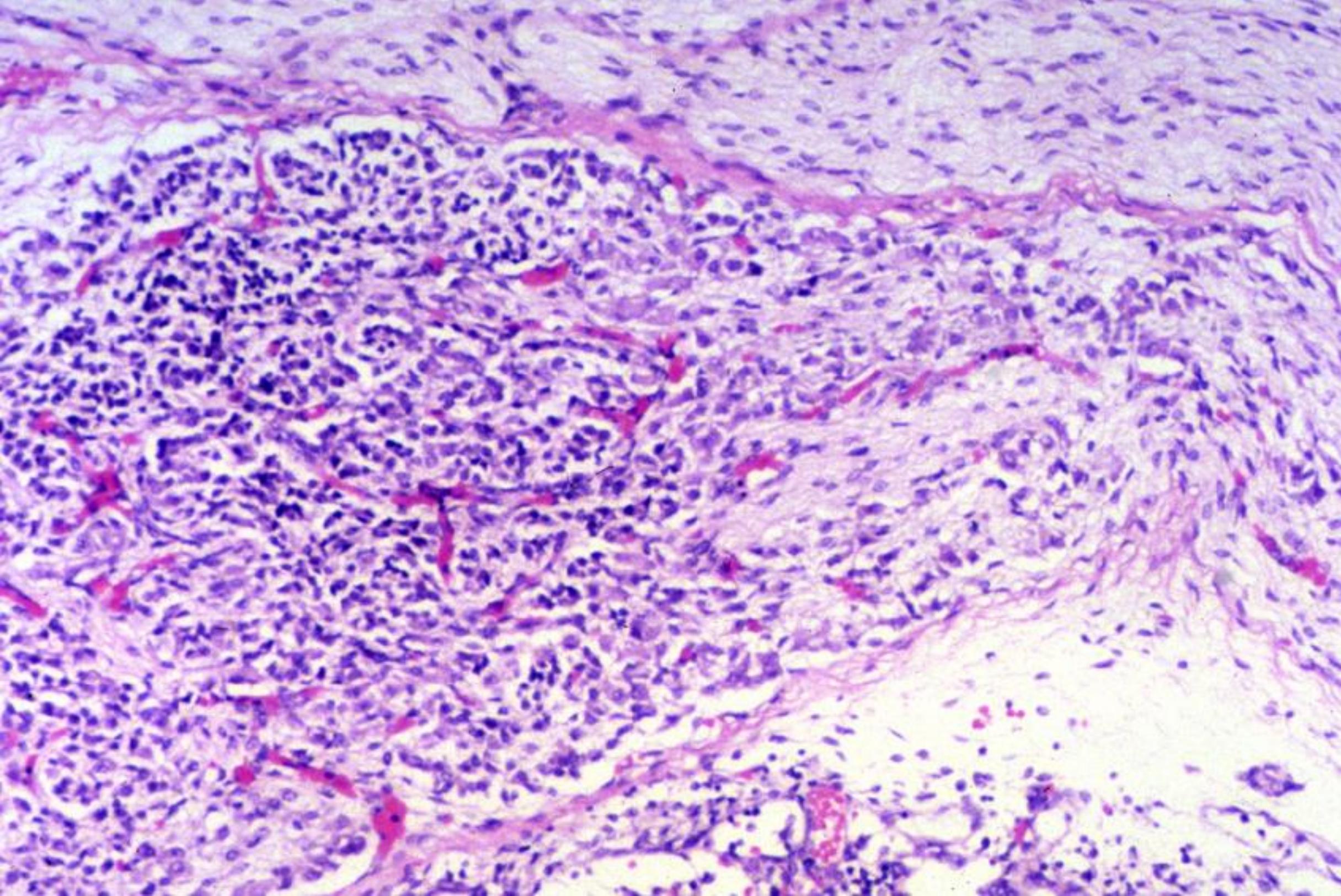
Li

AD

AO

AD





# International Neuroblastoma Pathology Classification

# Four Categories of Peripheral Neuroblastic Tumors

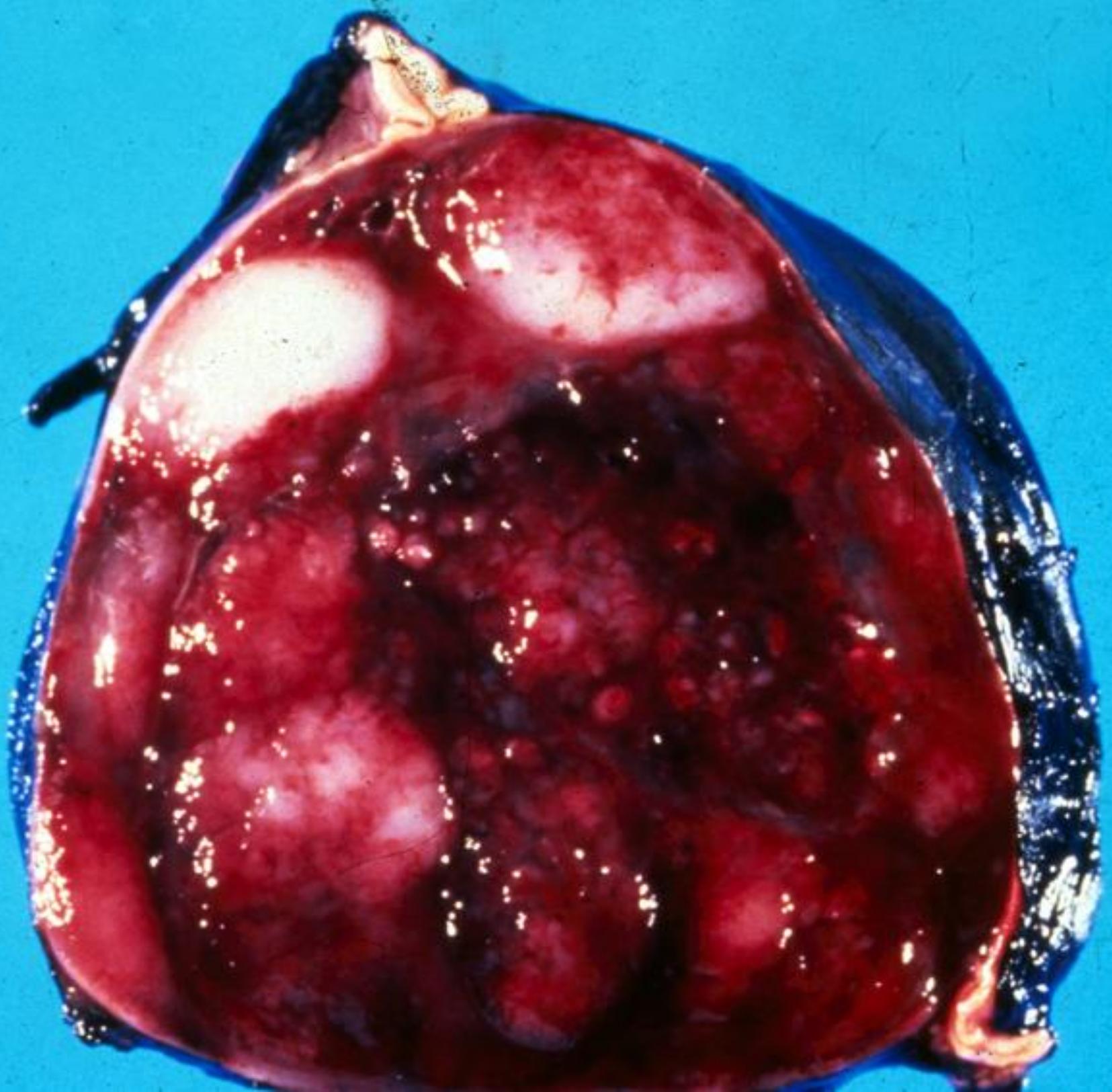
1. Neuroblastoma (Schwannian stroma-poor)
2. Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)
3. Ganglioneuroma (Schwannian stroma-dominant)
4. Ganglioneuroblastoma, Nodular  
(composite, Schwannian stroma-rich/stroma-dominant and stroma-poor)

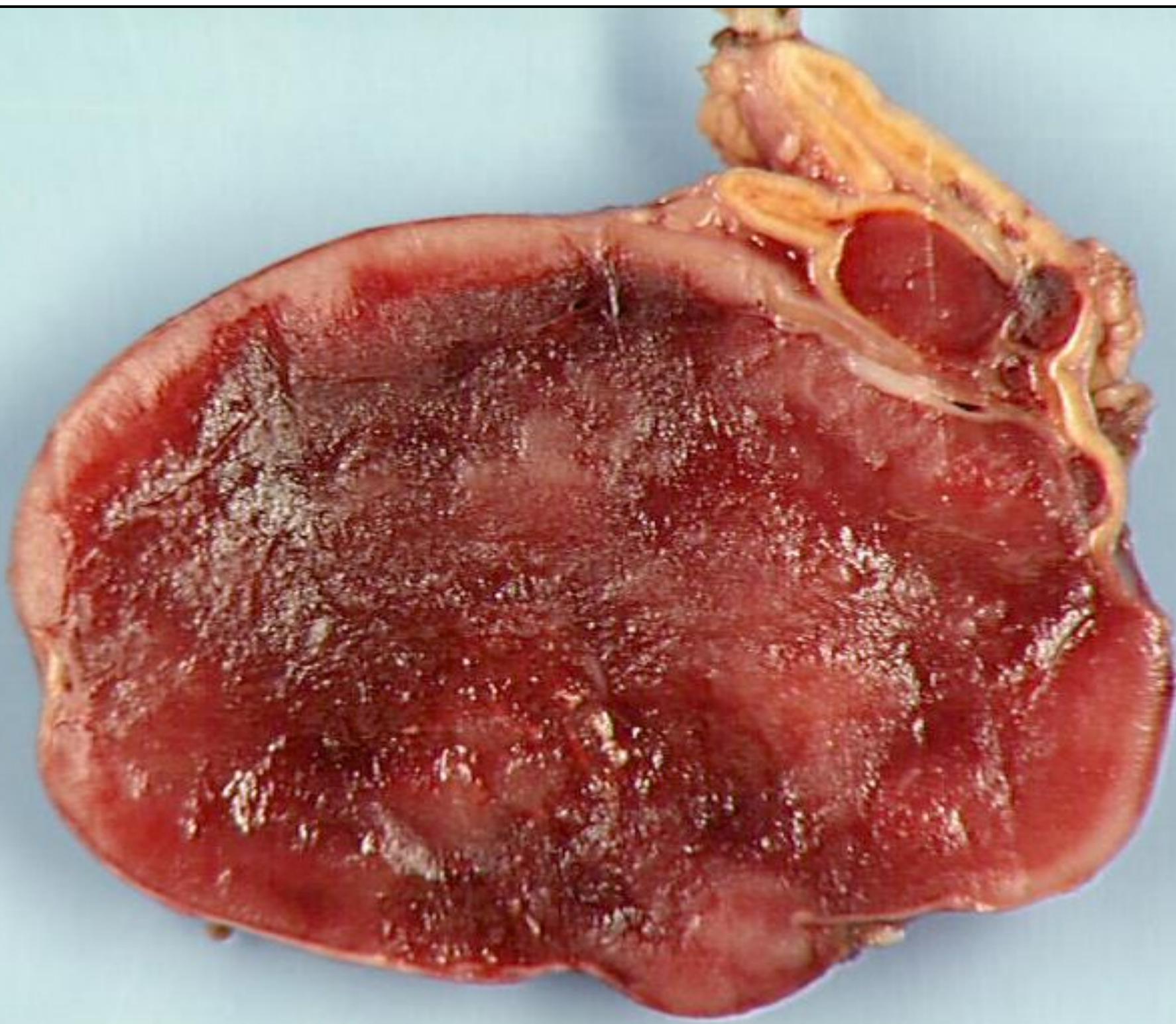
# Neuroblastoma (Schwannian stroma-poor)

Undifferentiated subtype

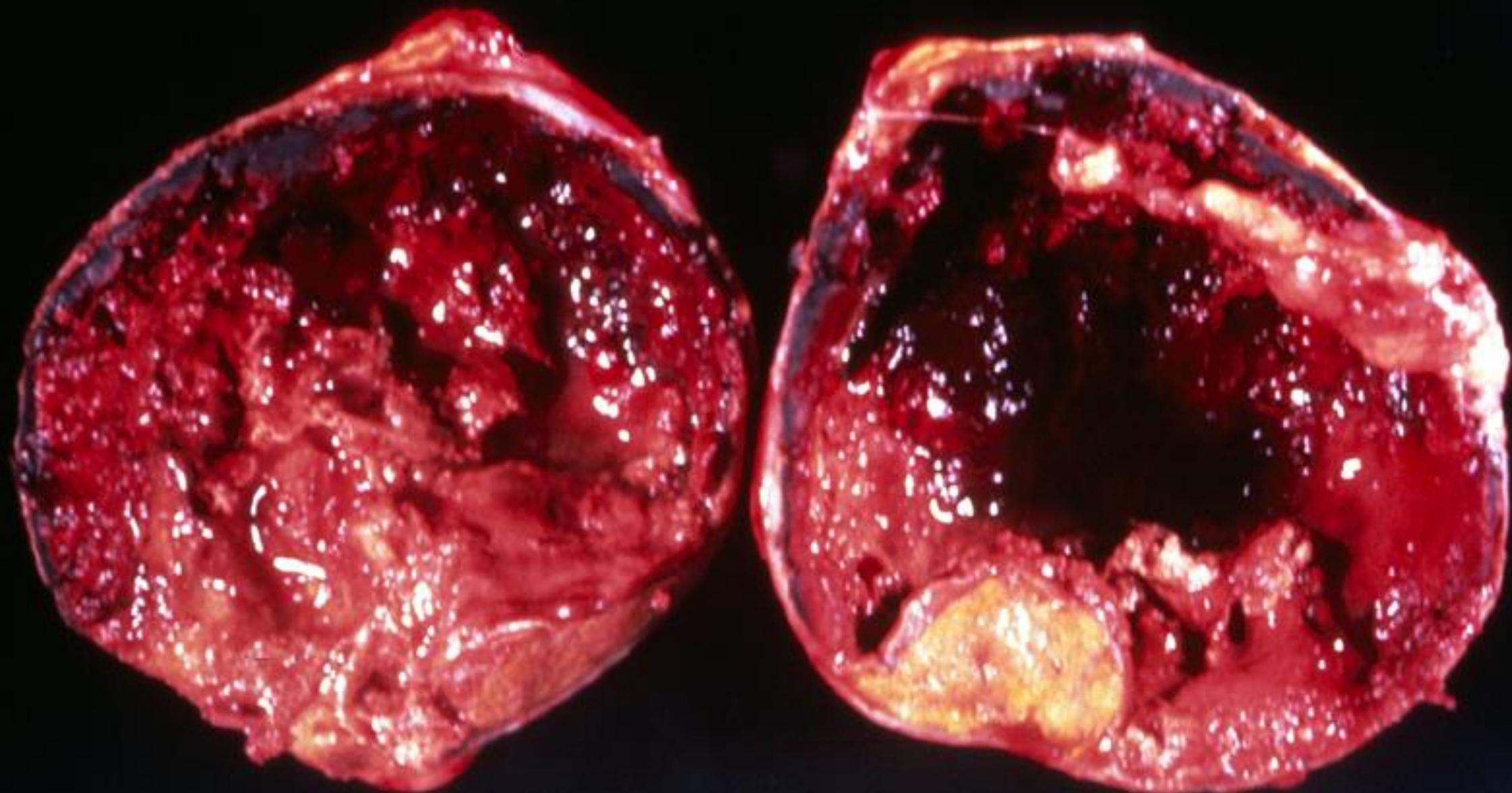
Poorly differentiated subtype

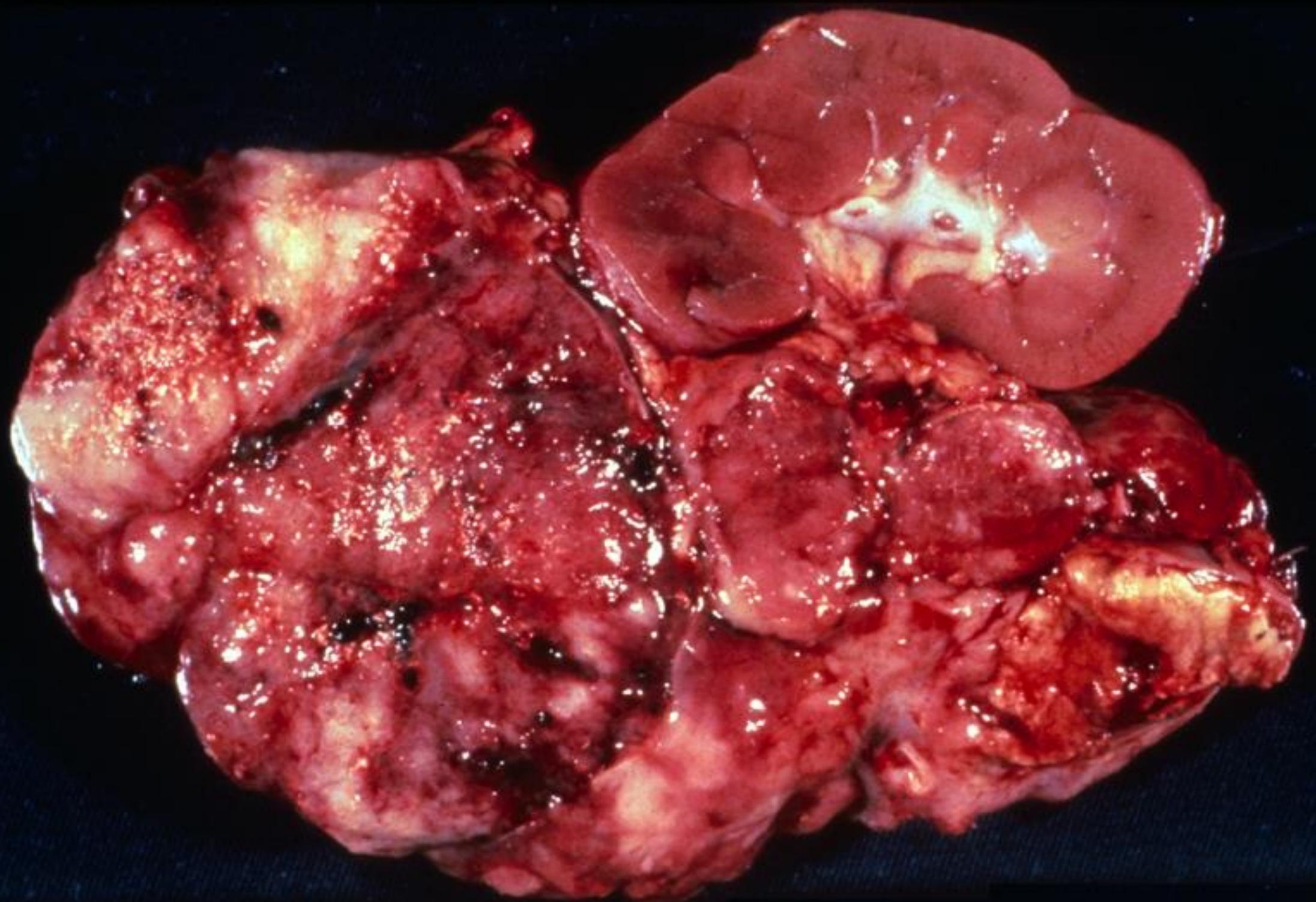
Differentiating subtype





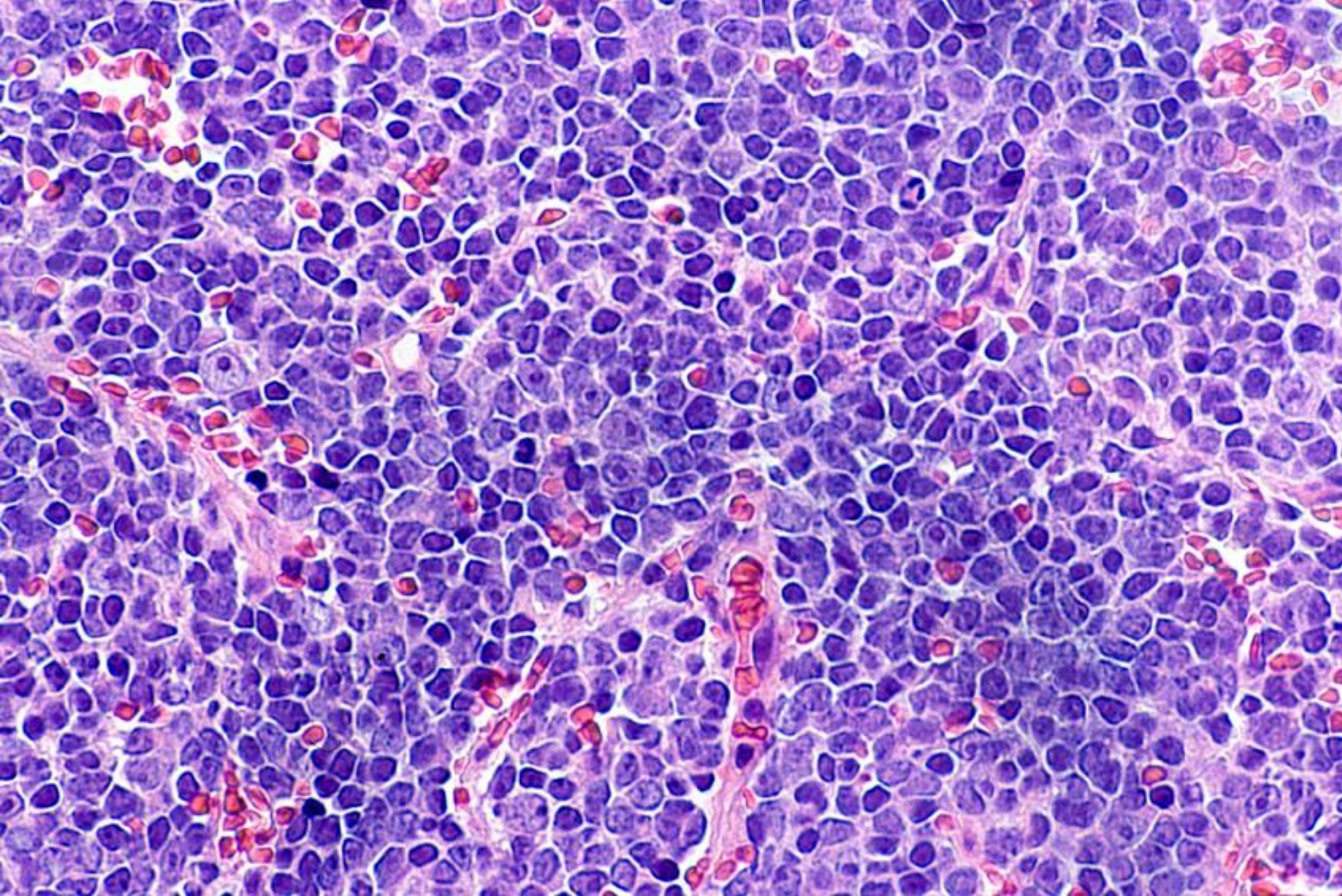


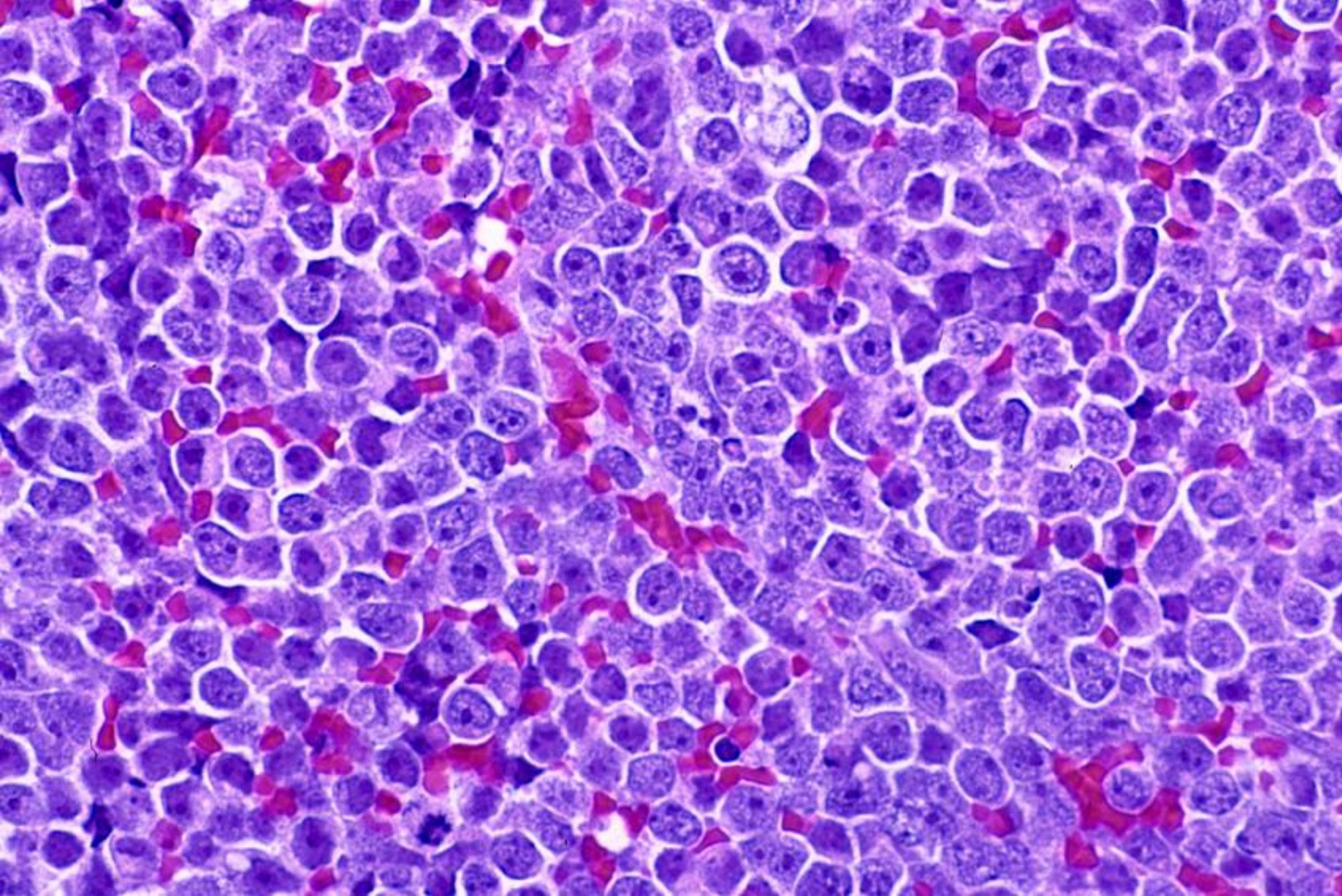


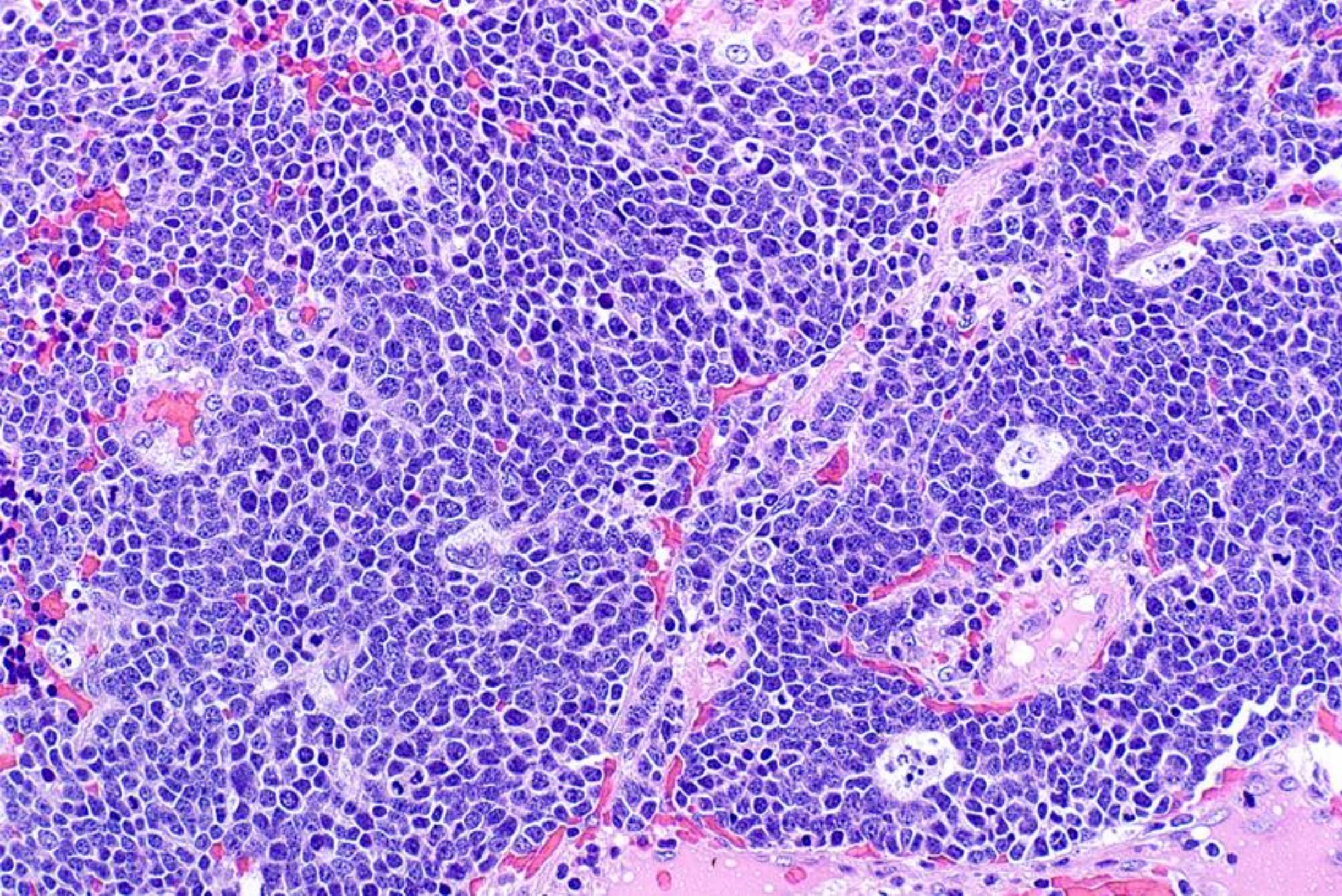


# Neuroblastoma (Schwannian stroma-poor)

Undifferentiated Subtype

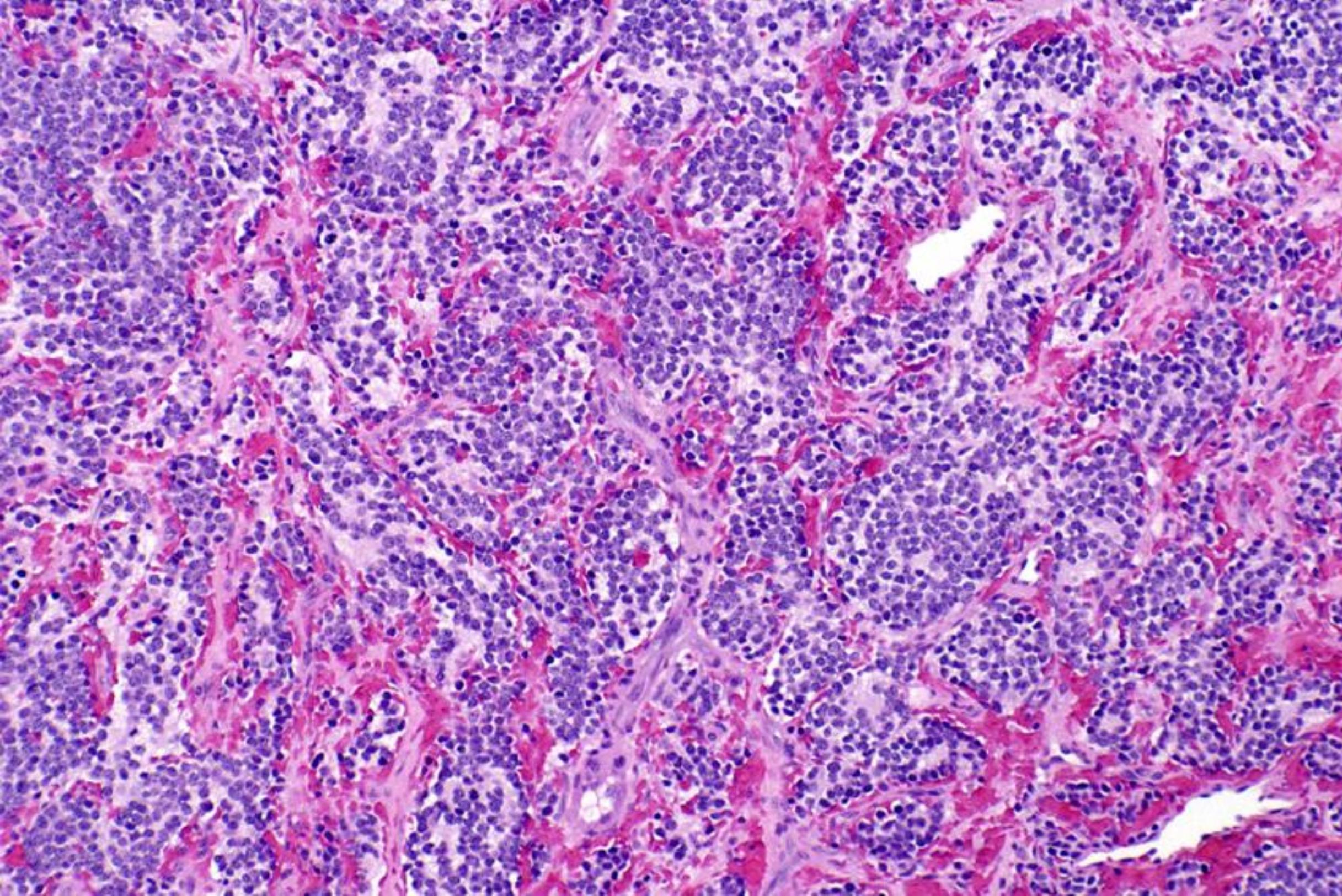


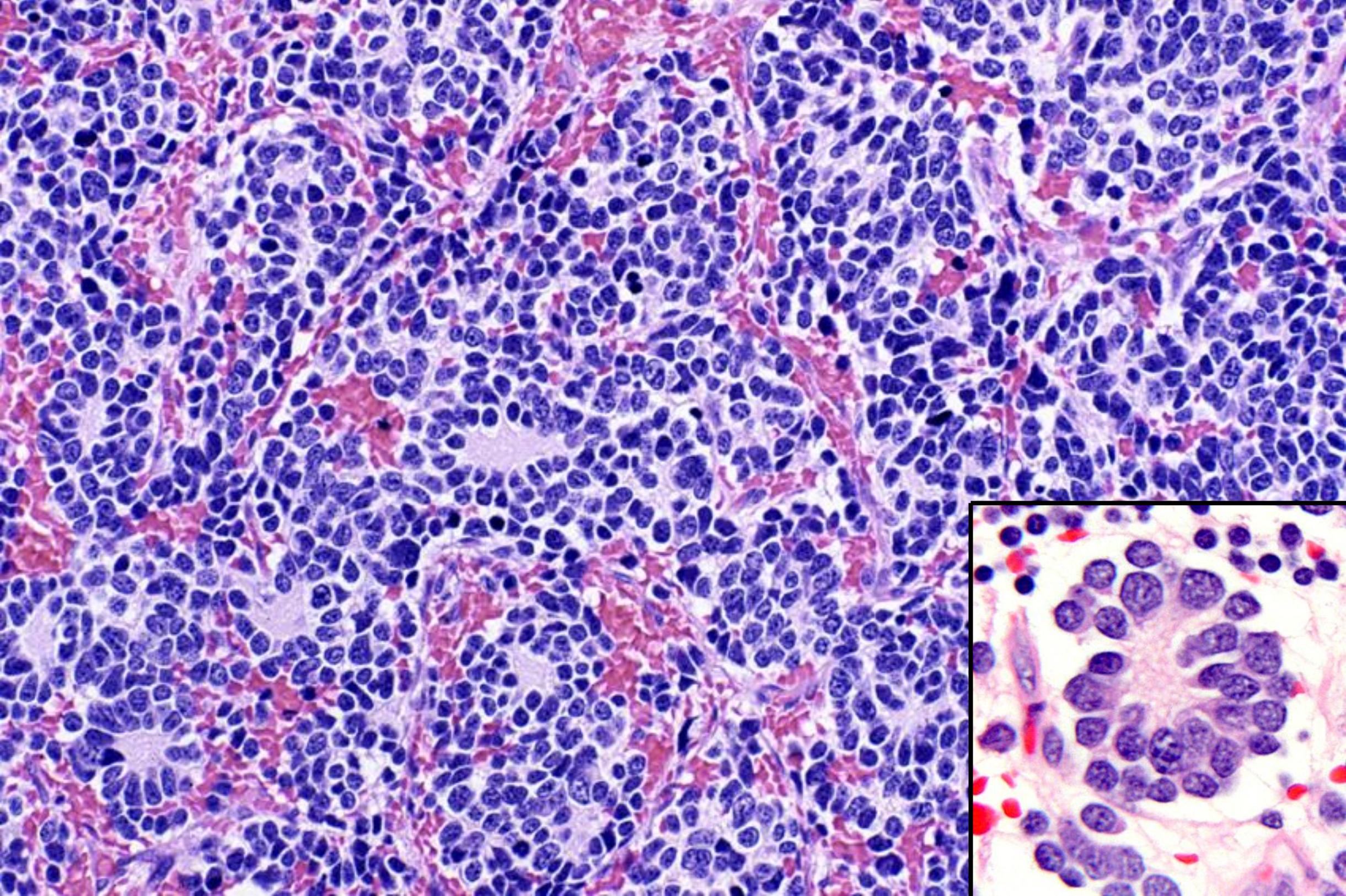


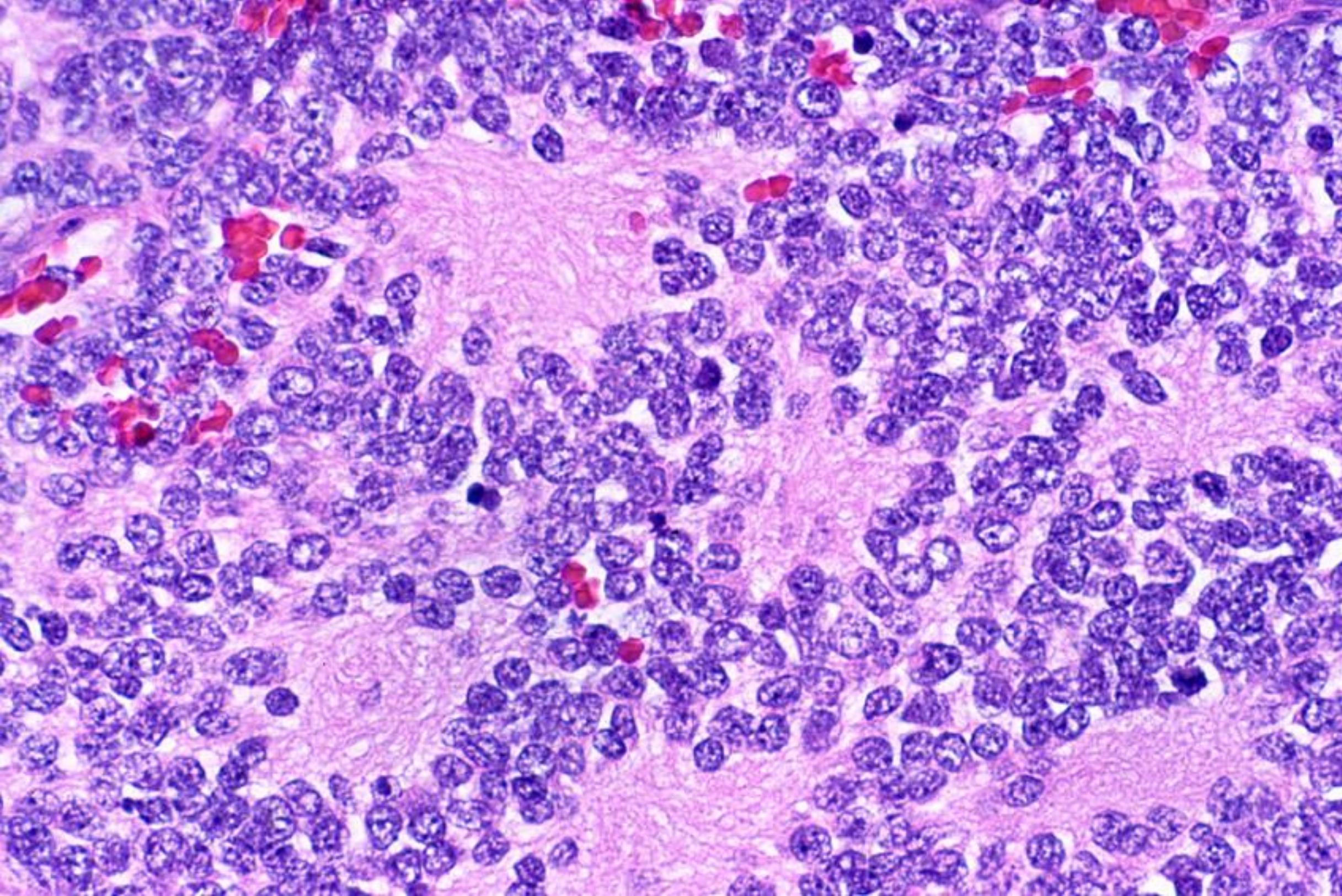


# Neuroblastoma (Schwannian stroma-poor)

Poorly differentiated Subtype

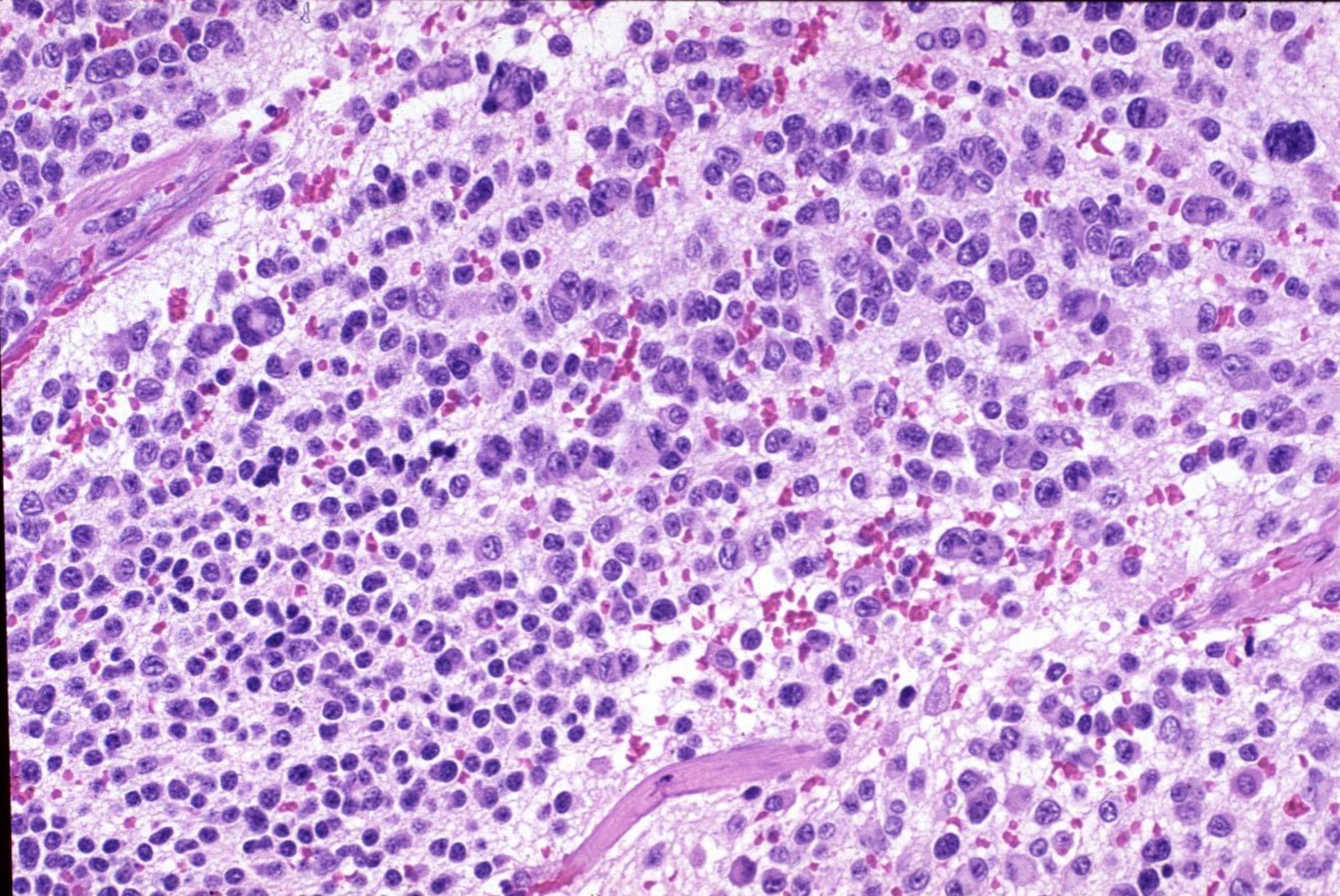


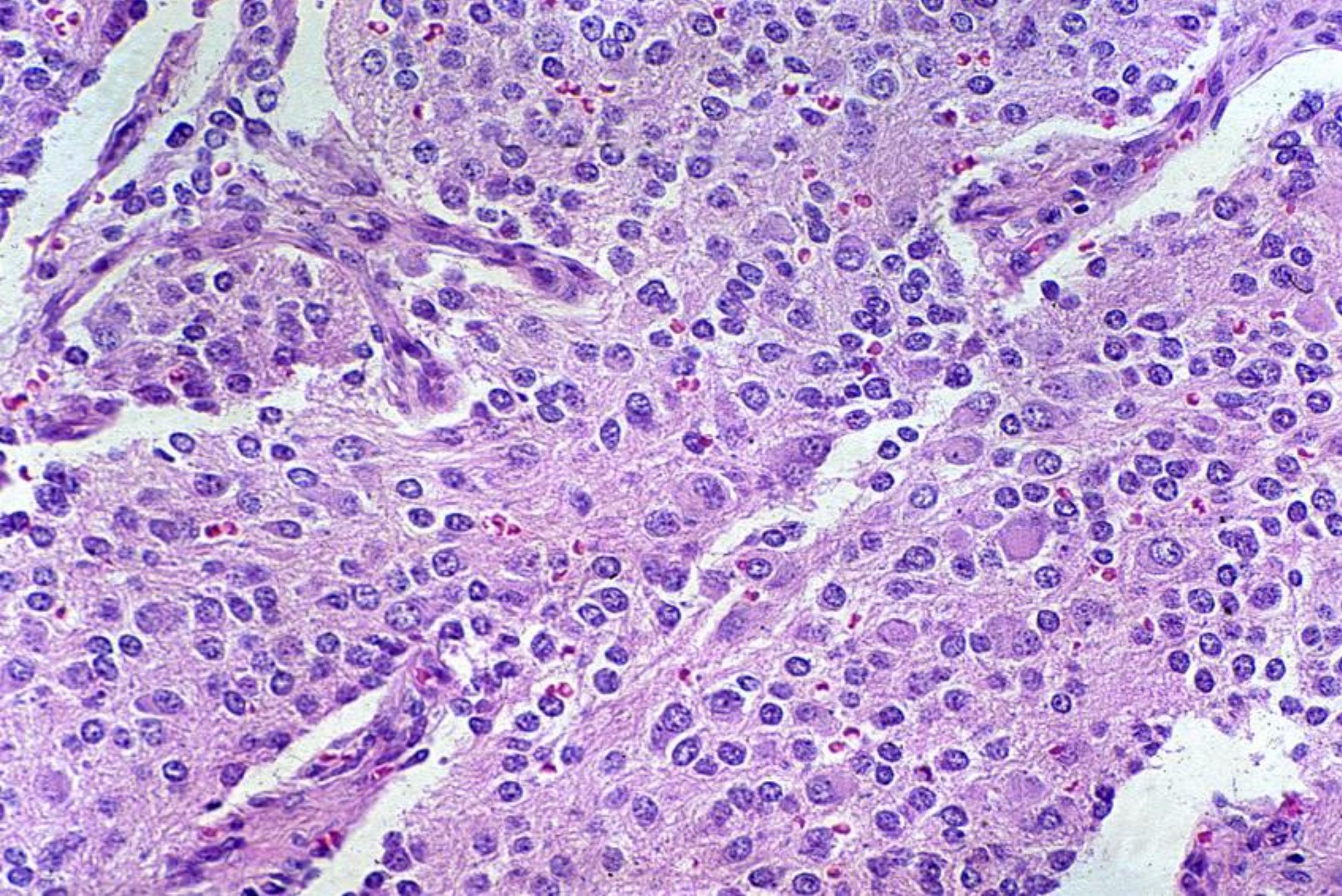




# Neuroblastoma (Schwannian stroma-poor)

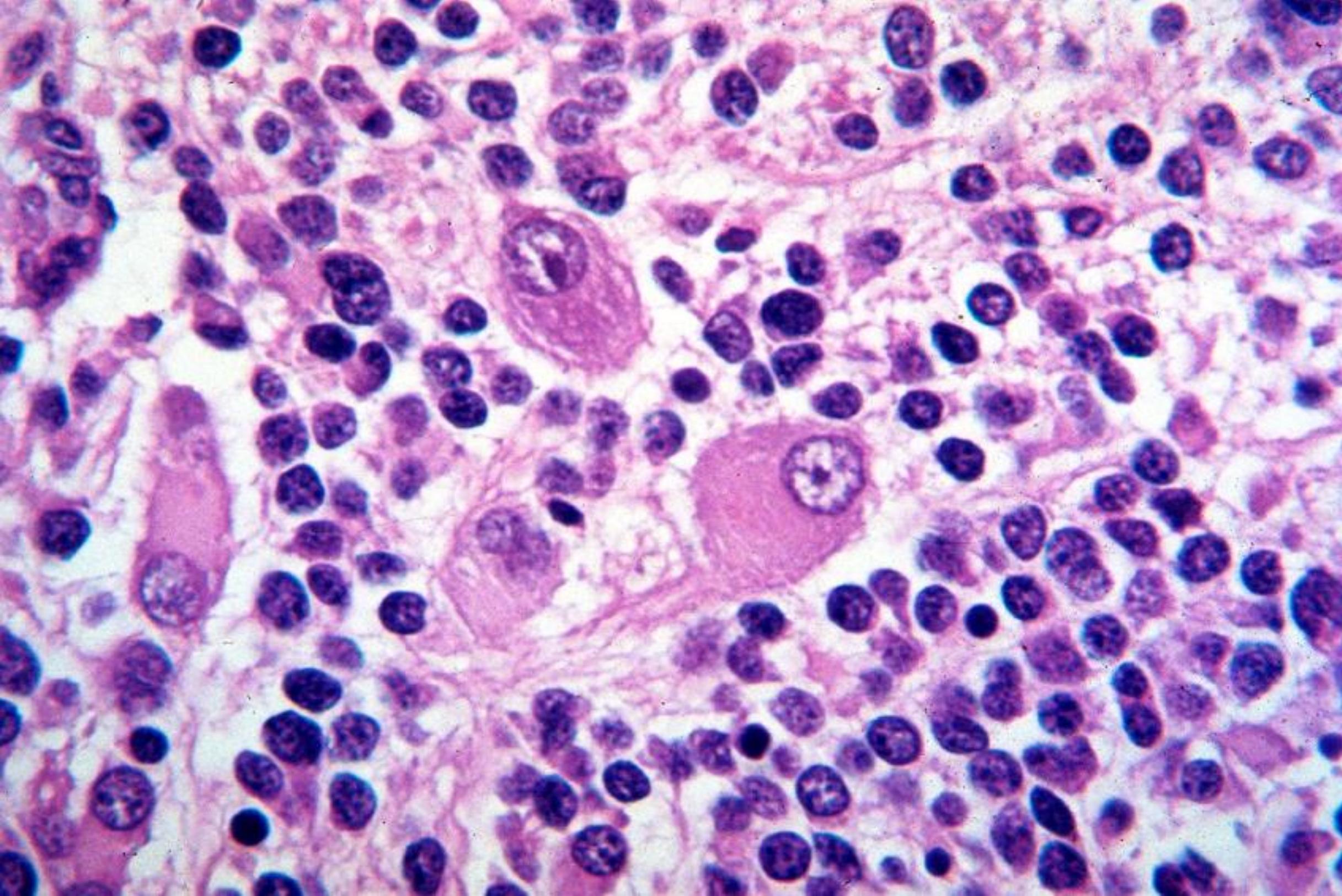
Transition between Poorly  
differentiated subtype to  
Differentiating subtype

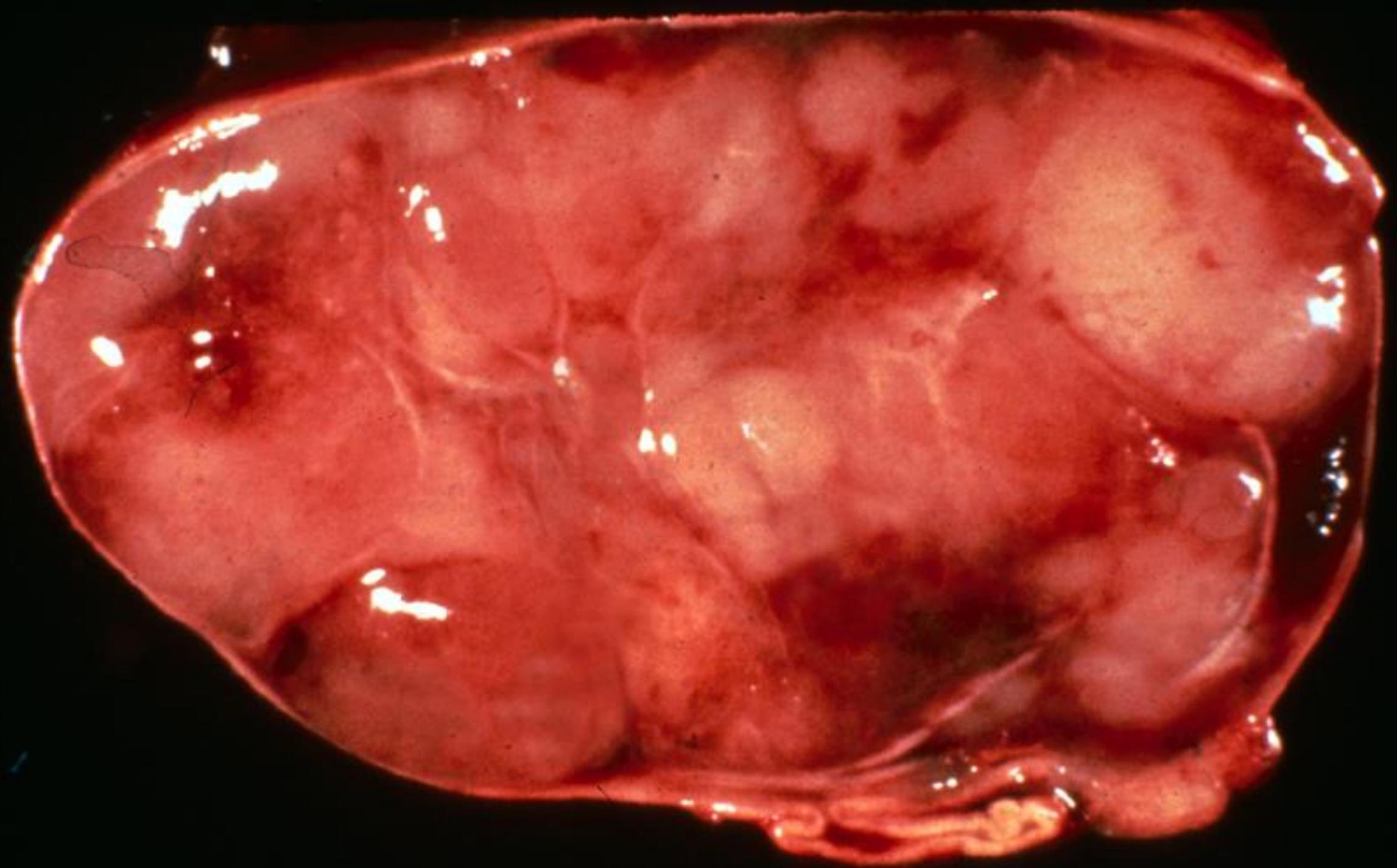


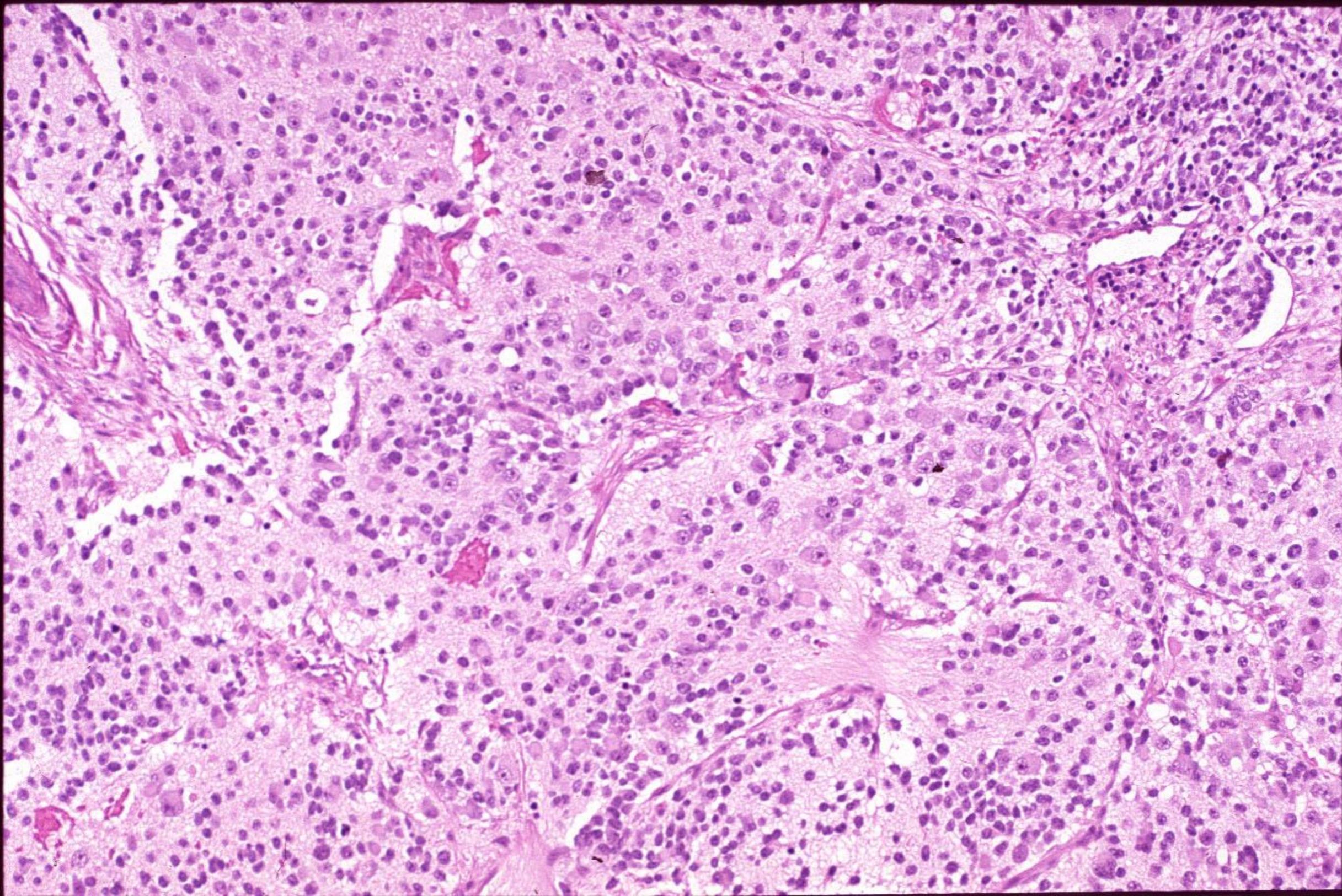


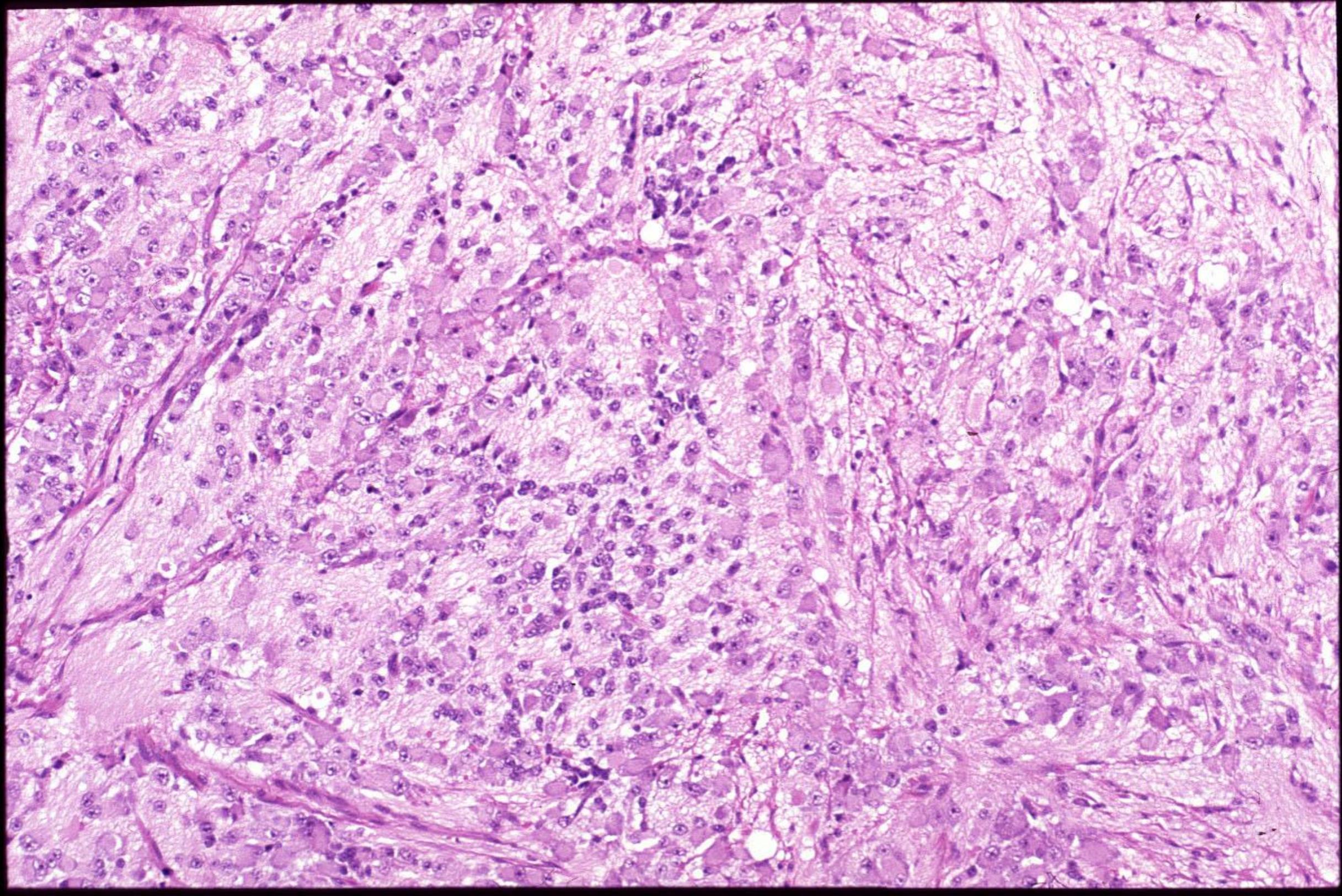
# Neuroblastoma (Schwannian stroma-poor)

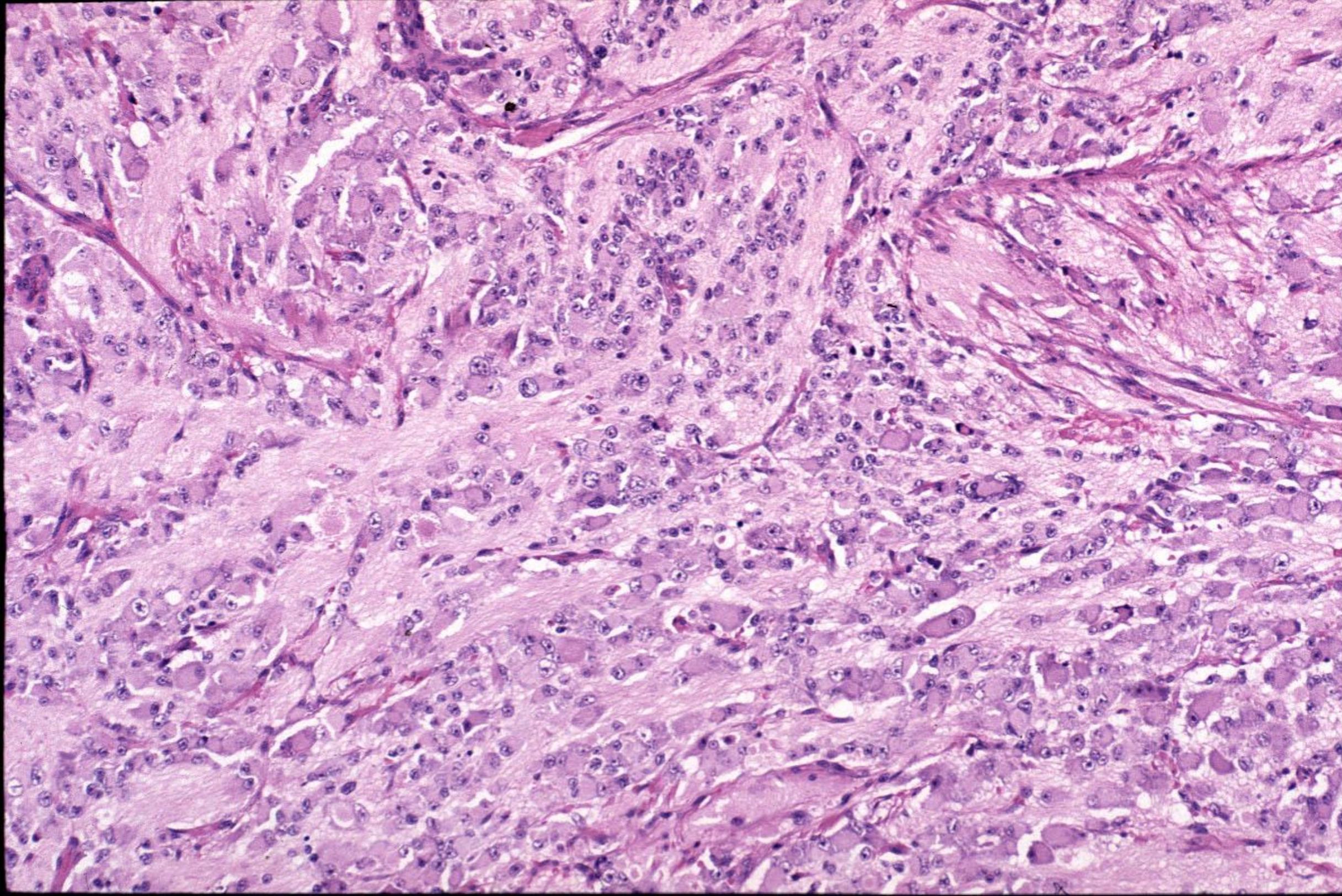
Differentiating Subtype

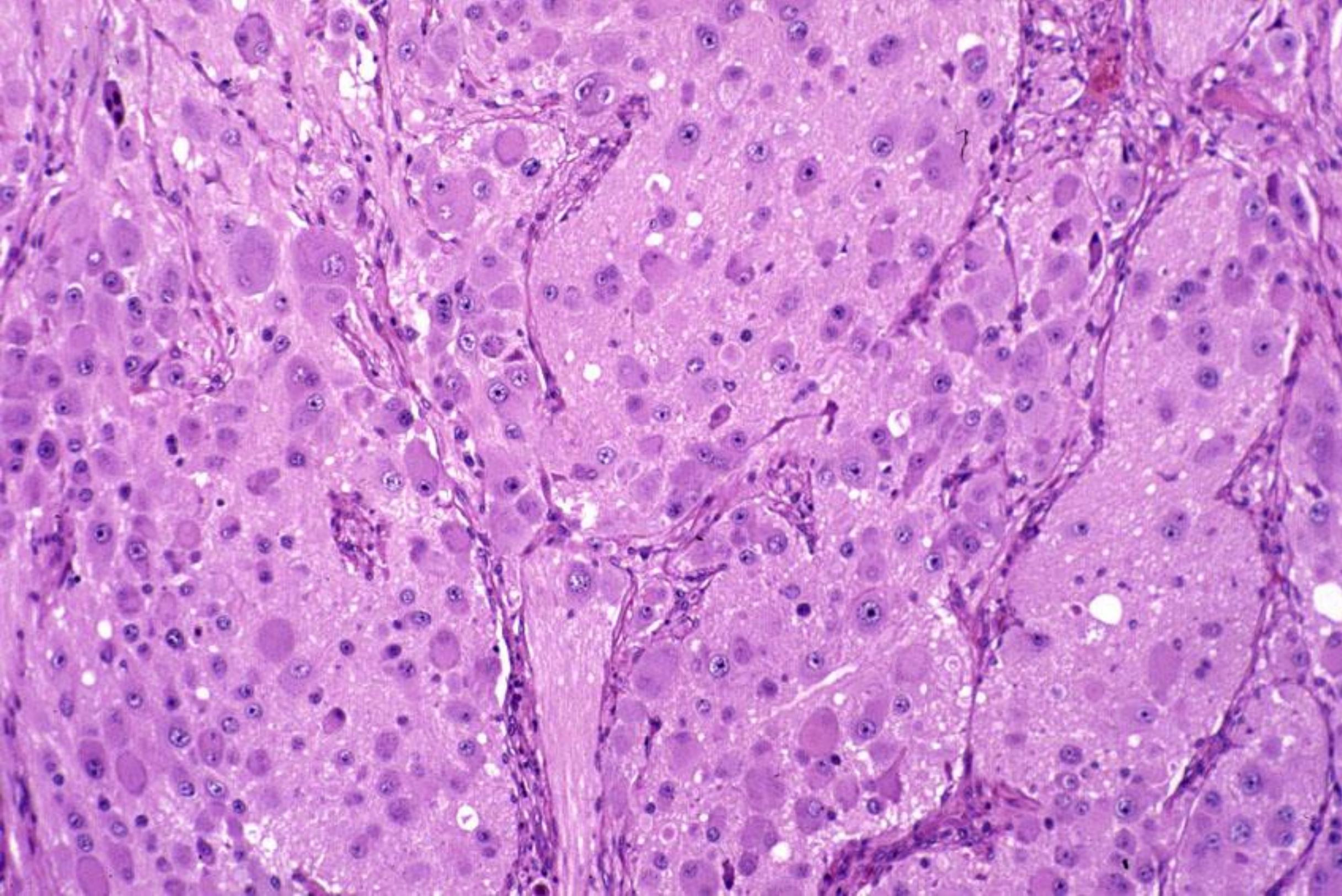


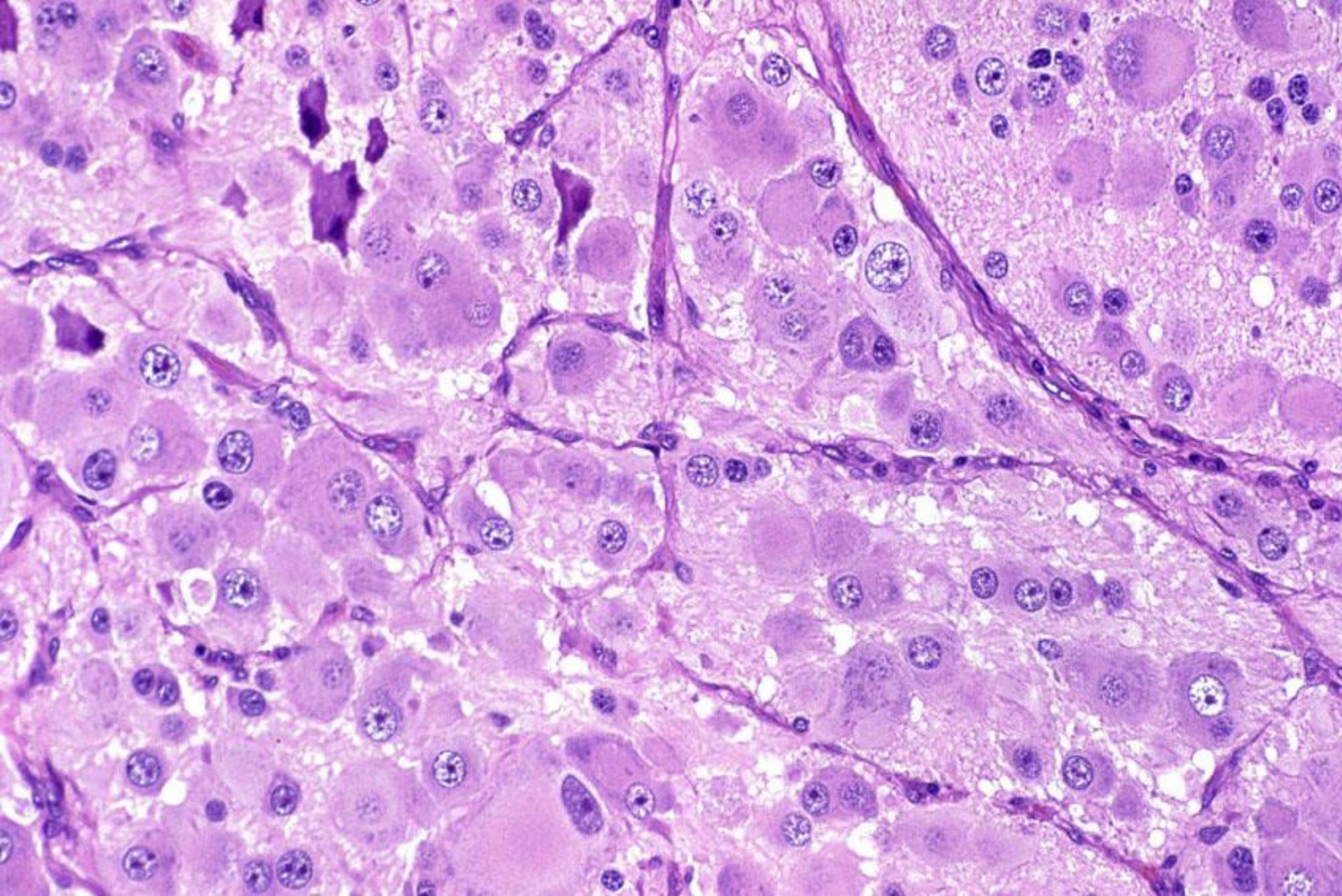












# Neuroblastoma (Schwannian stroma-poor)

Different Cellularity

Calcification

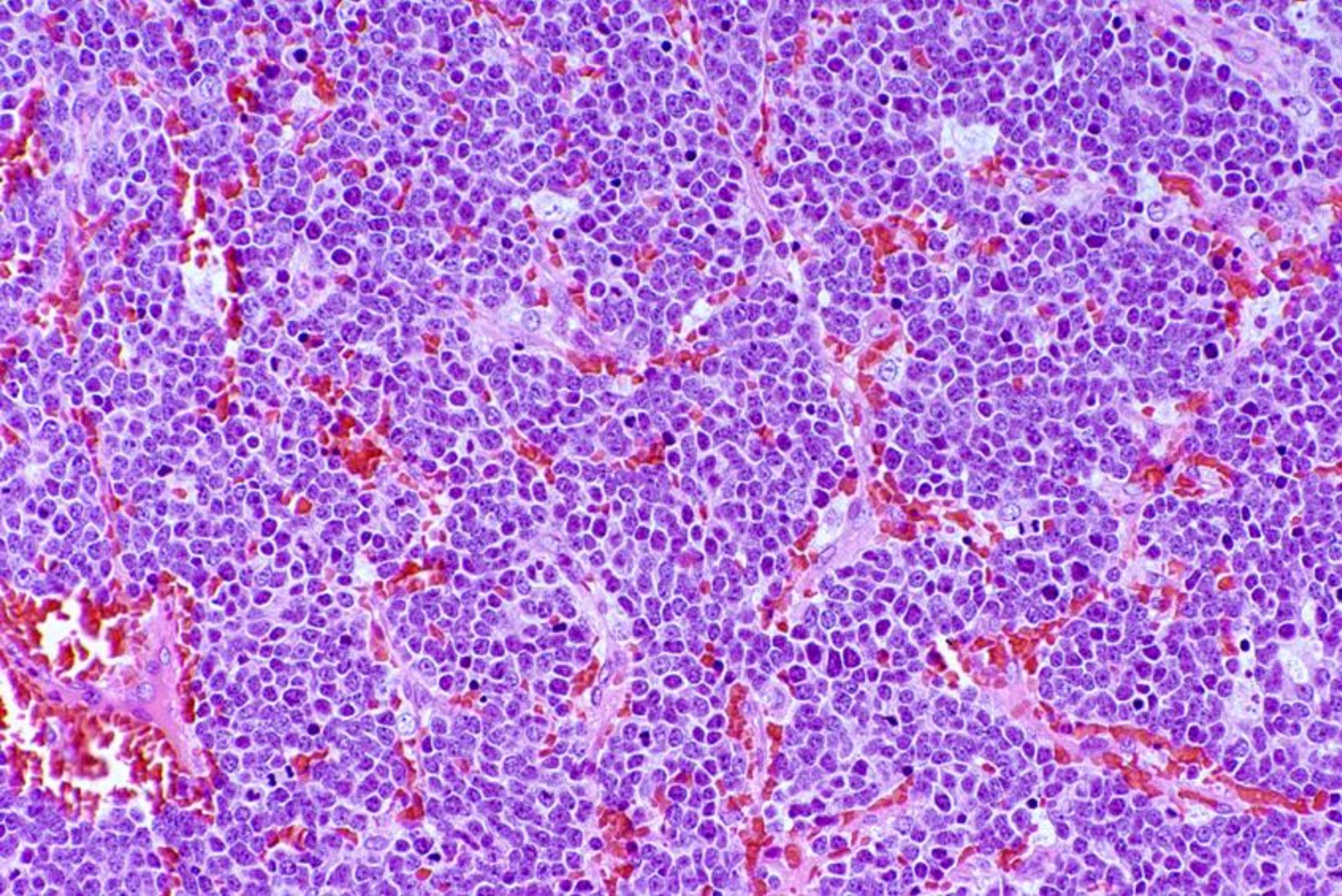
Multi-nucleated cells

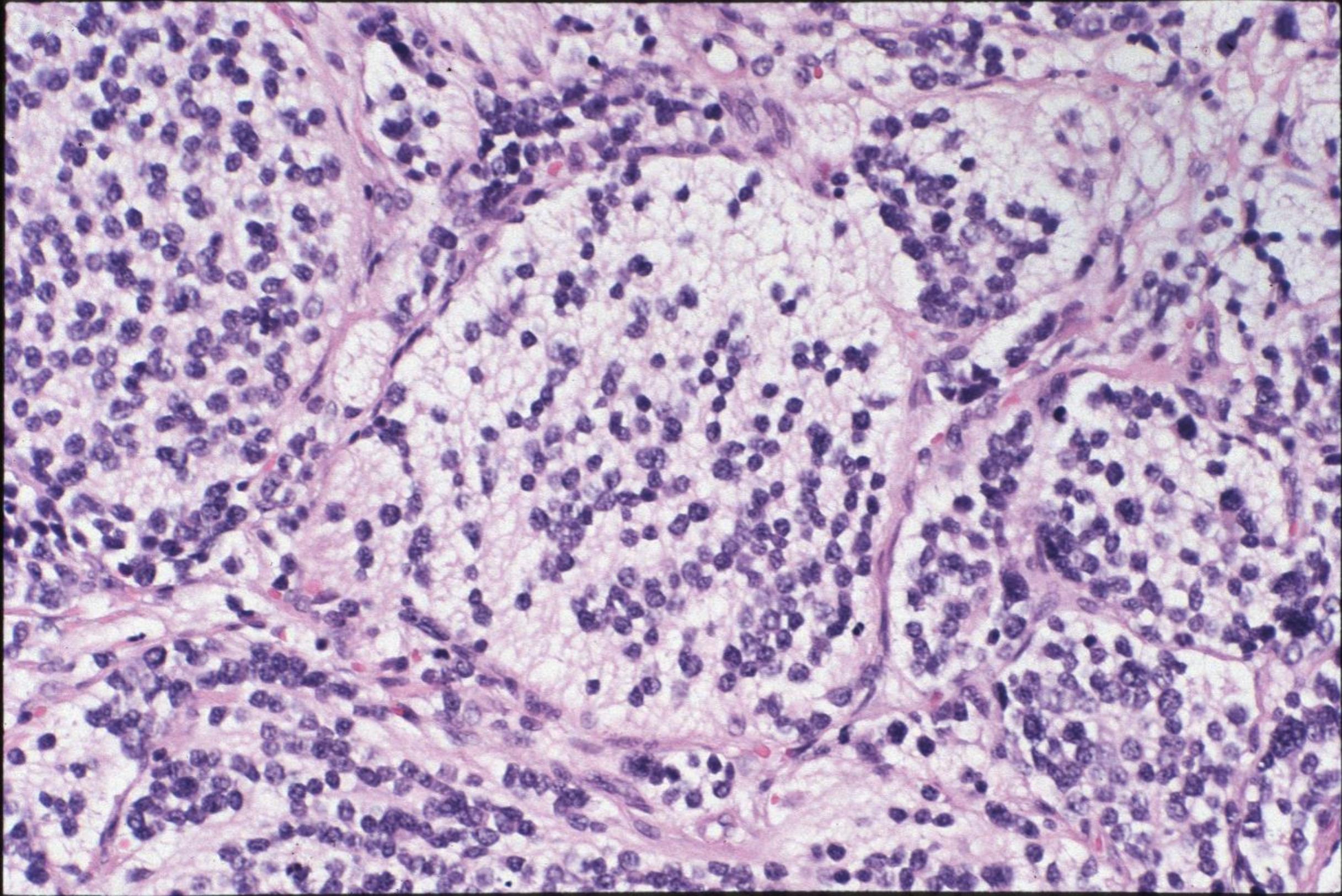
Melanin pigment

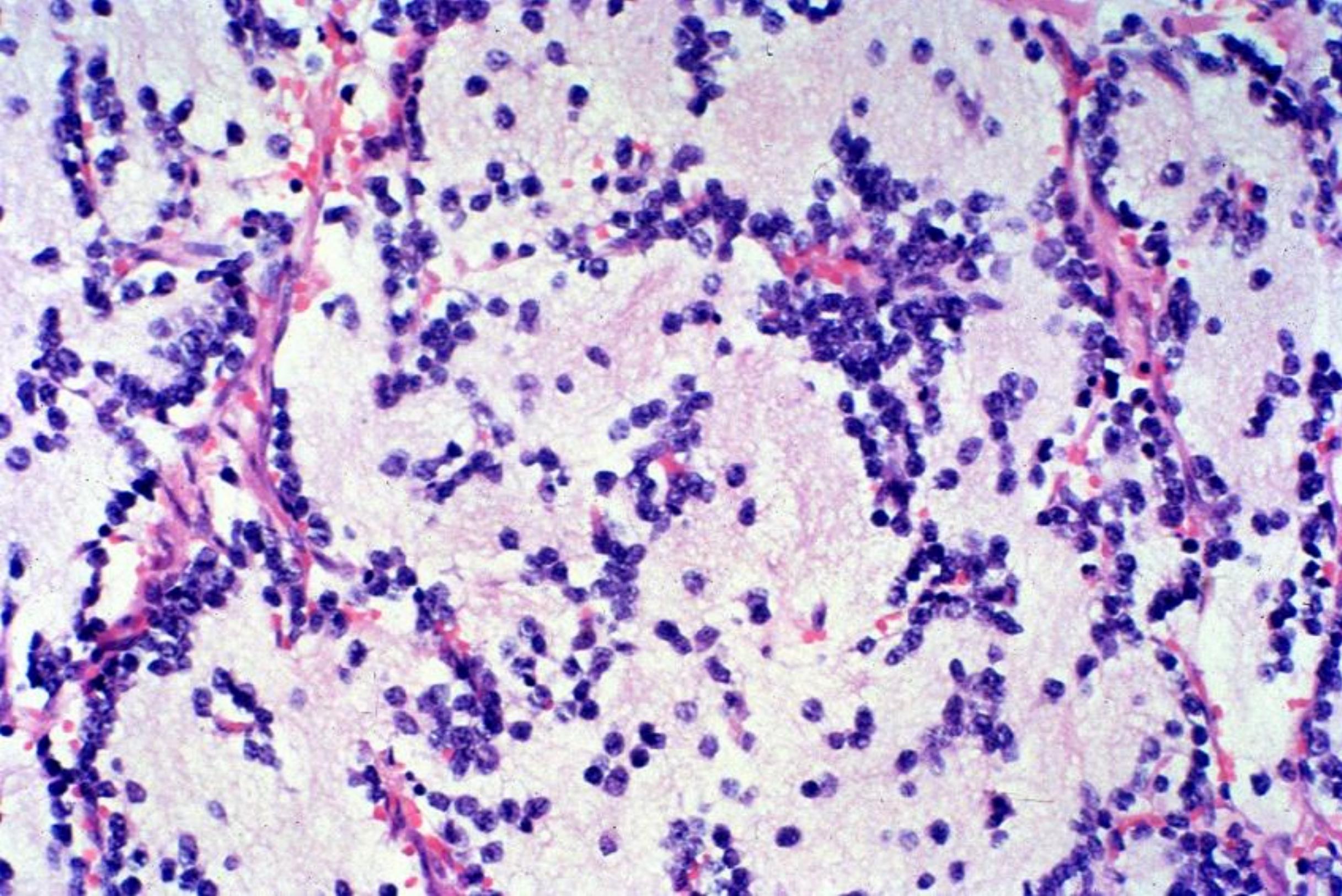
Mitosis

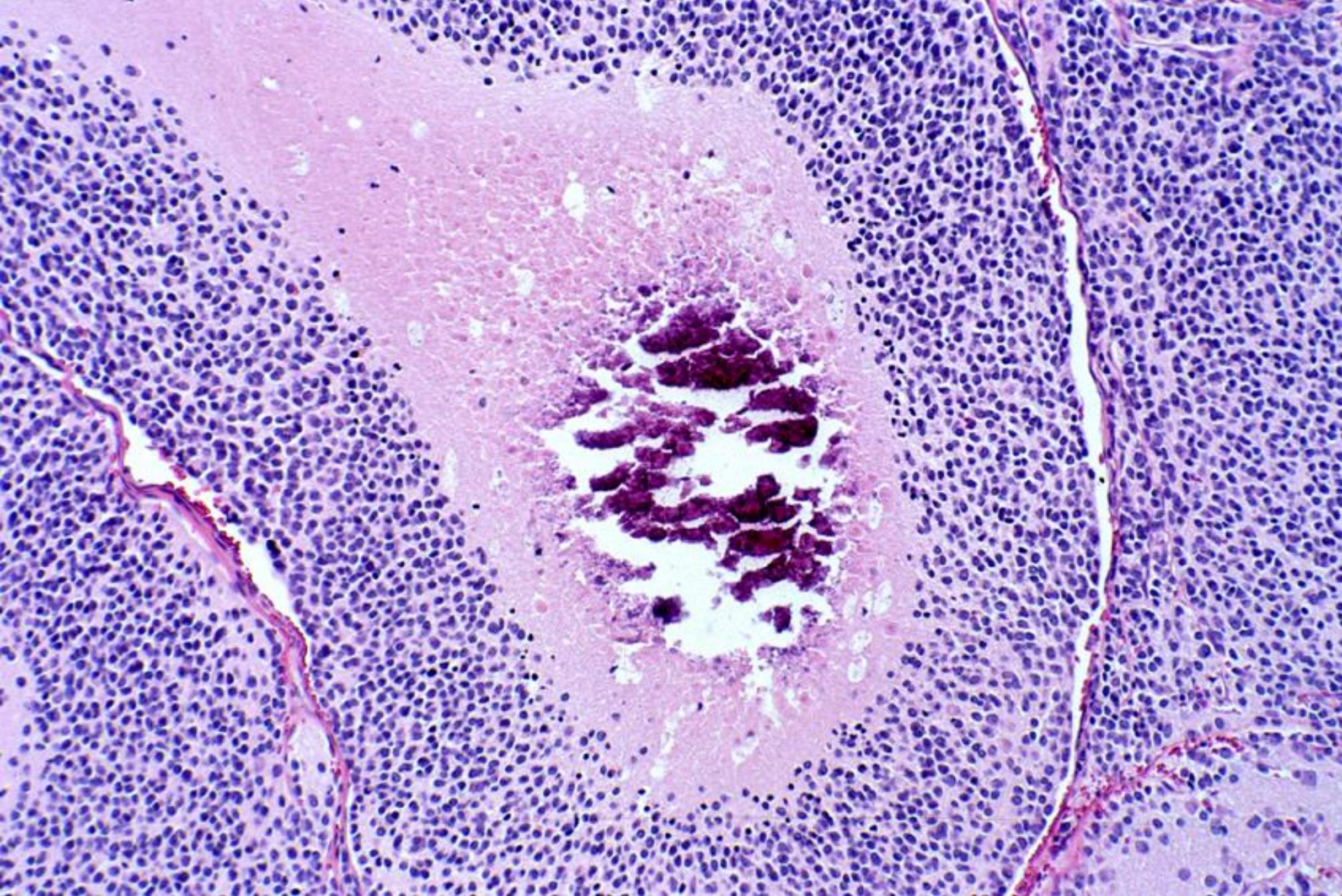
Mitosis-Karyorrhexis

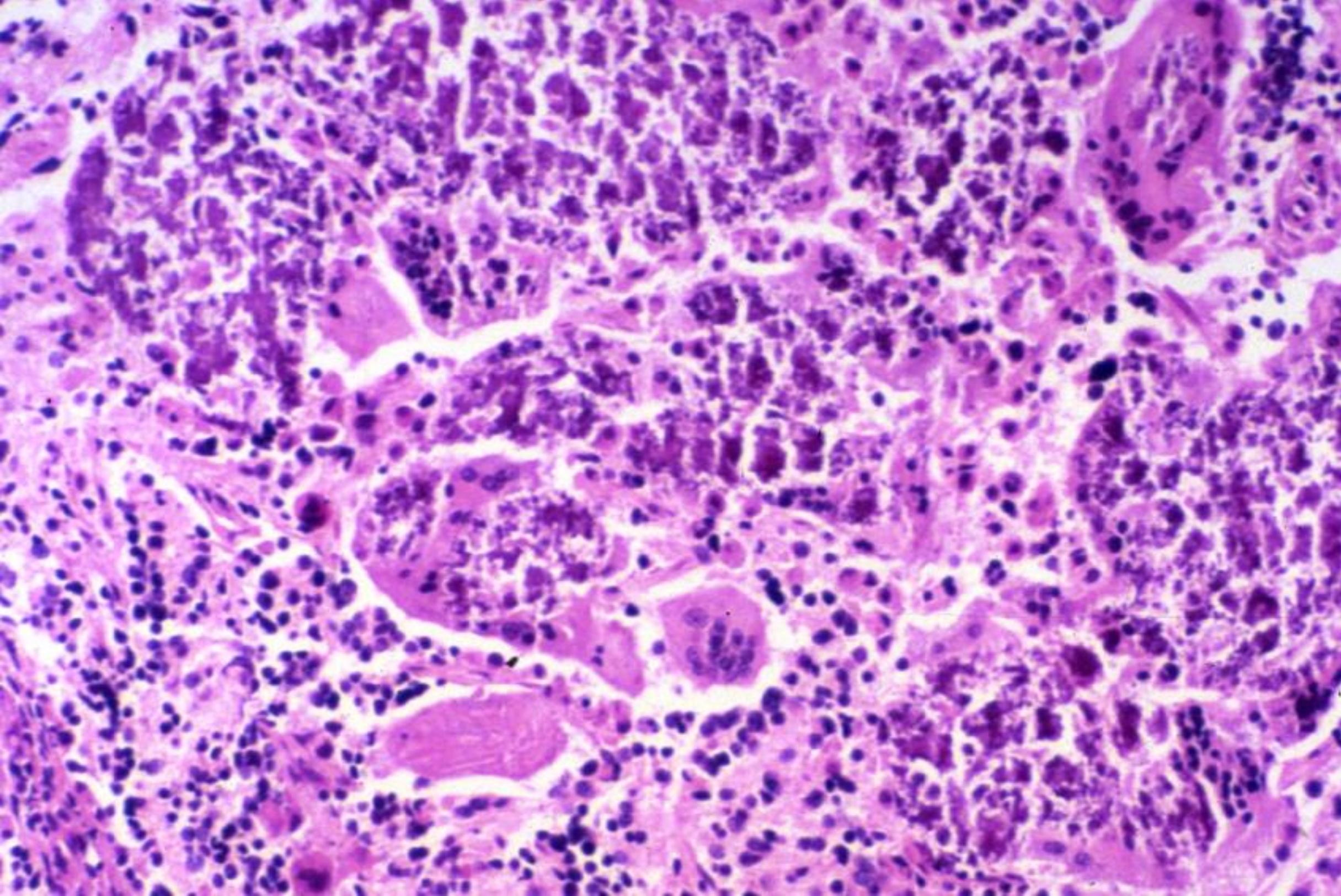
Apoptosis

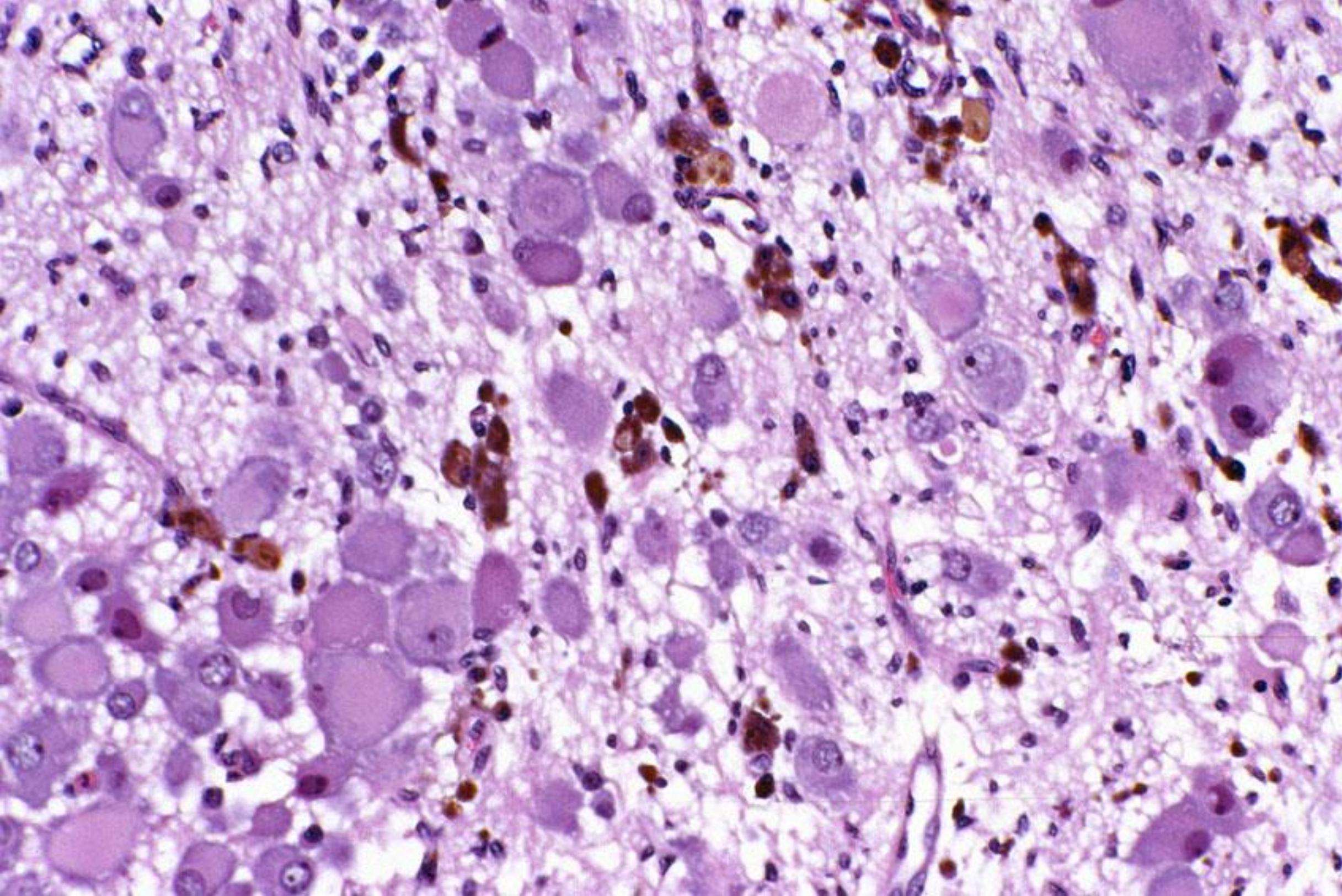


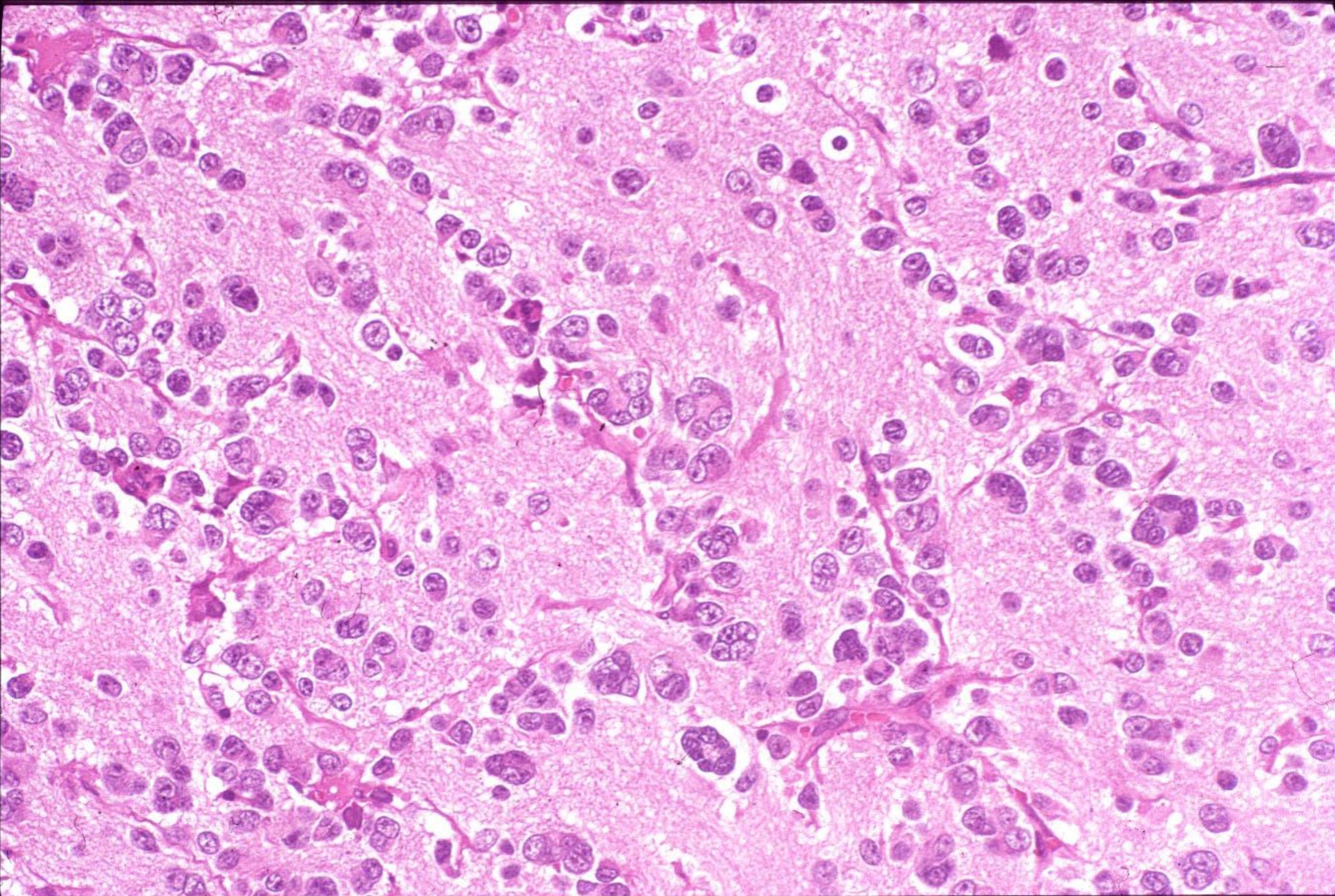


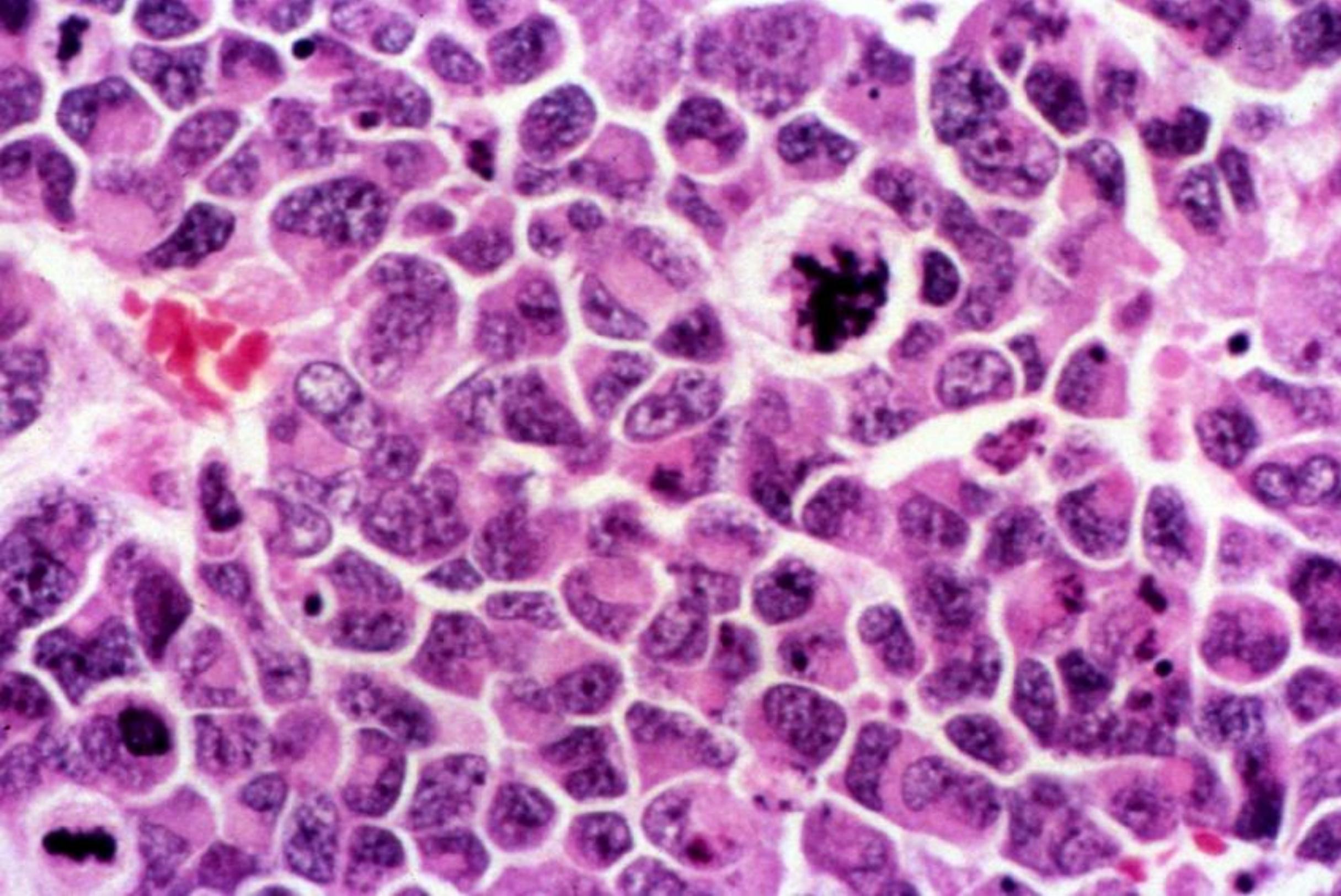


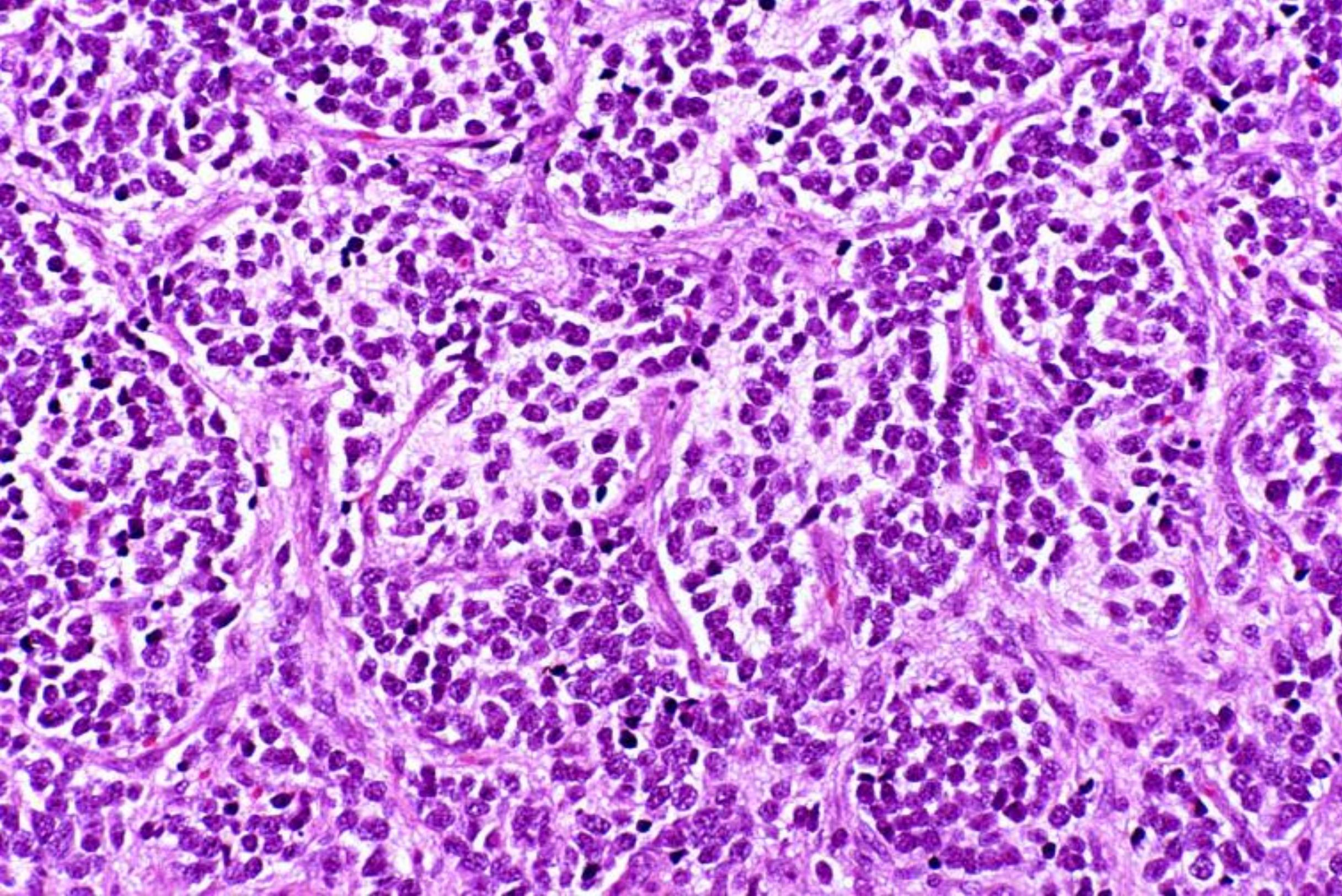


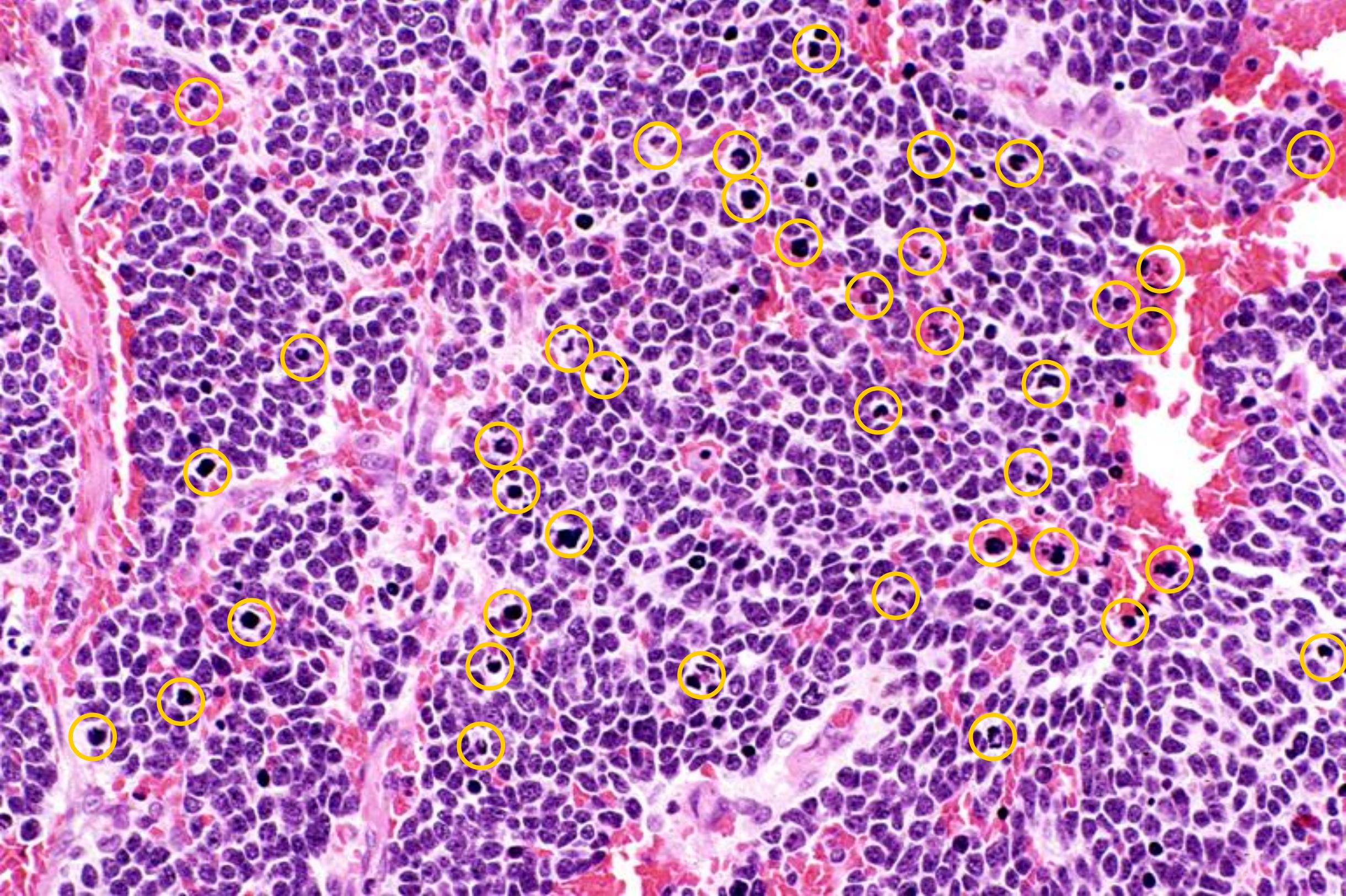


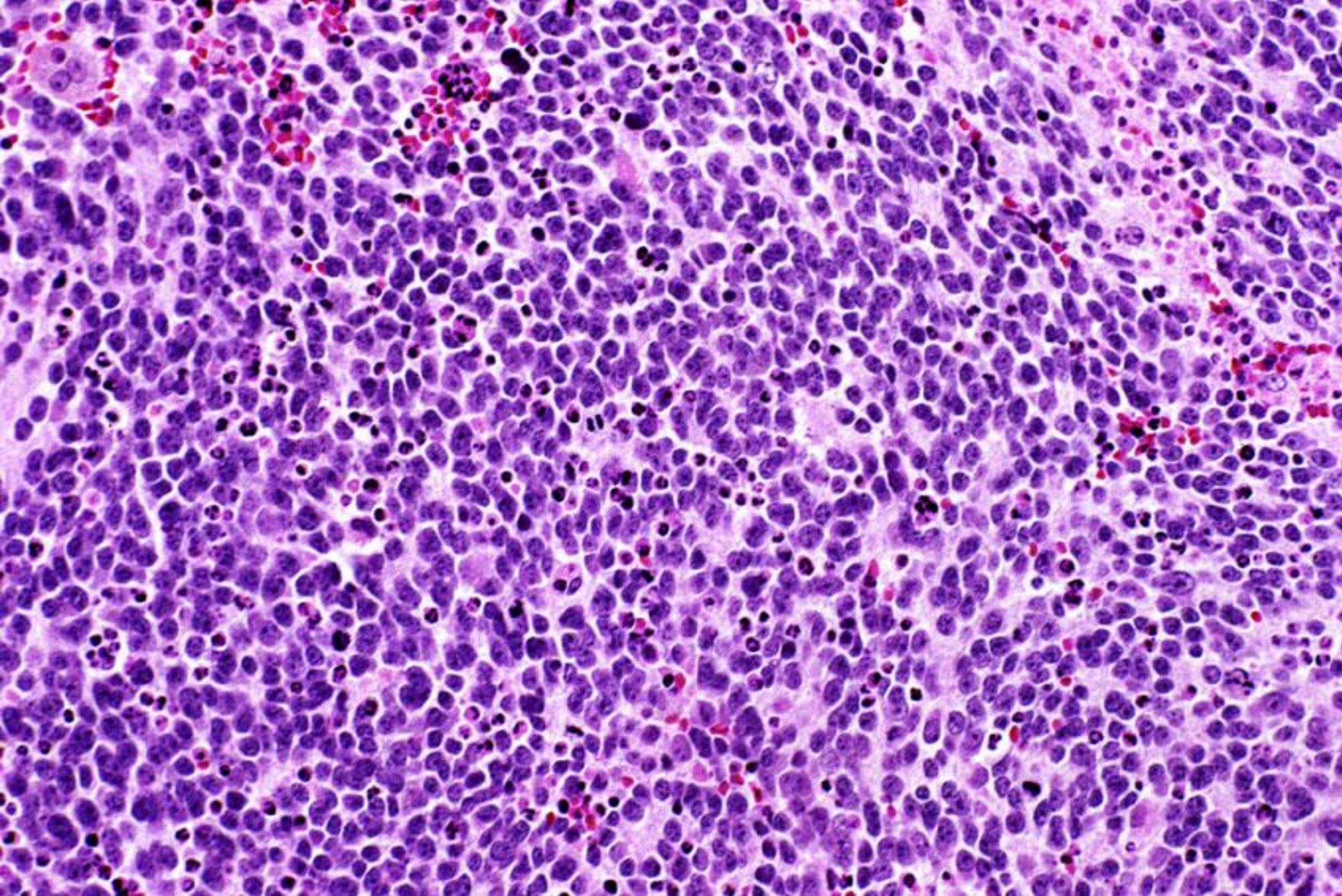


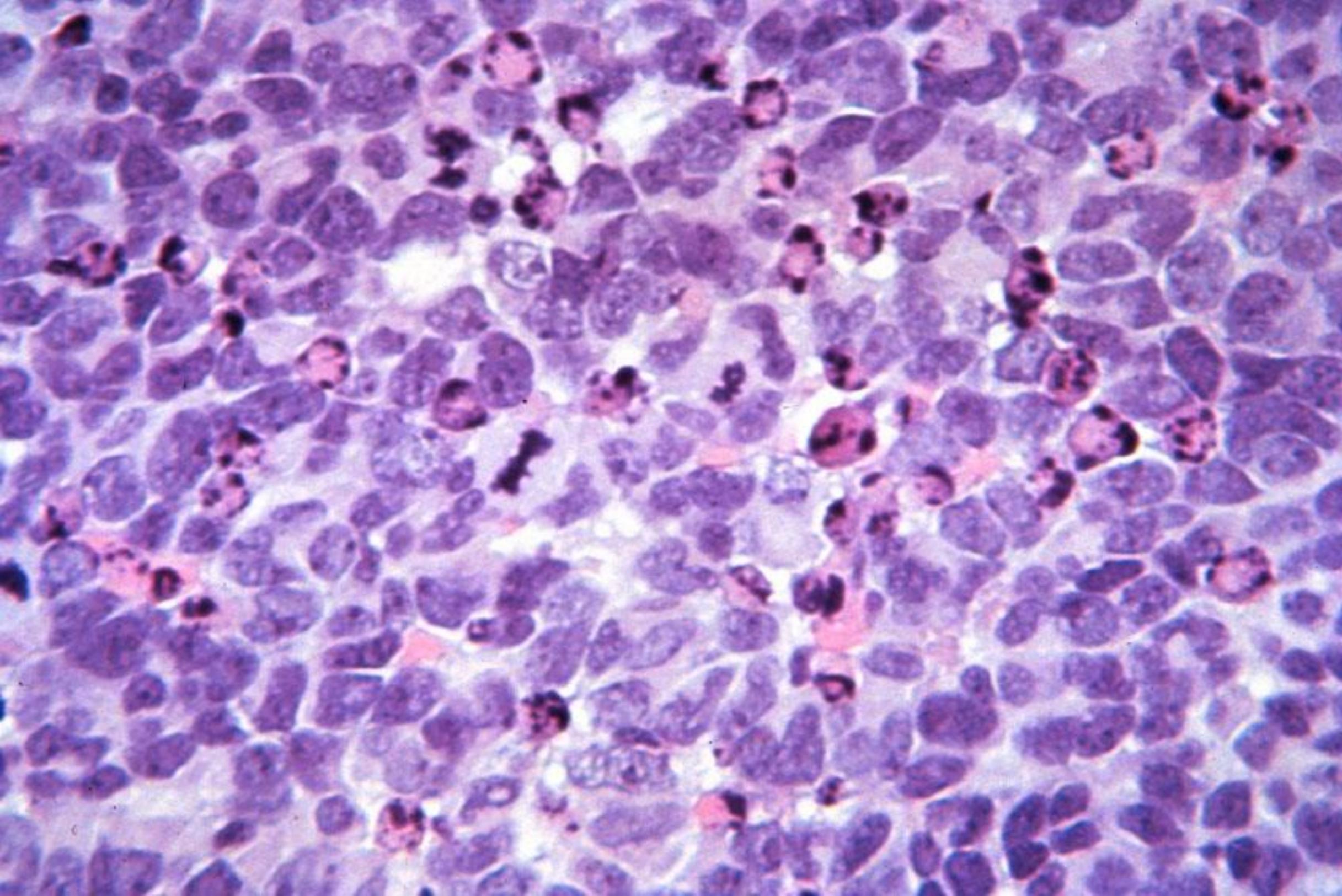


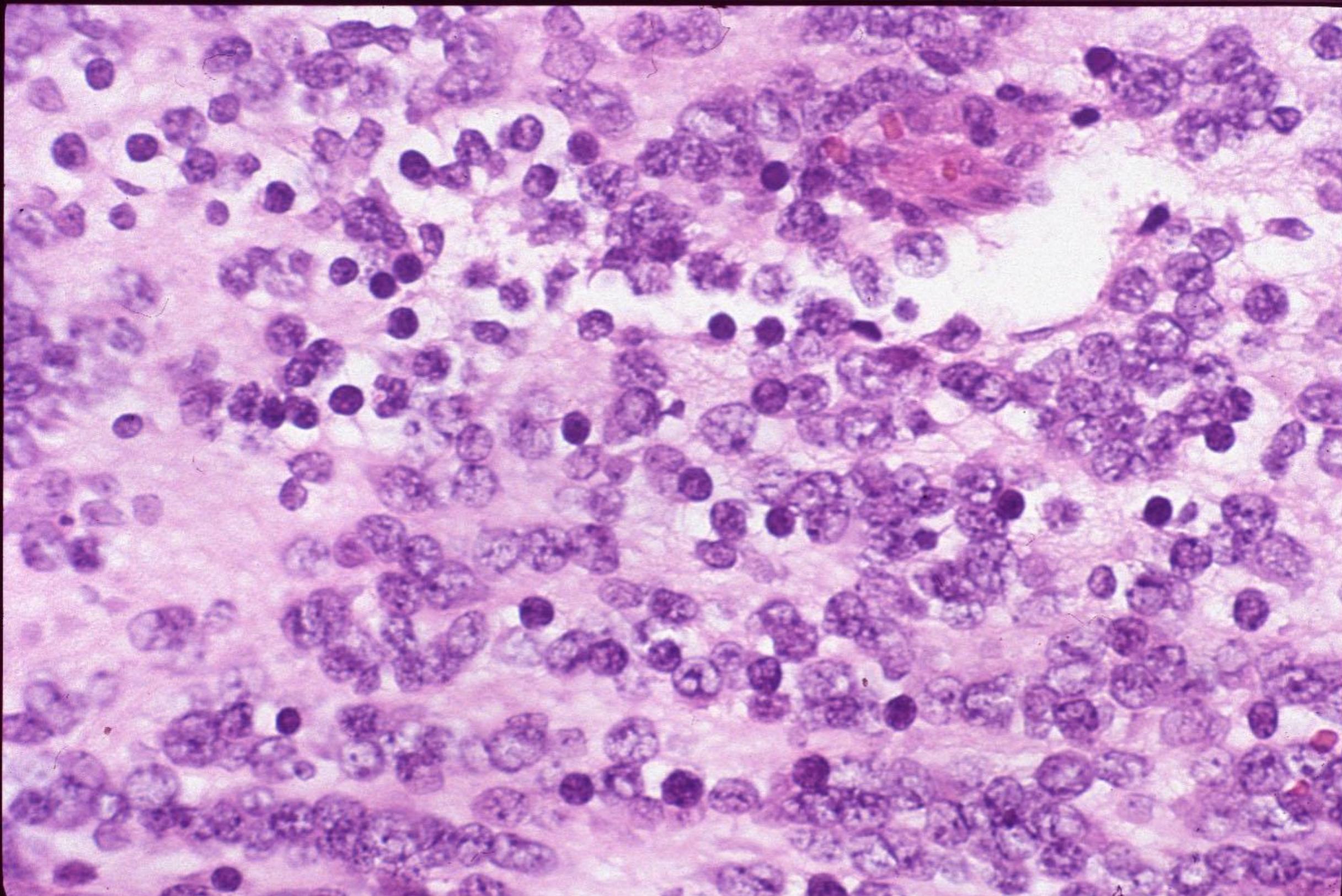


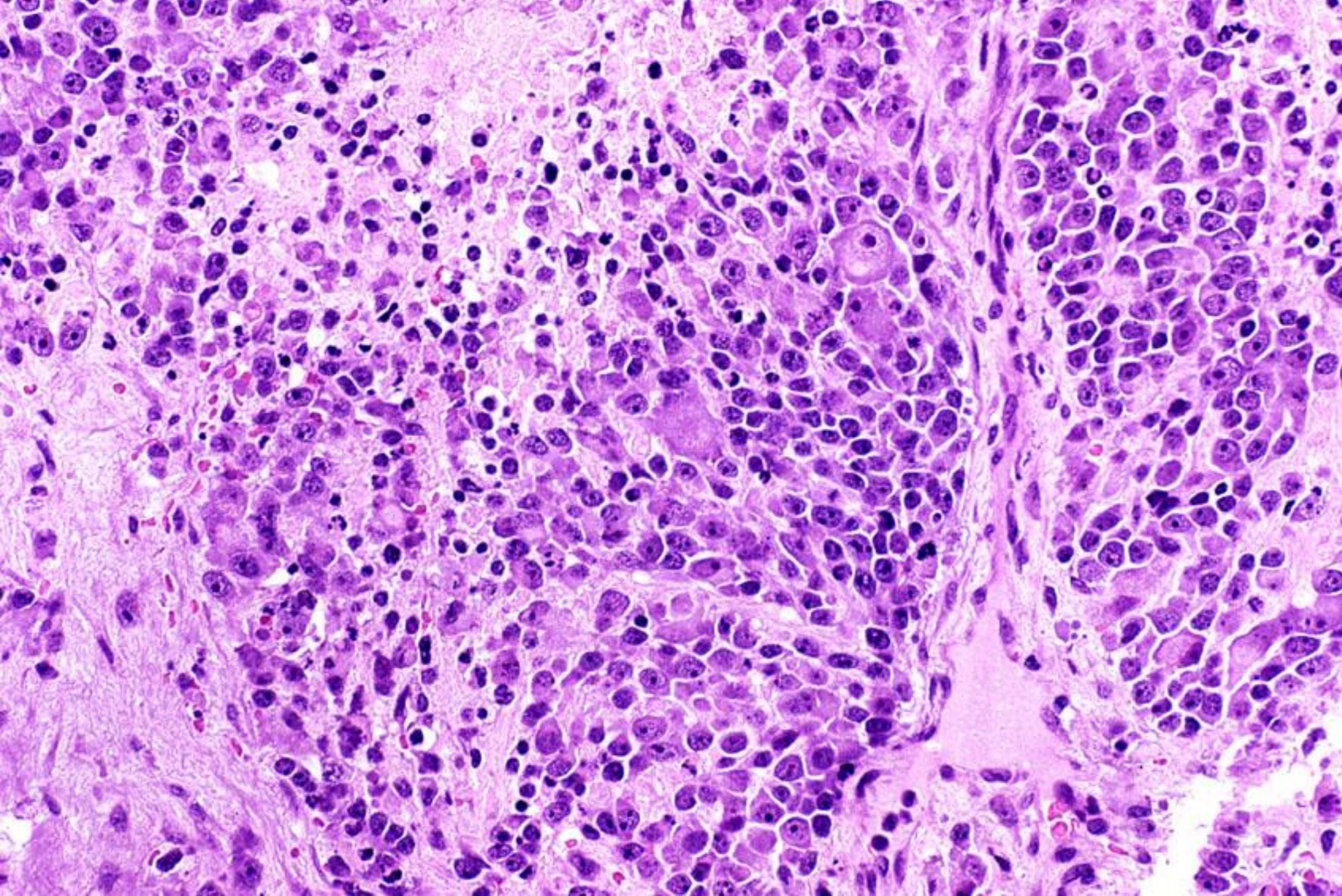






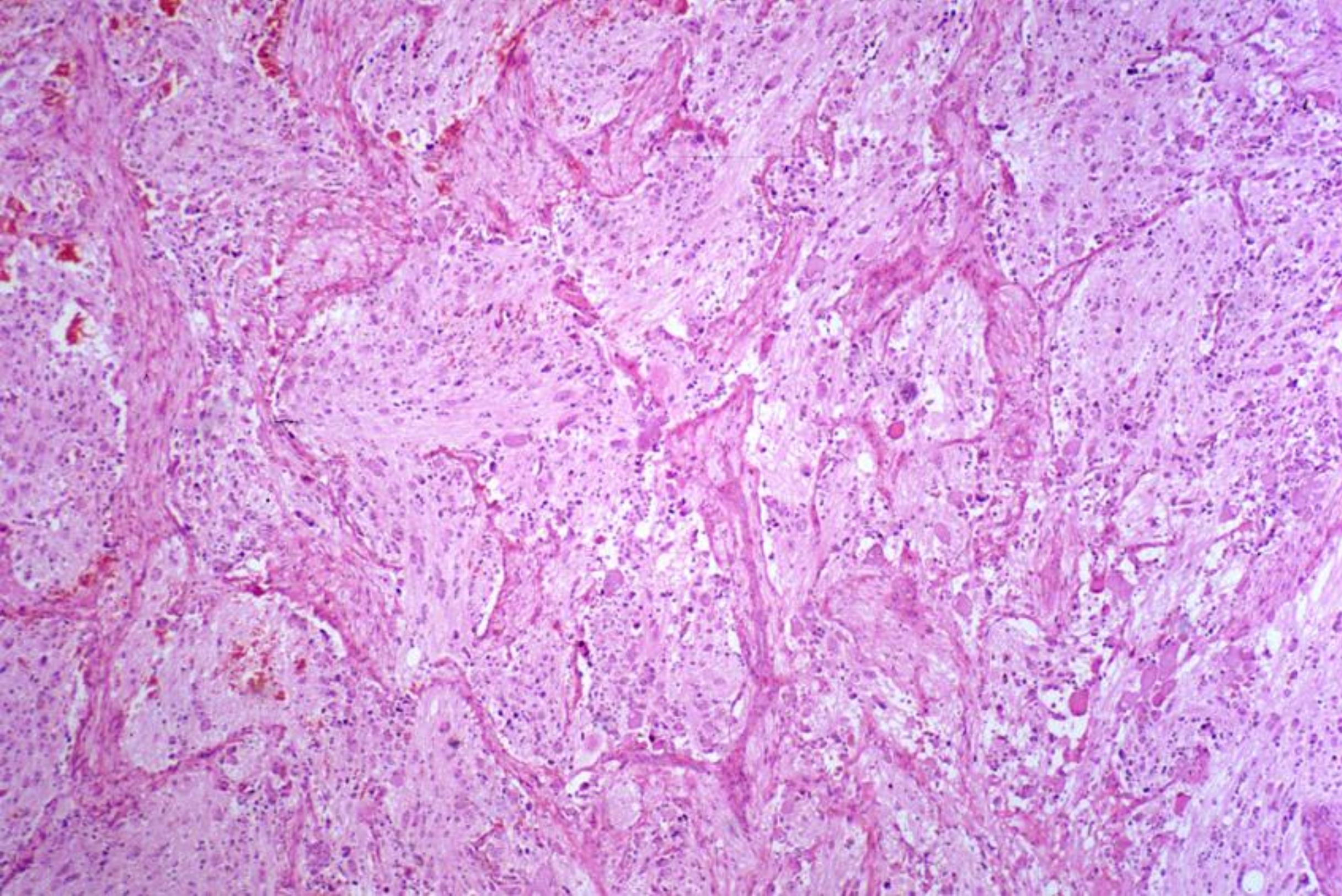


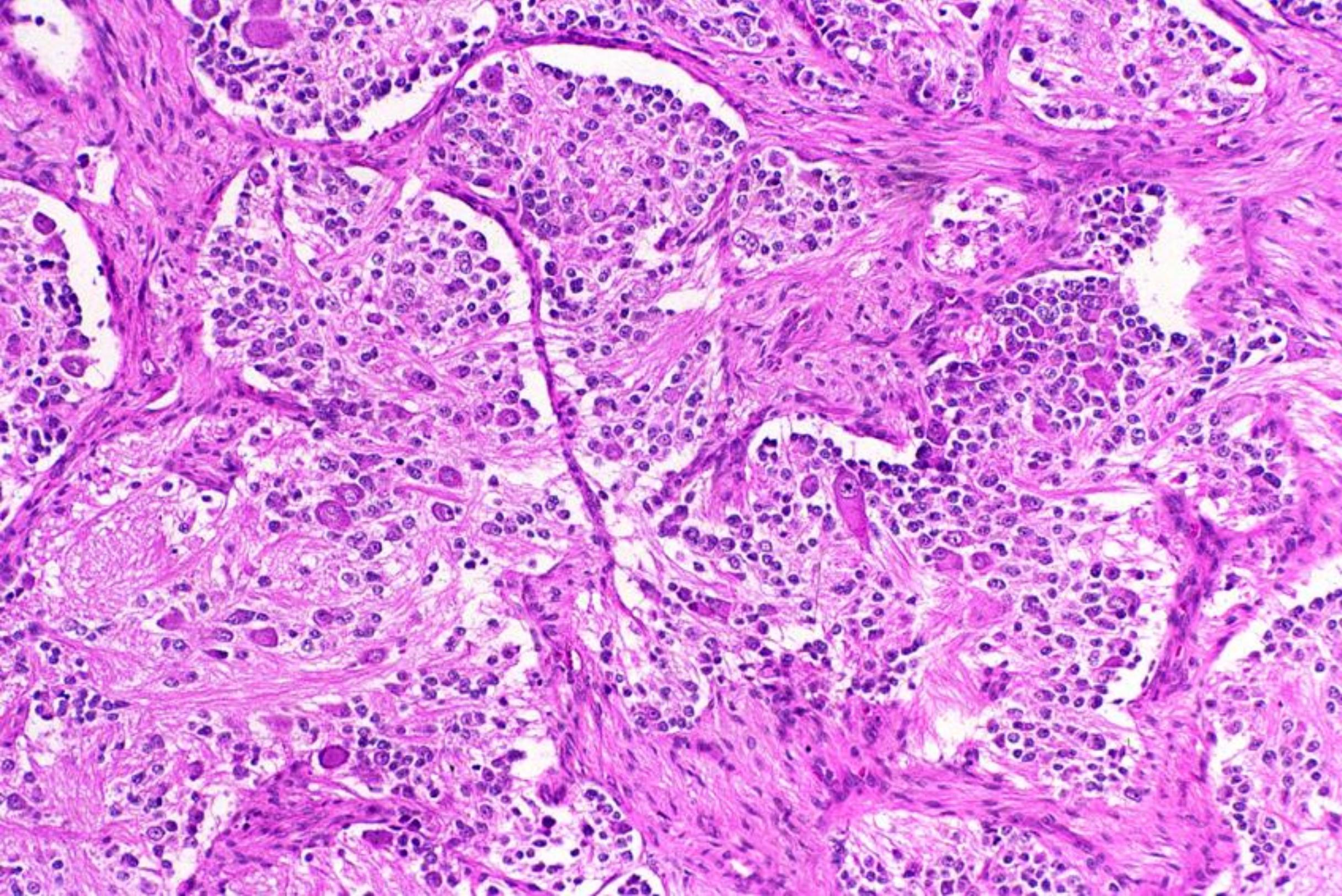


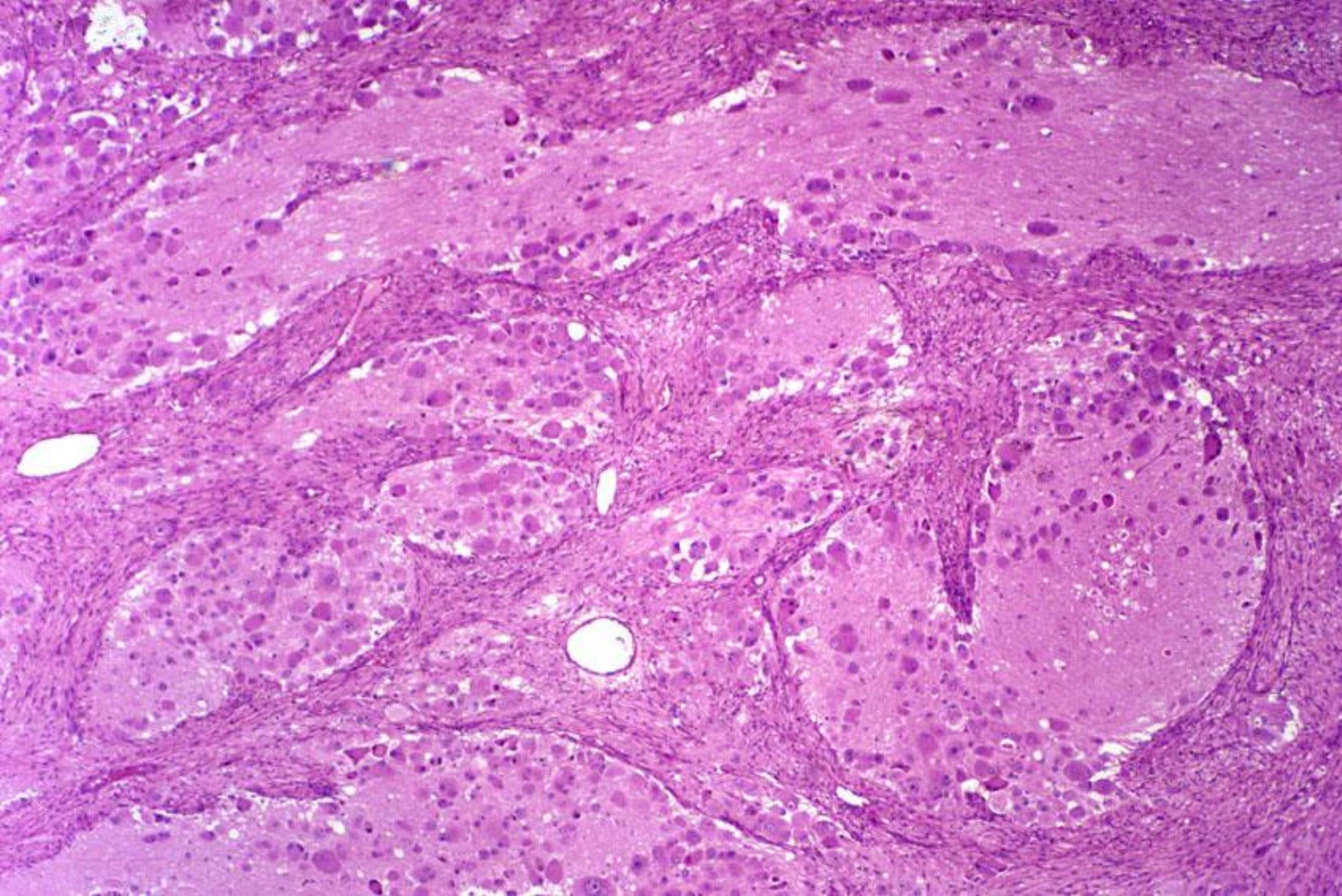


# Neuroblastoma (Schwannian stroma-poor)

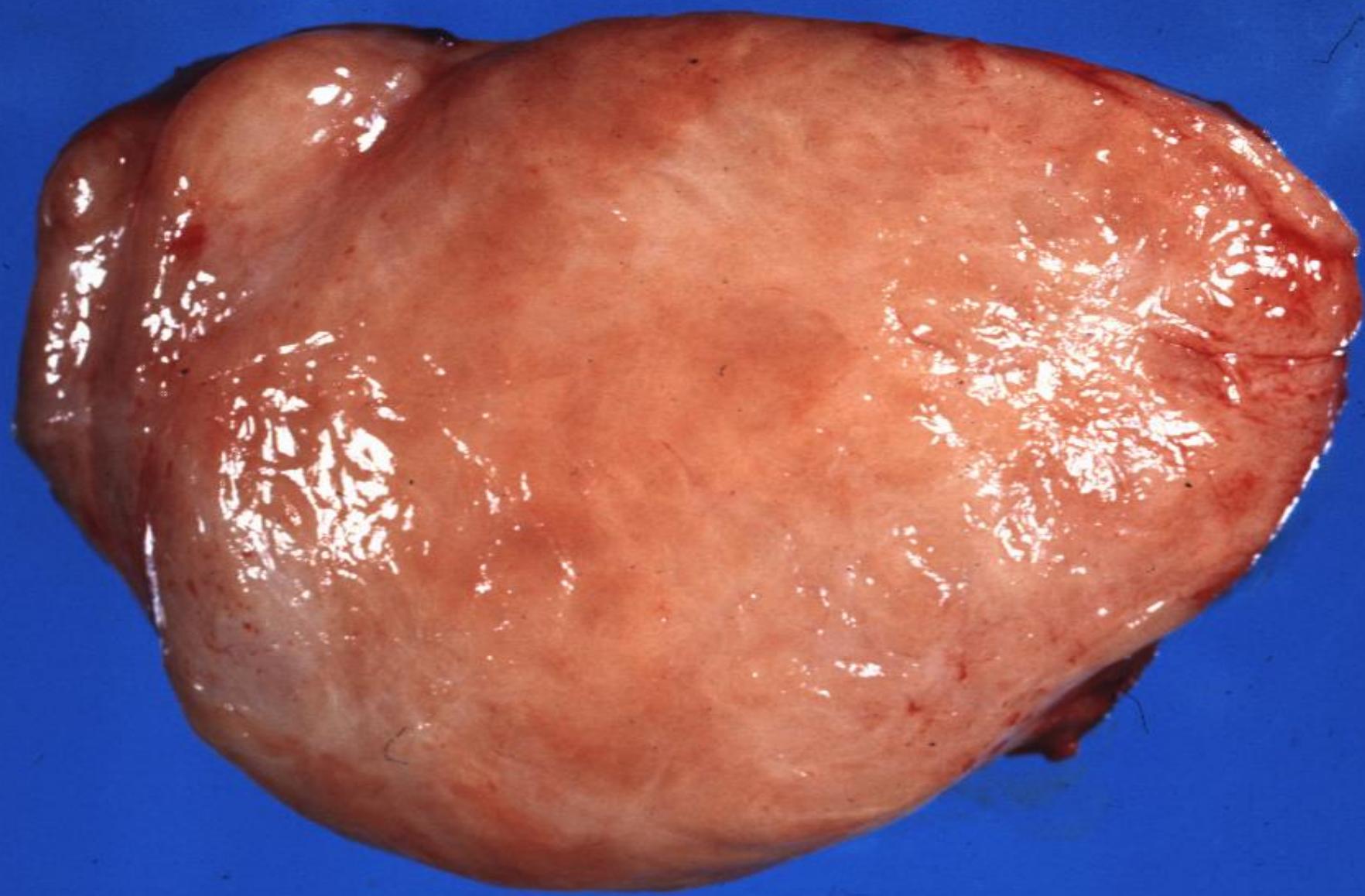
Transitional to  
Ganglioneuroblastoma, Intermixed  
(Schwannian stroma-Rich)

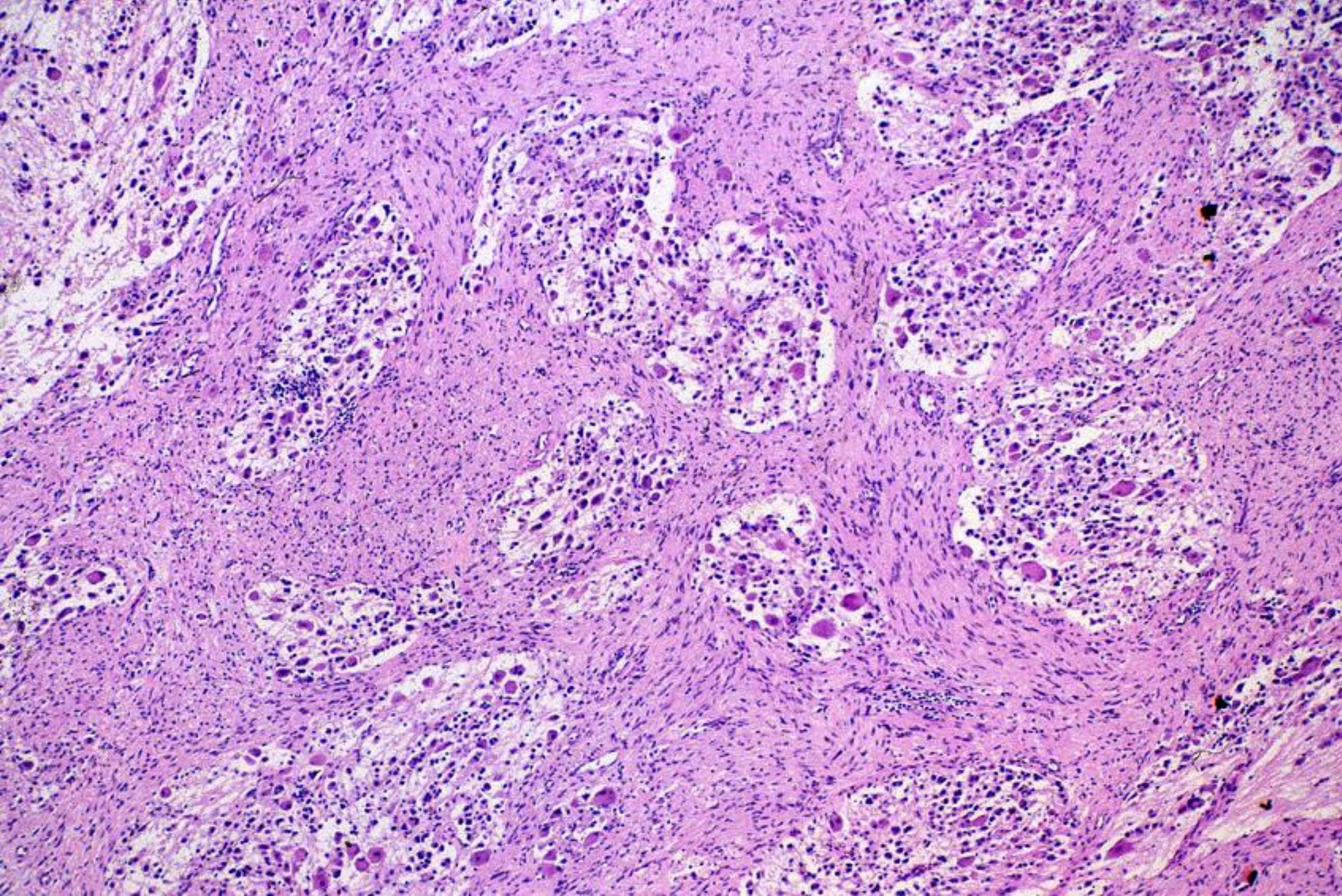


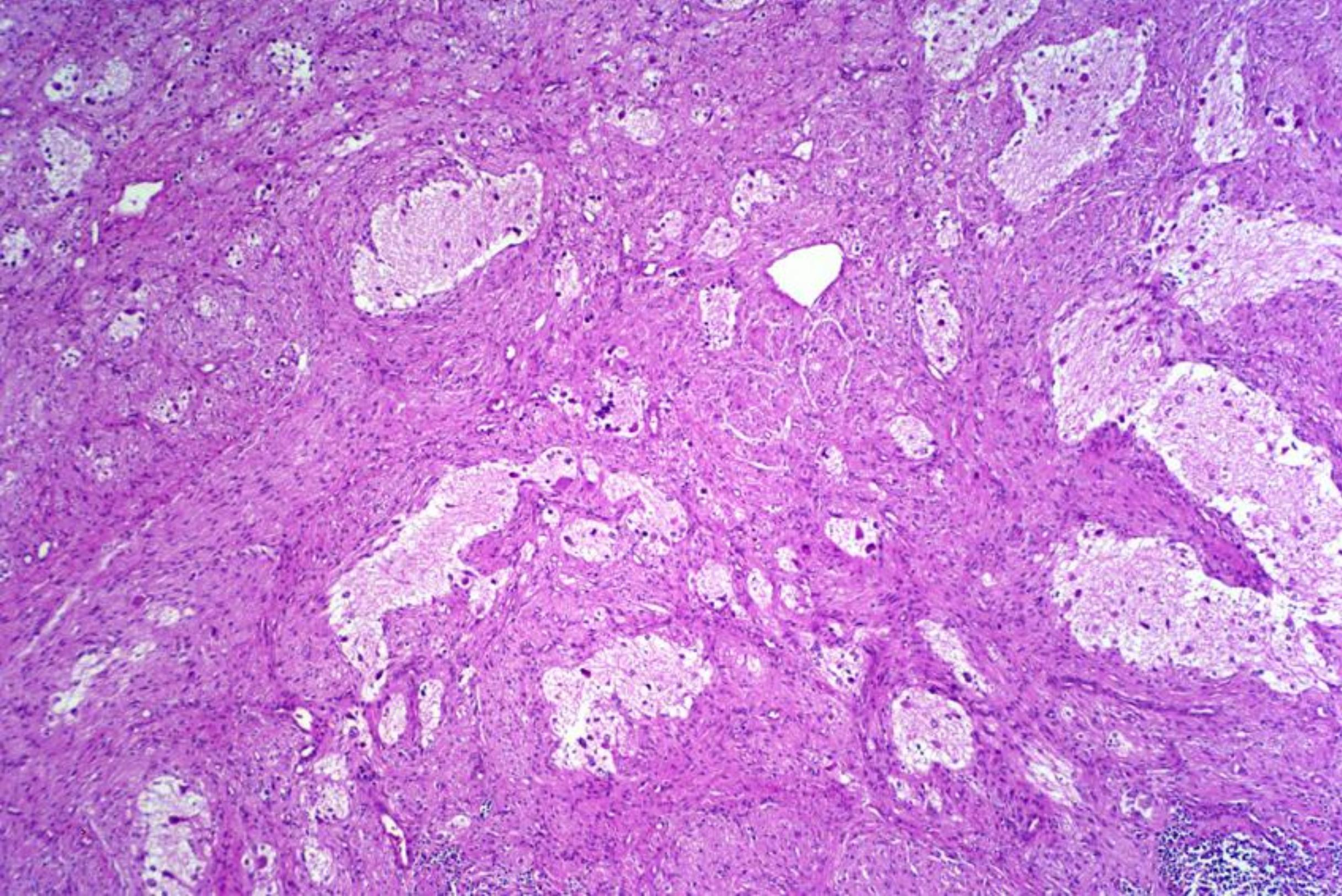


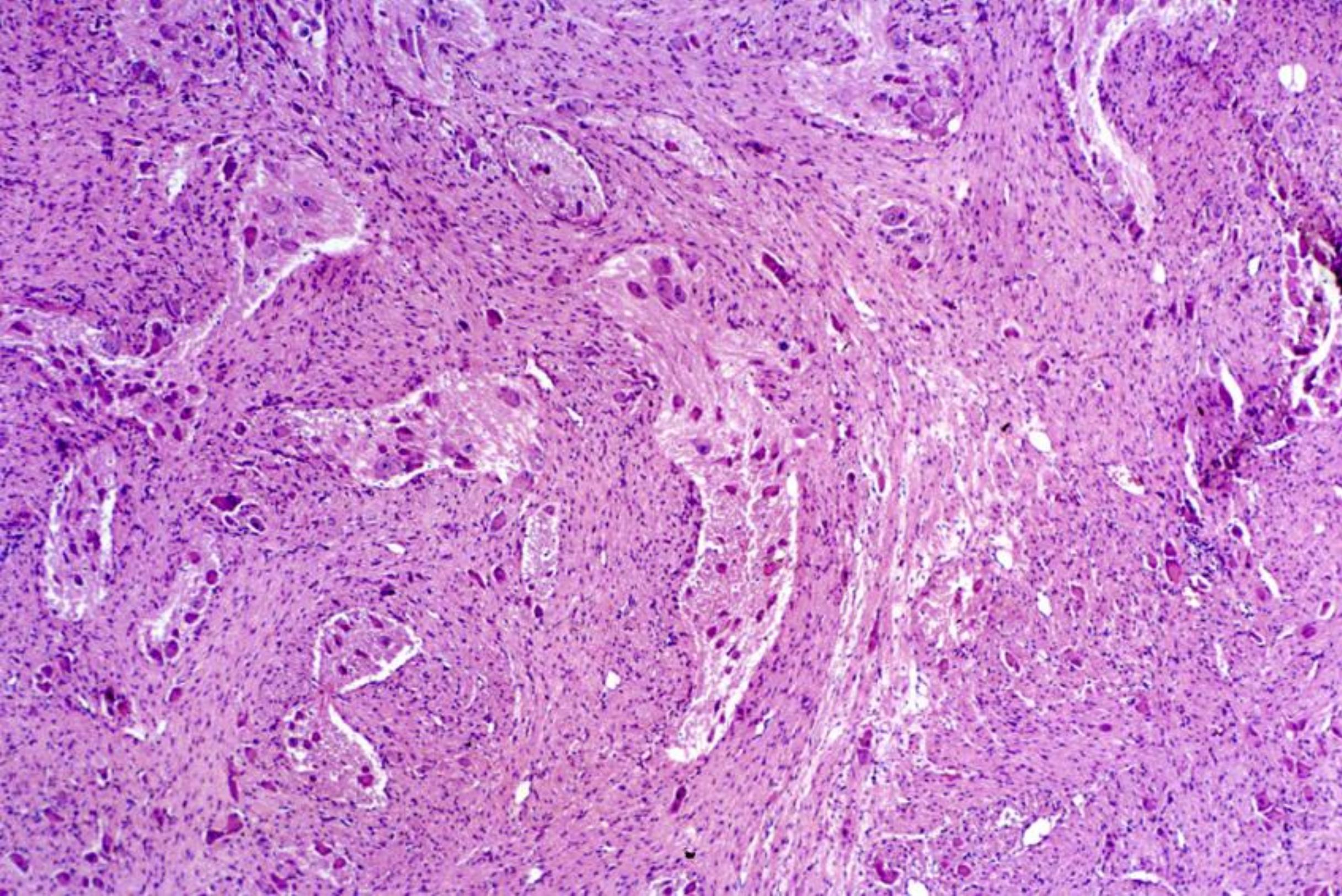


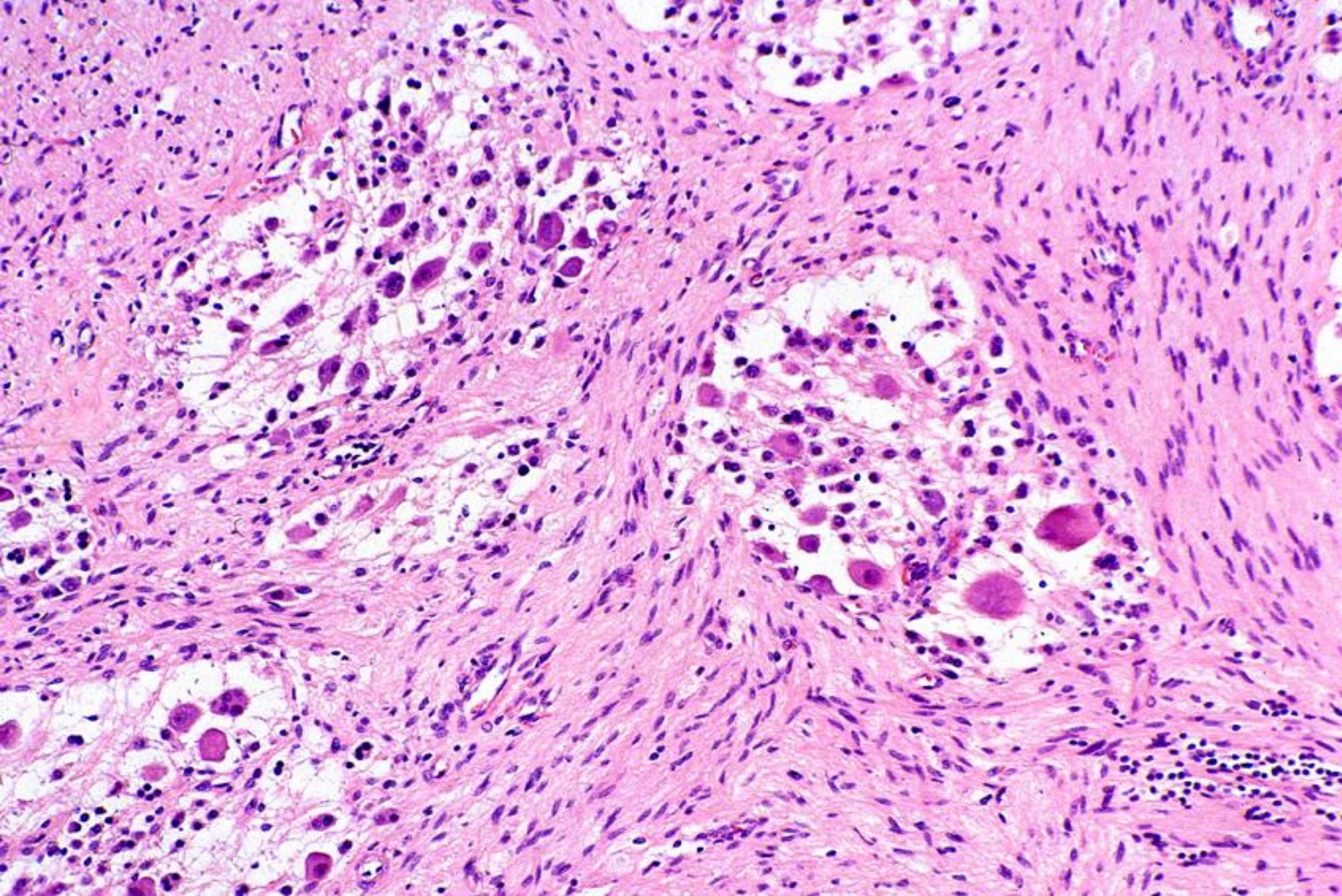
# Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)

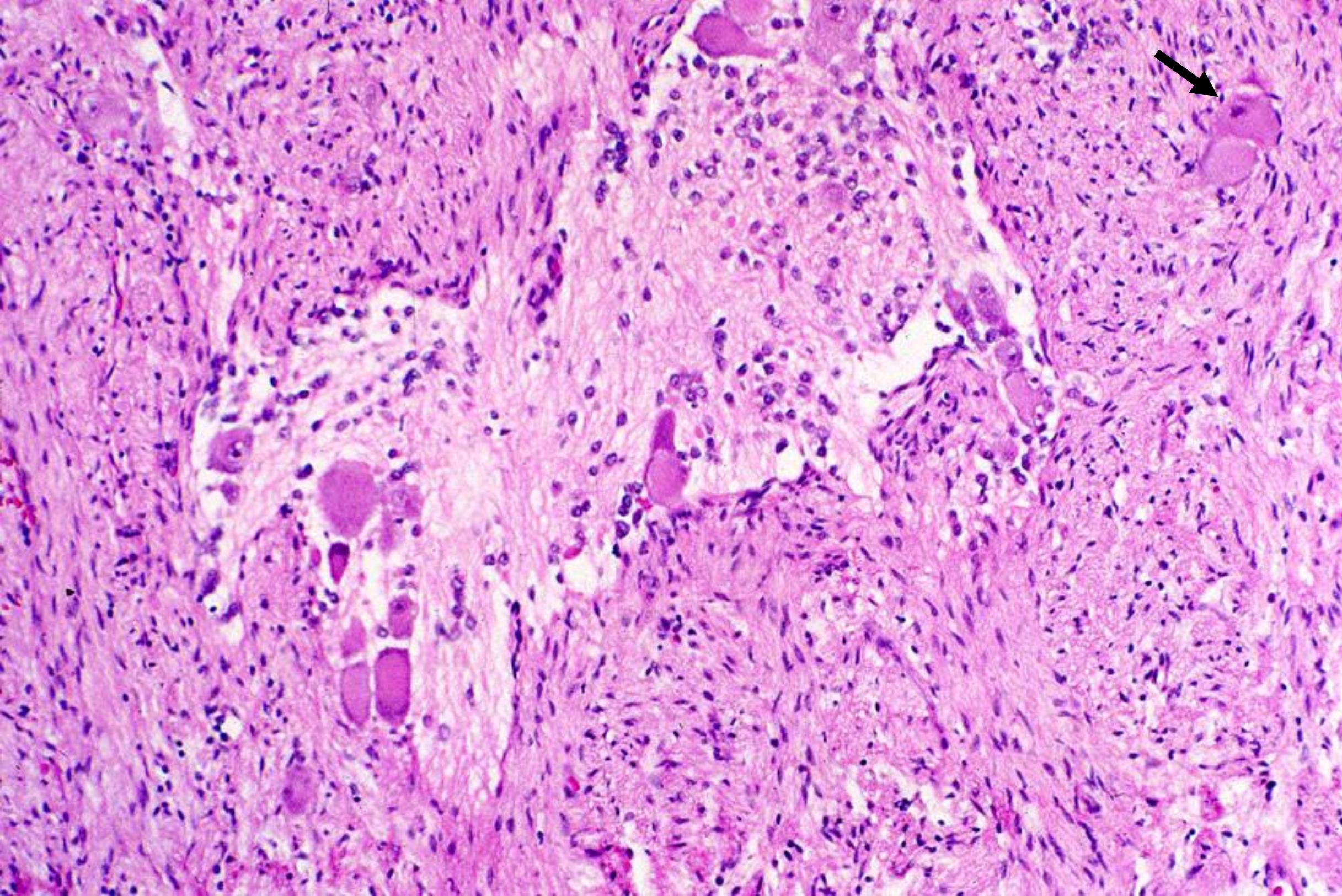








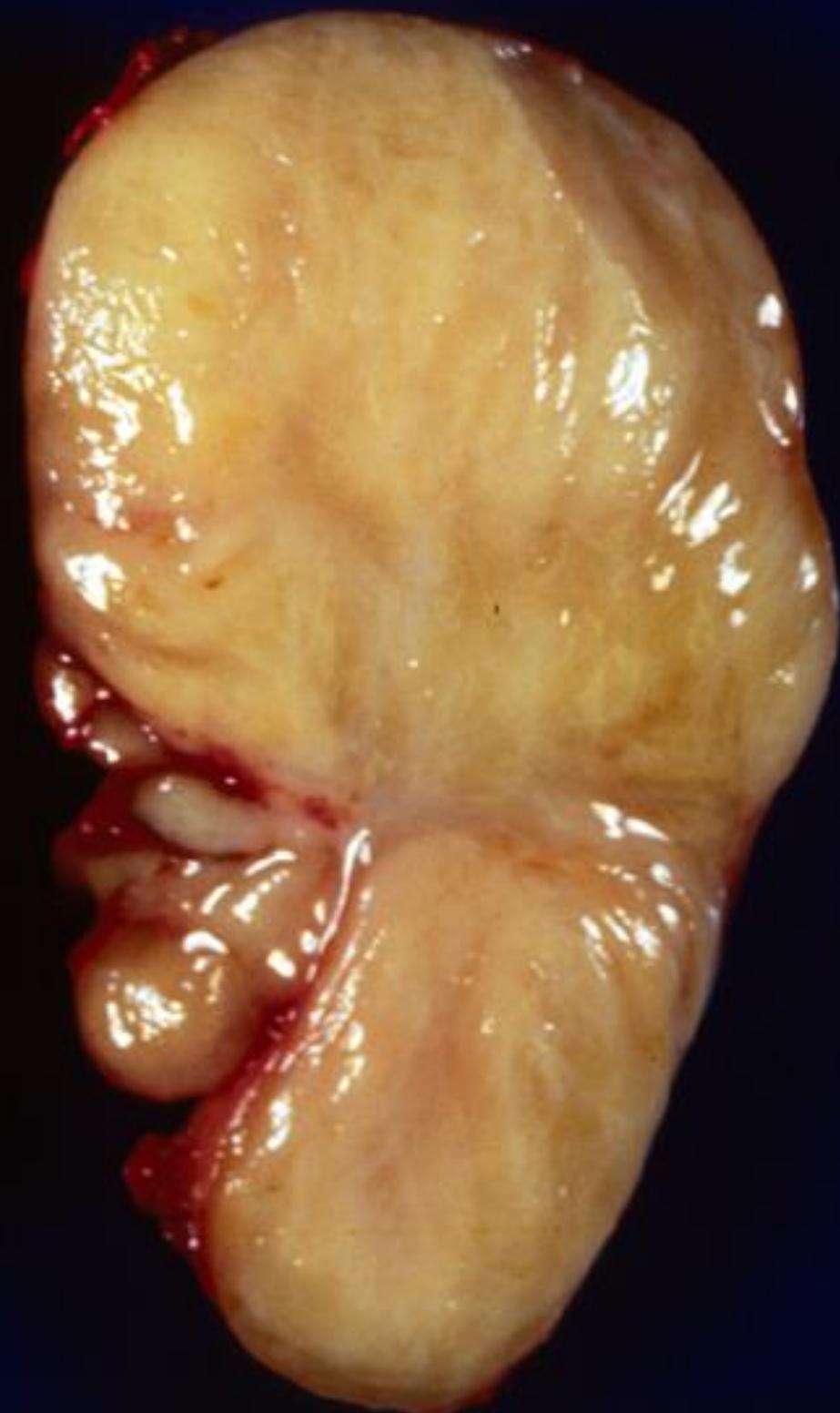


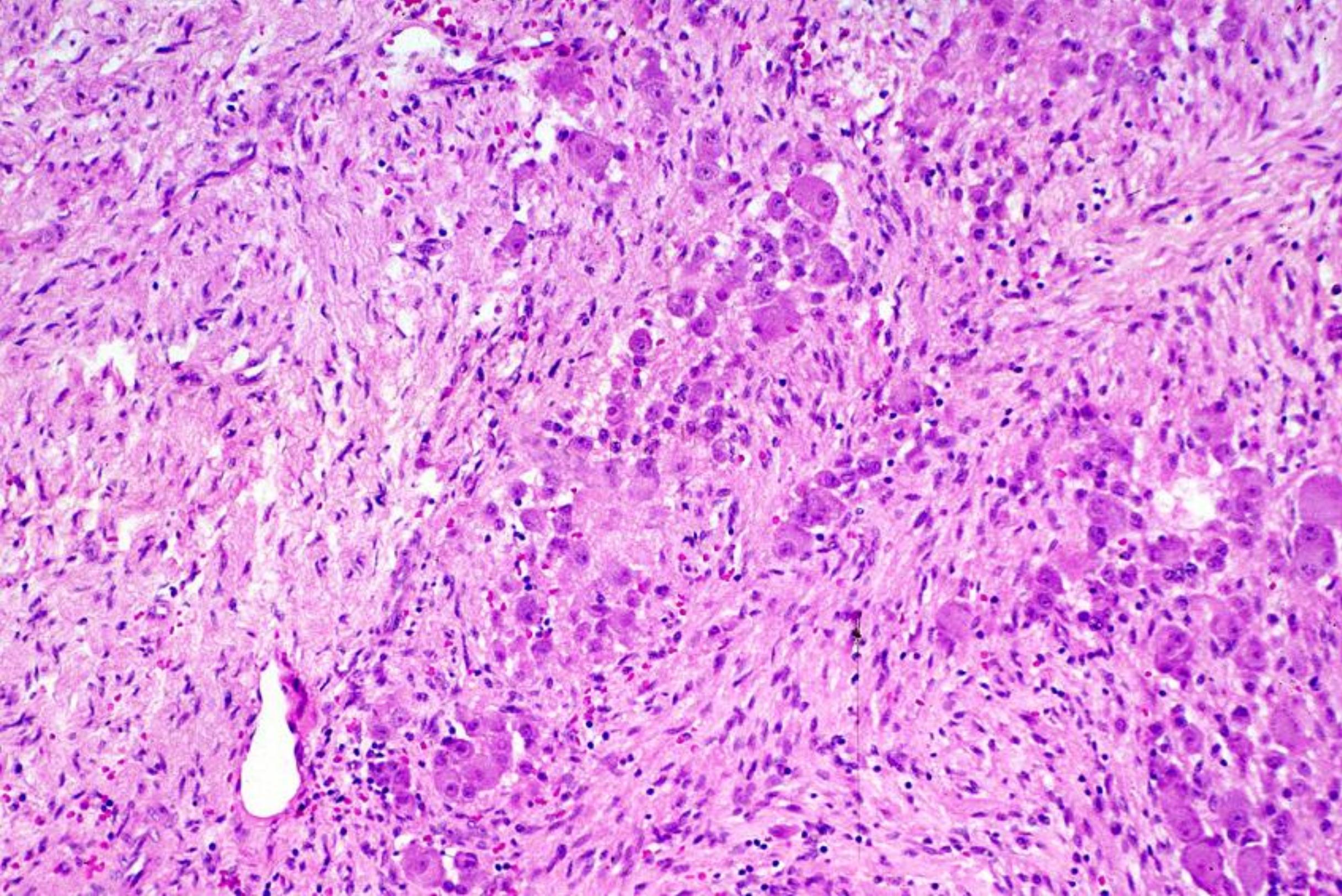


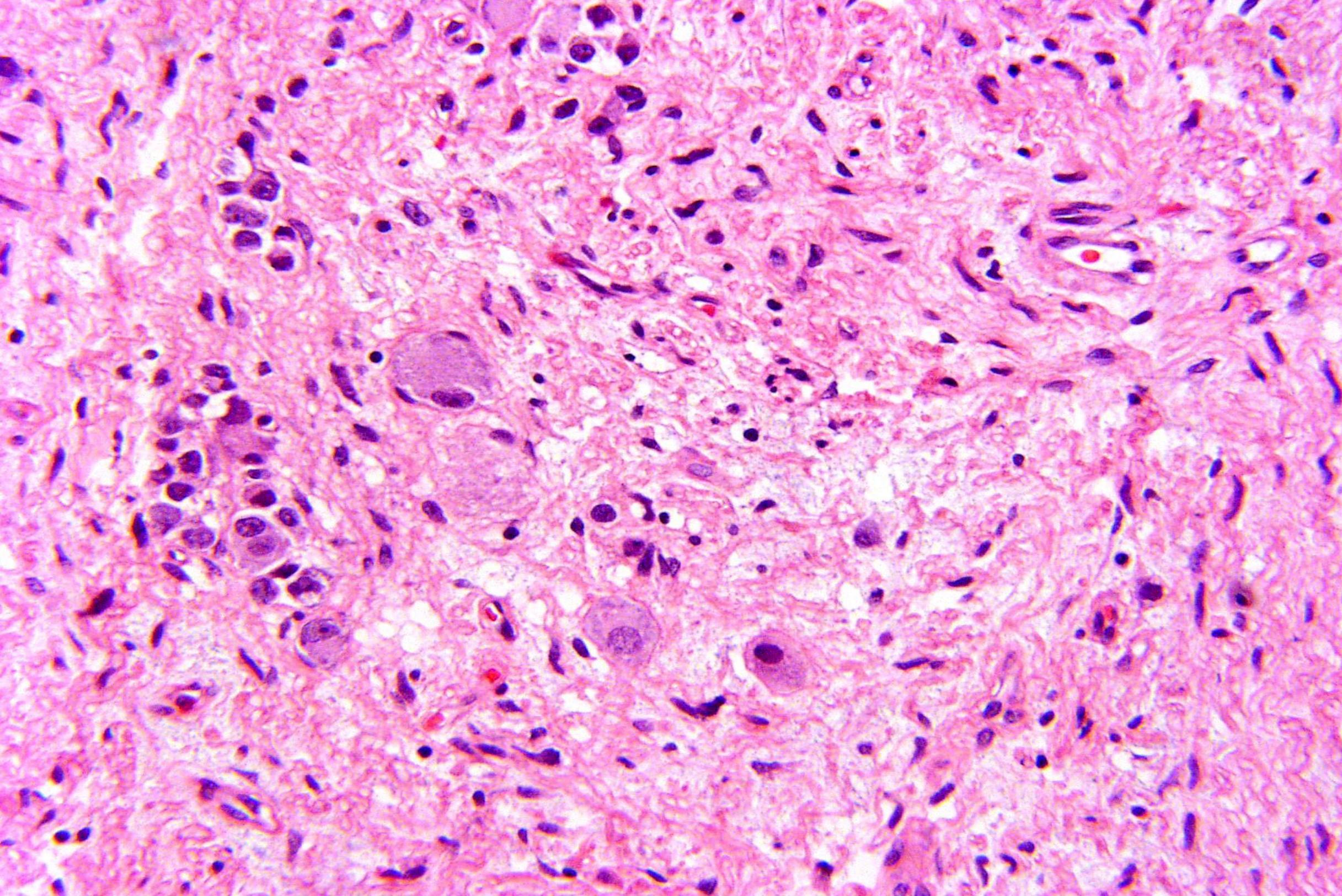
# Ganglioneuroma (Schwannian stroma-dominant)

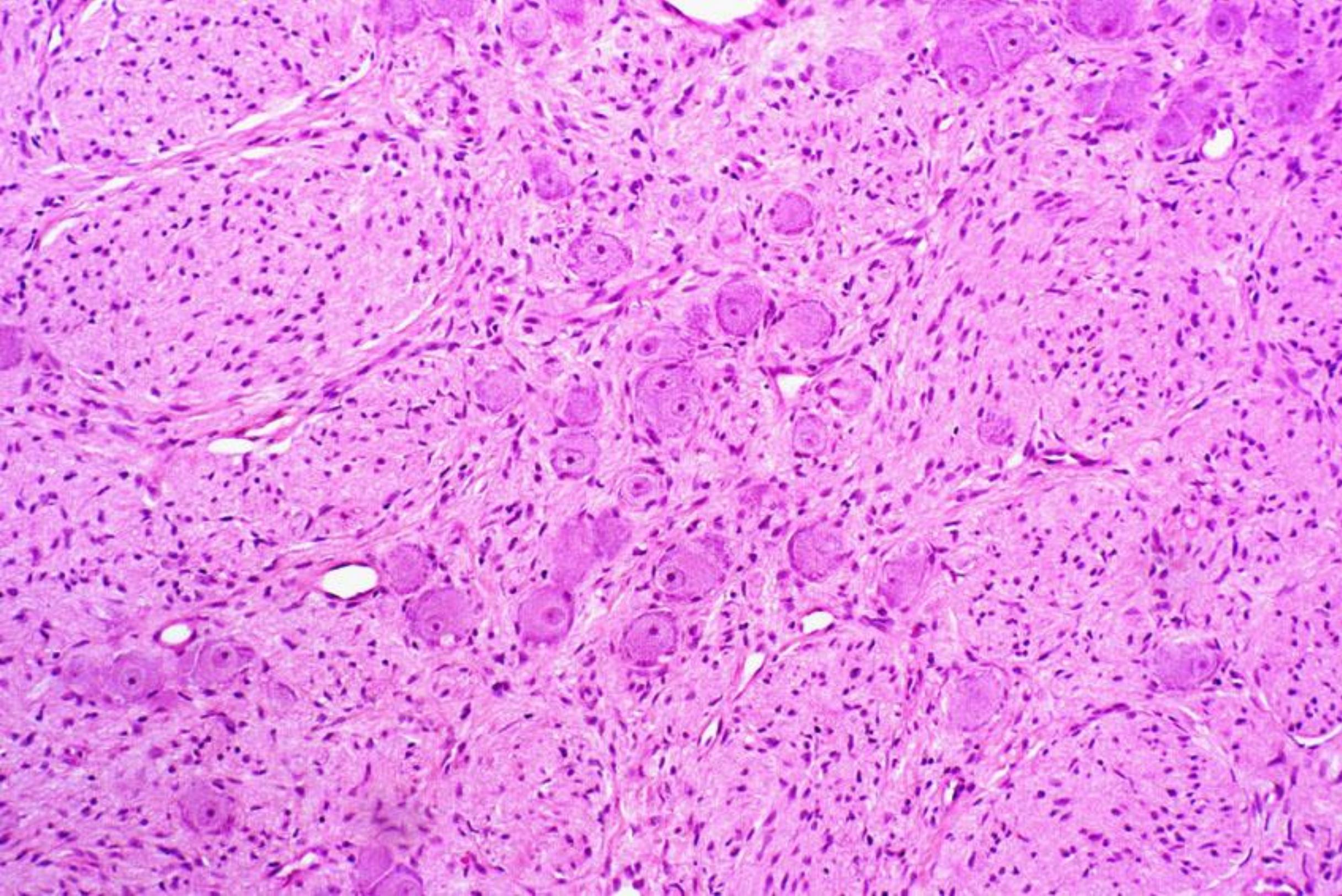
Maturing subtype

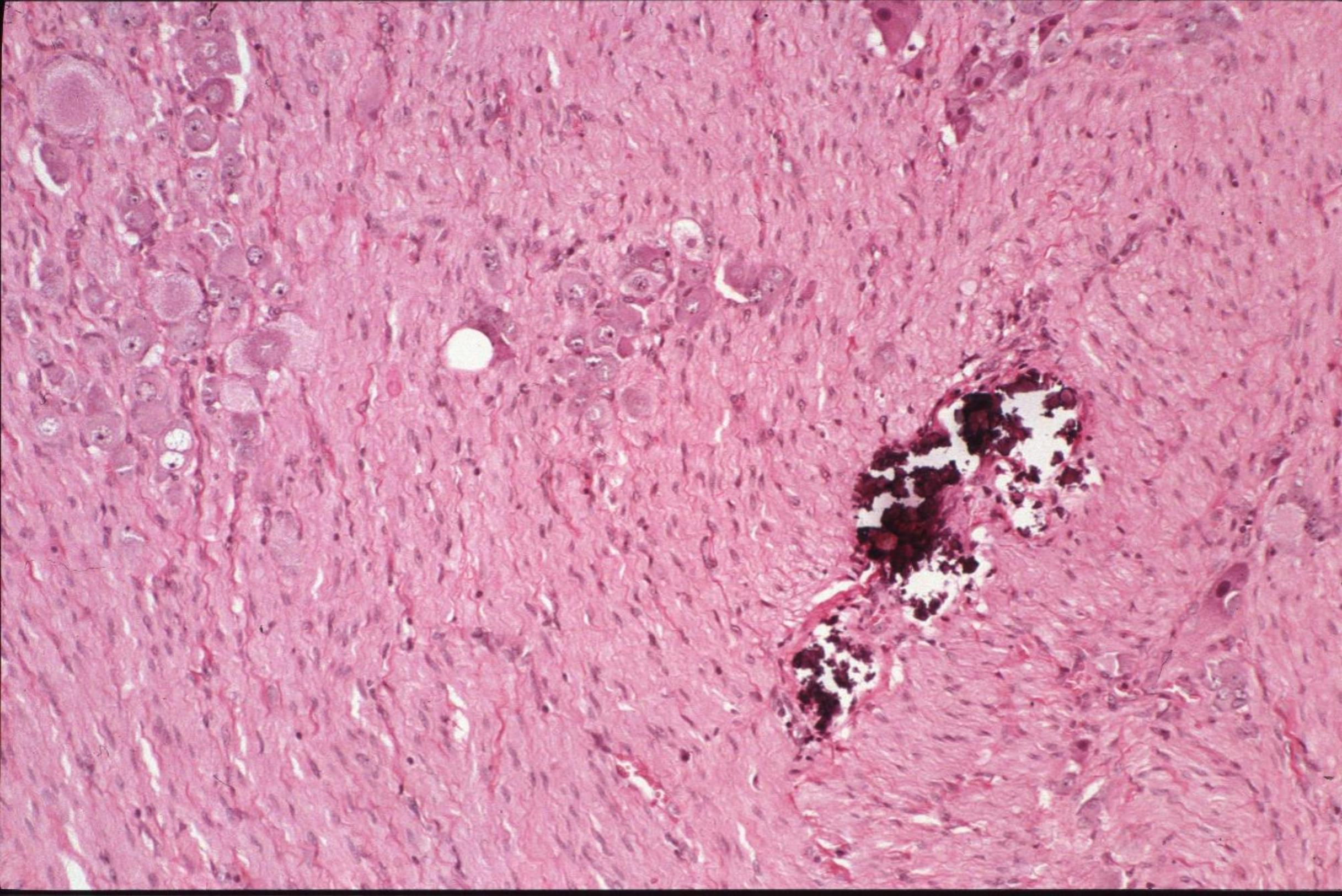
Mature subtype



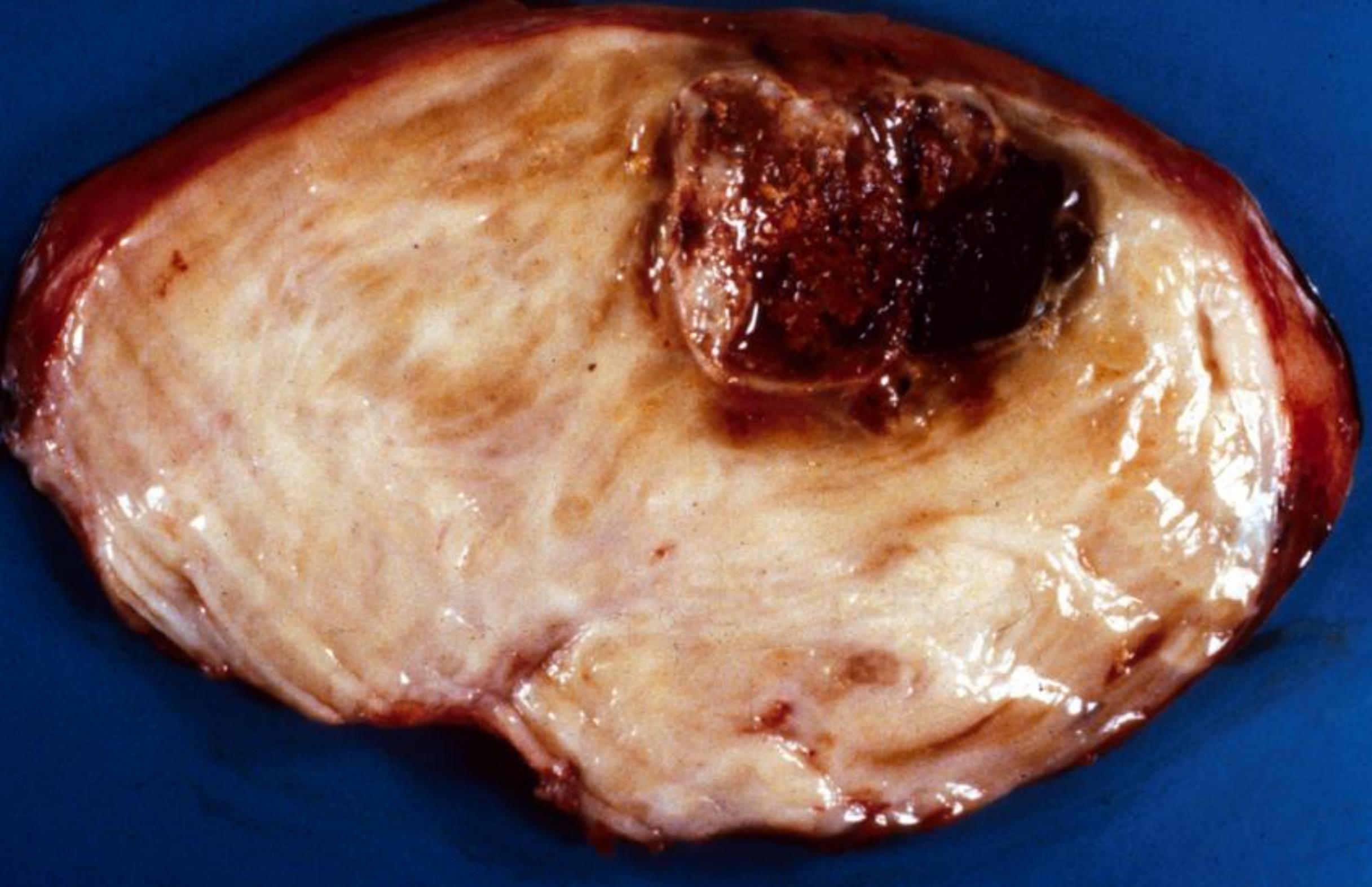


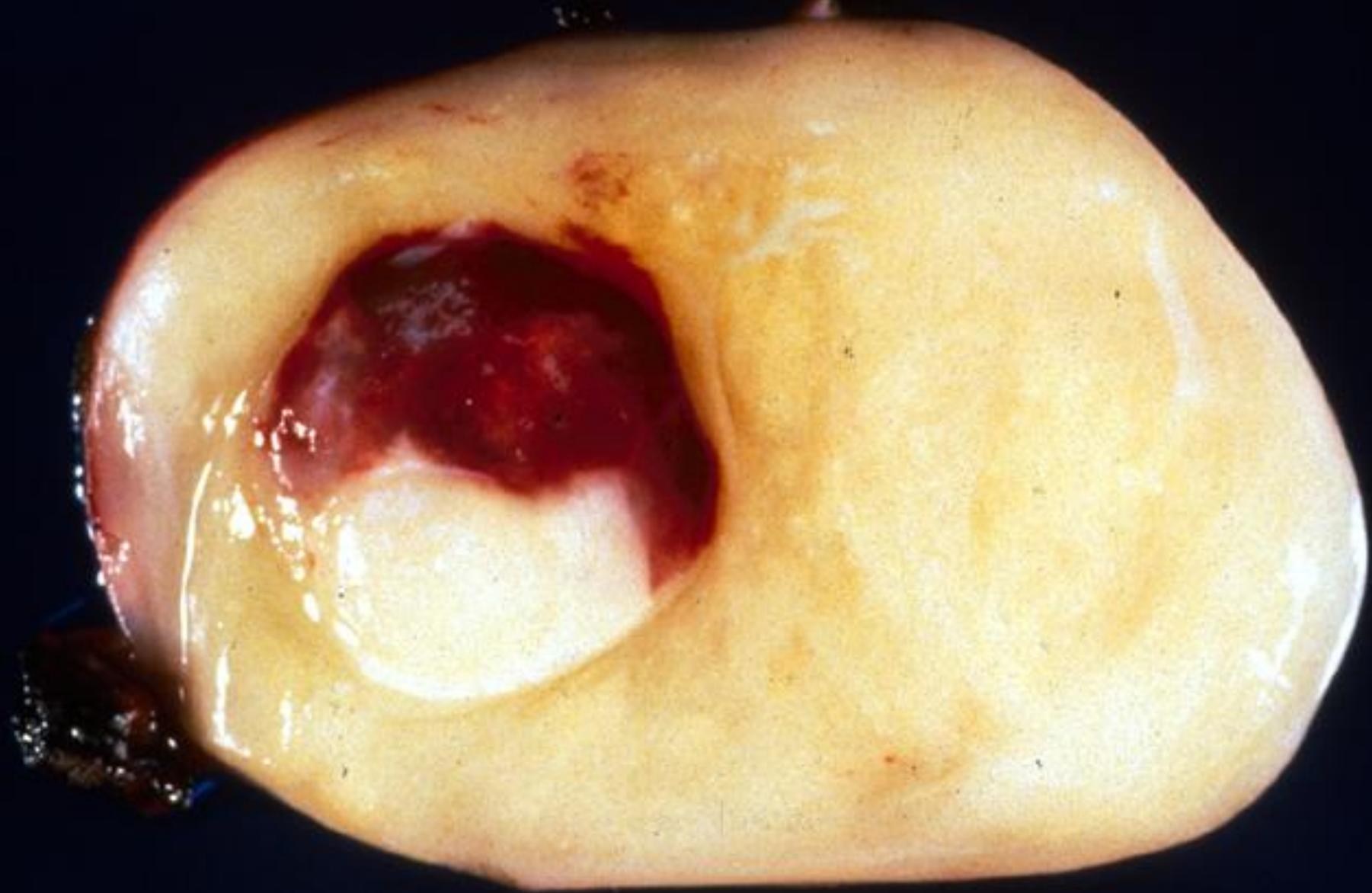


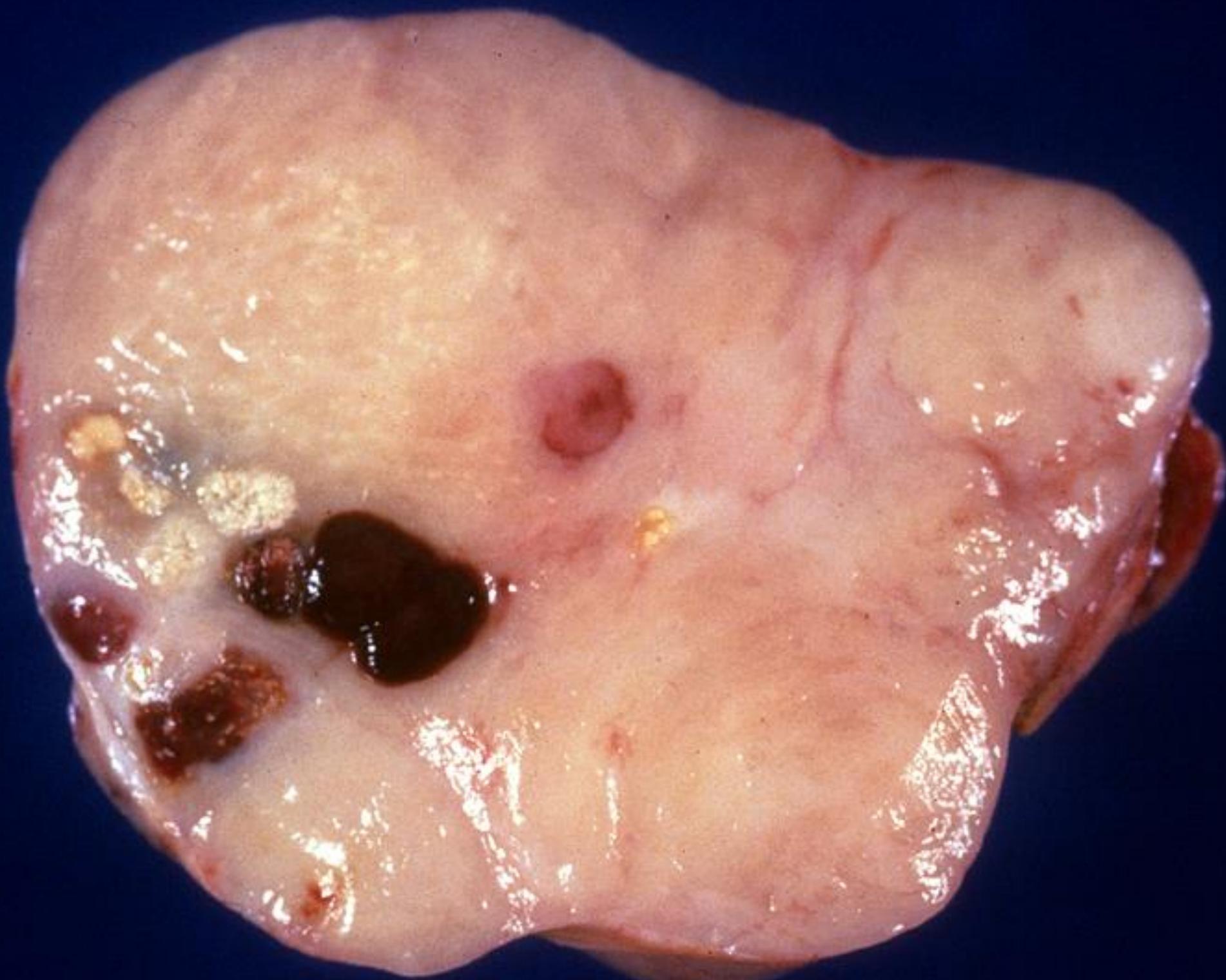




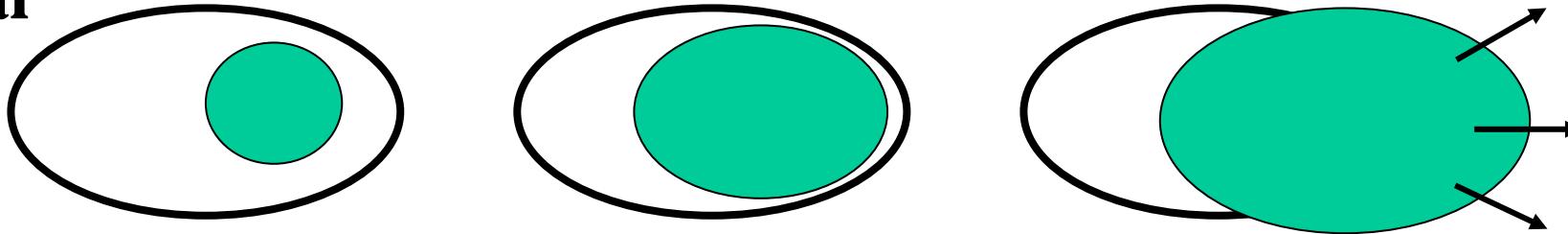
Ganglioneuroblastoma, Nodular  
(composite, Schwannian  
stroma-rich/stroma-dominant  
and stroma-poor)



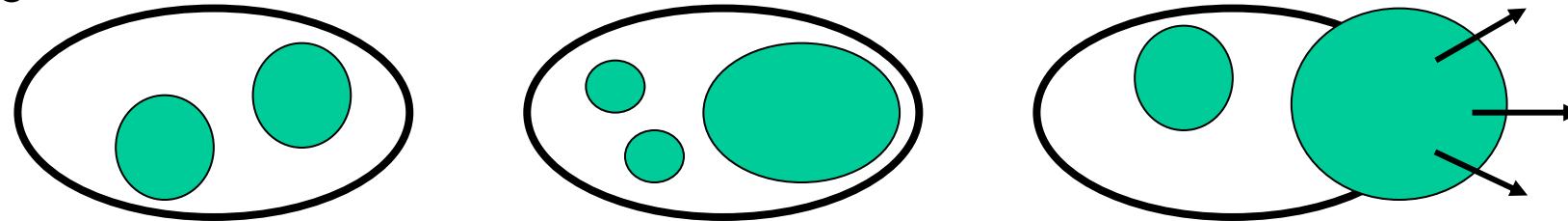




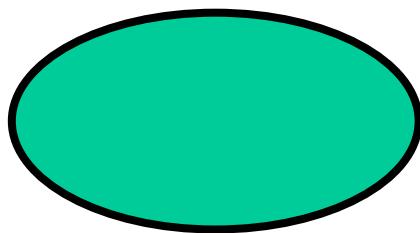
**Classical**



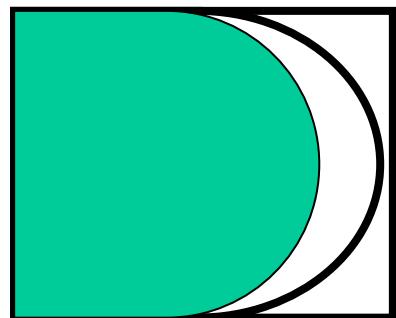
**Multiple**



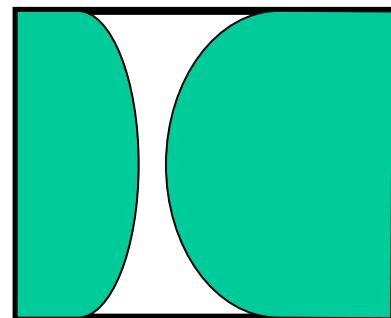
**Large Nodule(s)**



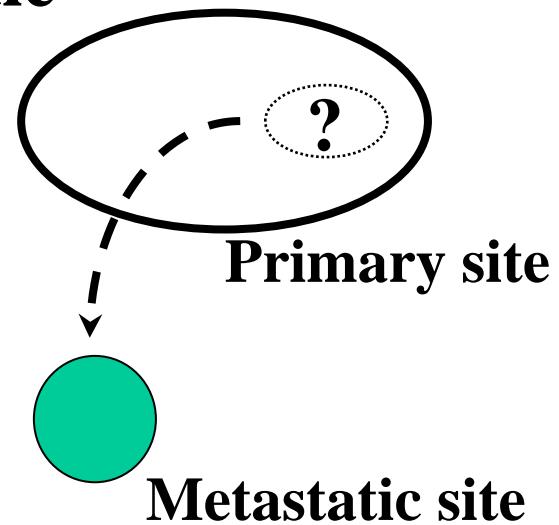
**a) Single**



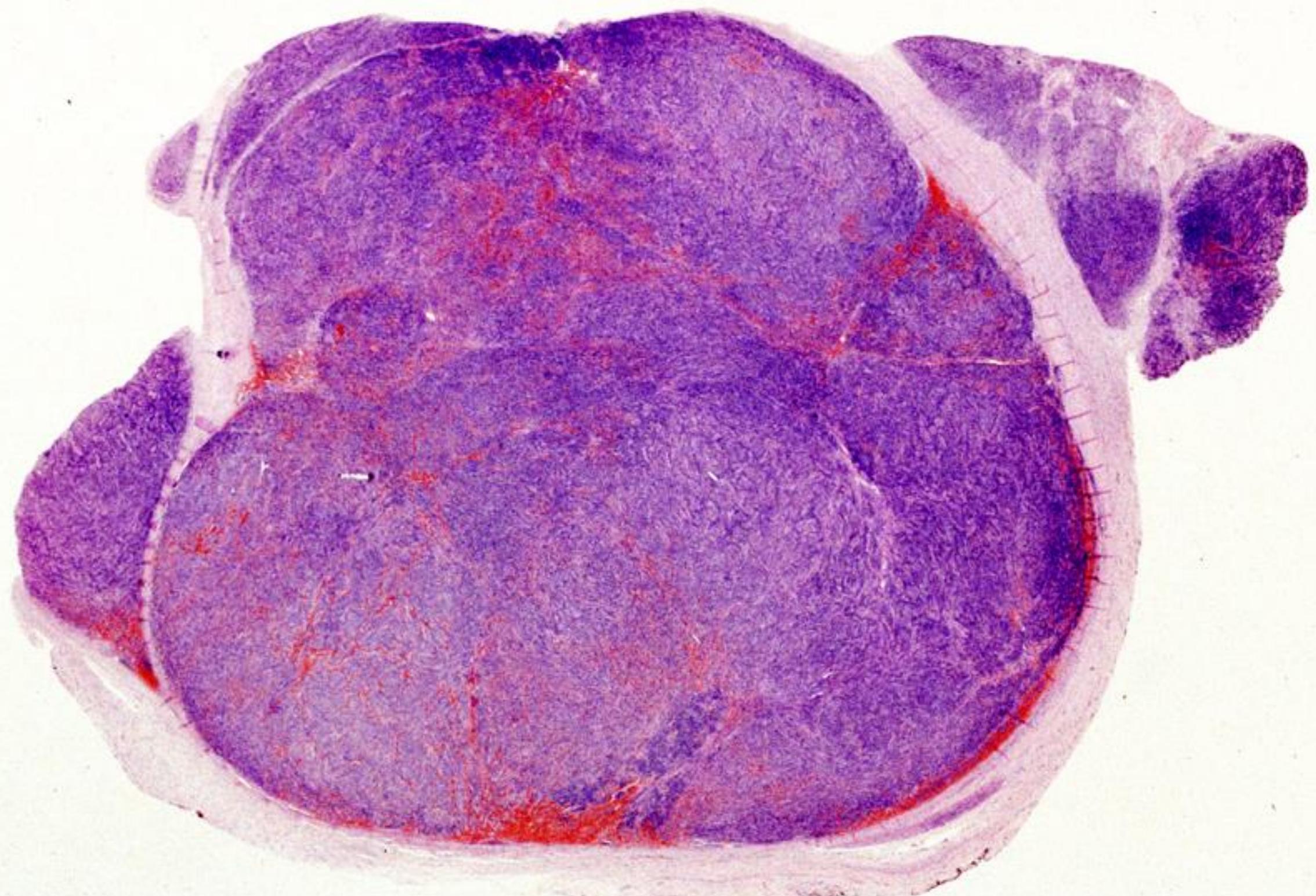
**b) Multiple**

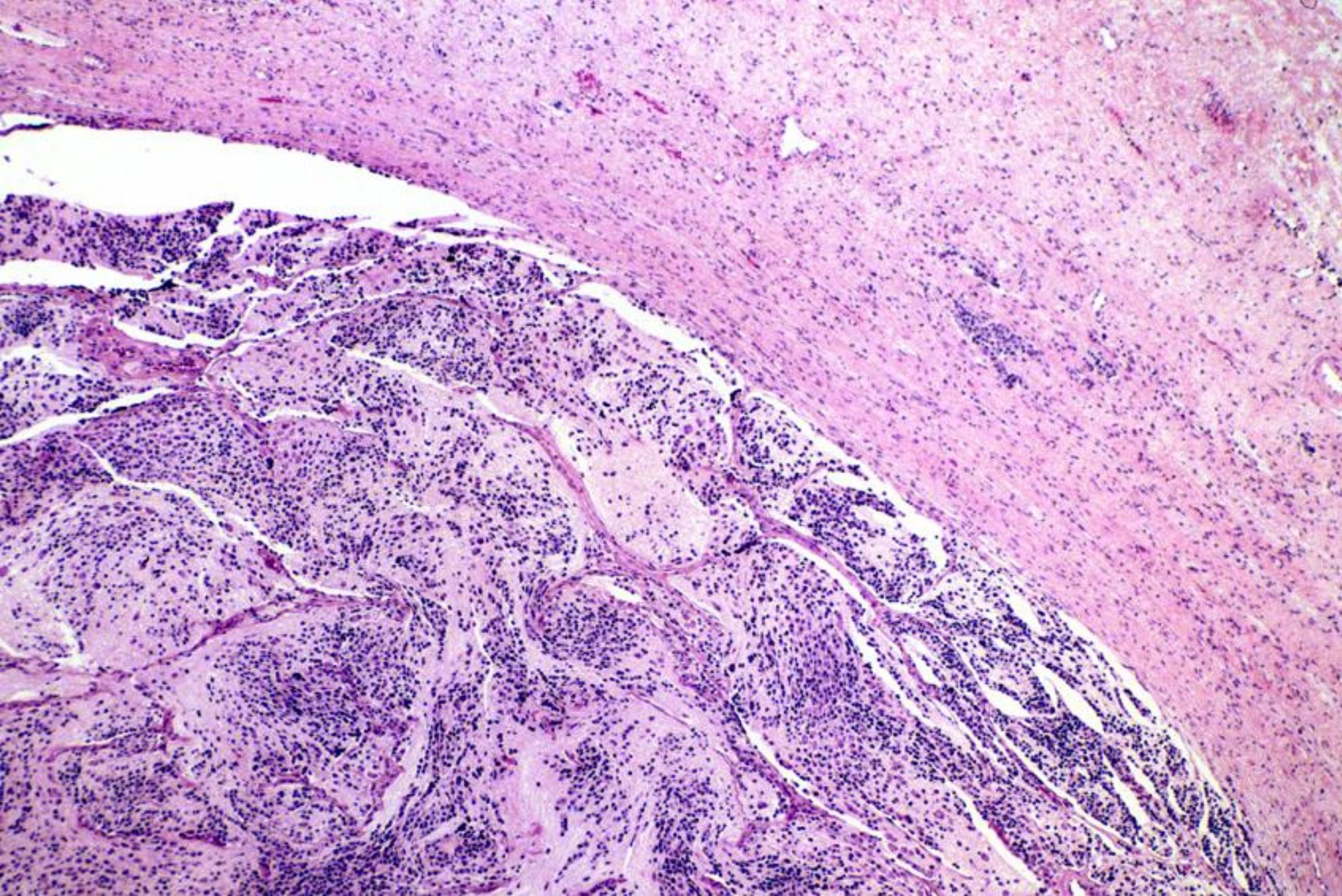


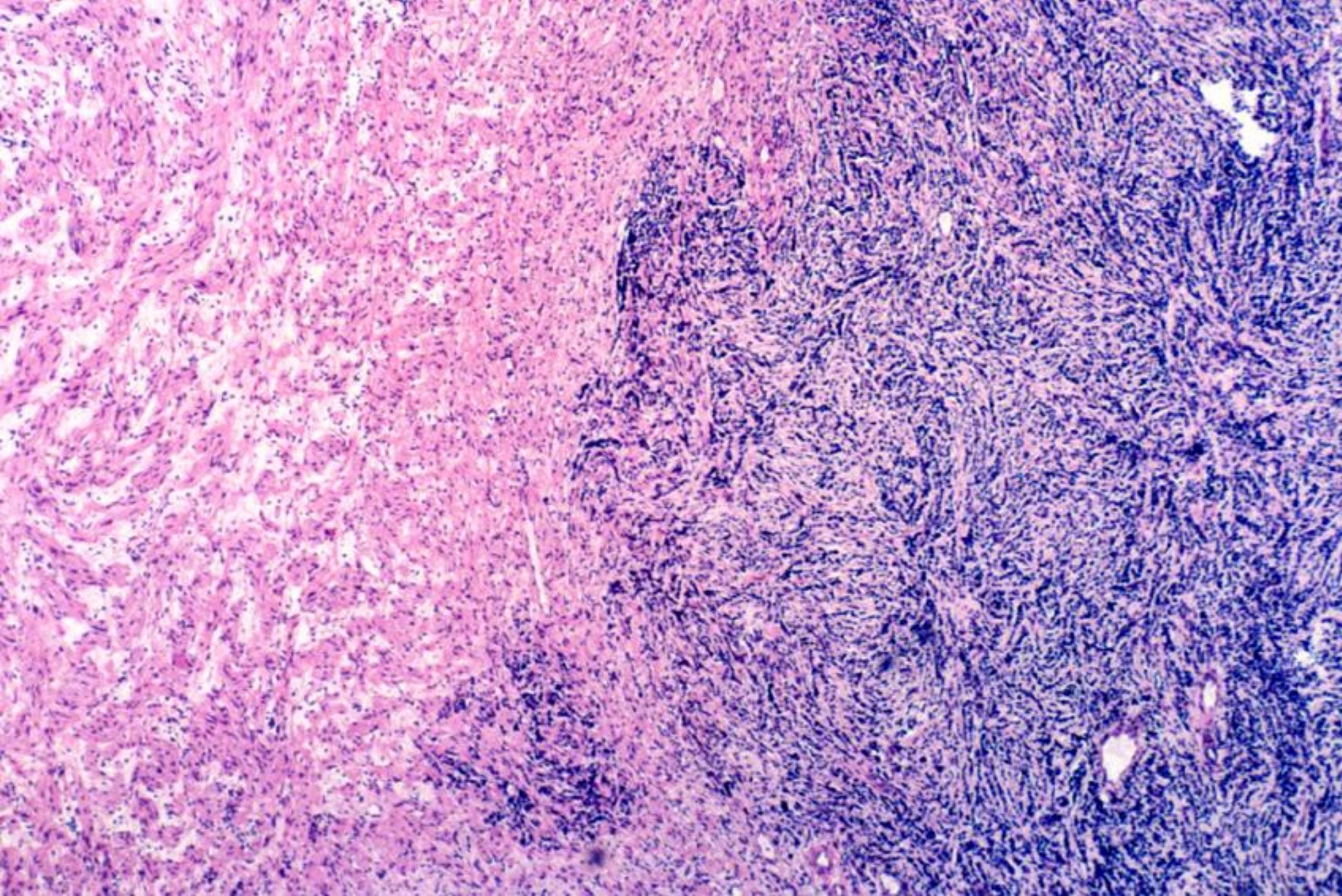
**No Nodule**

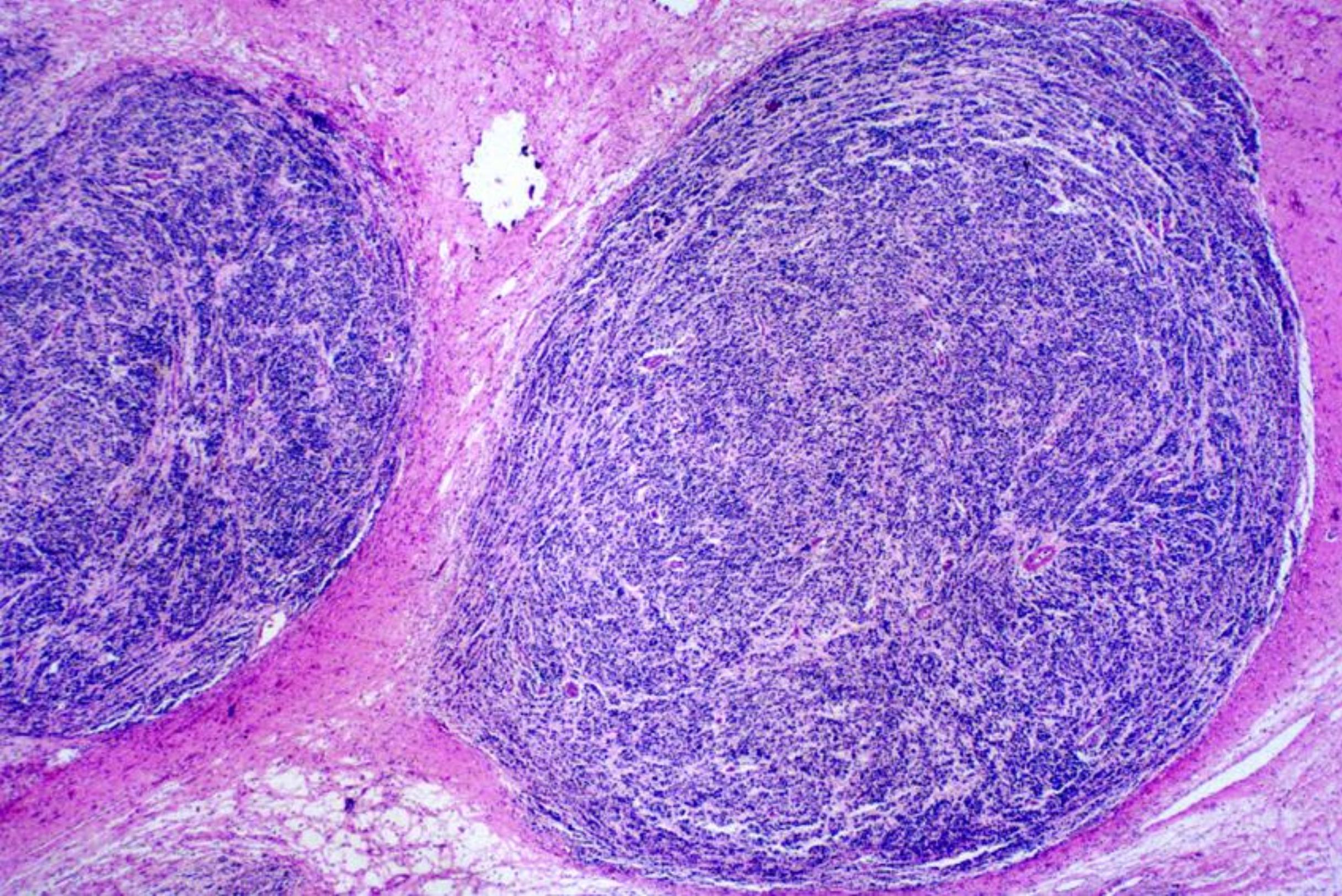


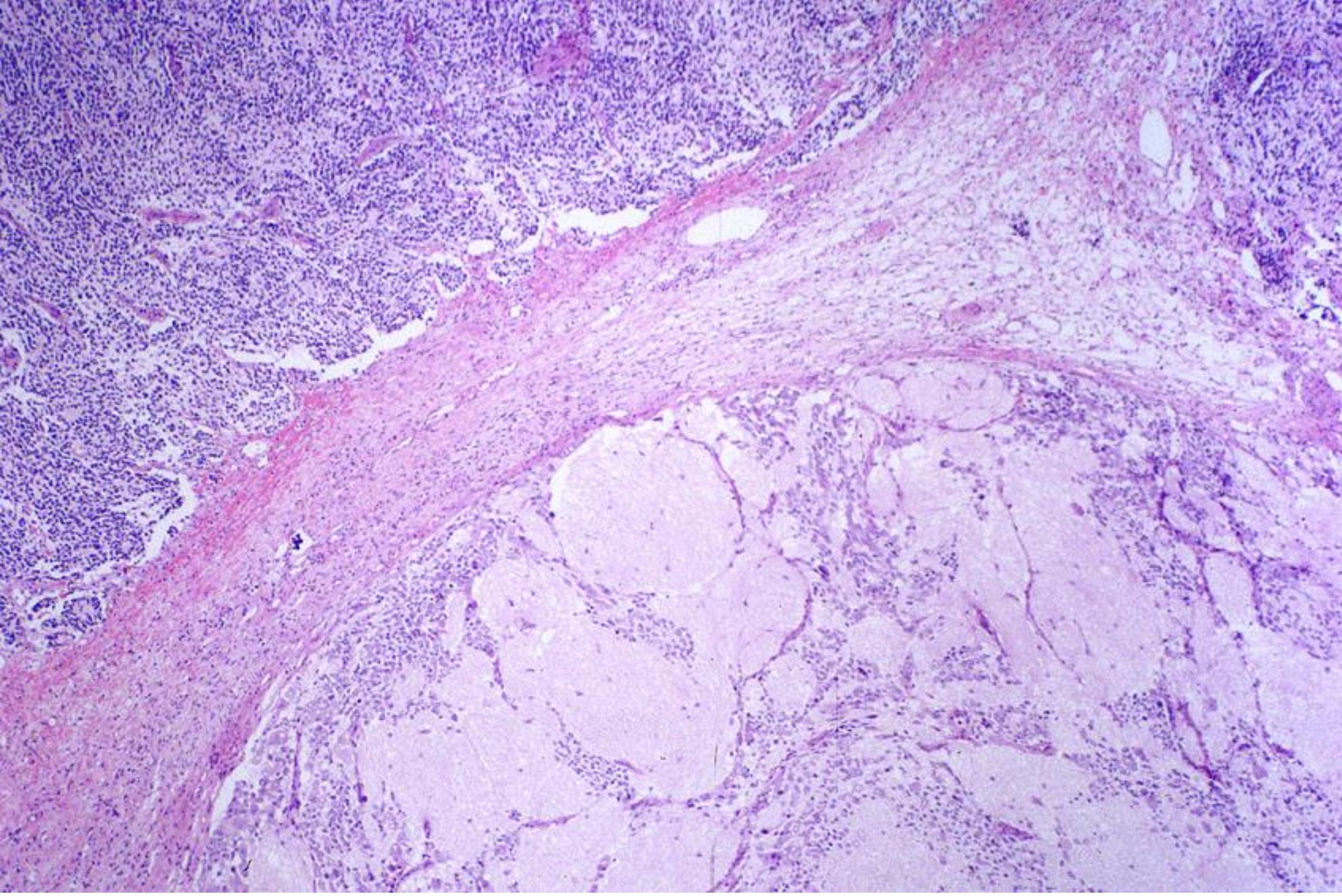


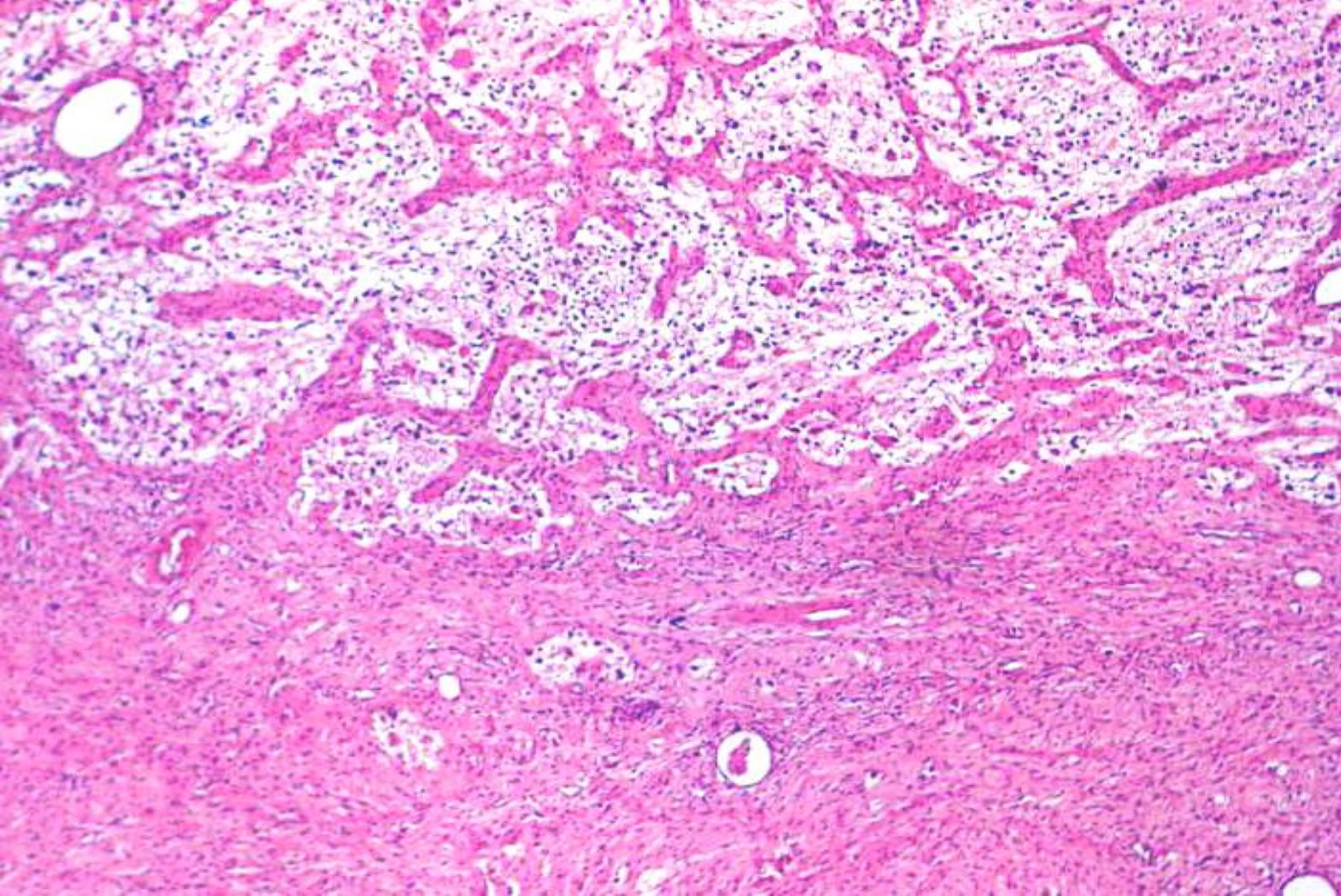


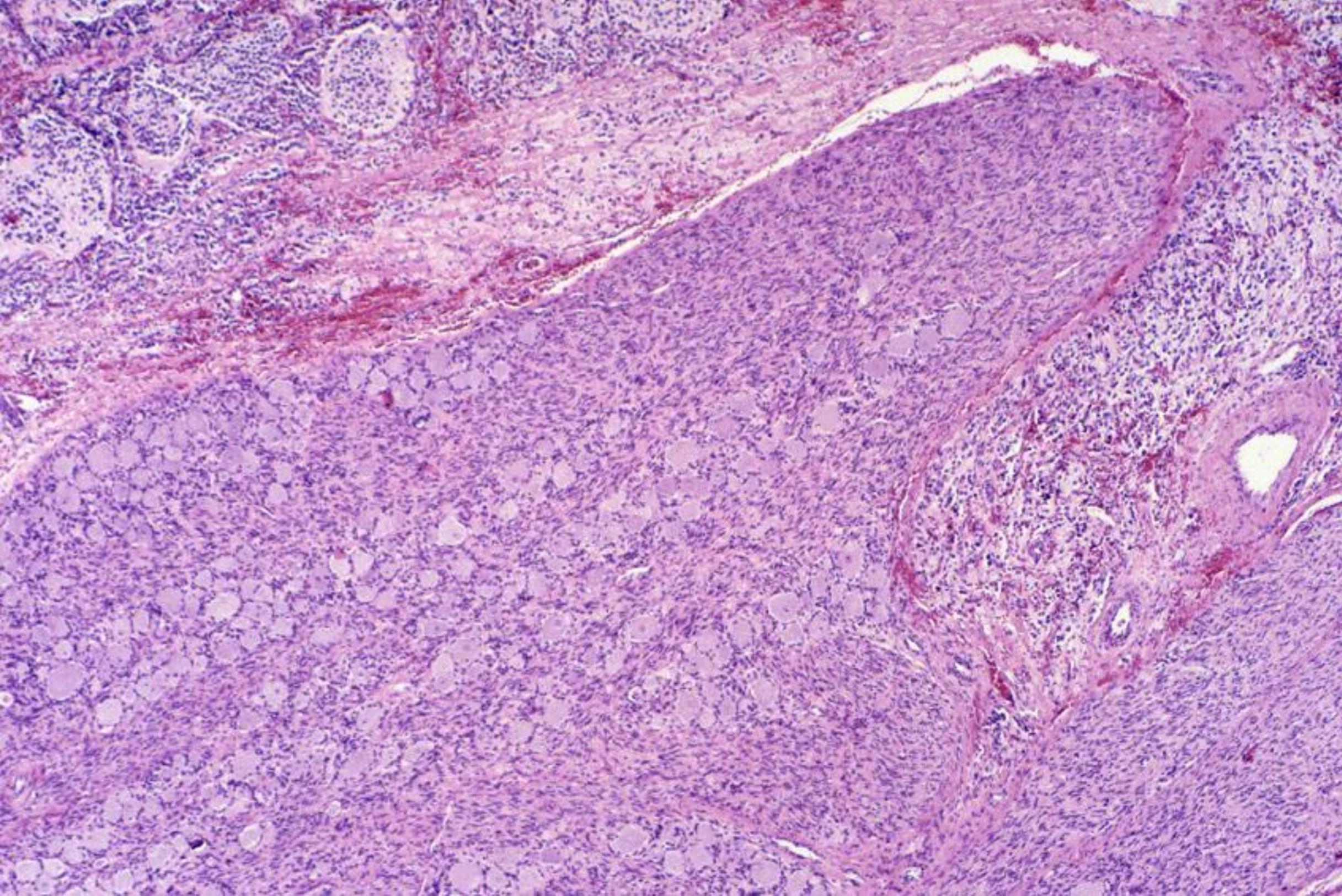












# Particular Features of Peripheral Neuroblastic Tumors

Embryonic rest/Neuroblastoma *in situ*

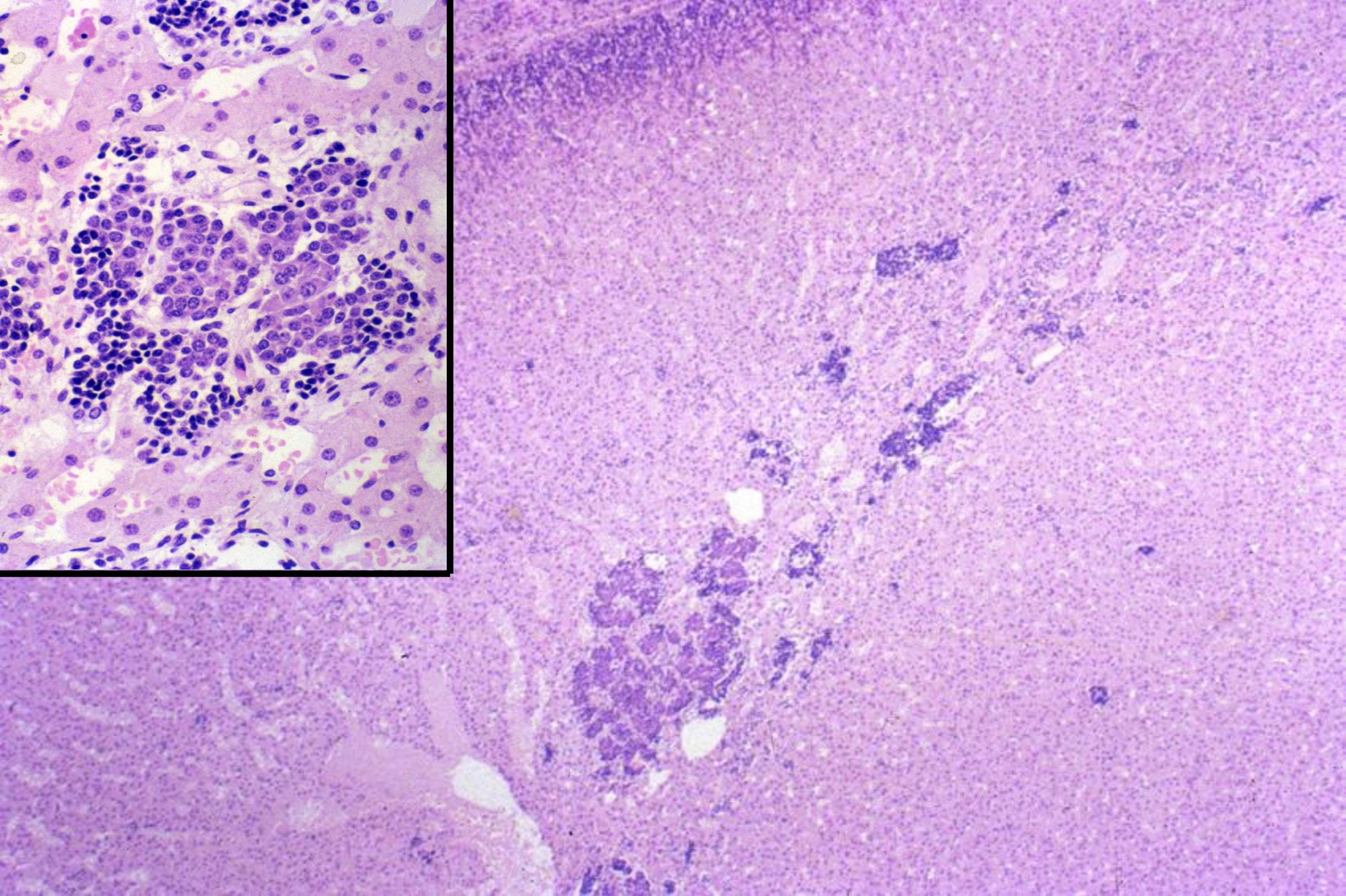
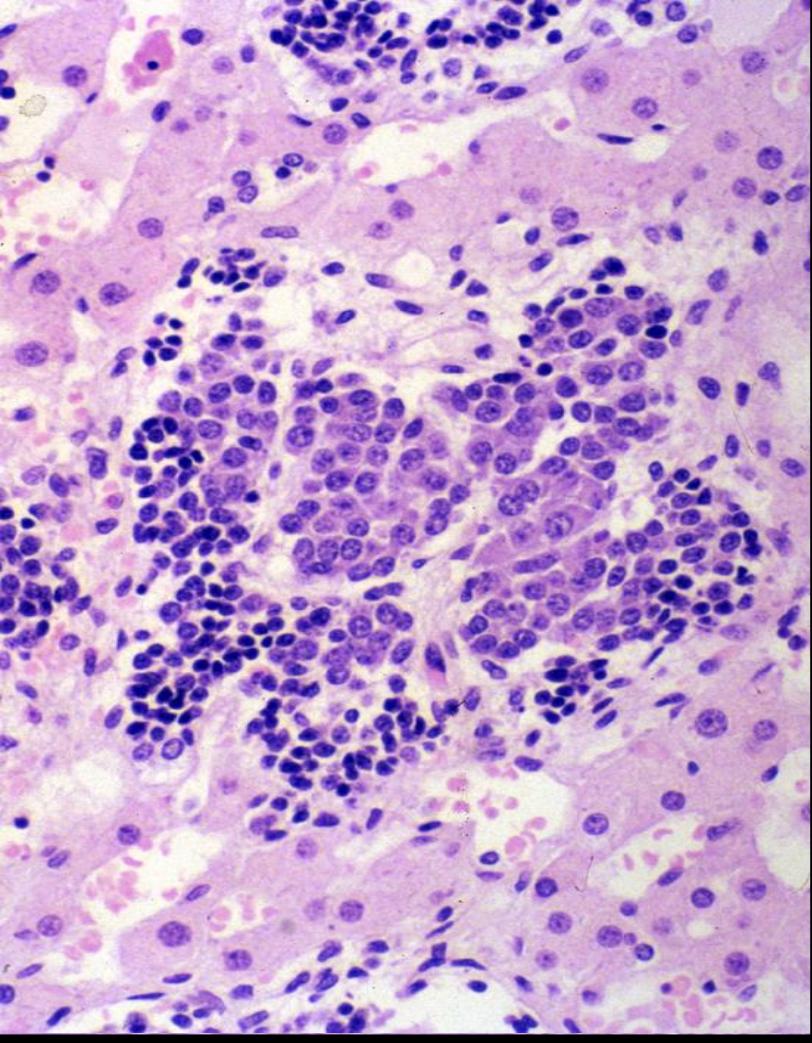
Stage 4S Disease

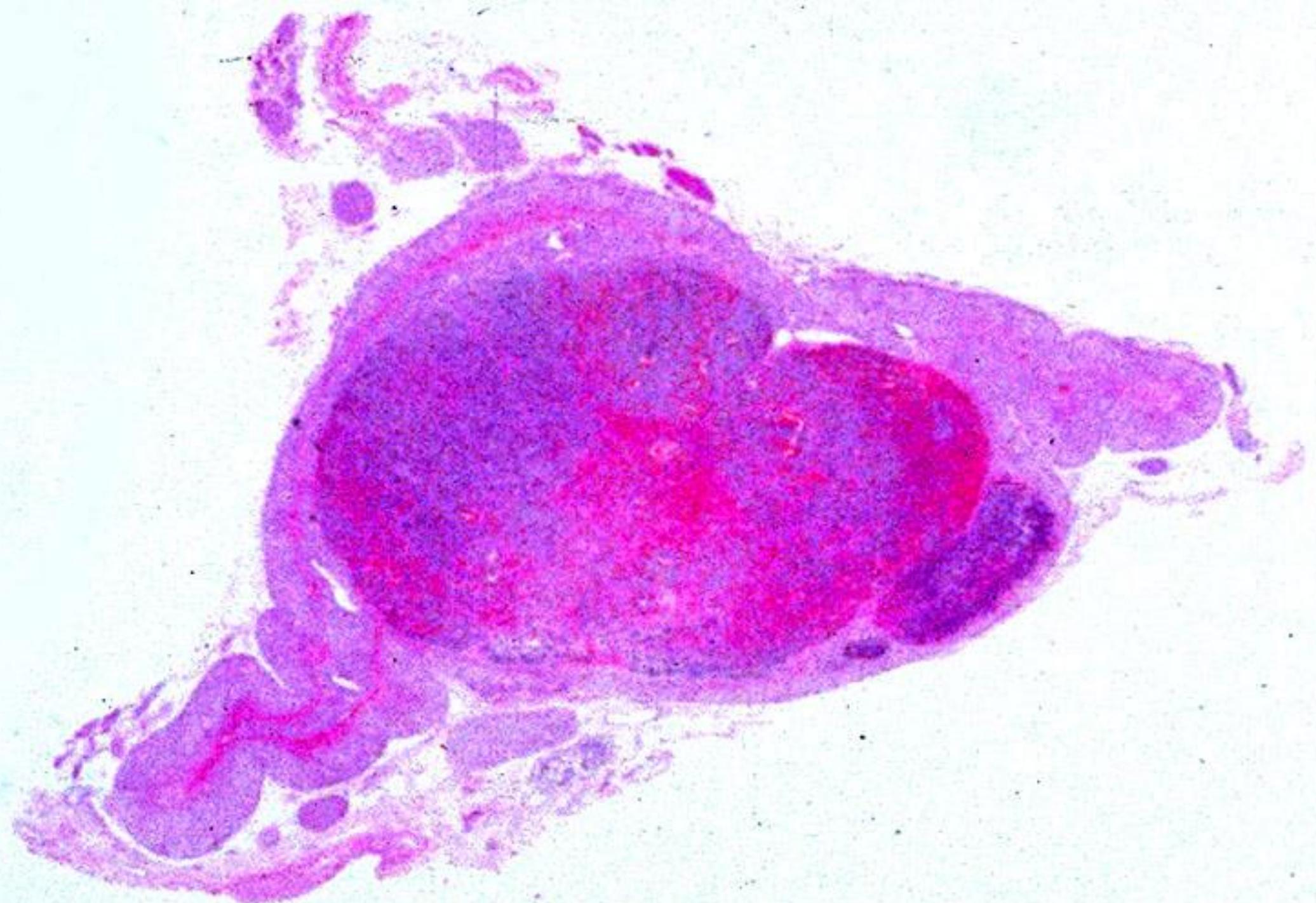
Cystic Neuroblastoma

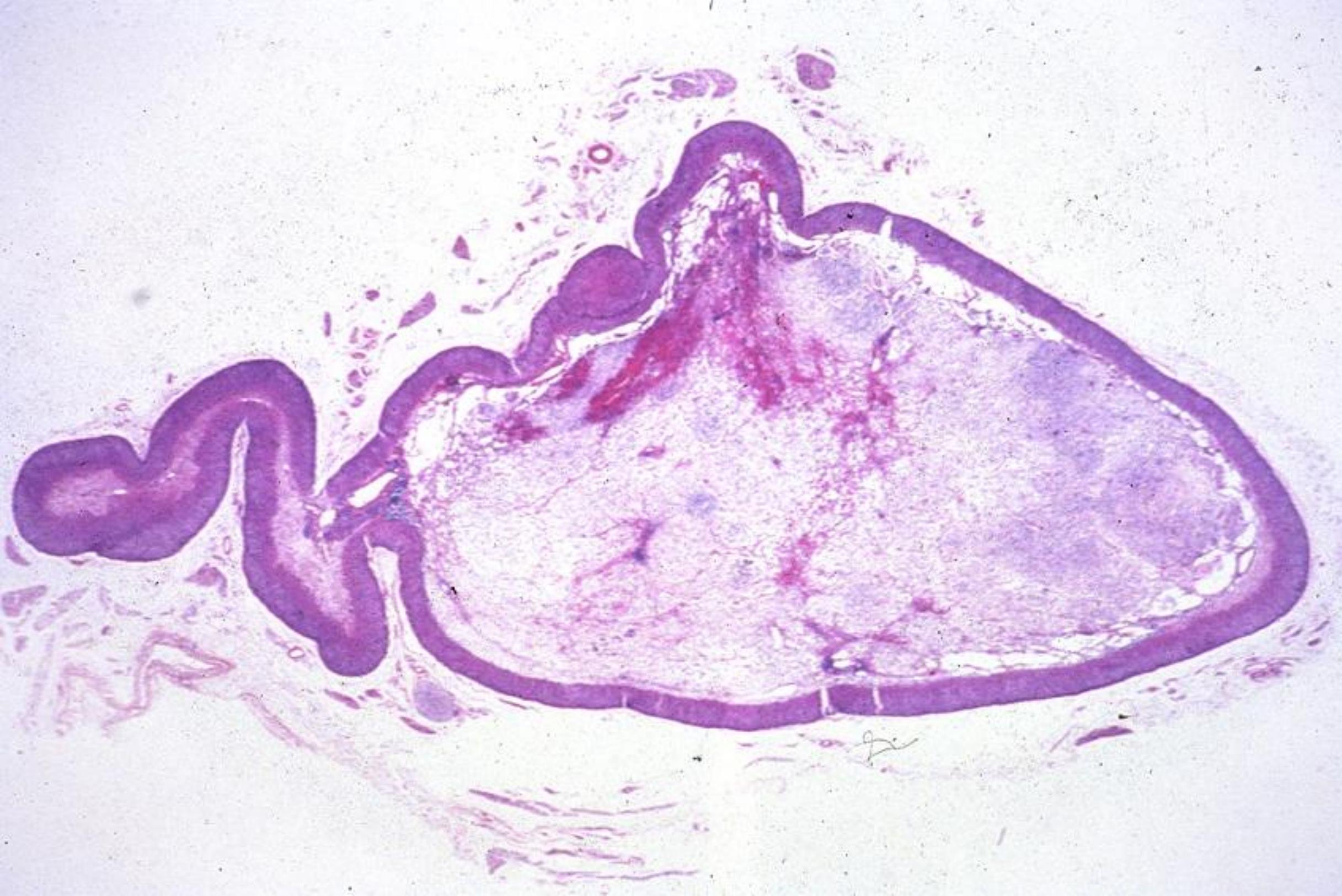
Angiomatoid Neuroblastoma

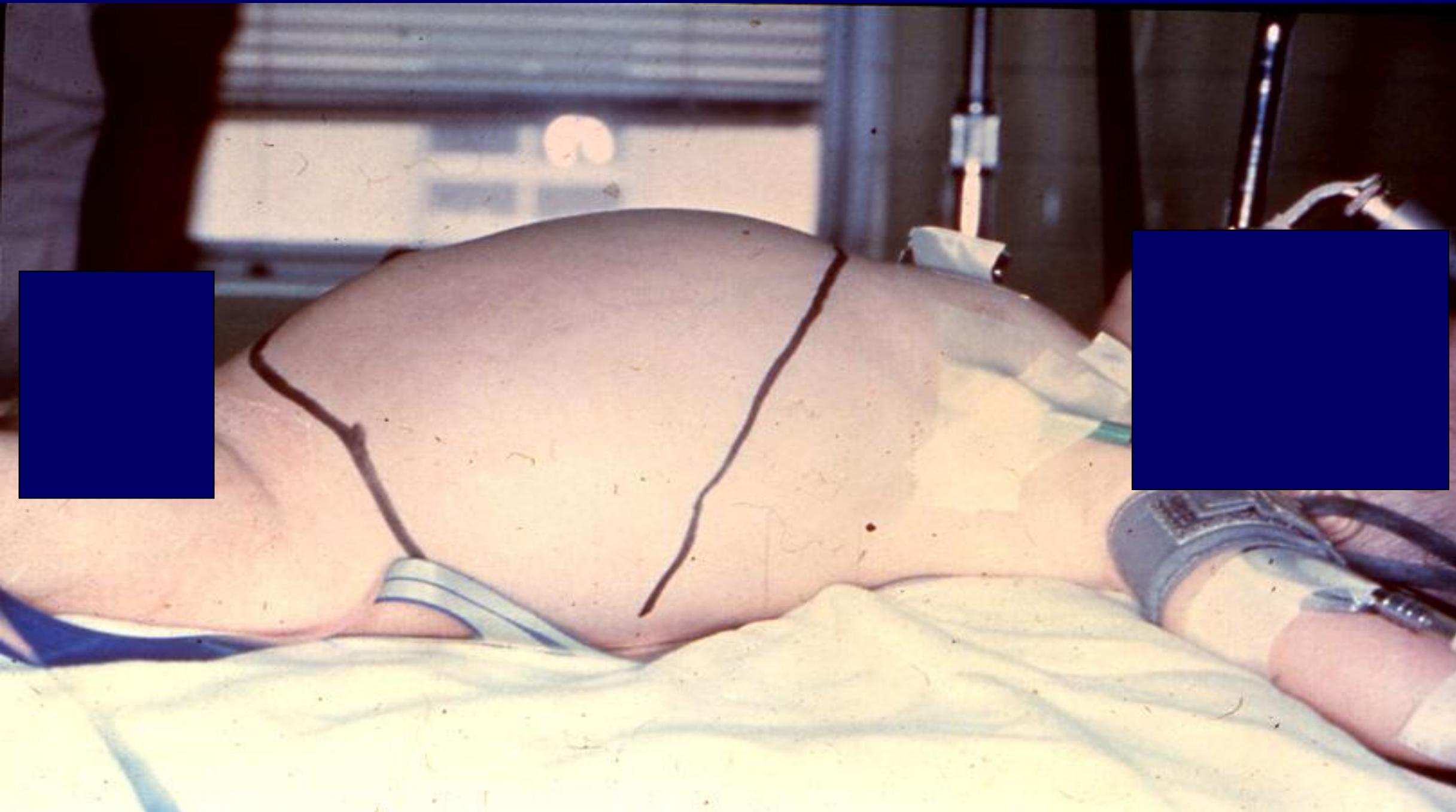
Neuroblastoma with OMA

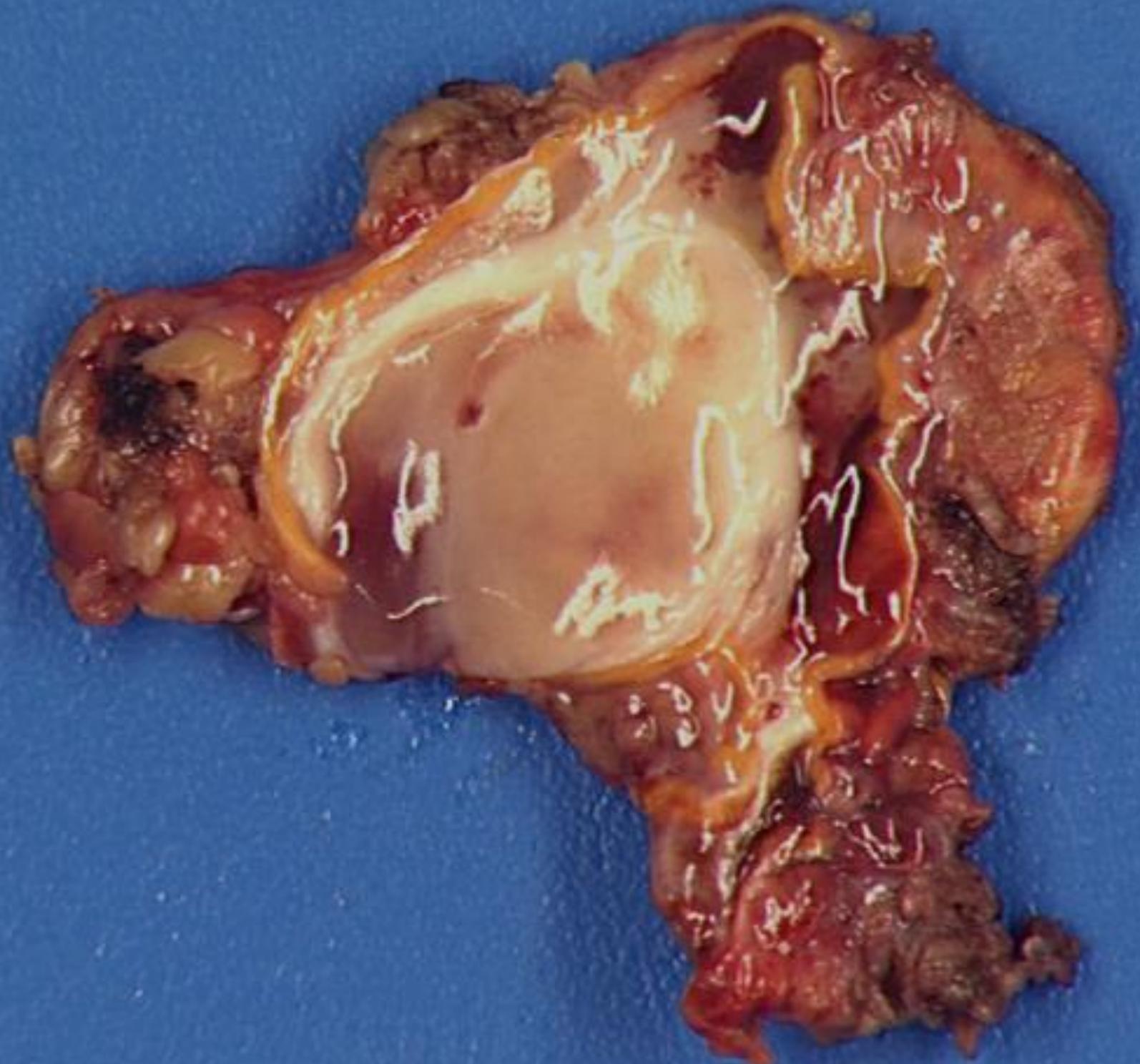
Neuroblastoma detected through Mass  
Screening

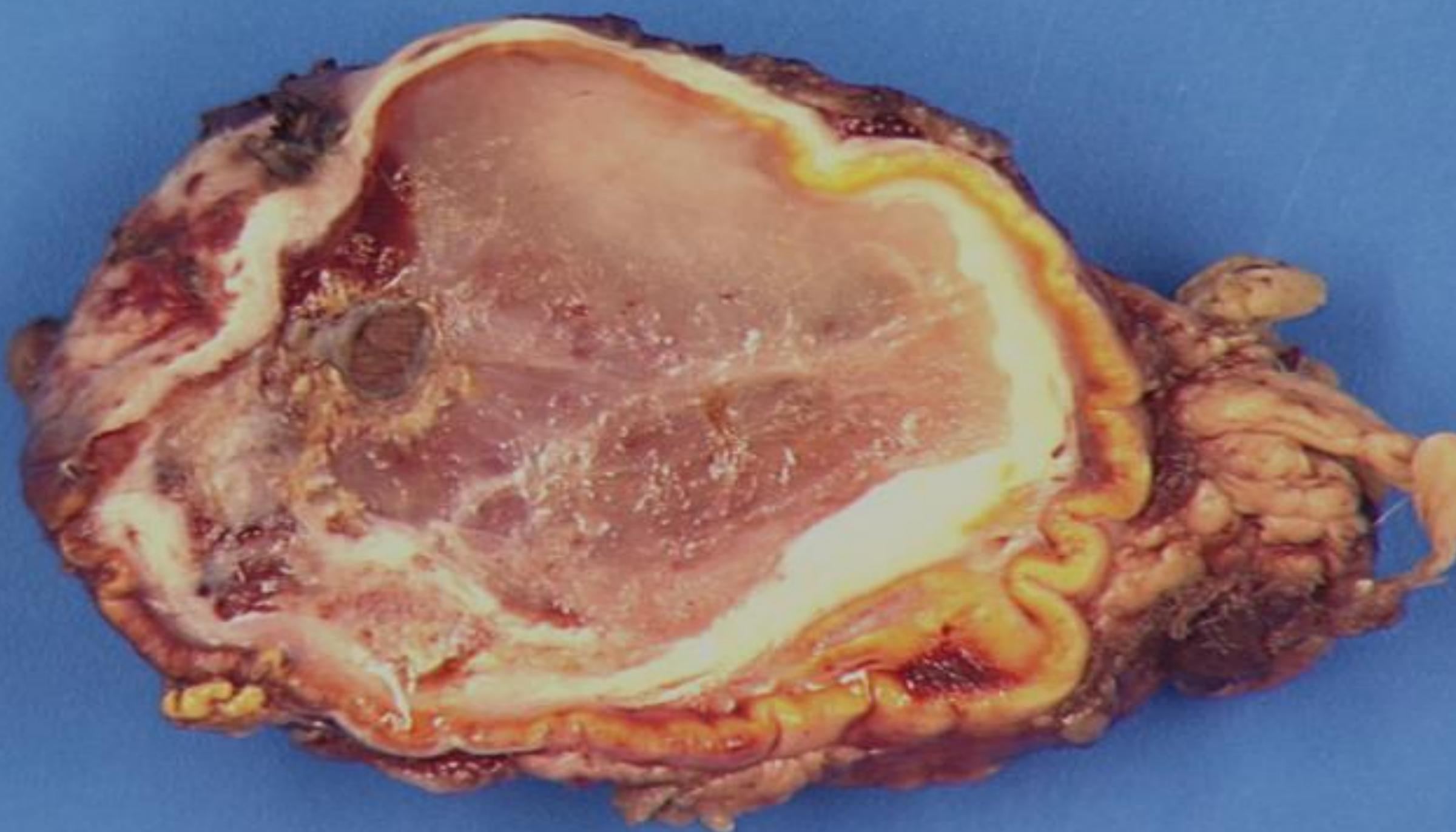


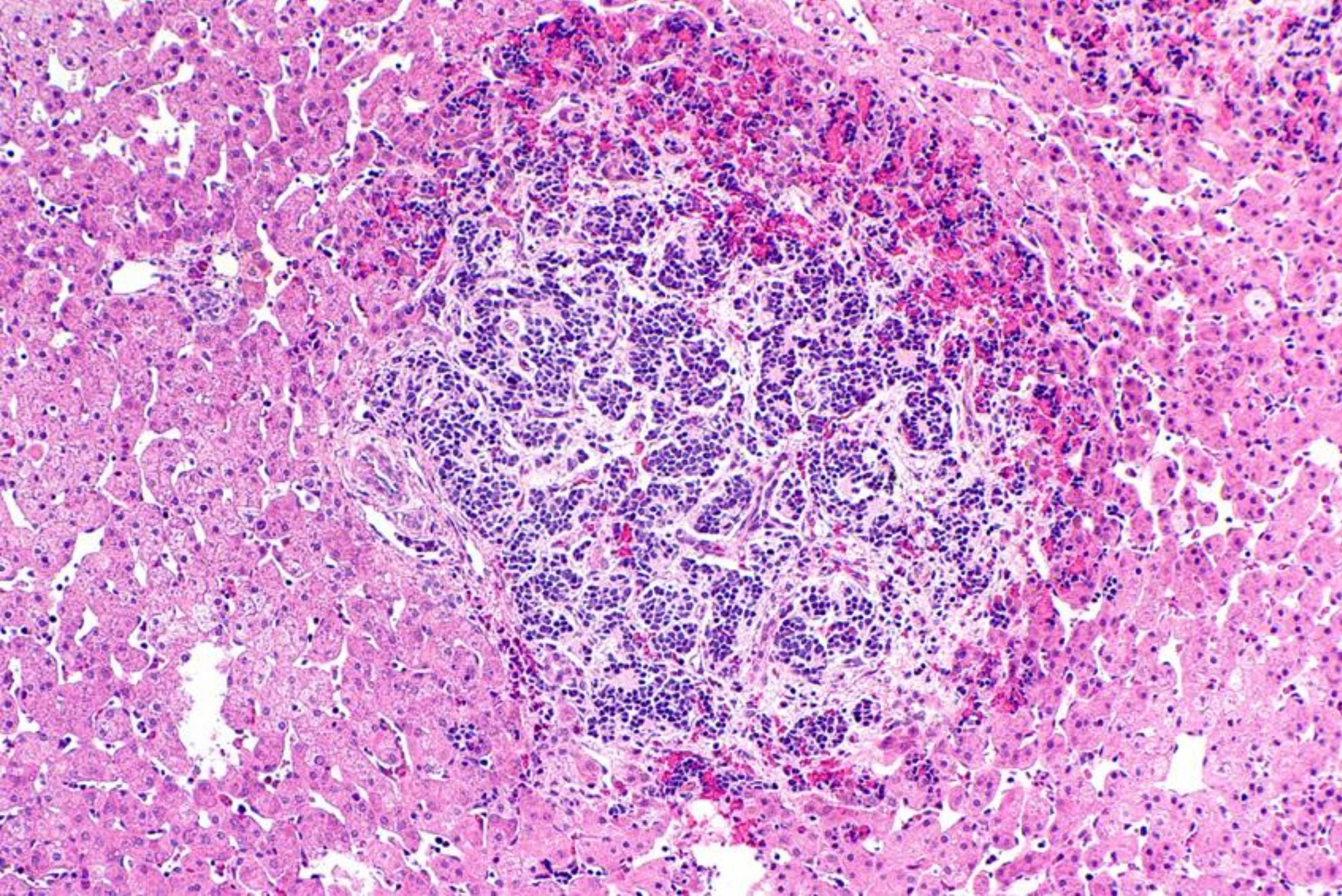


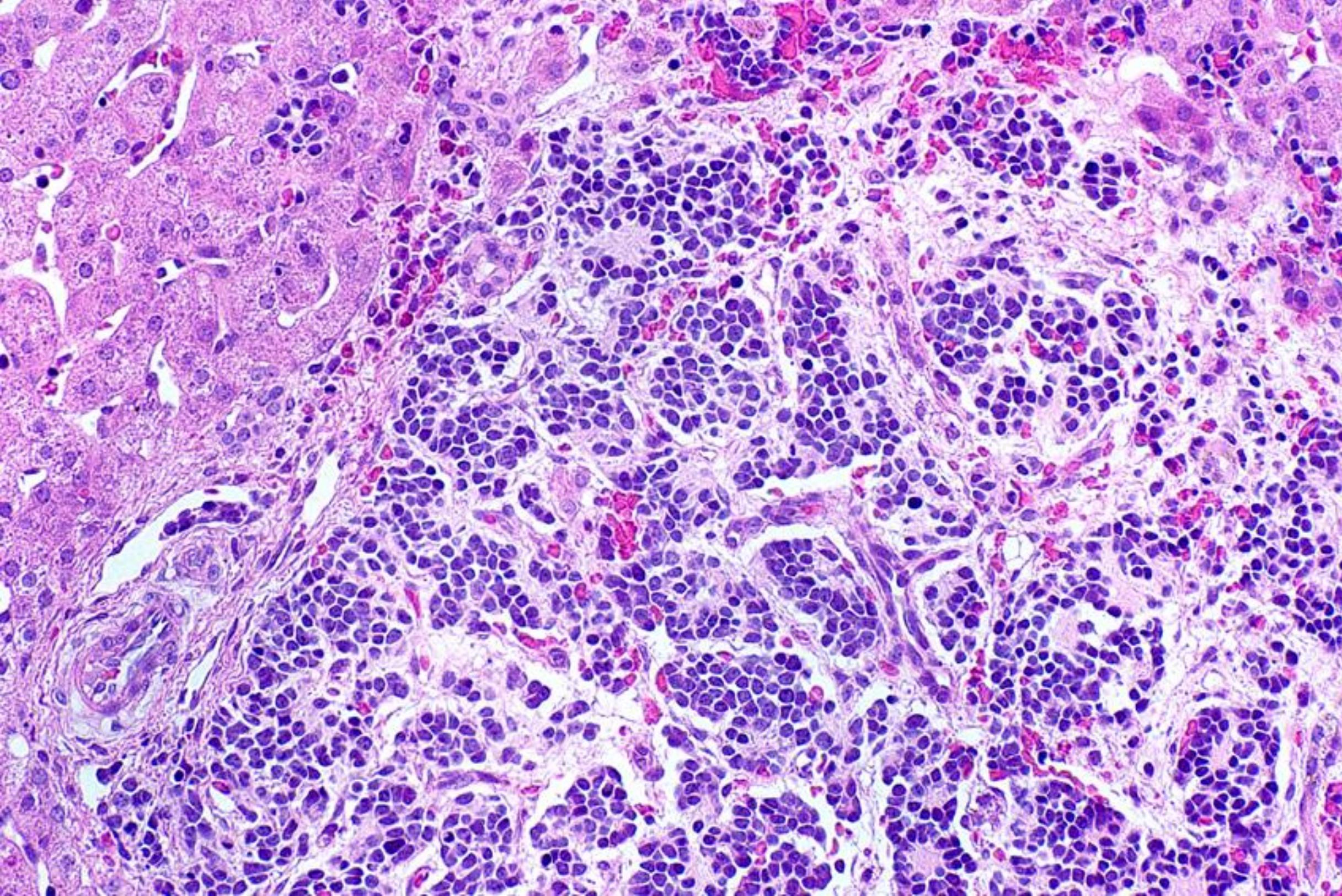


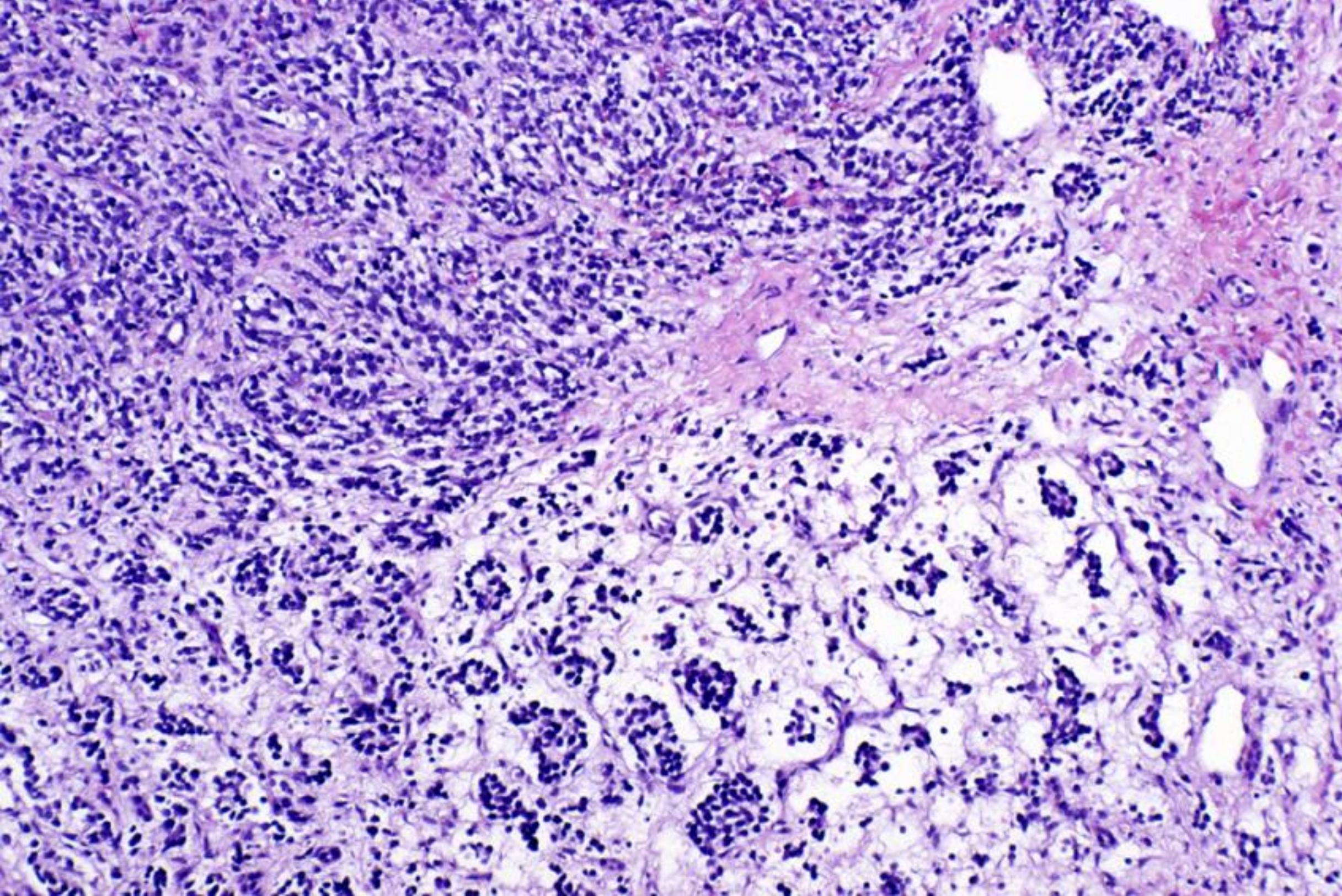


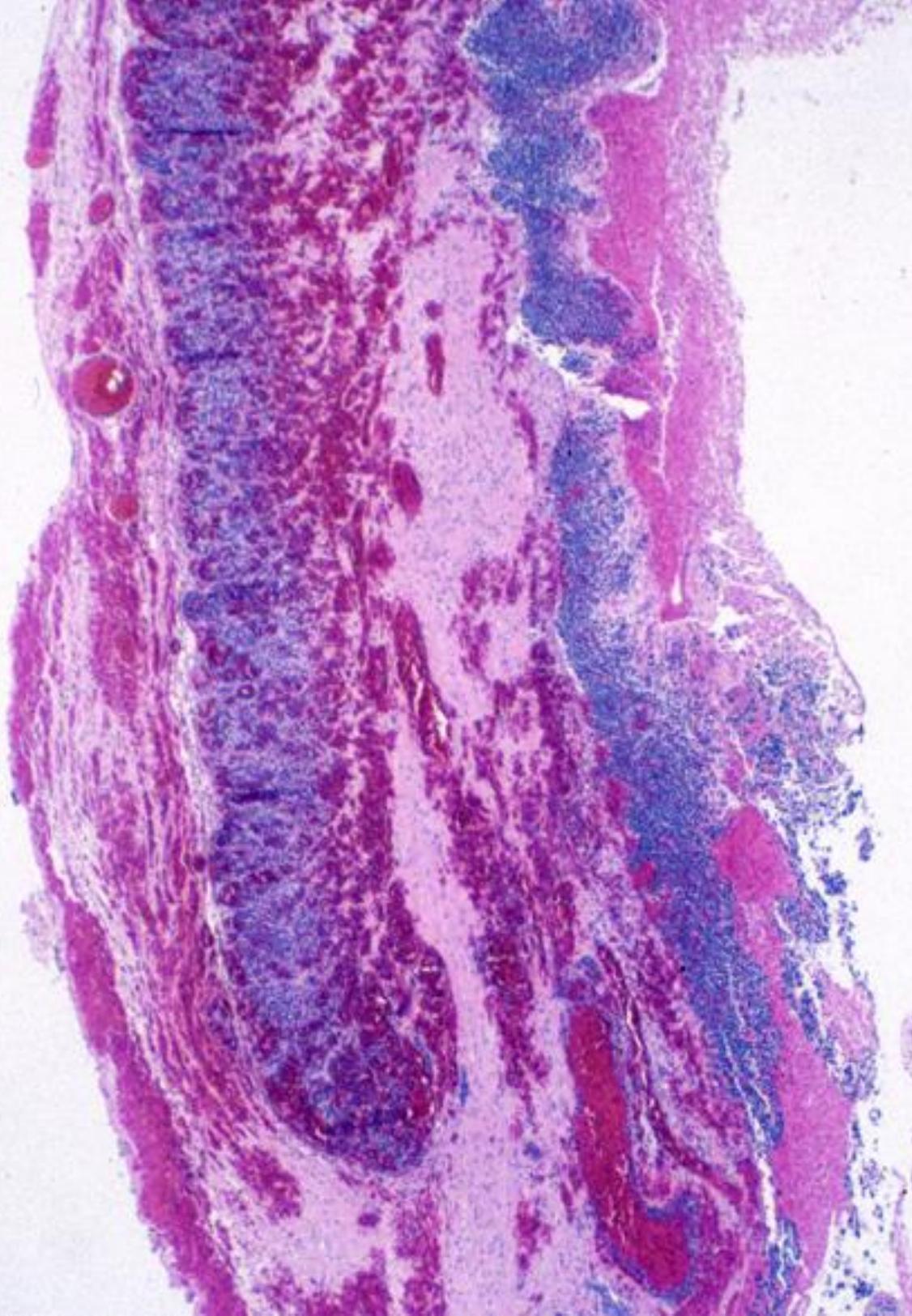




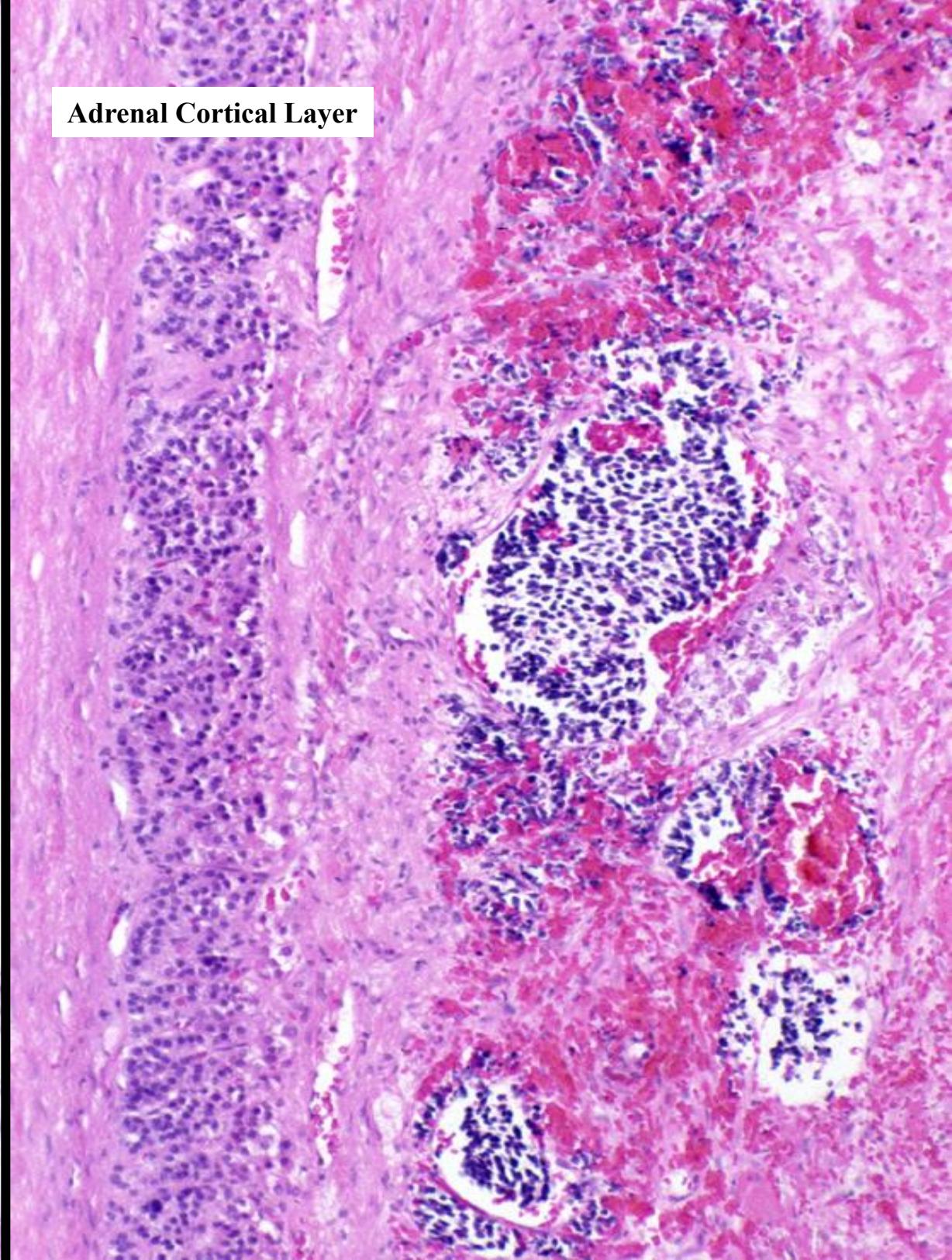


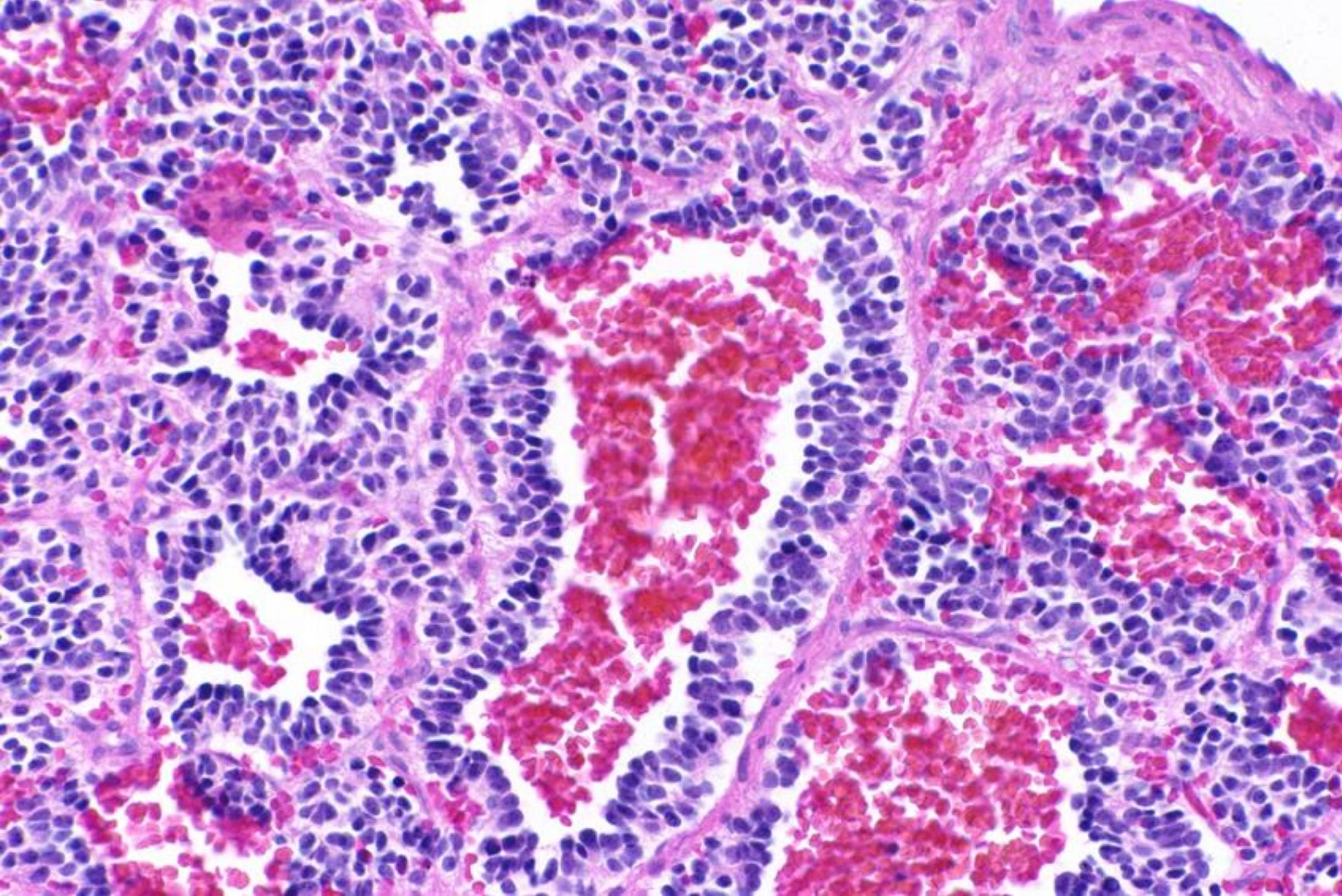




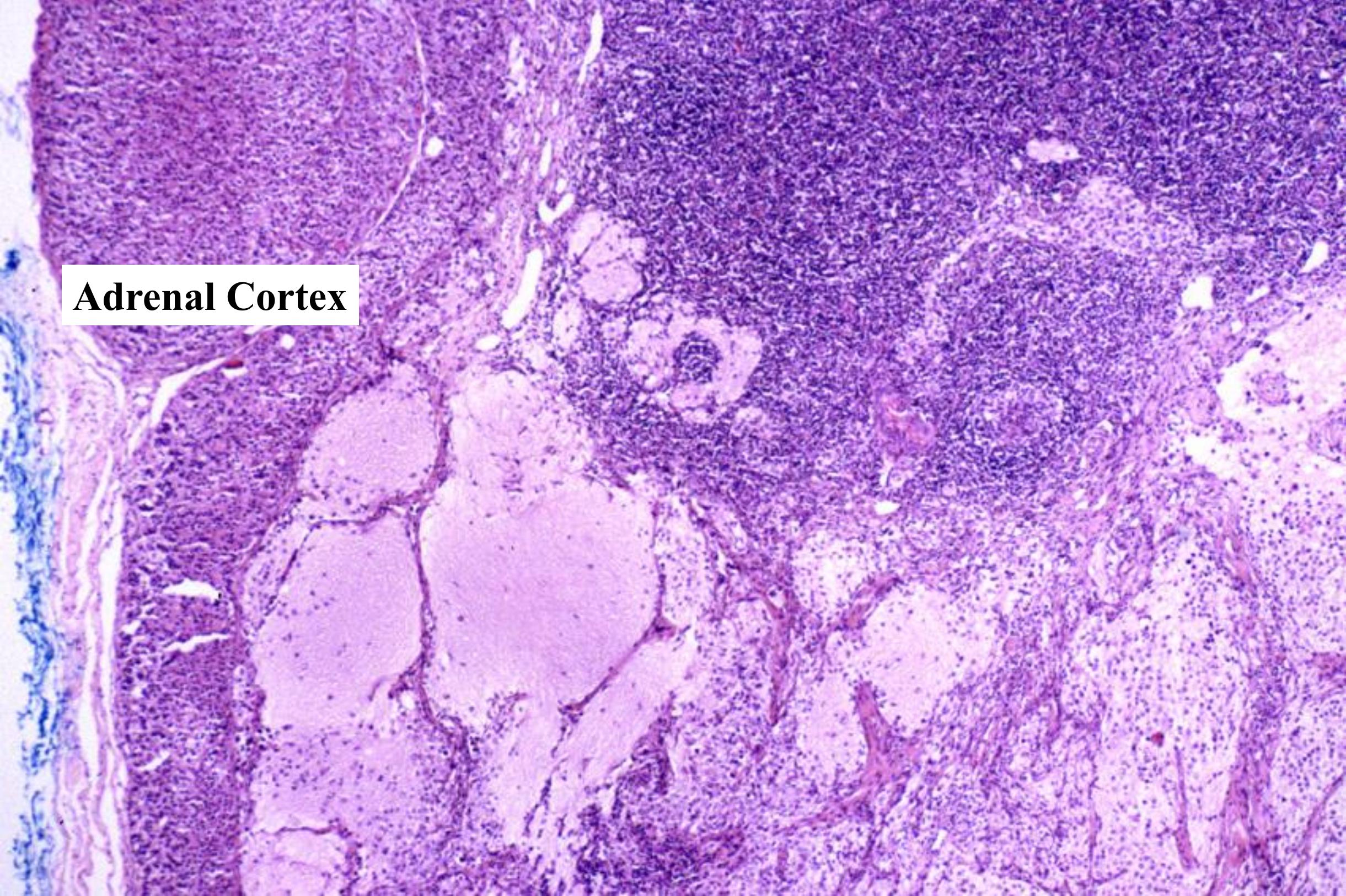


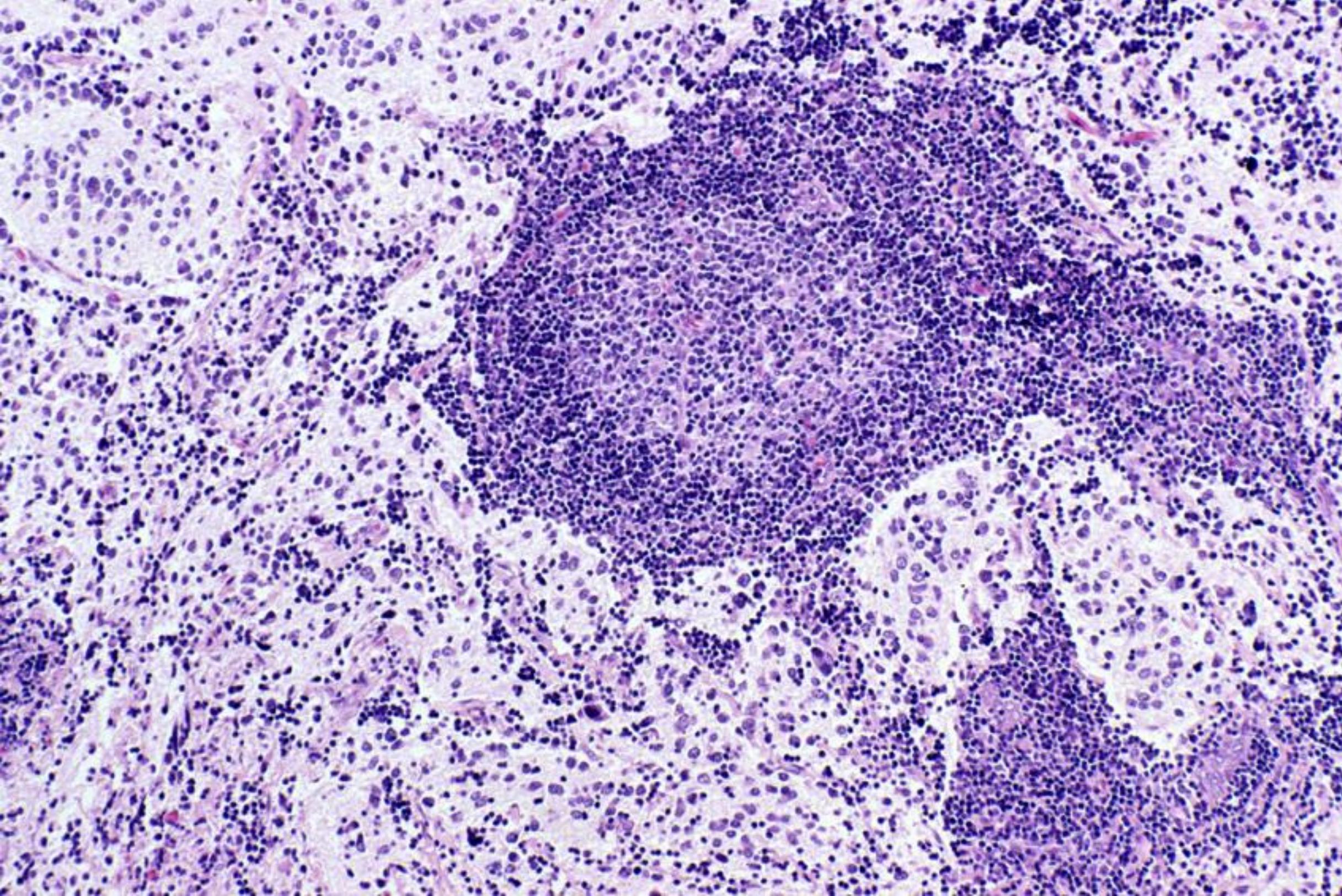
Adrenal Cortical Layer

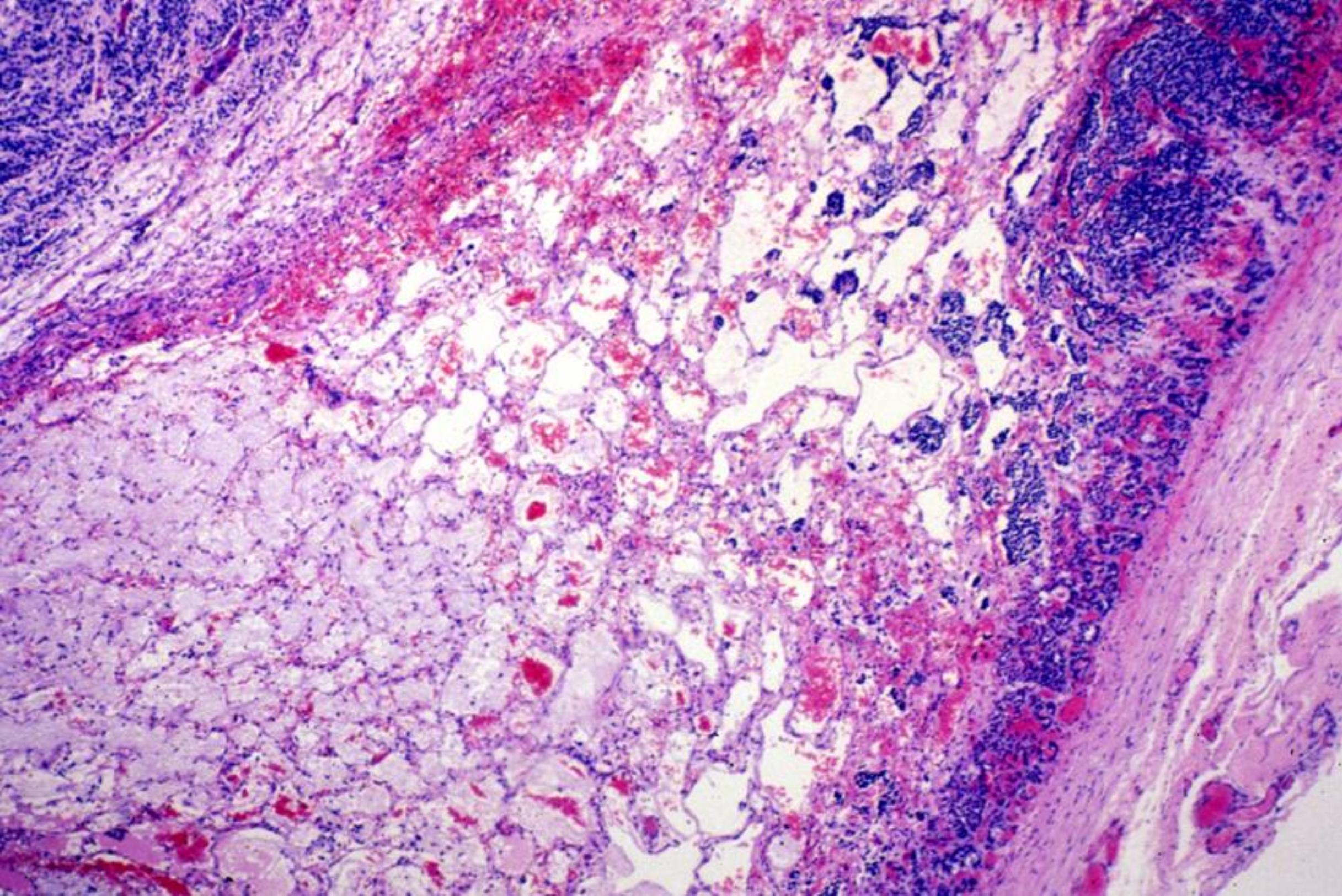


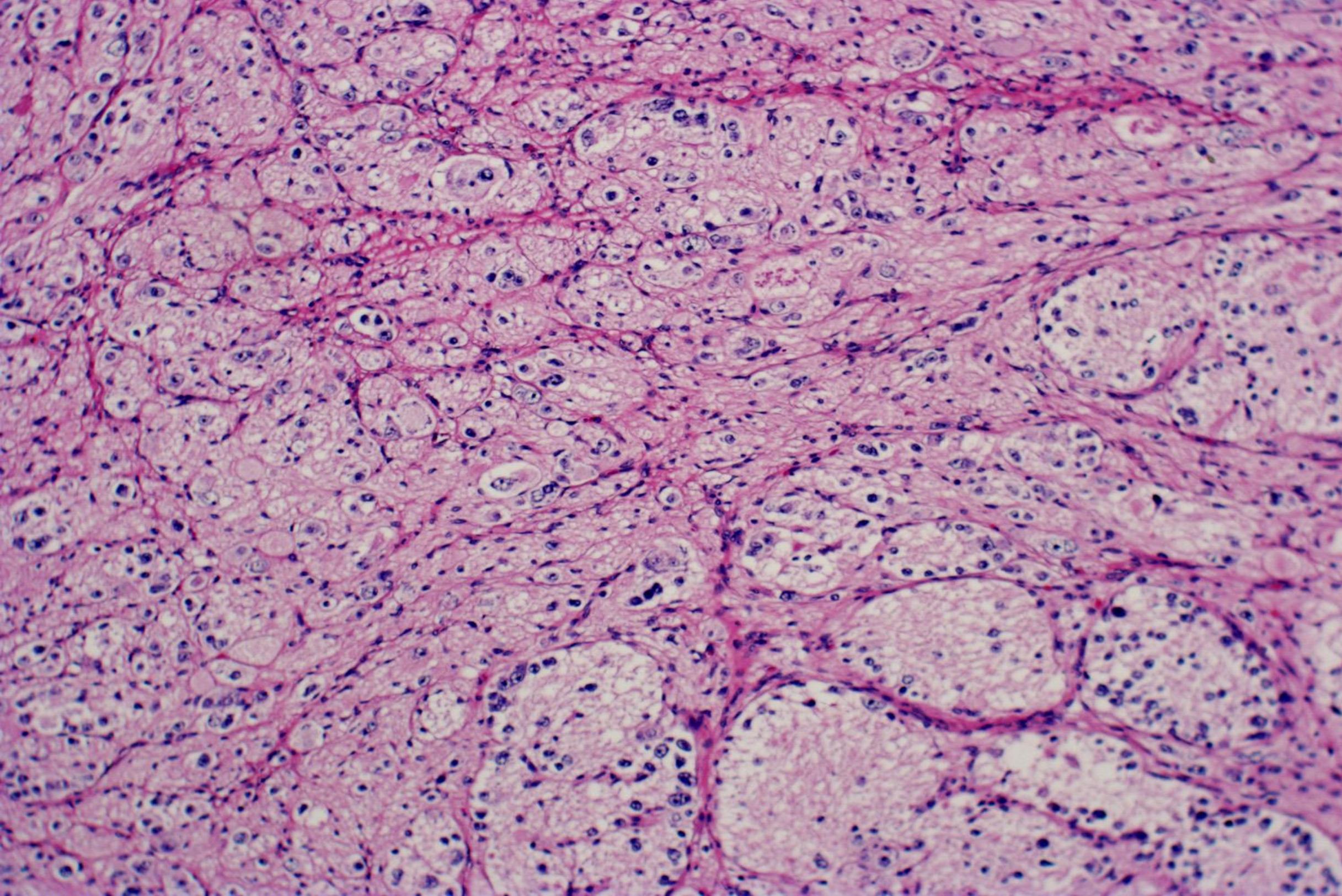


**Adrenal Cortex**









# Unusual Features of Peripheral Neuroblastic Tumors

Pleomorphic neuroblastoma

Focal area of pleomorphic cells

Fusiform/Spindle cell neuroblastoma

Diffuse pattern

Pseudoalveolar (pseudopapillary) pattern

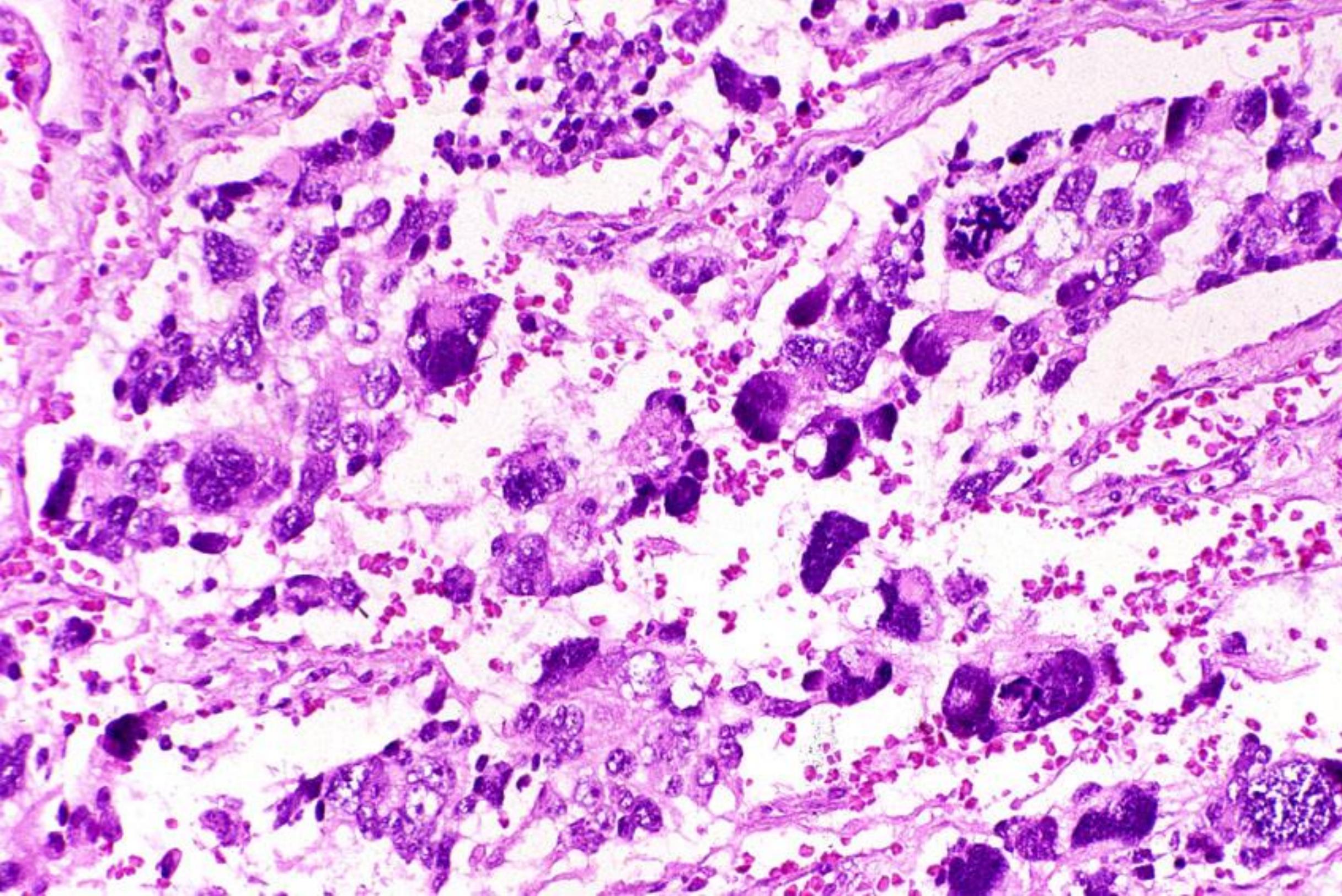
Nuclear inclusions of cytoplasmic material

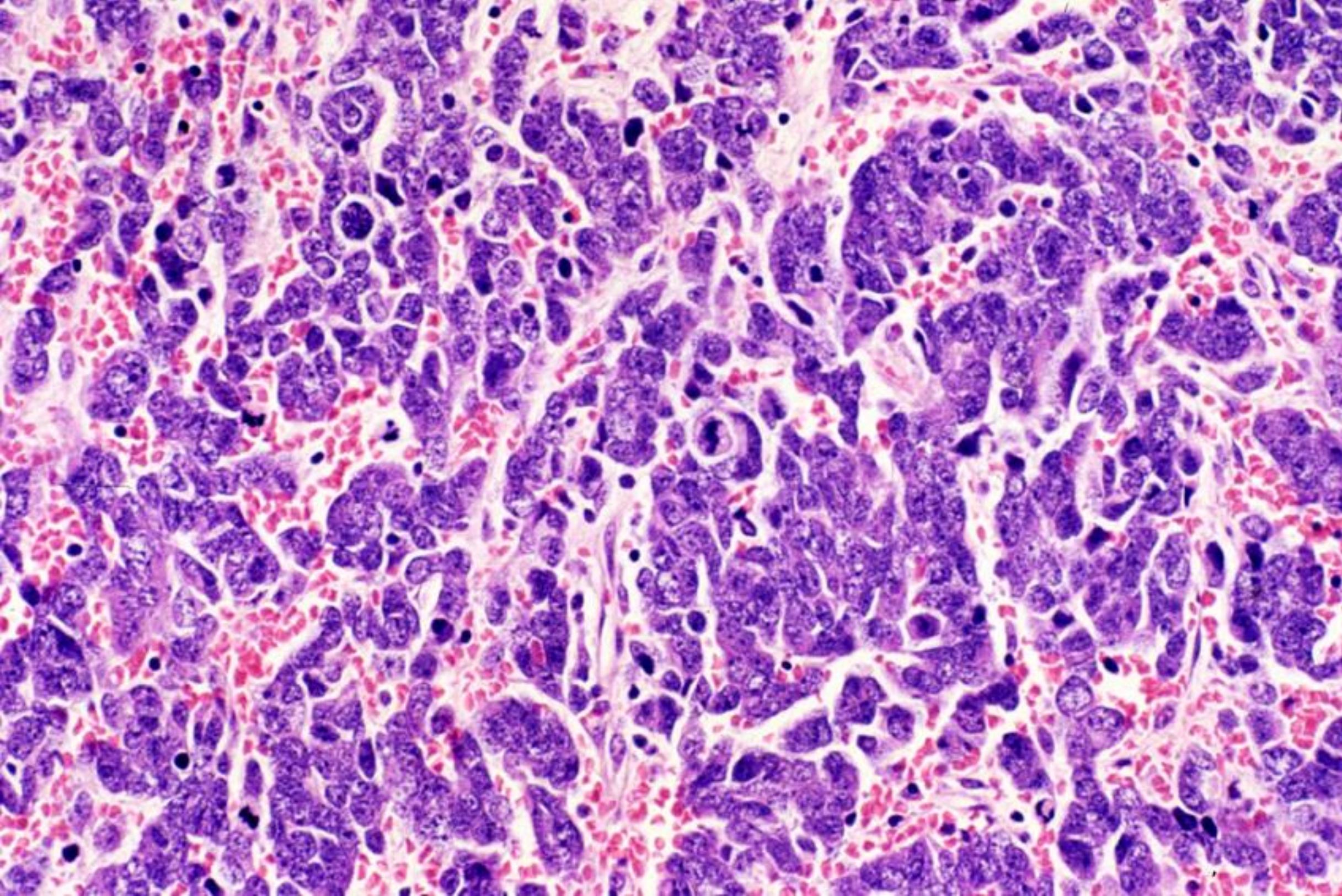
Rhabdoid cells in neuroblastoma

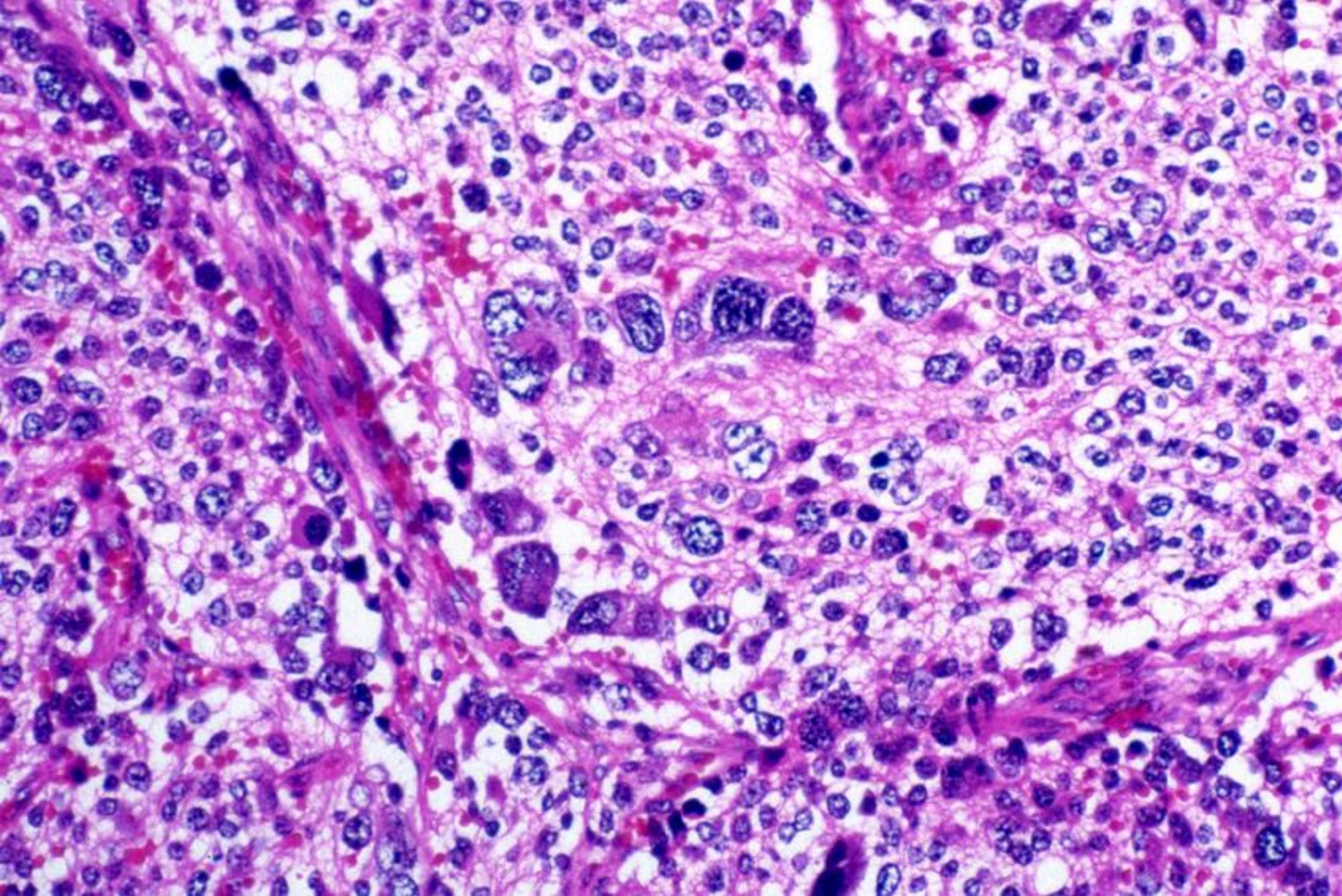
Prominent vascular proliferation

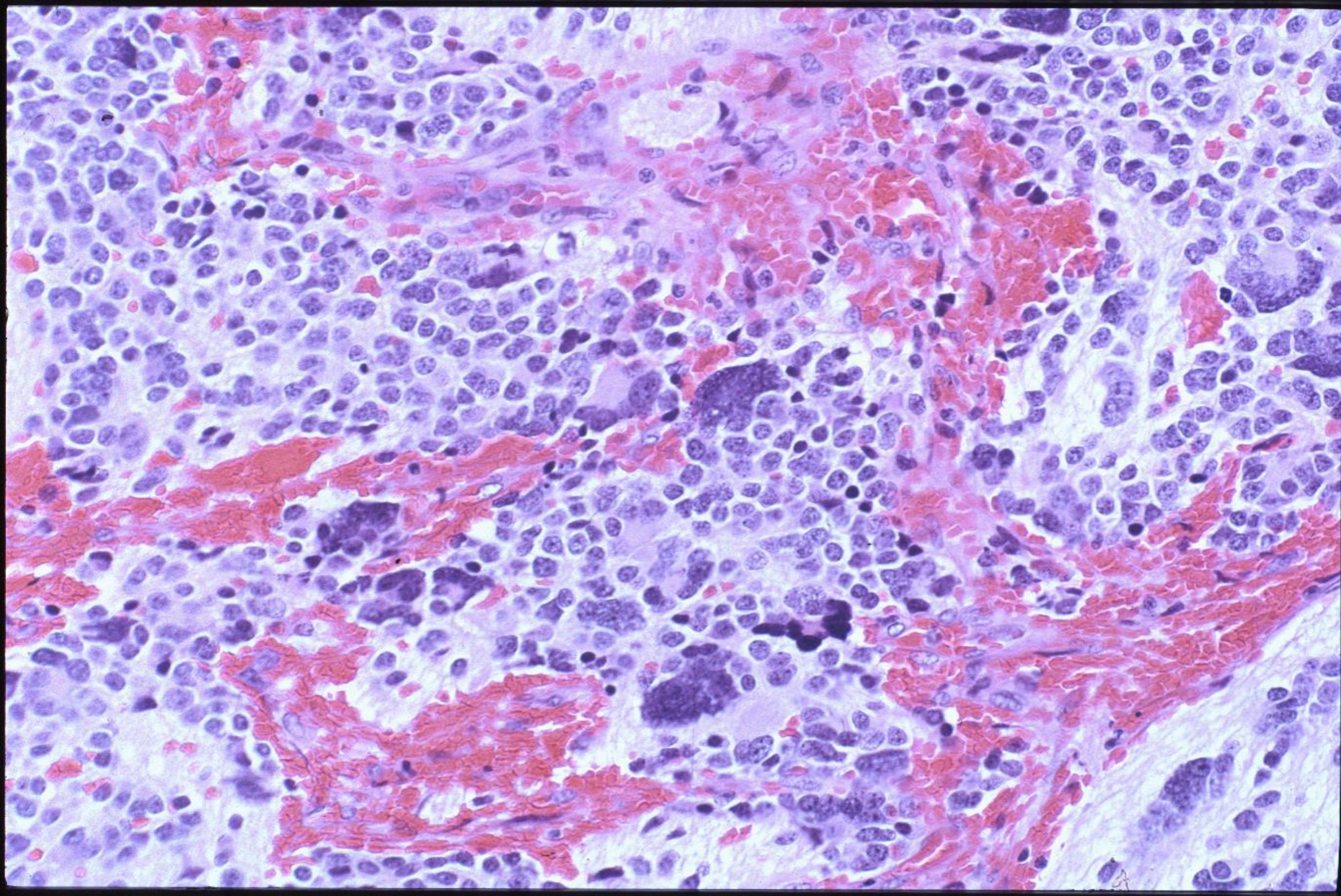
Desmoplastic reaction

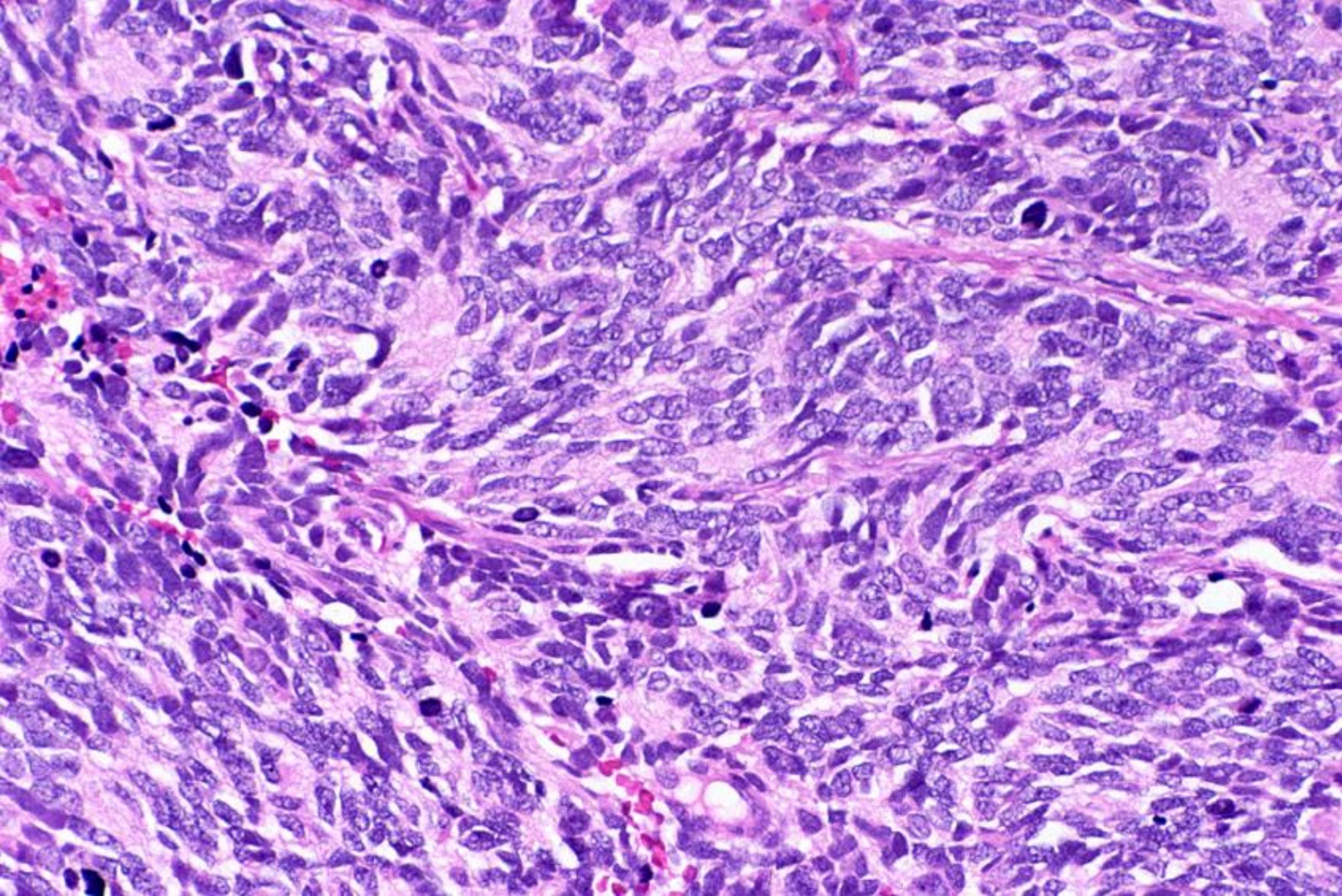
Sarcoid reaction

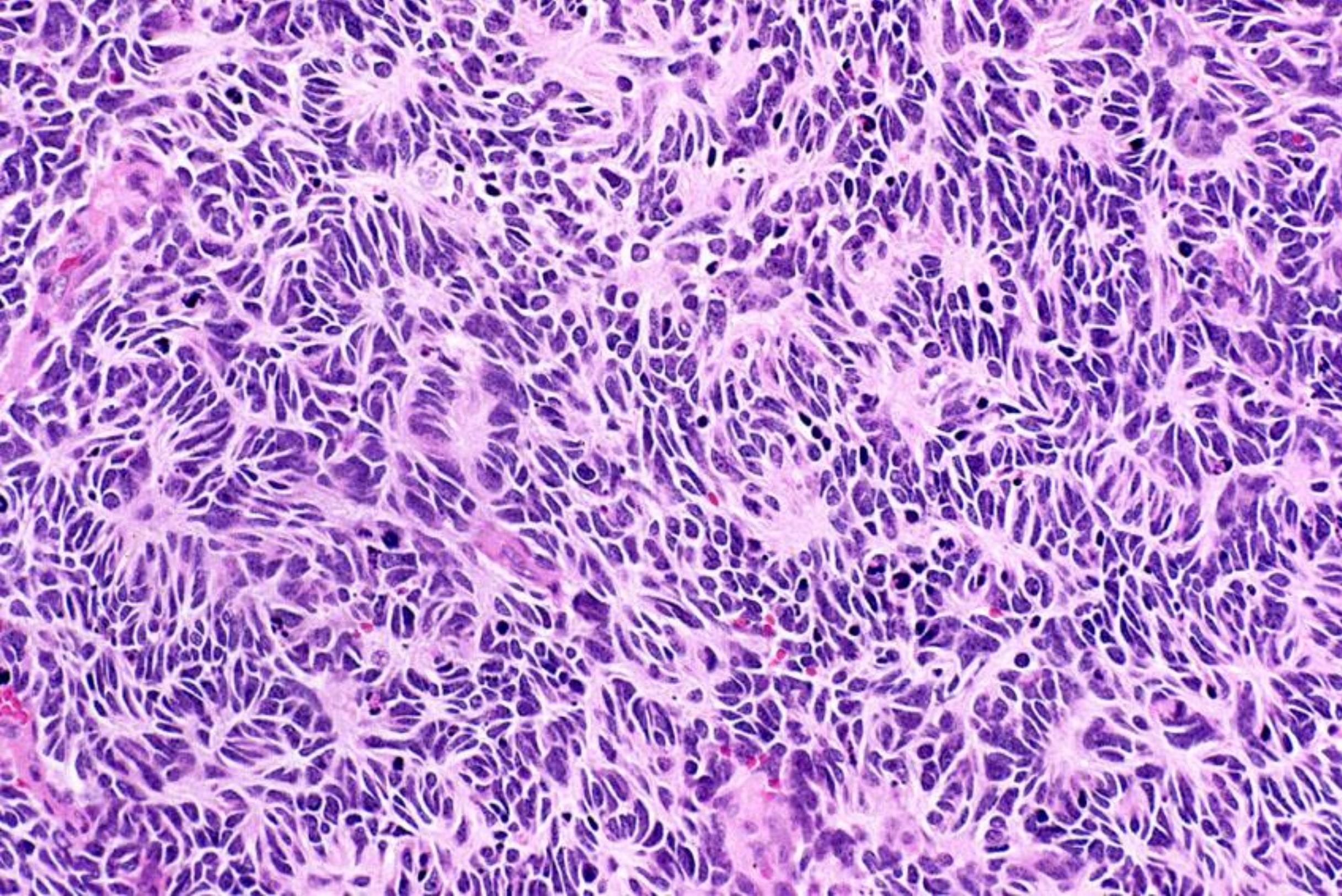


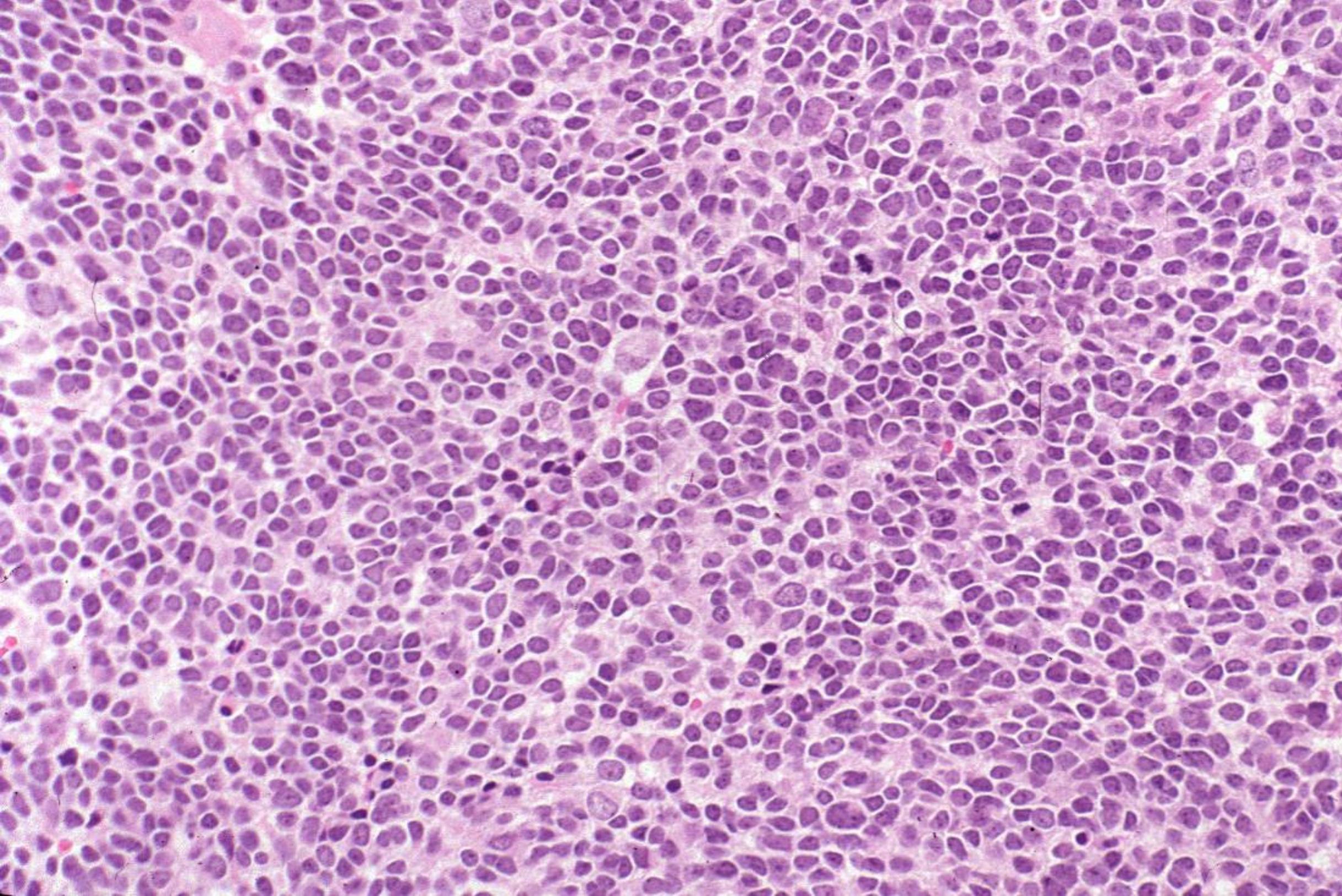


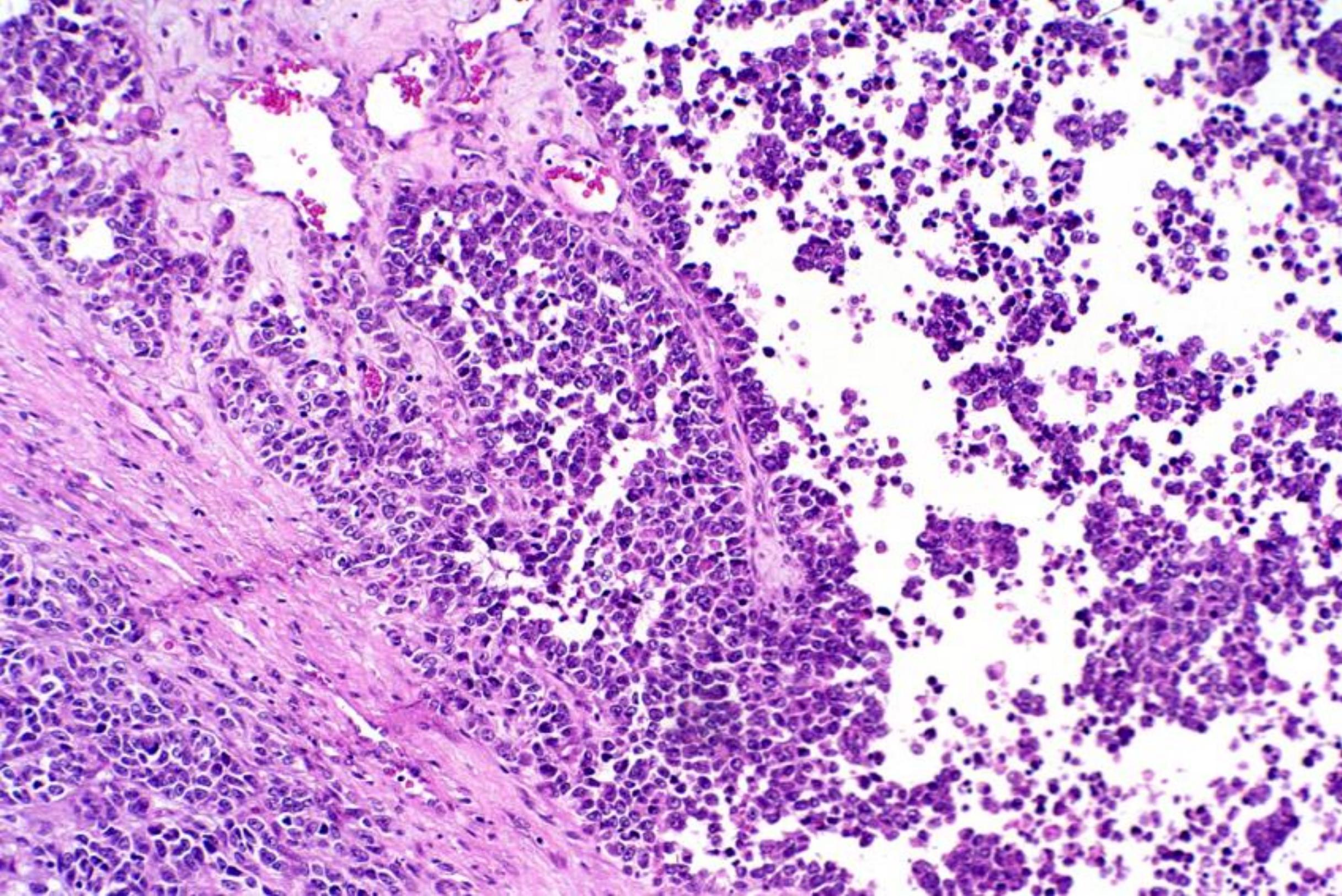


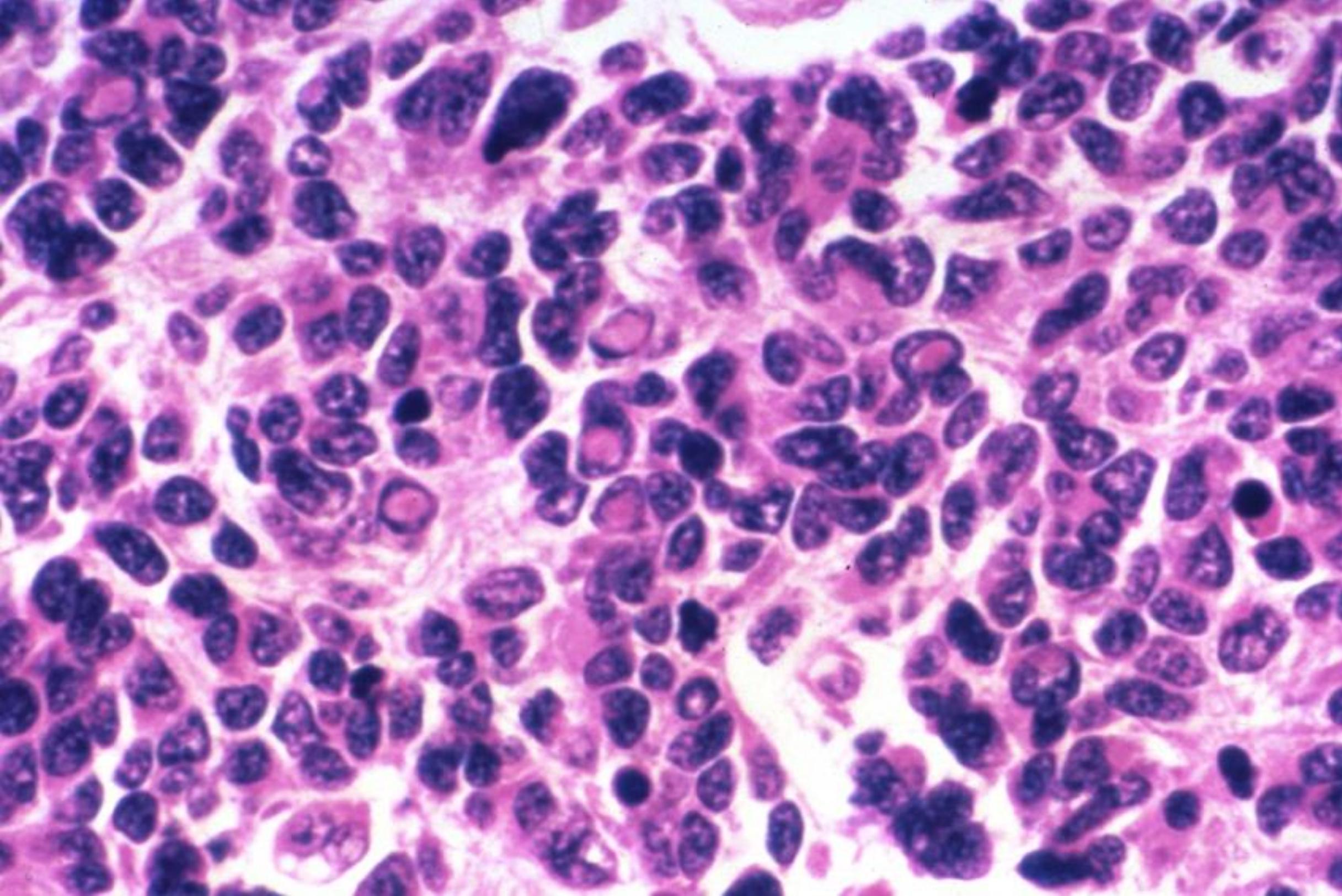


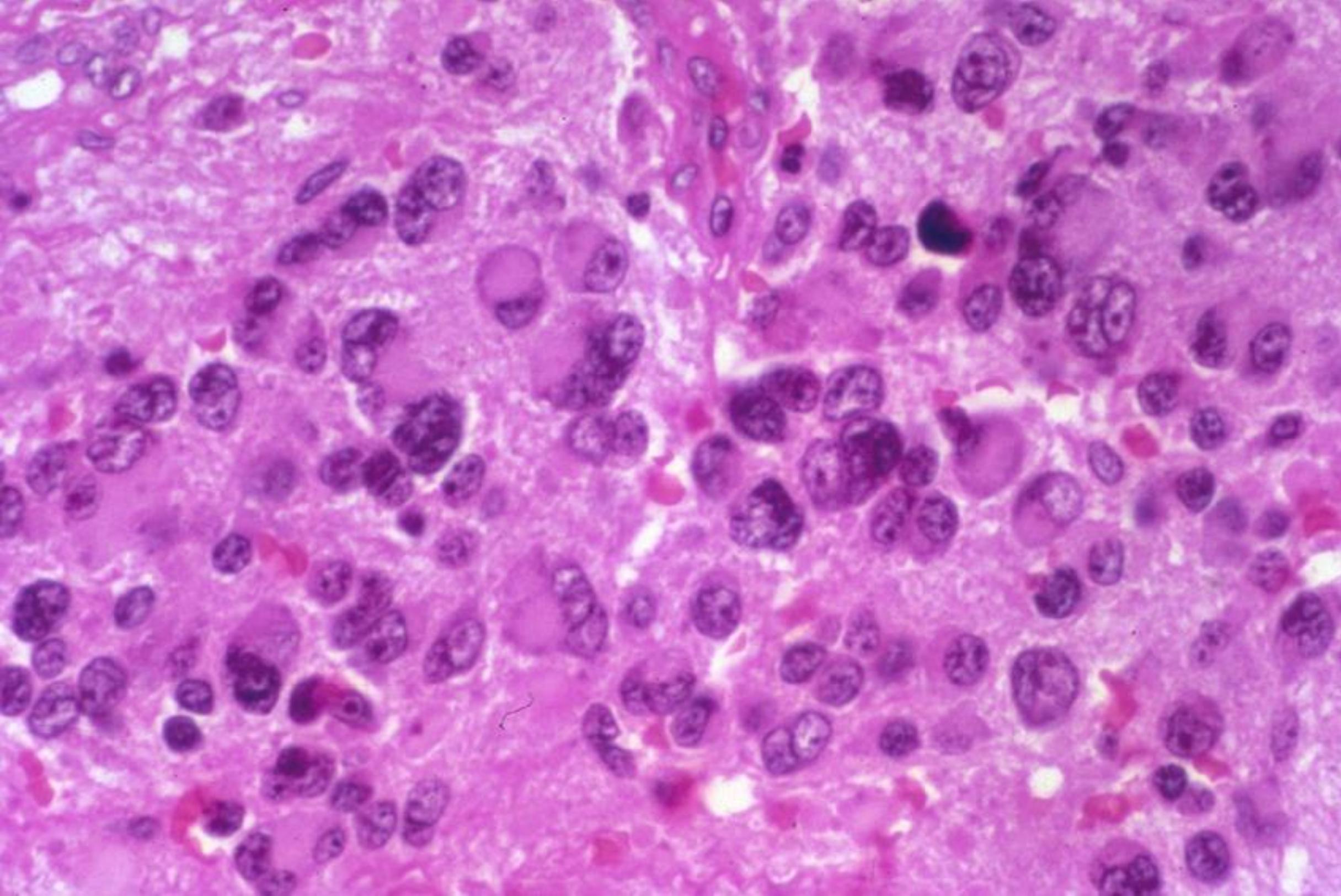


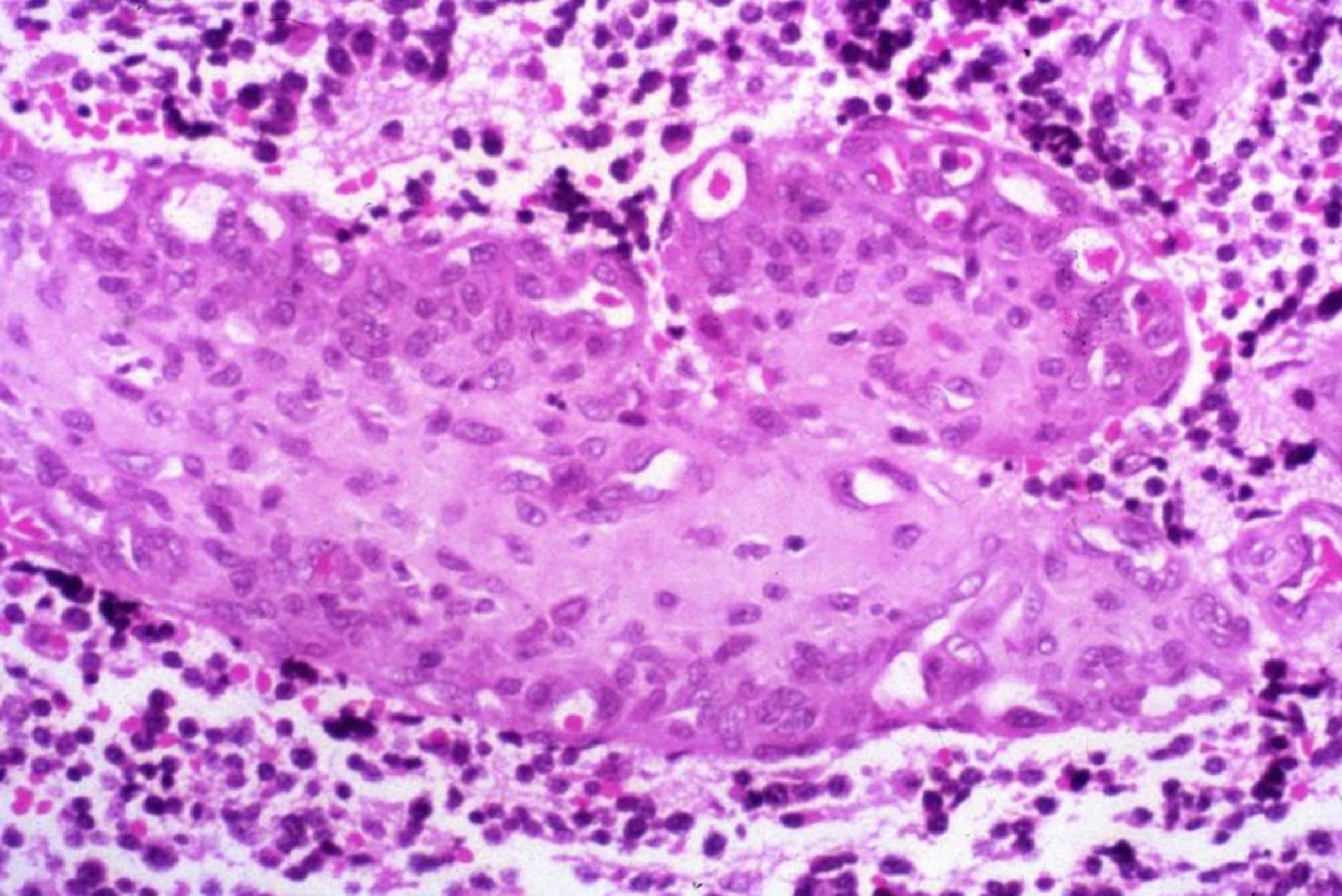


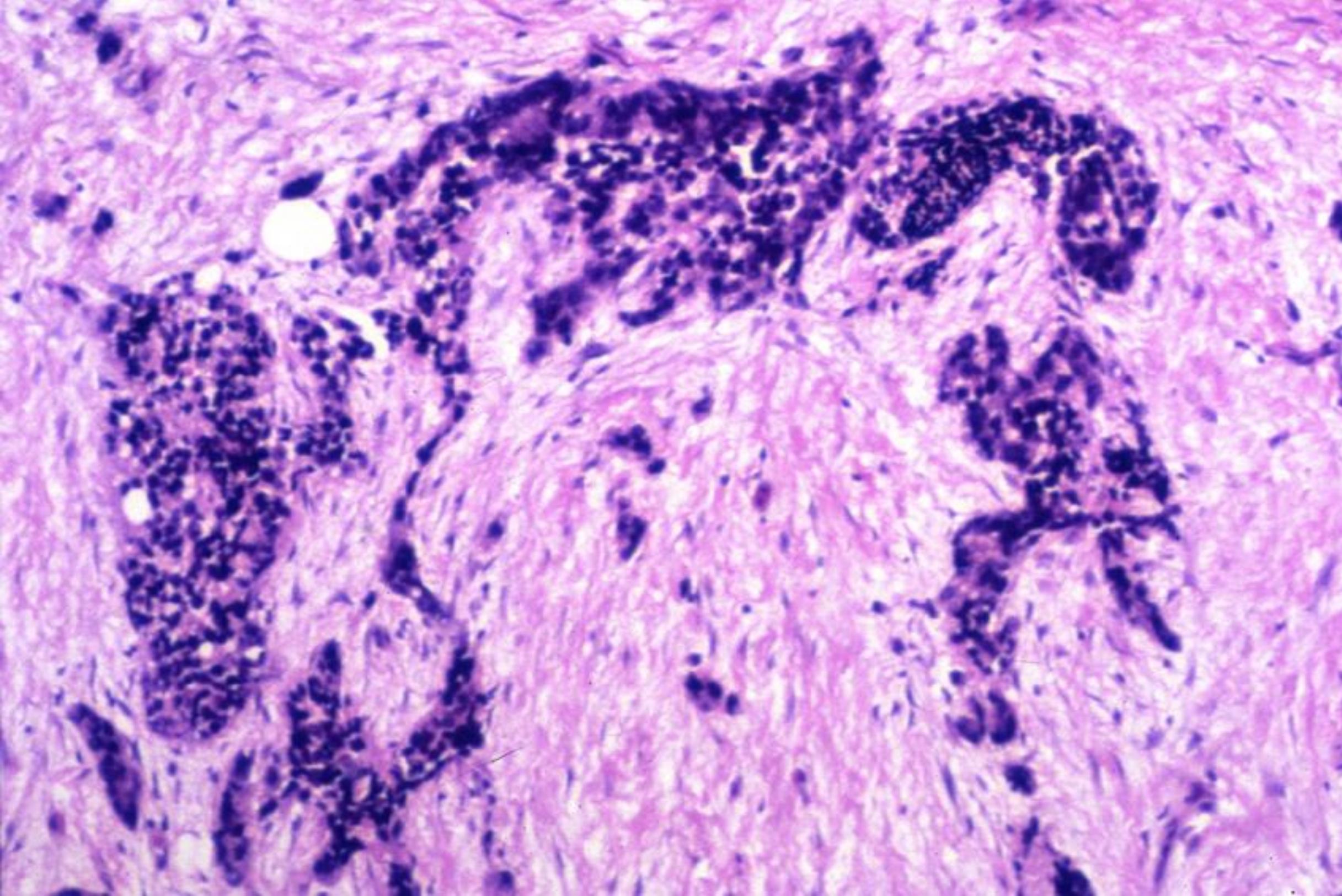


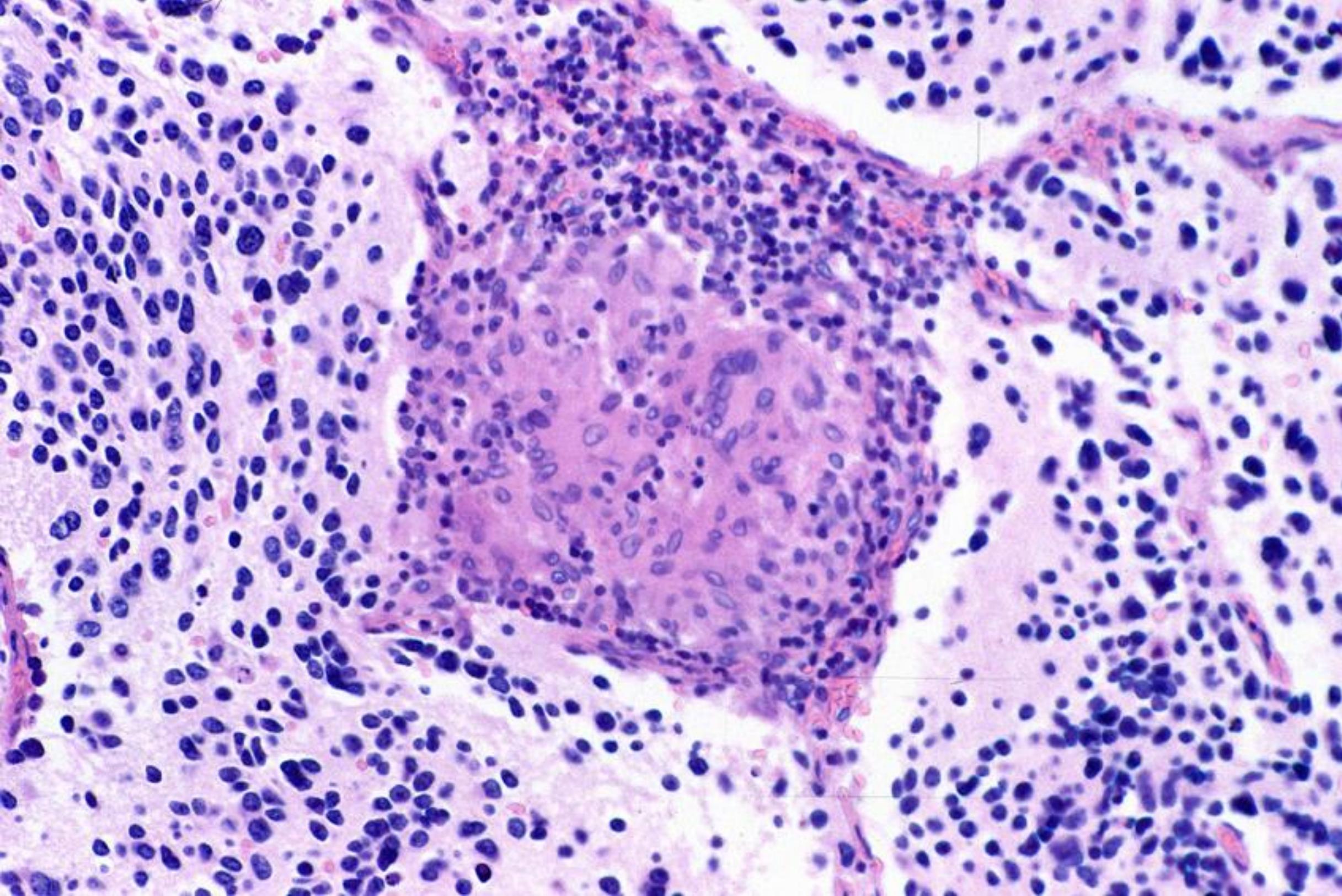




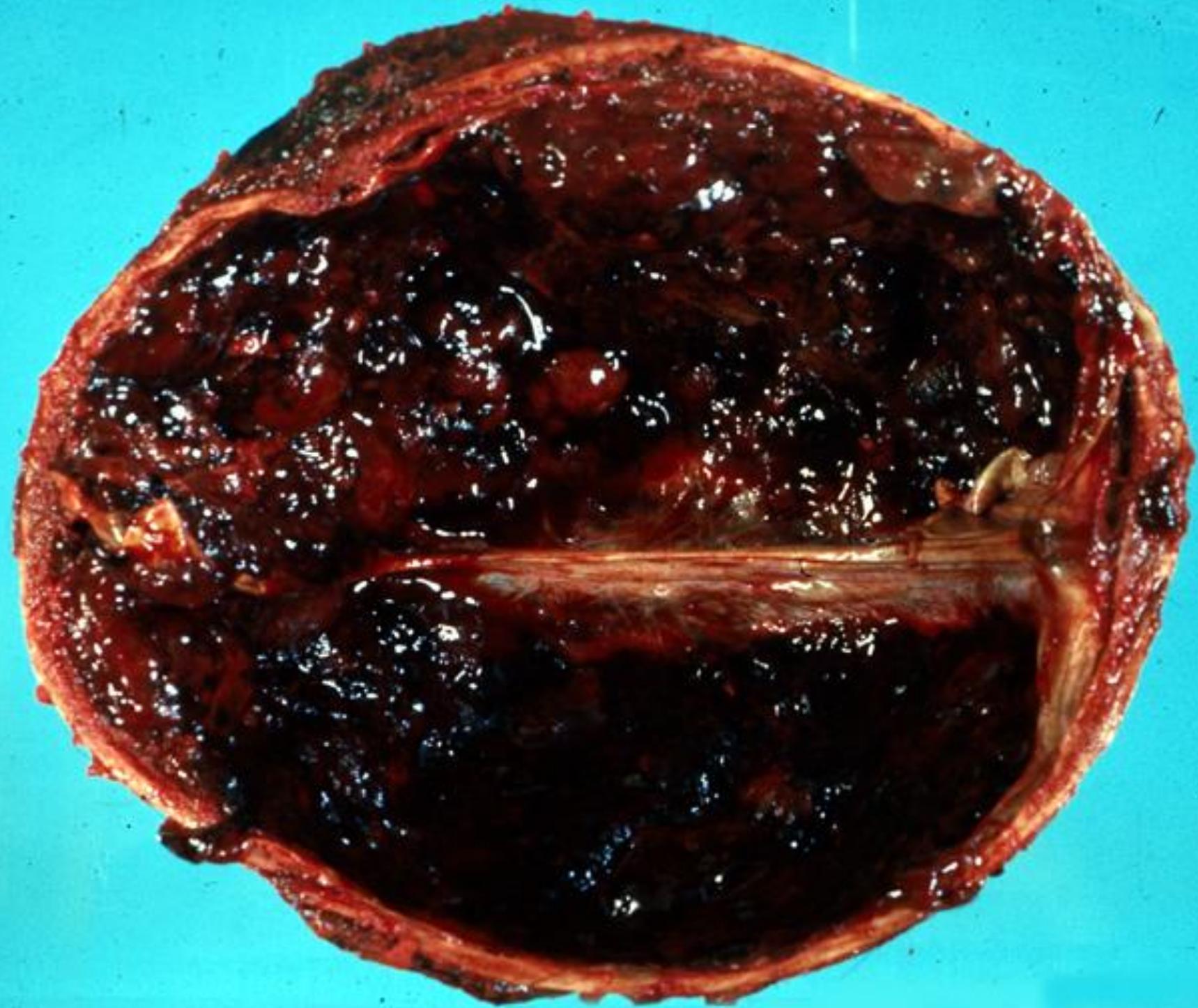




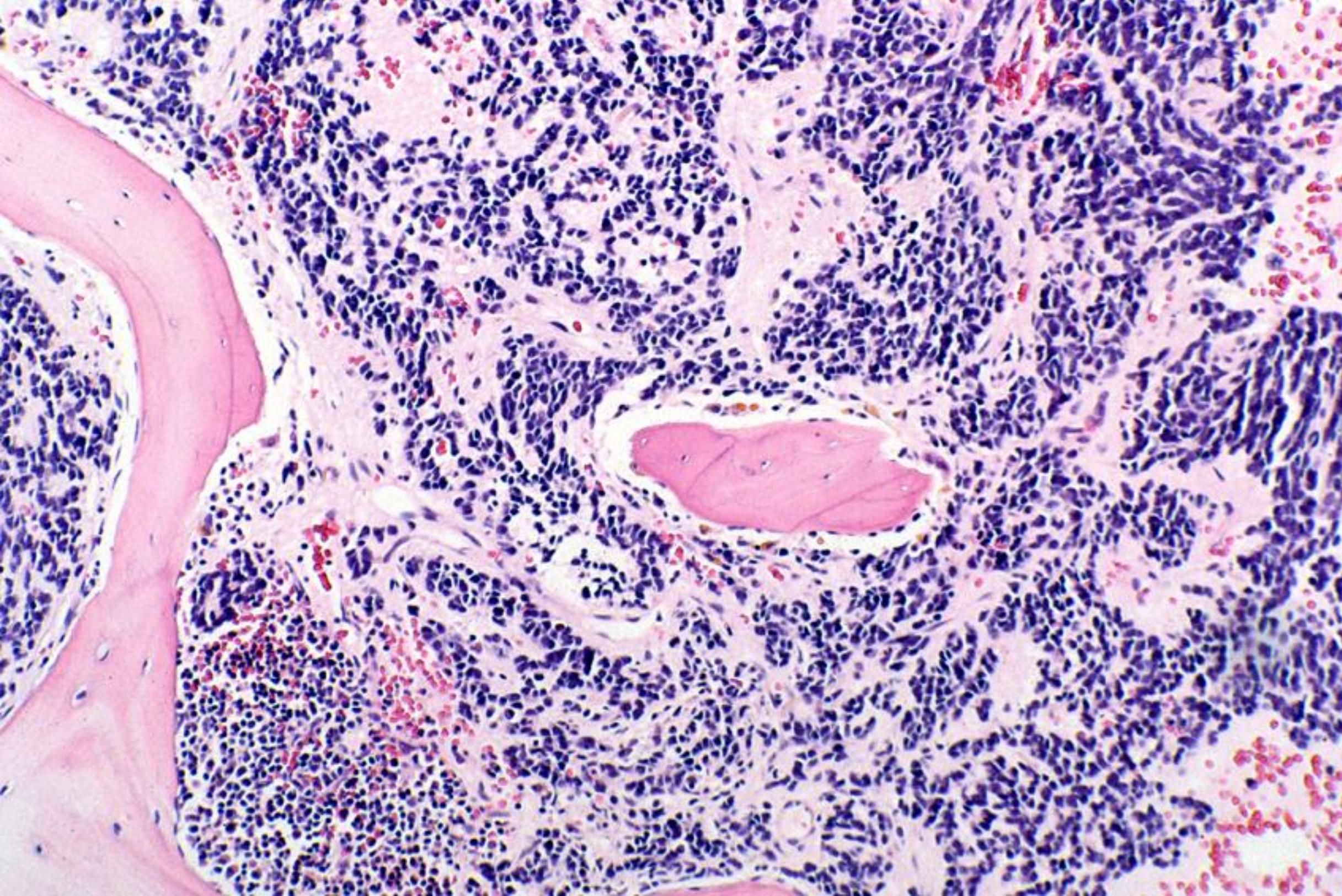


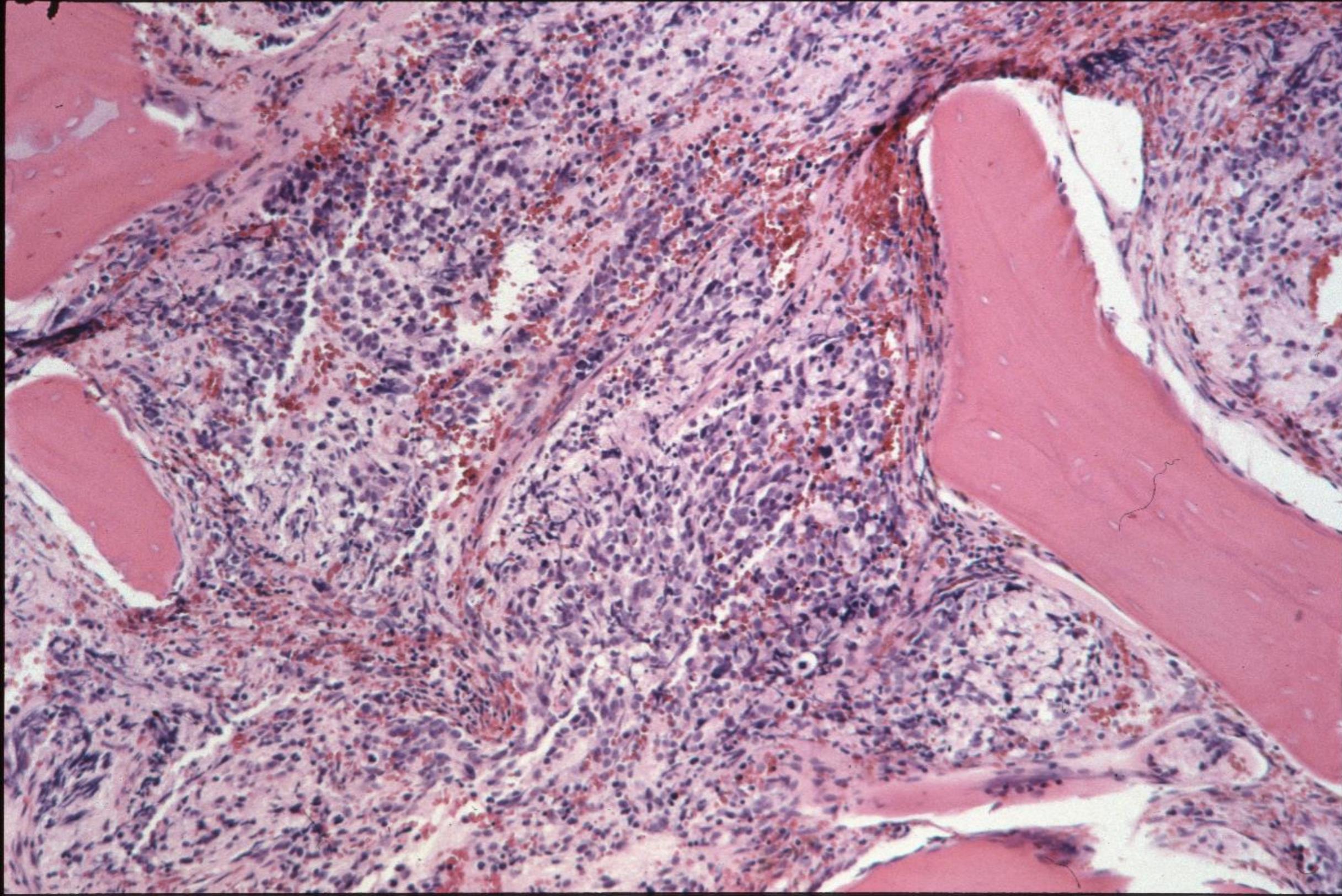


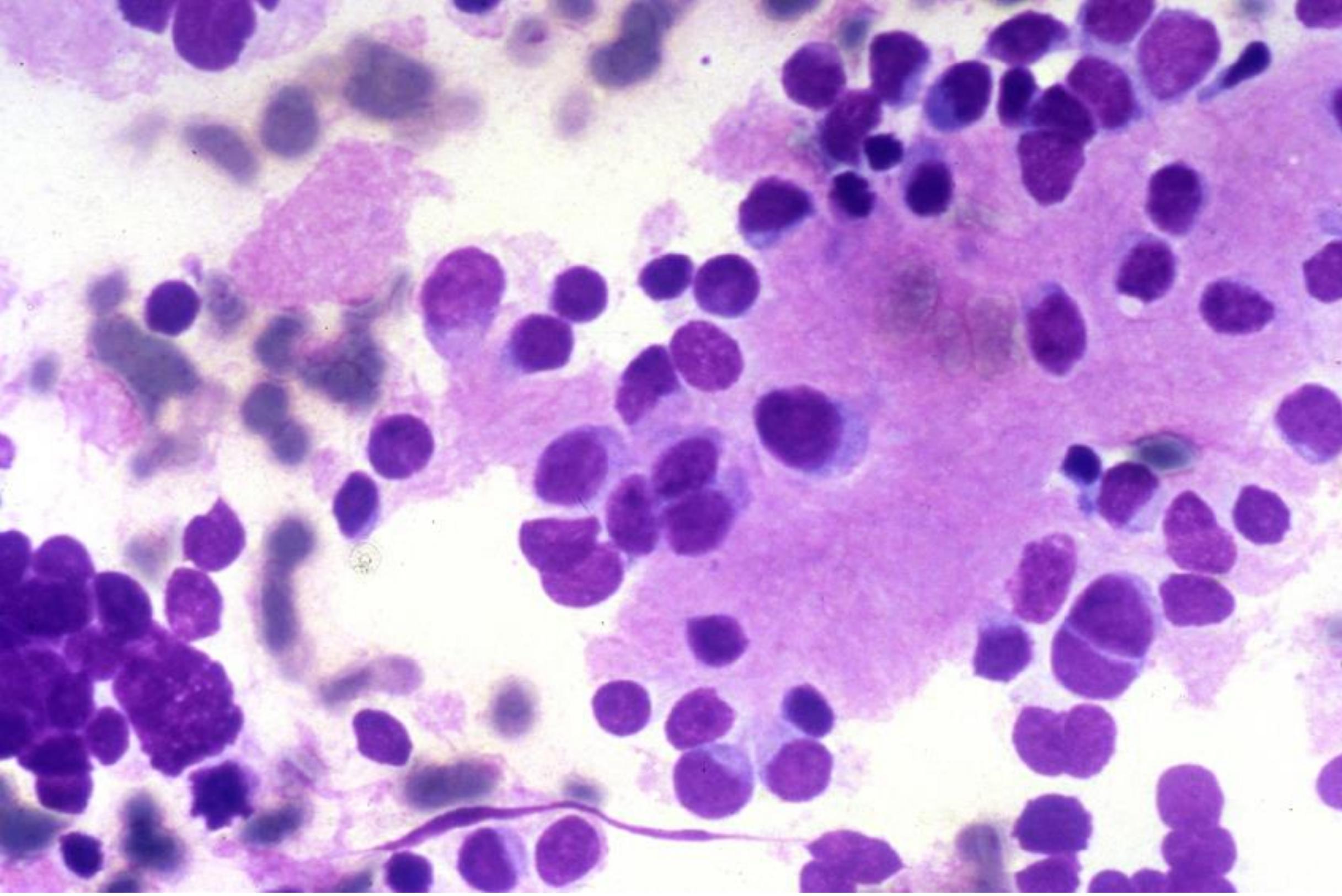
# Metastatic Disease

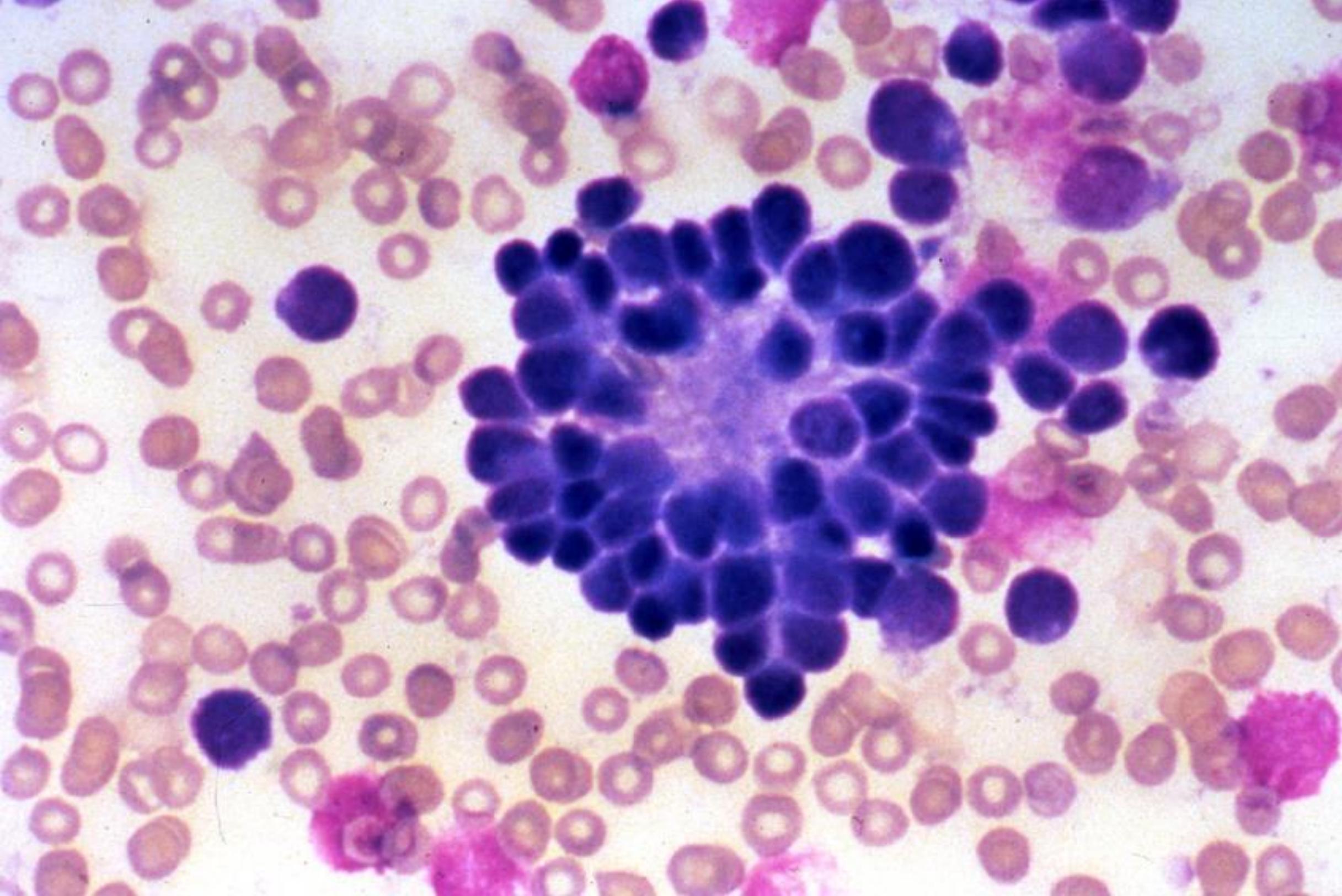


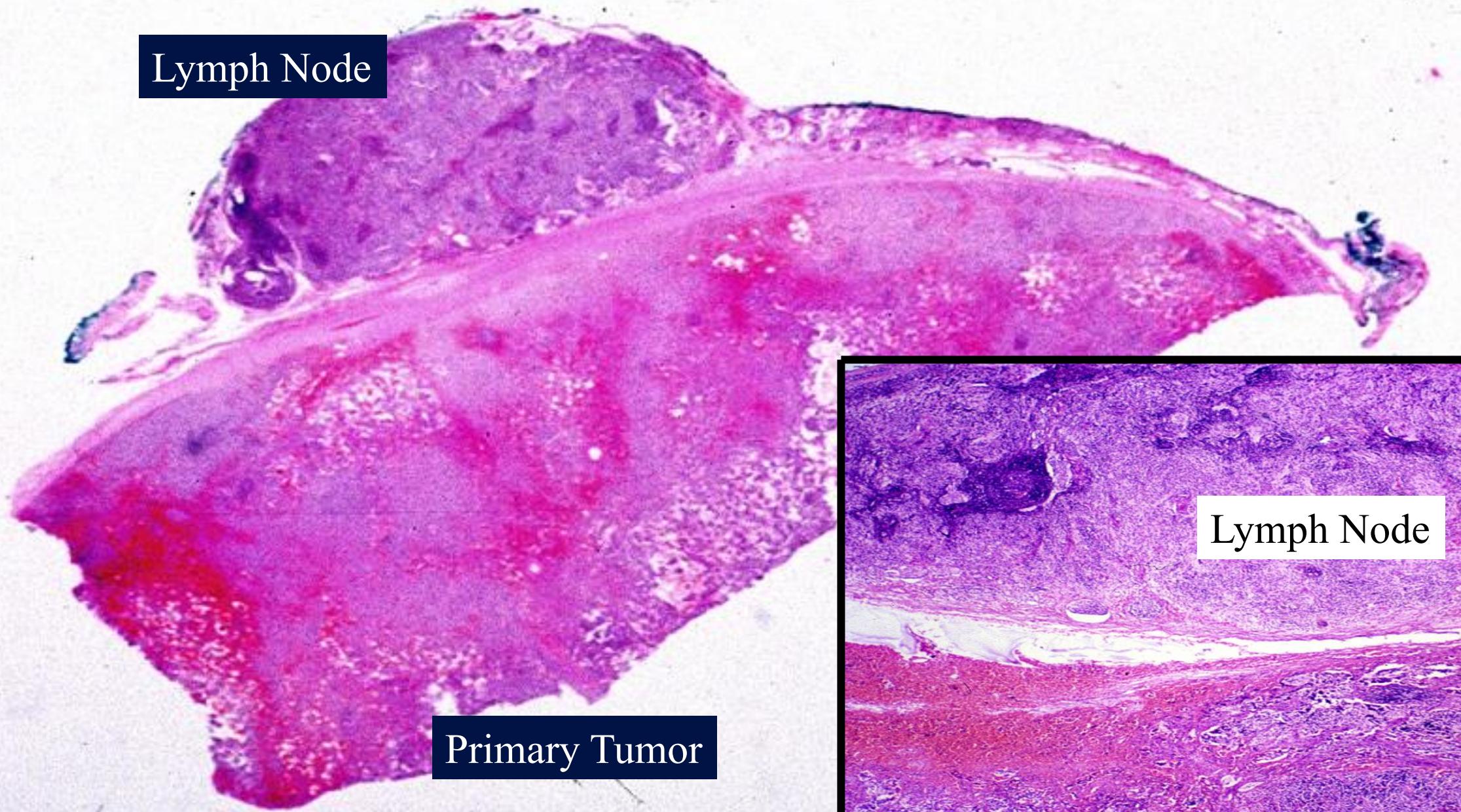










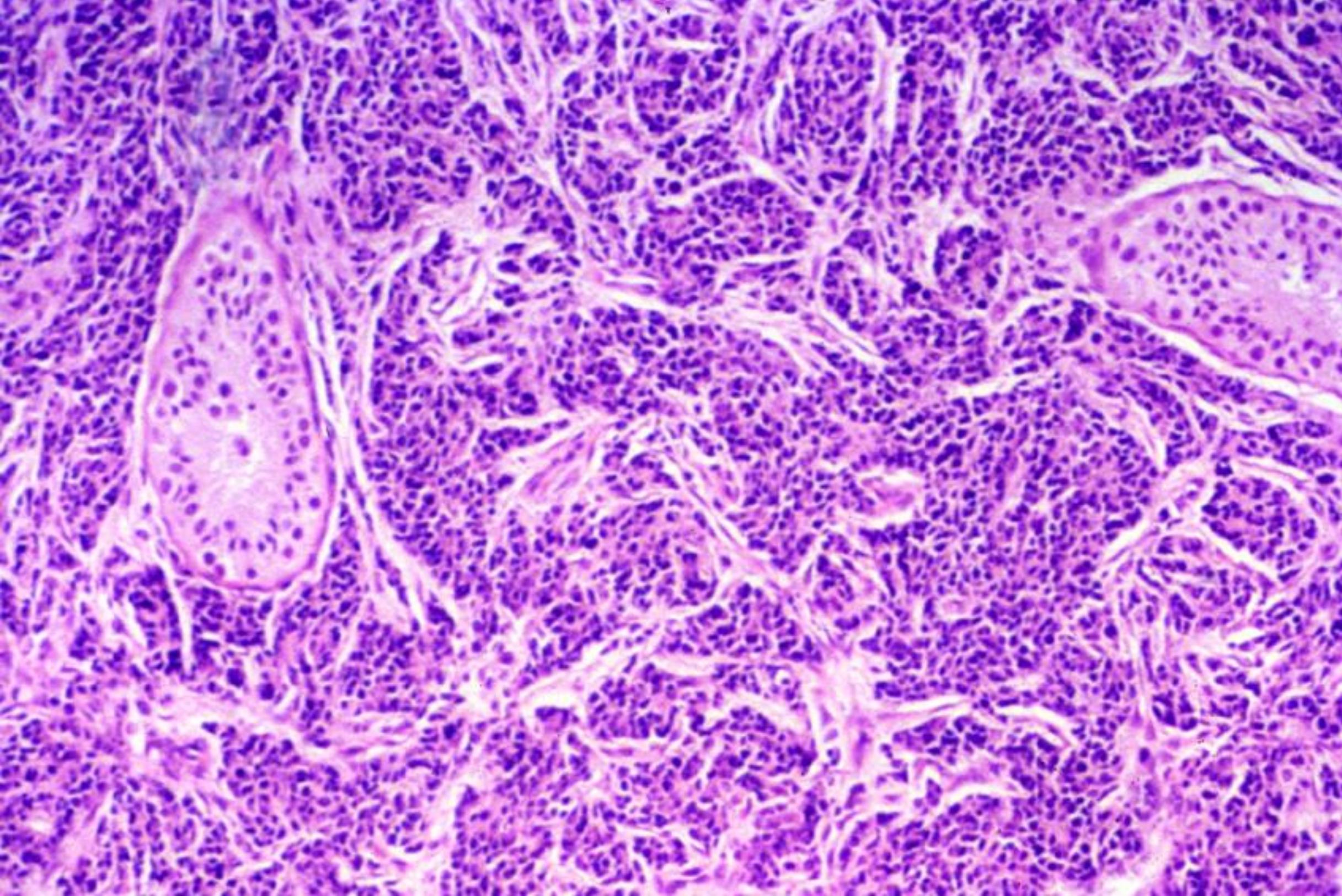


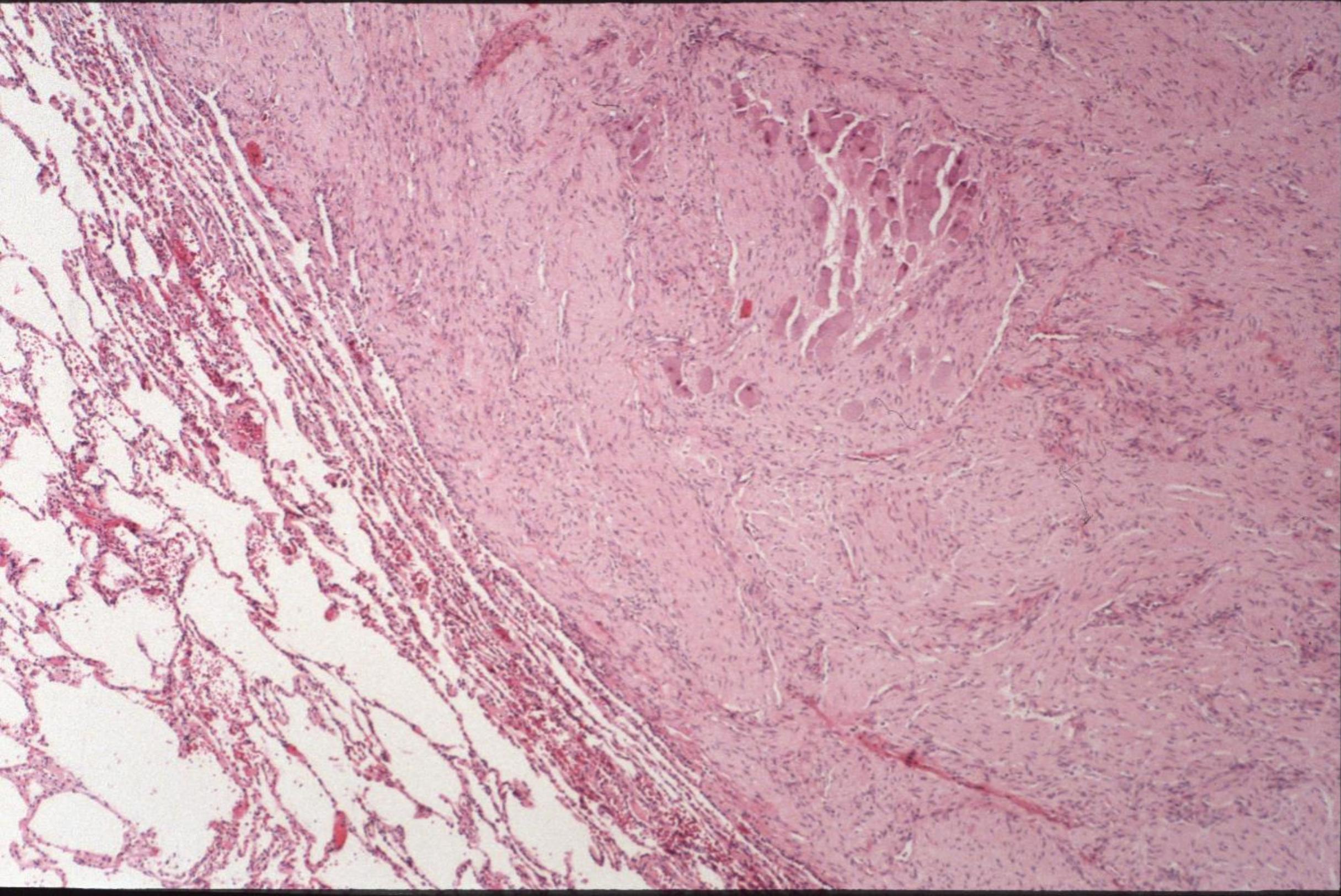
Lymph Node

Primary Tumor

Lymph Node

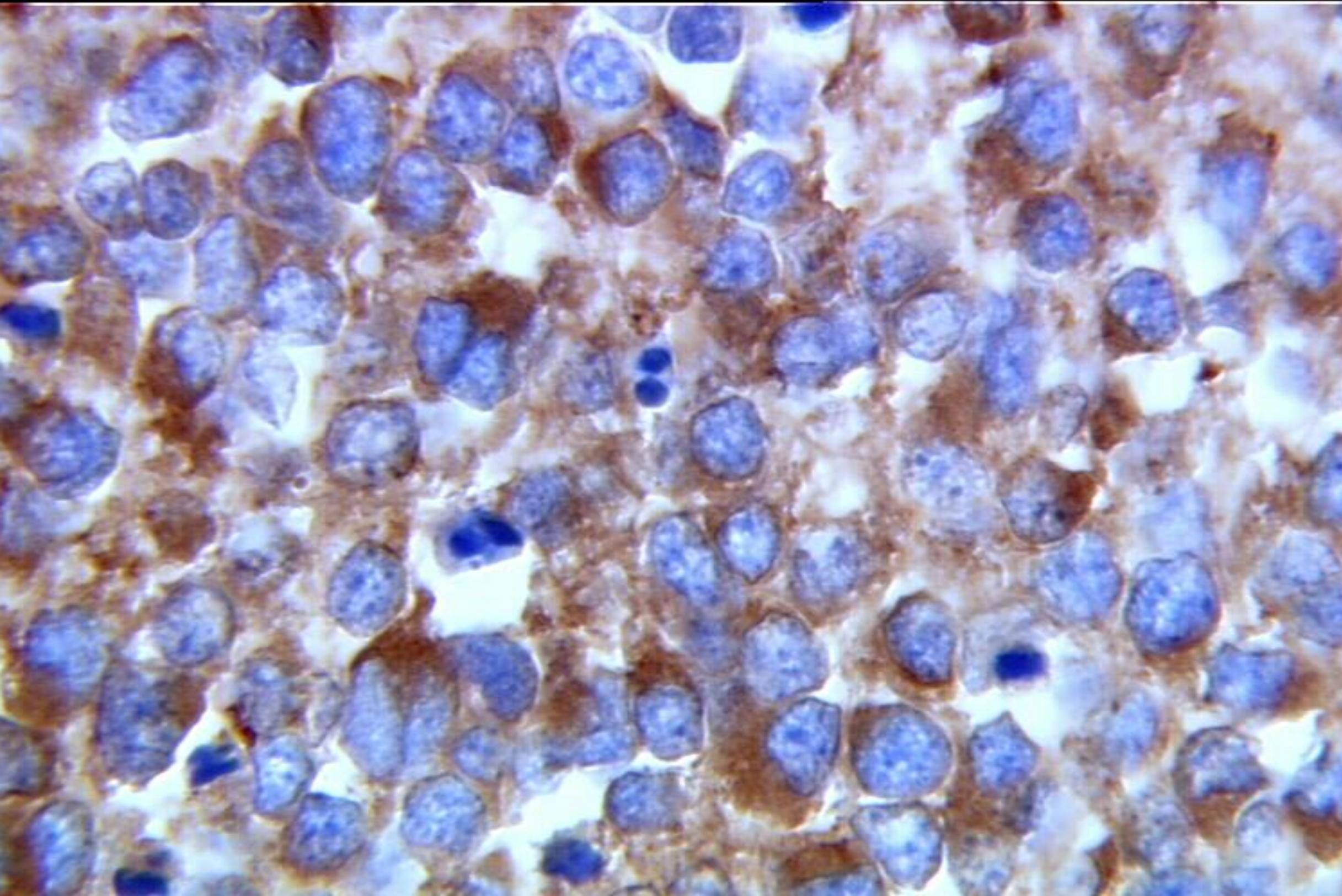
Primary Tumor

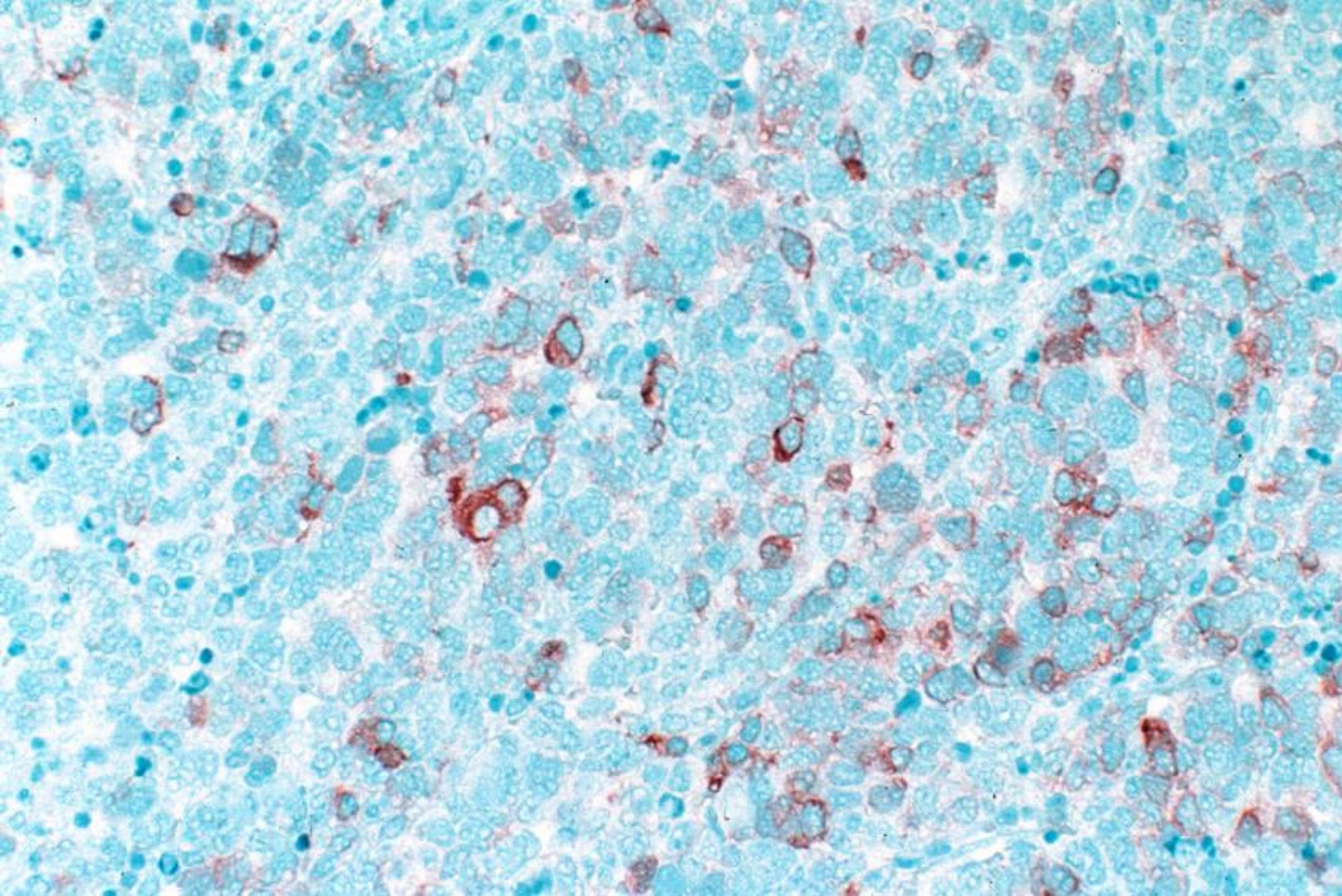


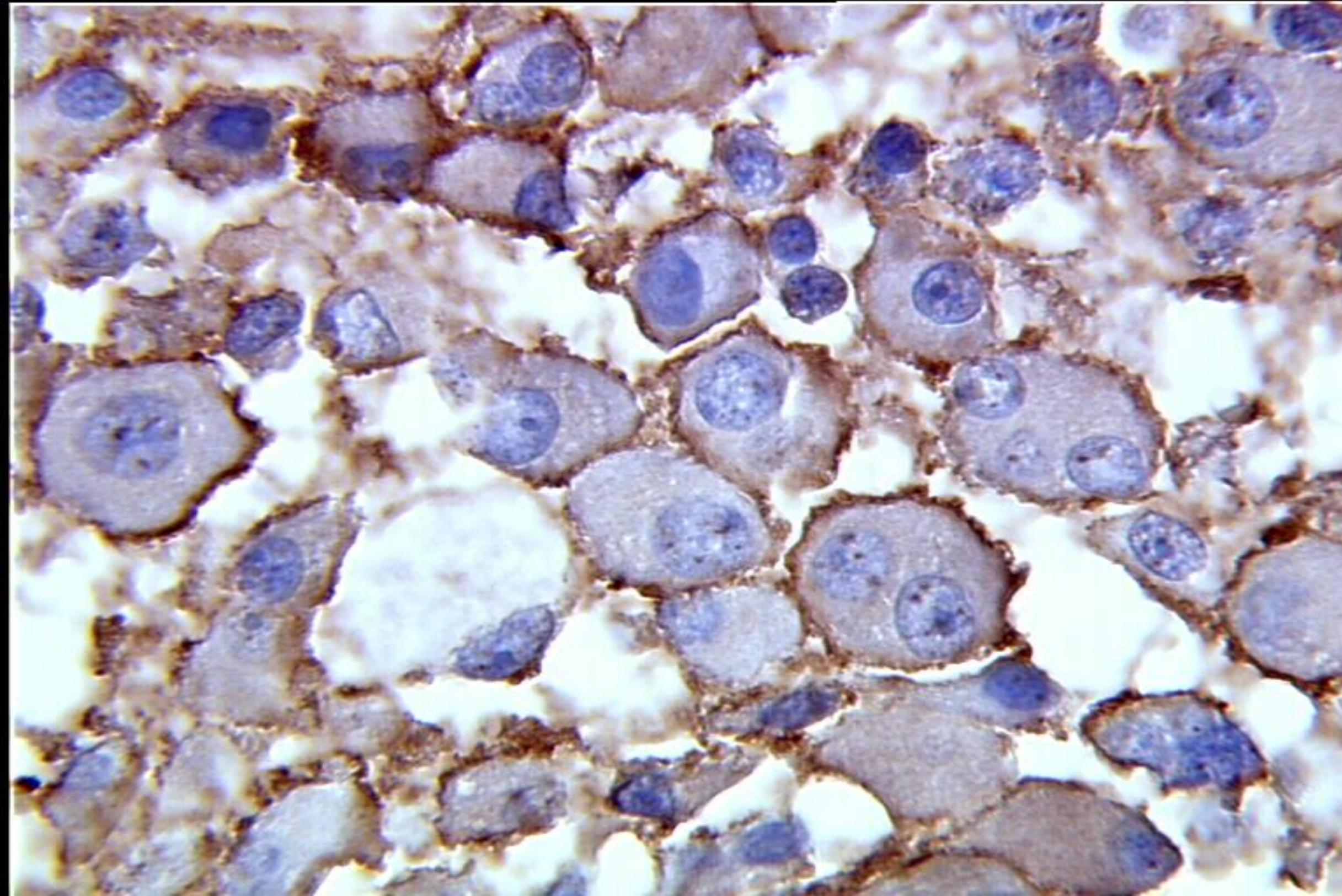


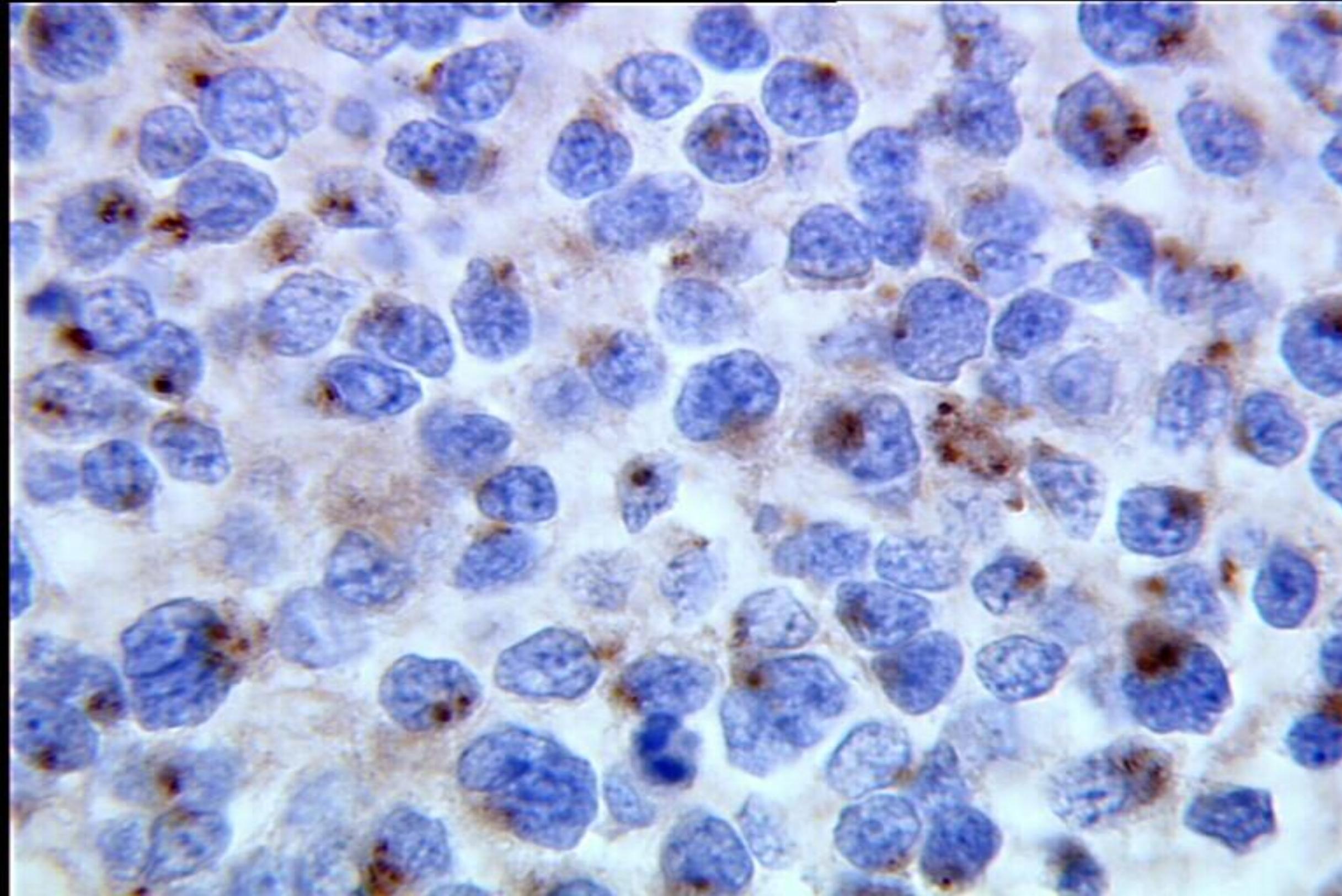
# Immunostaining

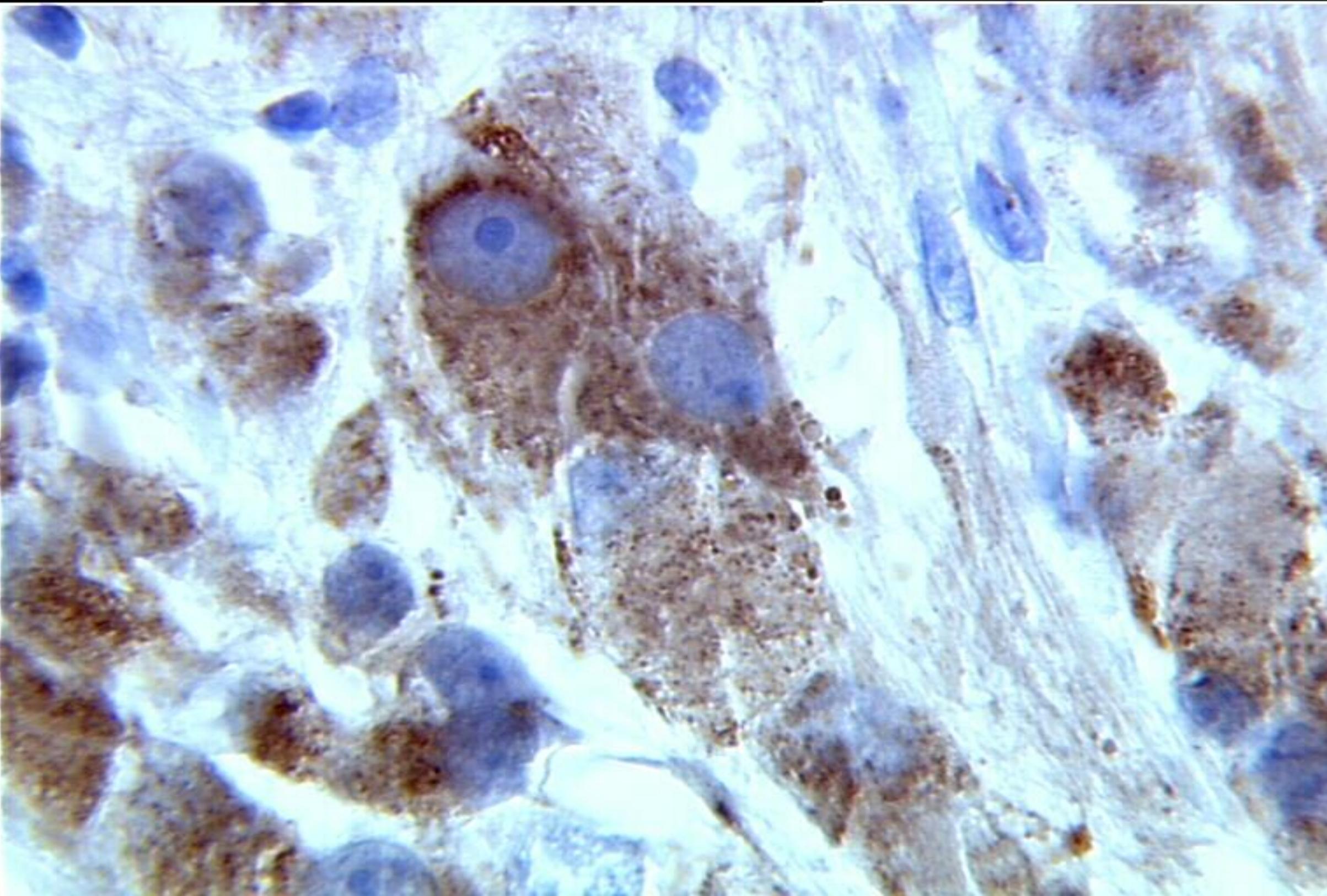
<i>Peripheral Neuroblastic Tumors</i>		<i>TH</i>	<i>PGP 9.5</i>	<i>NSE</i>	<i>CD 45</i>	<i>Desmin</i>	<i>MyoD1/ Myogenin</i>	<i>CD99</i>	<i>S 100 (<math>\beta</math>)</i>
Tumor cell types	Reactive cell types								
<i>Neuroblasts</i> <i>Differentiating neuroblasts</i> <i>Ganglionic cells</i>		+	+	+	-	-	-	-	-
	<b><i>Schwann cells</i></b>	-	-	-	-	-	-	-	+
	<i>Lymphocytes, if present</i>	-	-	-	+	-	-	-/+	-
<i>Peripheral Neuroblastic Tumors</i>						<b><i>CD 44 *</i></b>	<b><i>TrkA **</i></b>		
Prognostic markers						+			
<i>Better Prognosis Tumors</i>									+
<i>Poor Prognosis Tumors</i>						-			-
<i>Peripheral Neuroblastic Tumors, differential diagnosis</i>		<i>TH</i>	<i>Vimentin</i>	<i>PGP 9.5</i>	<i>CD 45</i>	<i>Desmin</i>	<i>MyoD1/ Myogenin</i>	<i>CD99</i>	
<i>Neuroblastoma (Schwannian stroma- poor)</i>		+	+/-	+	-	-	-	-	-
<i>Ewing's/pPNET</i>		-	+	+	-	-	-	-	+
<i>Rhabdomyosarcoma</i>		-	+/-	-	-	+	+	+	-
<i>Non-Hodgkin Lymphoma (lymphoblastic type)</i>		-	+/-	-	+	-	-	-	+/-

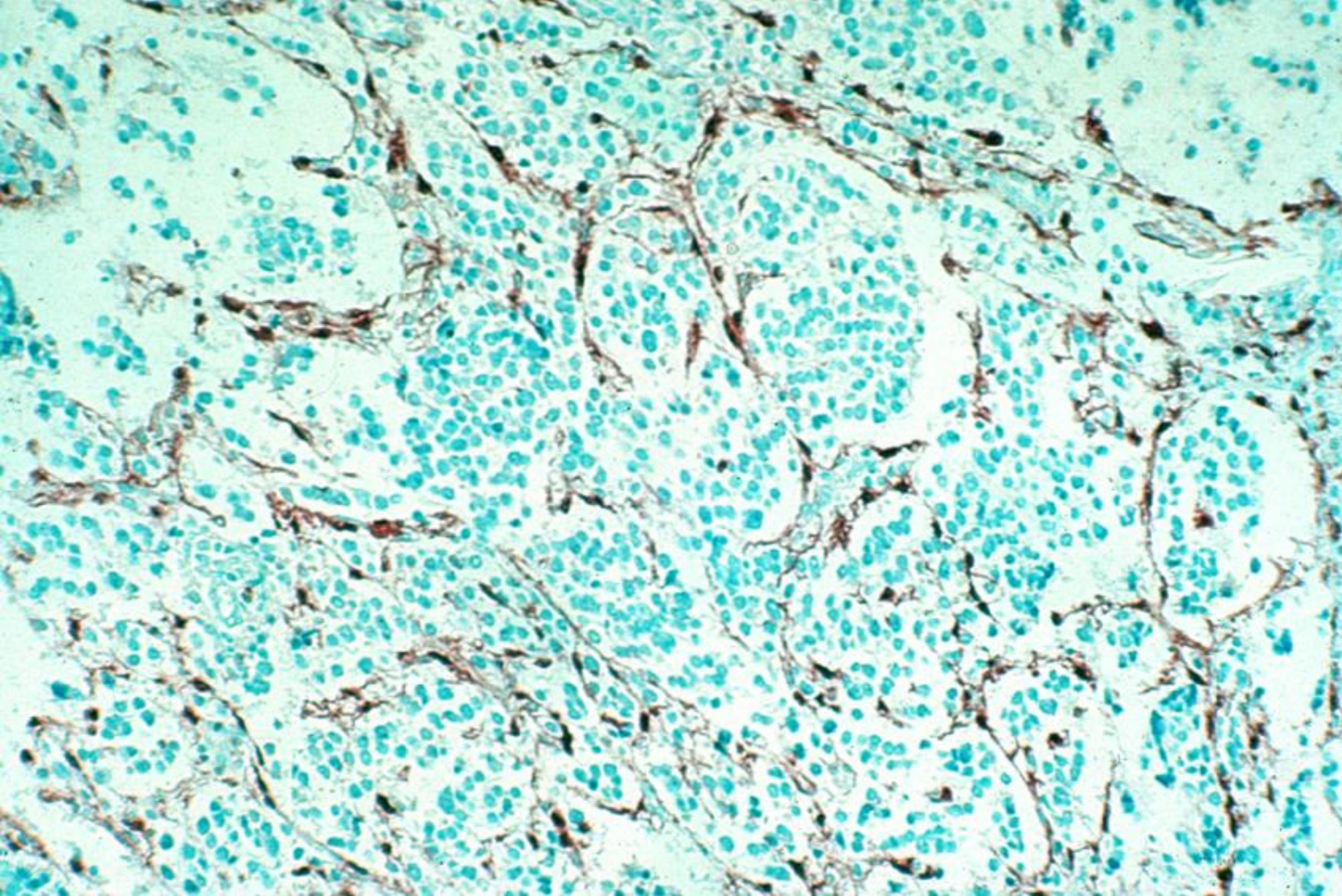


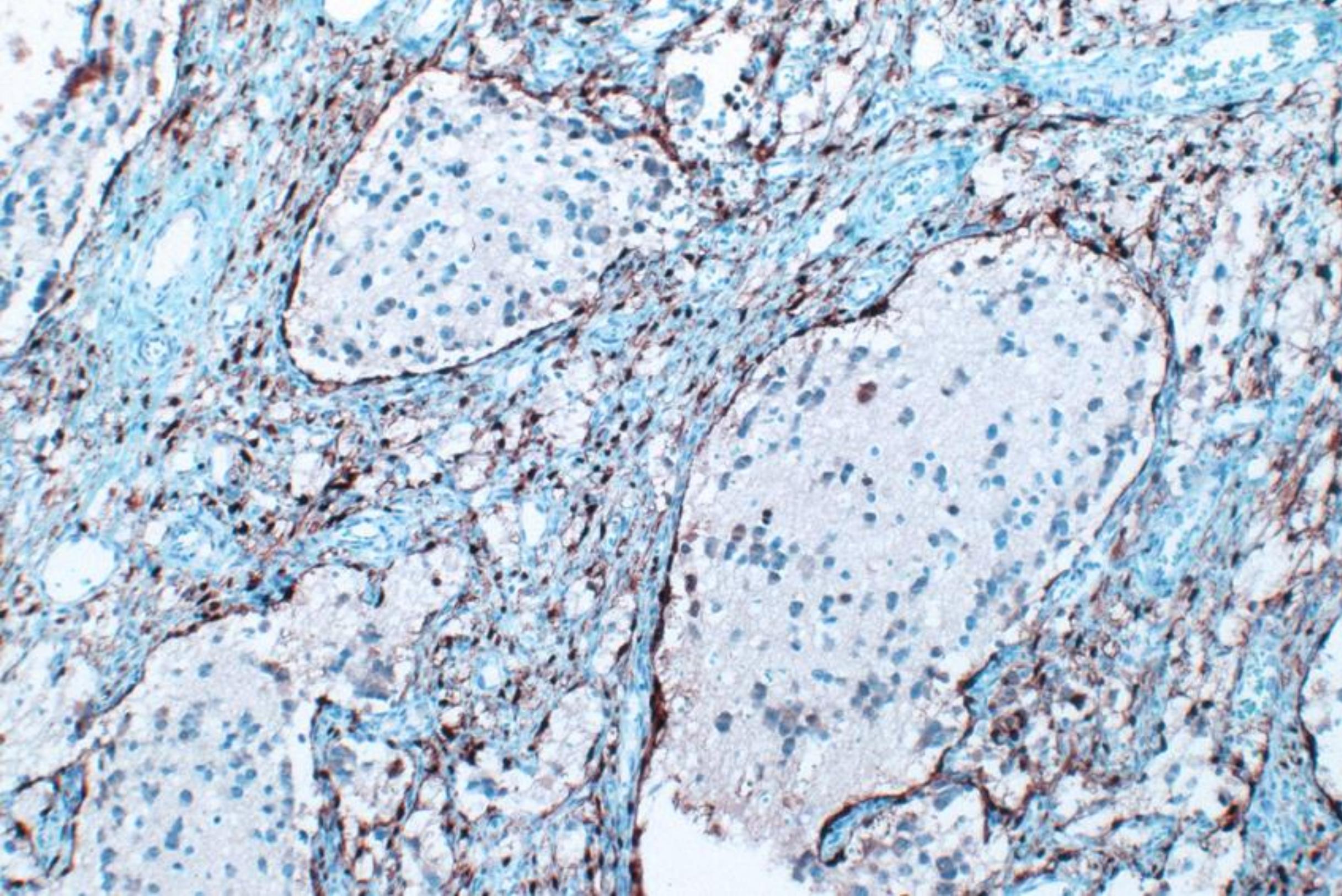


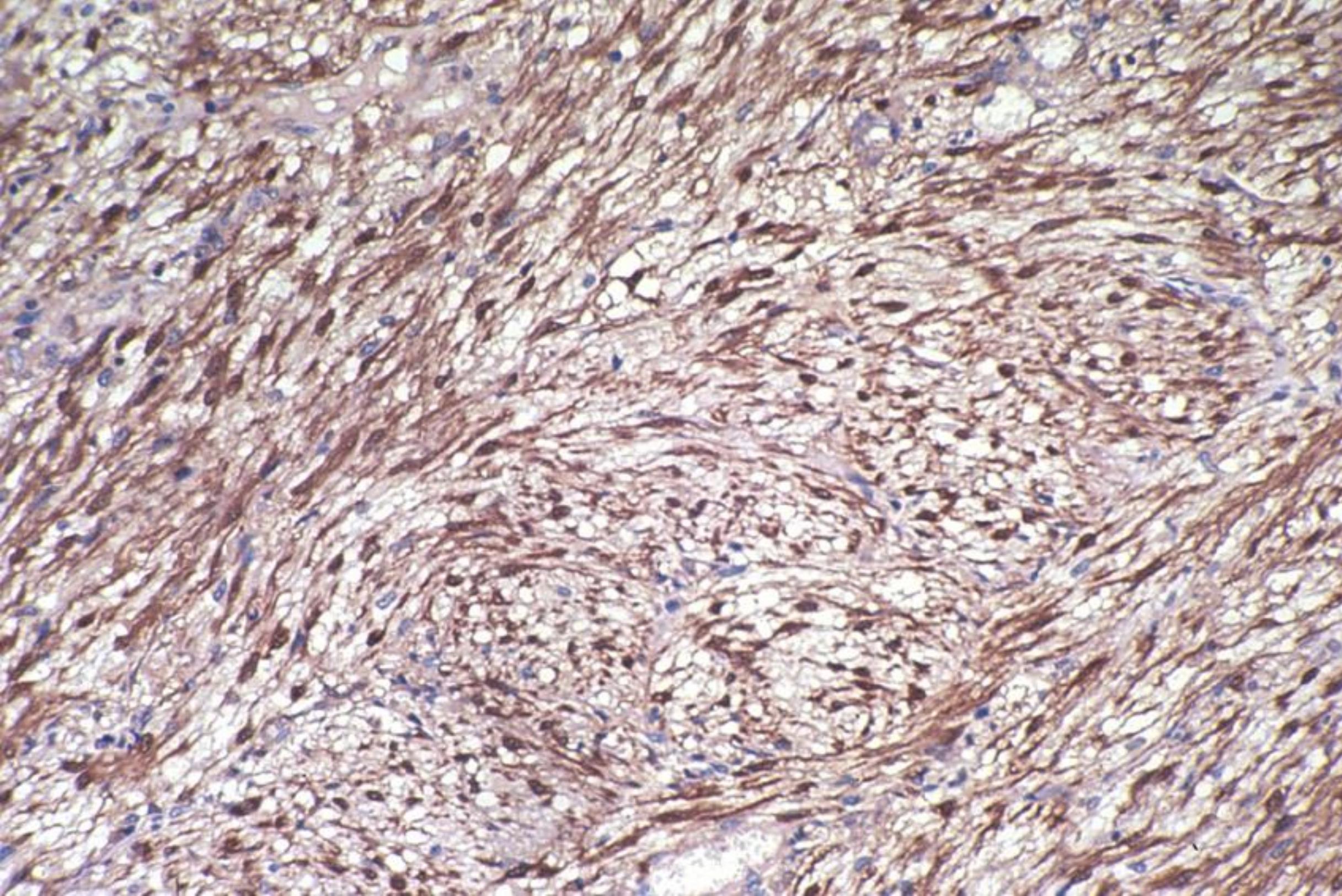












# Genetic Properties

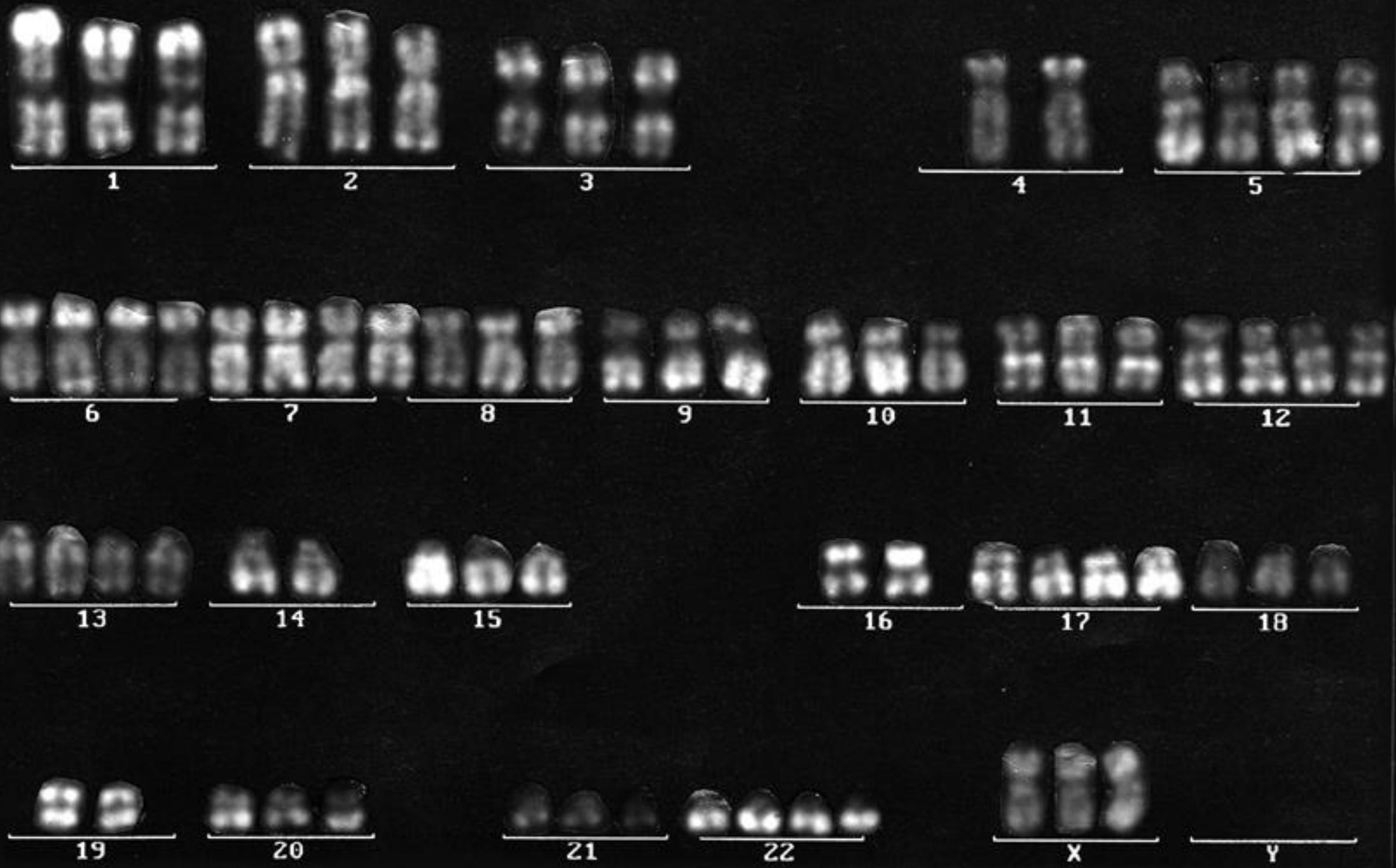
Karyotype

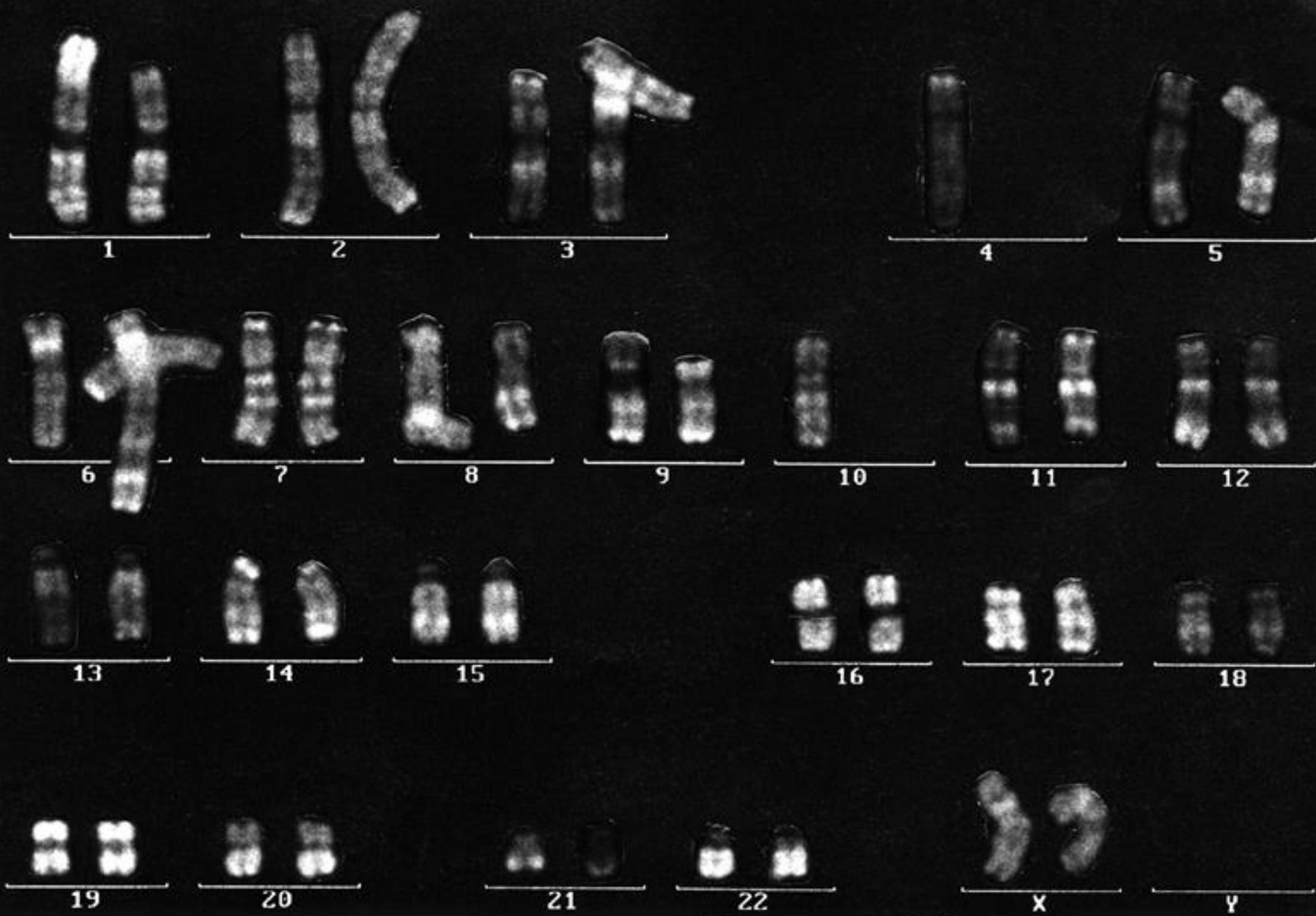
MYCN amplification

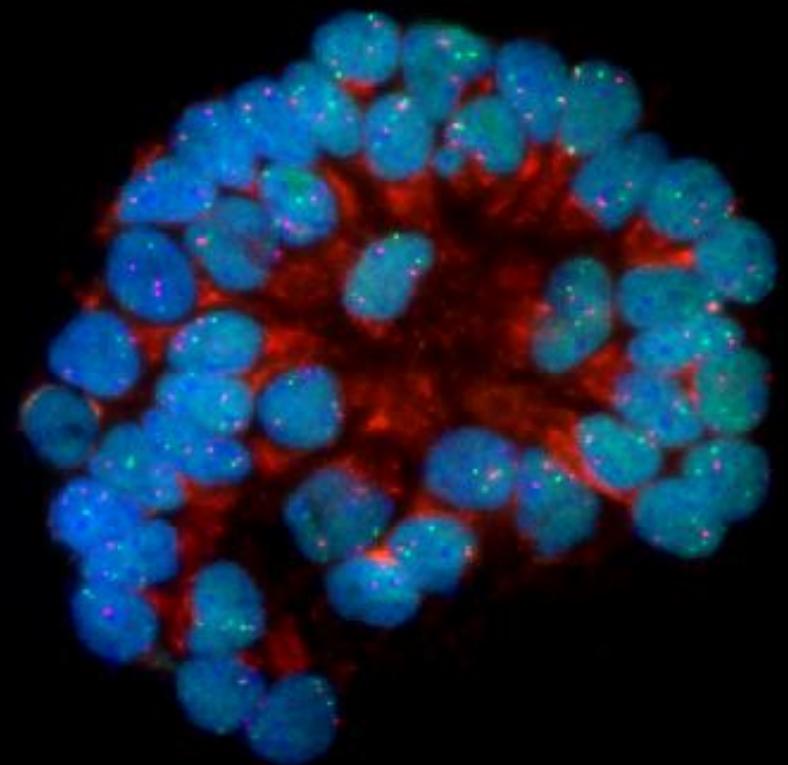
Deletion of chromosome 1p

Gain of chromosome 17q

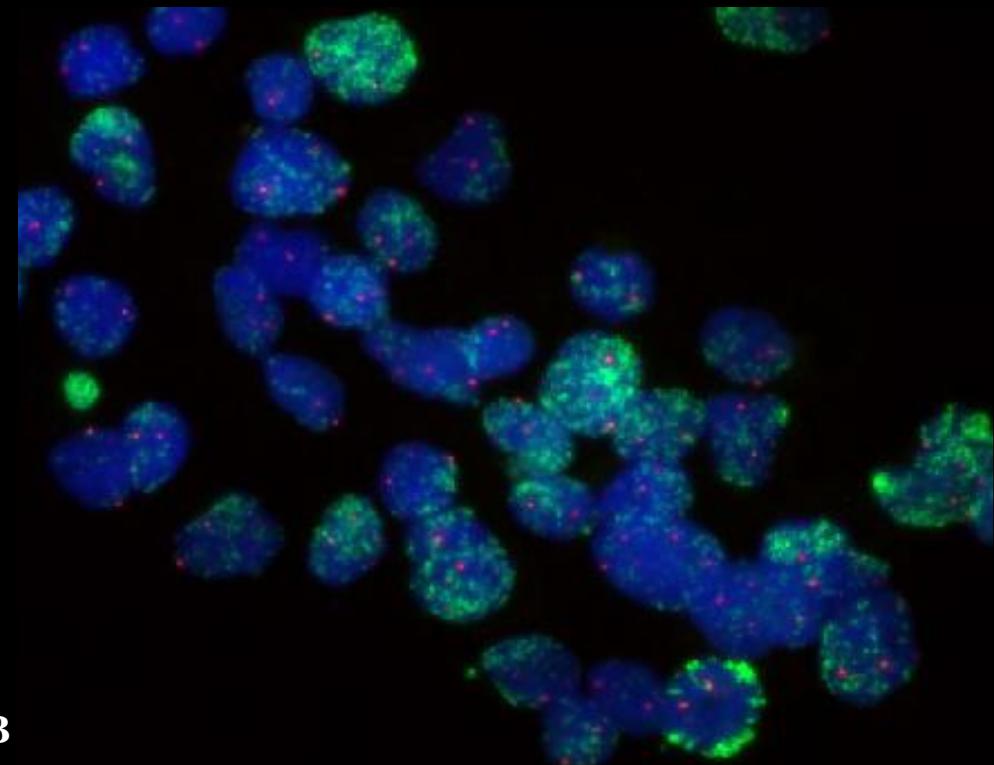
Ganglion cells and Schwann cells



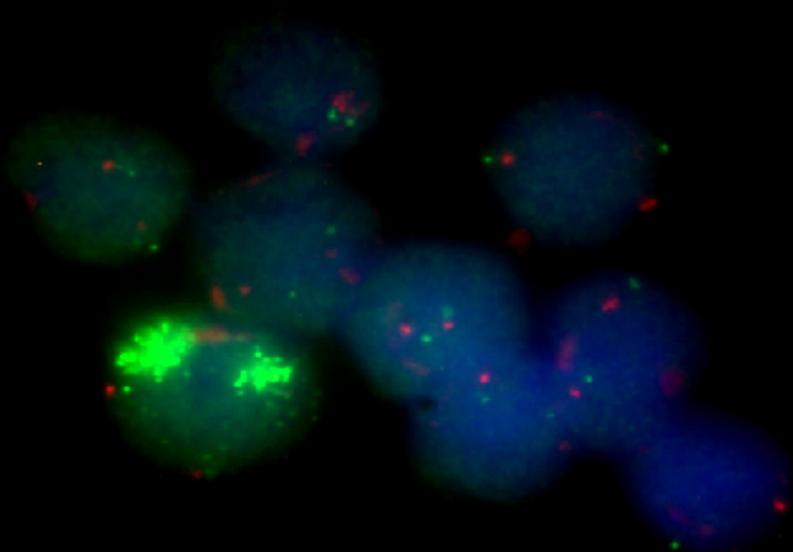




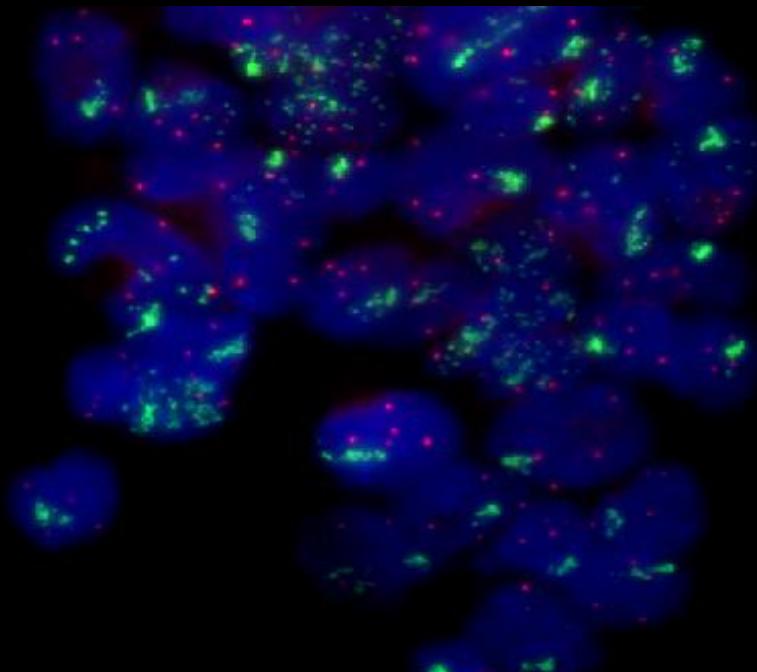
A



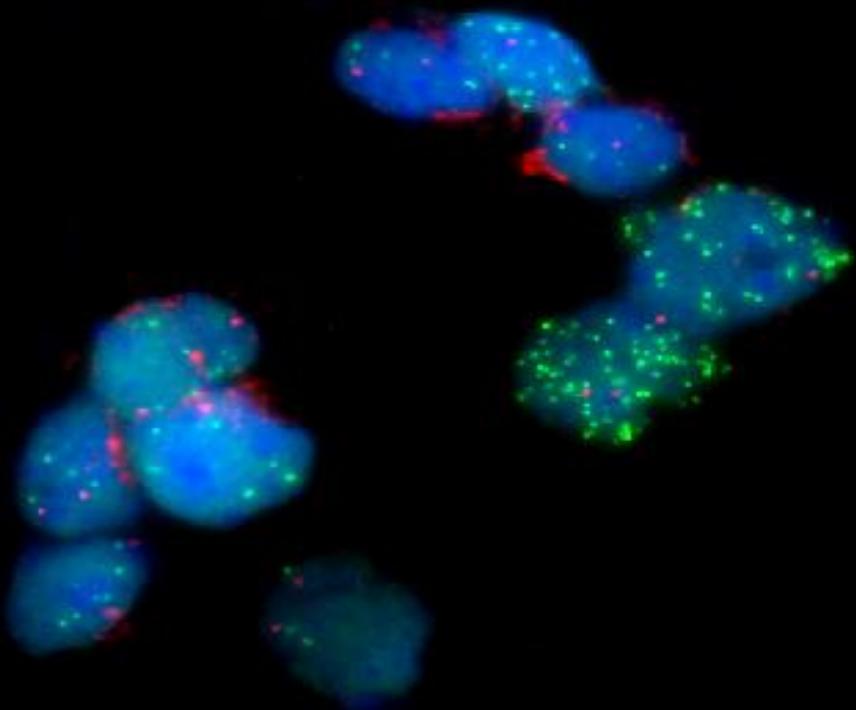
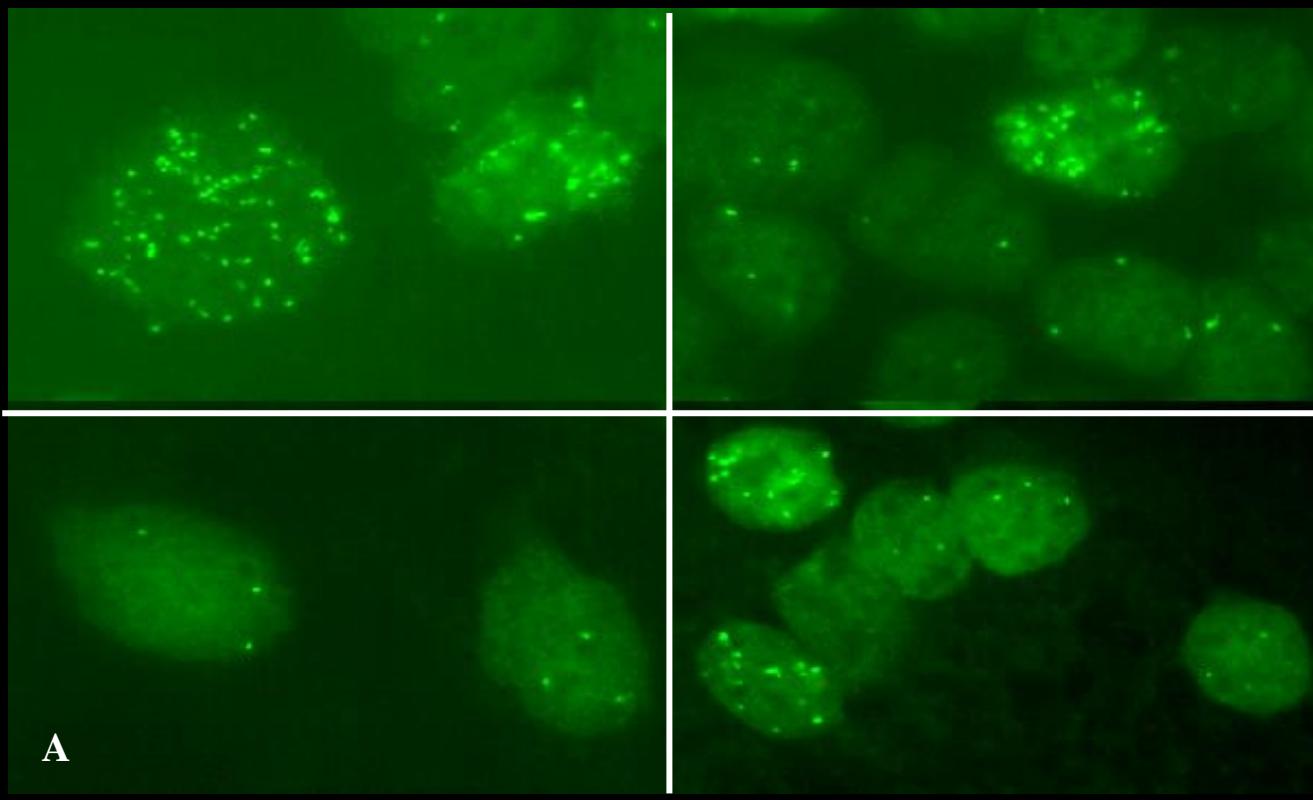
B

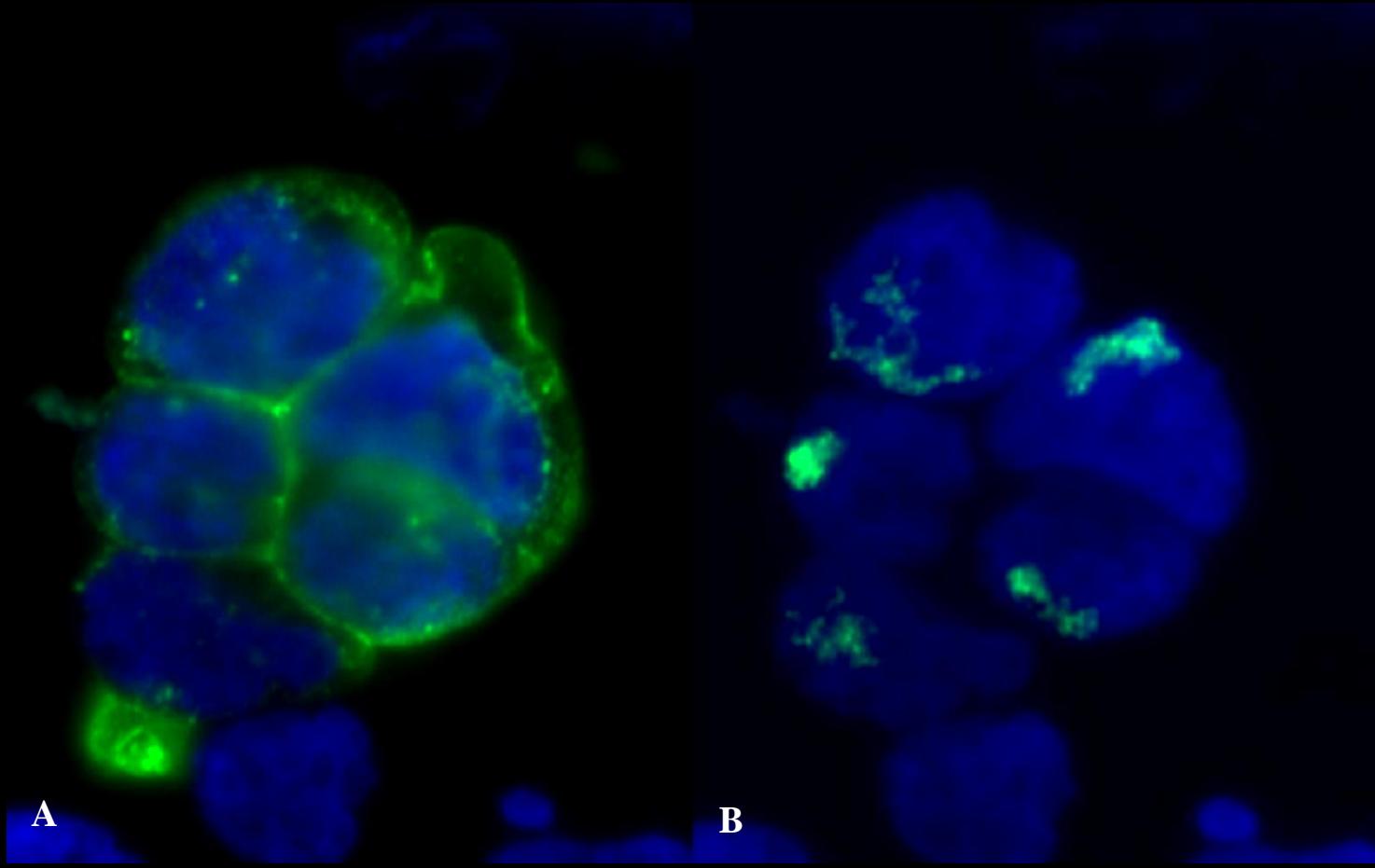


C



D

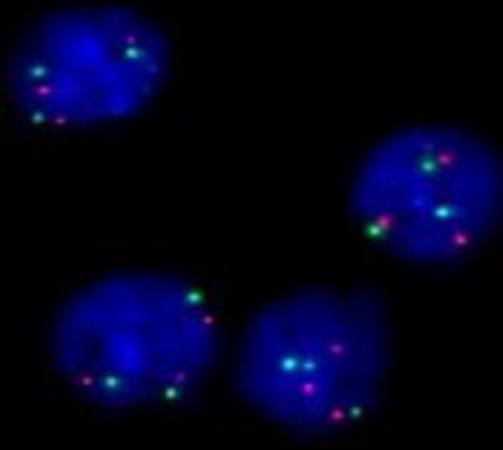




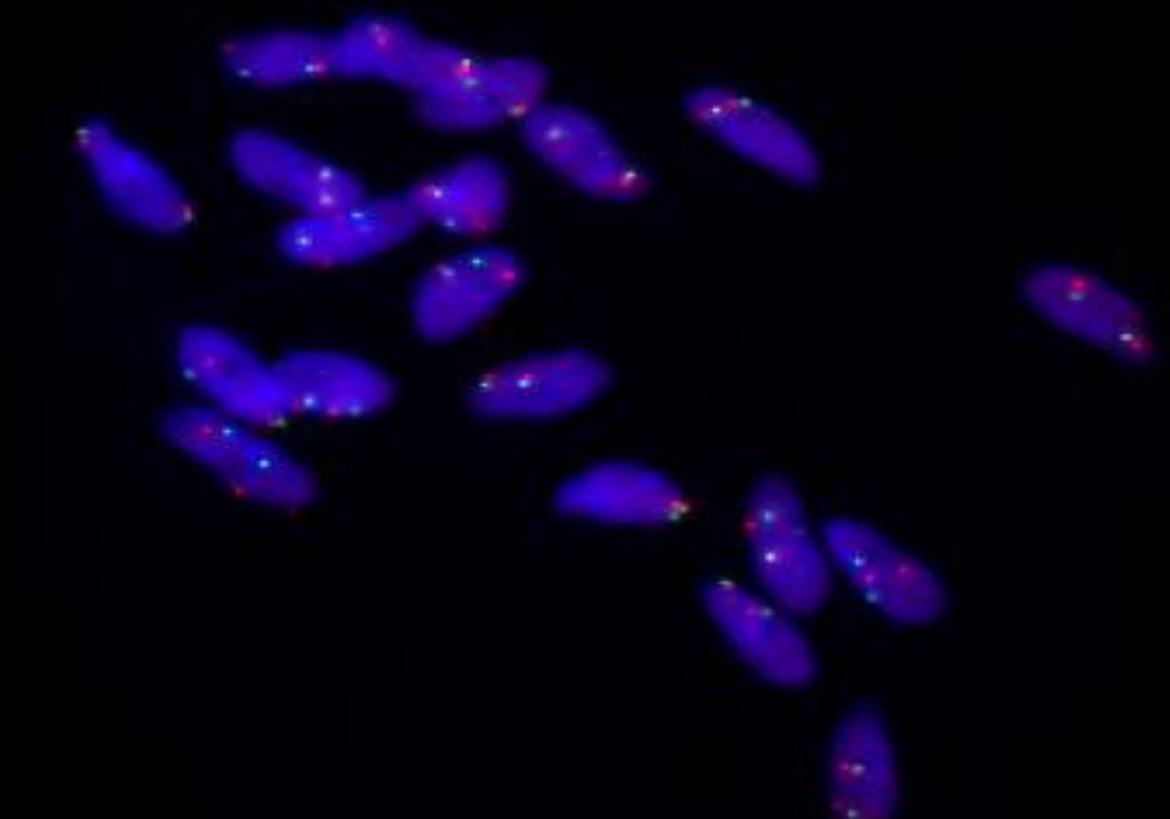
A

B

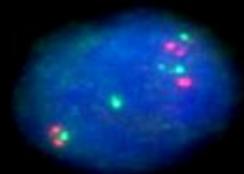
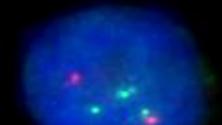
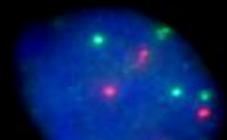
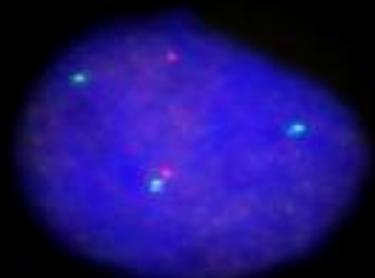
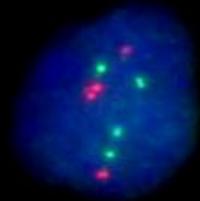
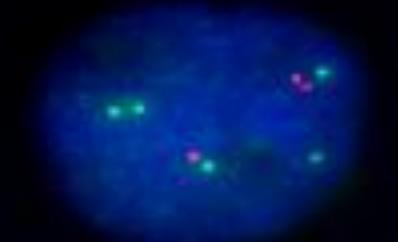




A



B

**A****B****C****D****E**

# Pathology Checklist

**Morphologic Features**  
(as described in Shimada et al. CANCER 1999;86:349-63)

**(I) Tumor Type**

- Neuroblastoma (Schwannian stroma-poor)-----I I  
Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)-----I I  
Ganglioneuroma (Schwannian stroma-dominant)-----I I  
Ganglioneuroblastoma, Nodular (Composite, Schwannian stroma-rich/stroma-dominant and stroma-poor)-----I I

Primary tumor showing "Ganglioneuroblastoma, Intermixed" or "Ganglioneuroma" appearance with concurrent metastatic nodule(s) of Neuroblastoma is classified as "Ganglioneuroblastoma, Nodular".

**(II) For Neuroblastoma (Schwannian stroma-poor) and stroma-poor portion of the Ganglioneuroblastoma, Nodular\***

**1) Neuroblastic differentiation**

- a) Undifferentiated (Totally undifferentiated, difficult in making the diagnosis by routine H&E examination, alone)-----I I  
b) Poorly differentiated (<5% differentiating neuroblasts)-----I I  
c) Differentiating (>5% differentiating neuroblasts)-----I I

Differentiating neuroblasts = neuroblastic cells having synchronously maturing nucleus and cytoplasm

**2) MKI (mitosis-karyorrhexis index)**

- a) low (<2% or <100/5,000 cells)-----I I  
b) intermediate (2-4% or 100-200/5,000 cells)-----I I  
c) high (>4% or >200/5,000 cells)-----I I

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\*List different histologies, if present, of nodular lesions separately (circle a, b, or c for each morphologic feature; codes, see above):

- Nodule 1:      neuroblastic differentiation (a, b, c);                  MKI (a, b, c)  
Nodule 2:      neuroblastic differentiation (a, b, c);                  MKI (a, b, c)  
Nodule 3:      neuroblastic differentiation (a, b, c);                  MKI (a, b, c)
- 

**(III) For Ganglioneuroma (Schwannian stroma-dominant)**

**1) Neuroblastic maturation towards ganglion cells**

- a) **Maturing** (mixture of completely and incompletely mature ganglion cells)-----I I  
b) **Mature** (complete maturation with satellite cells)-----I I

**(IV) Other Findings**

- Calcification:** yes-----I I  
no-----I I

**Comments:**

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Patient I.D.

Date of Birth

Date of Surgery/Biopsy

# International Neuroblastoma Pathology Classification

FH: favorable histology

UH: unfavorable histology

- For variant forms and prognostic evaluation of “**Ganglioneuroblastoma, Nodular**”, see CANCER 2003;98:2274-81.

