

## 頭部皮膚腫瘍

川崎医大総合医療センター  
病理科 物部 泰昌、藤原 英世

60代後半、男性。

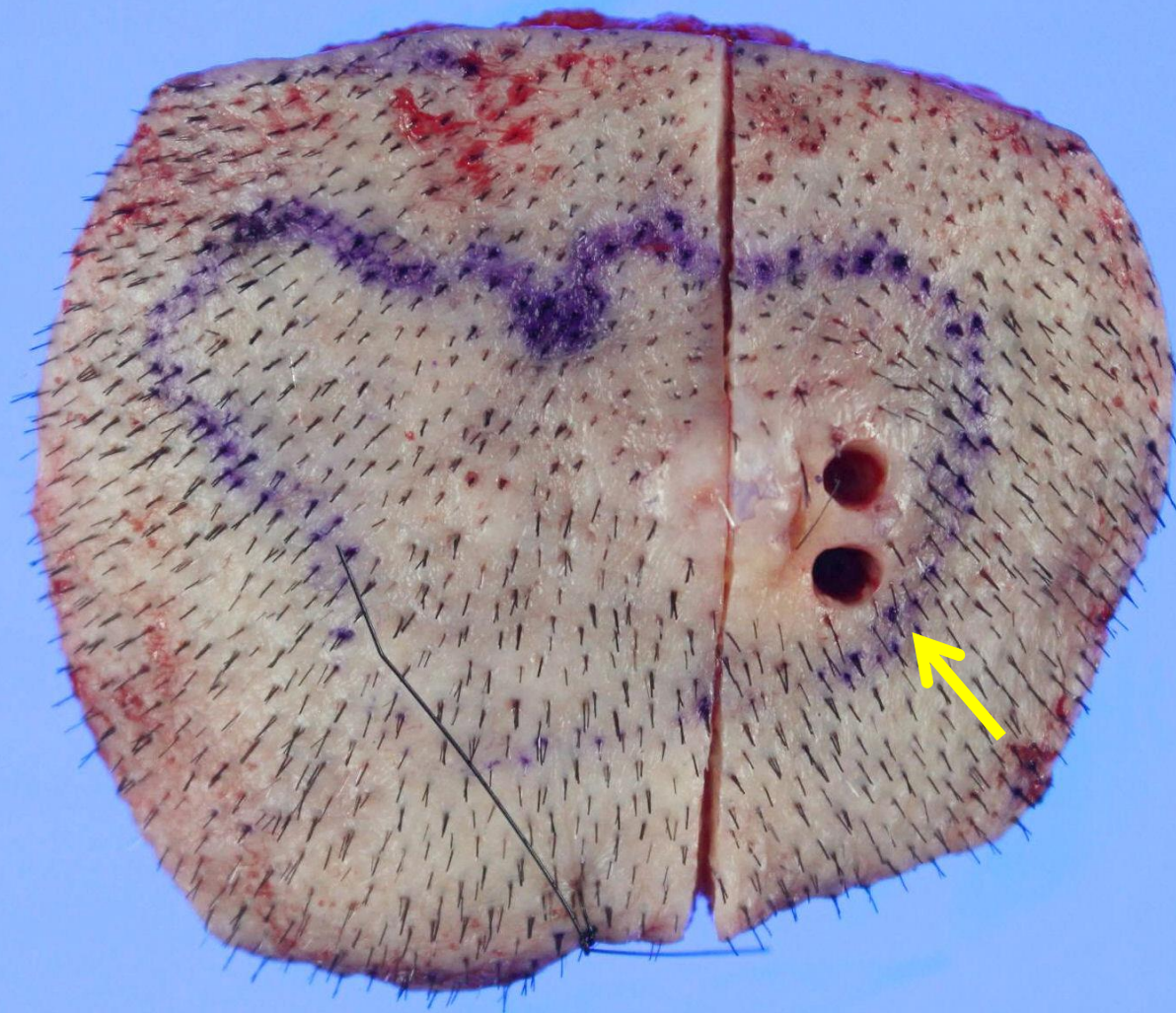
1年ほど前から頭頂部、やや左寄りに紅色調の皮膚結節病変(15mm)が出現。周辺にも”浸潤性に触れる”病変あり。さらに1～2か月前には前額部にも紅色の光沢をもった”浸潤性に触れる”病変が出現。皮膚生検では **Malignant small round cell tumor** で、シナプトフィジンが陽性より、**Merkel cell carcinoma** が疑われた。腫瘍摘出術と周辺の浸潤性病変の生検が施行された。

摘出された皮膚腫瘍の断面では境界不明瞭で、乳白色調の充実性の結節性腫瘍(15x10mm)で真皮から皮下組織にかけて増殖していた。 組織診断は？ 下図は頭部の皮膚病変図です。



頭頂部やや左寄りの  
紅色調の結節性病変





頭皮腫瘍切除標本(生検後)

術後2ヶ月後

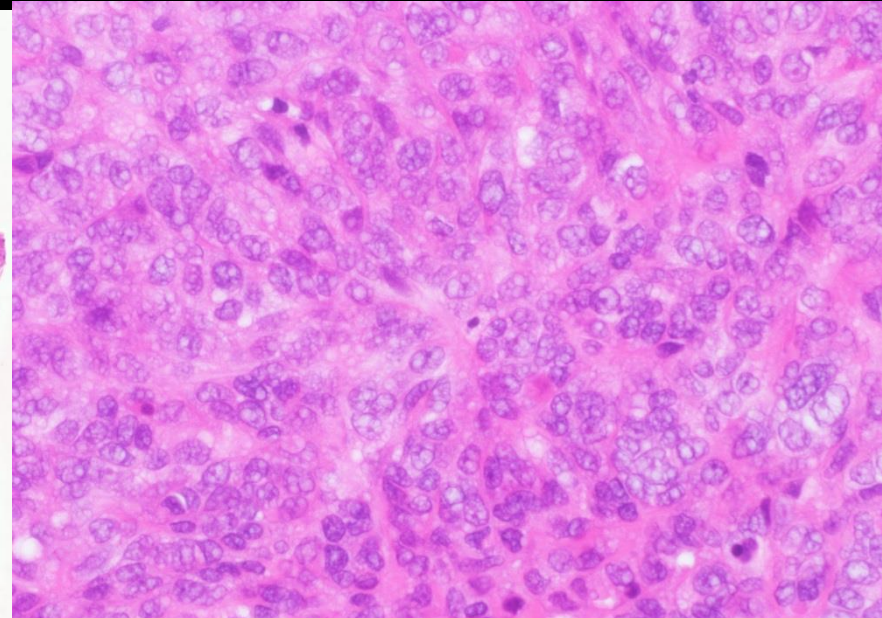
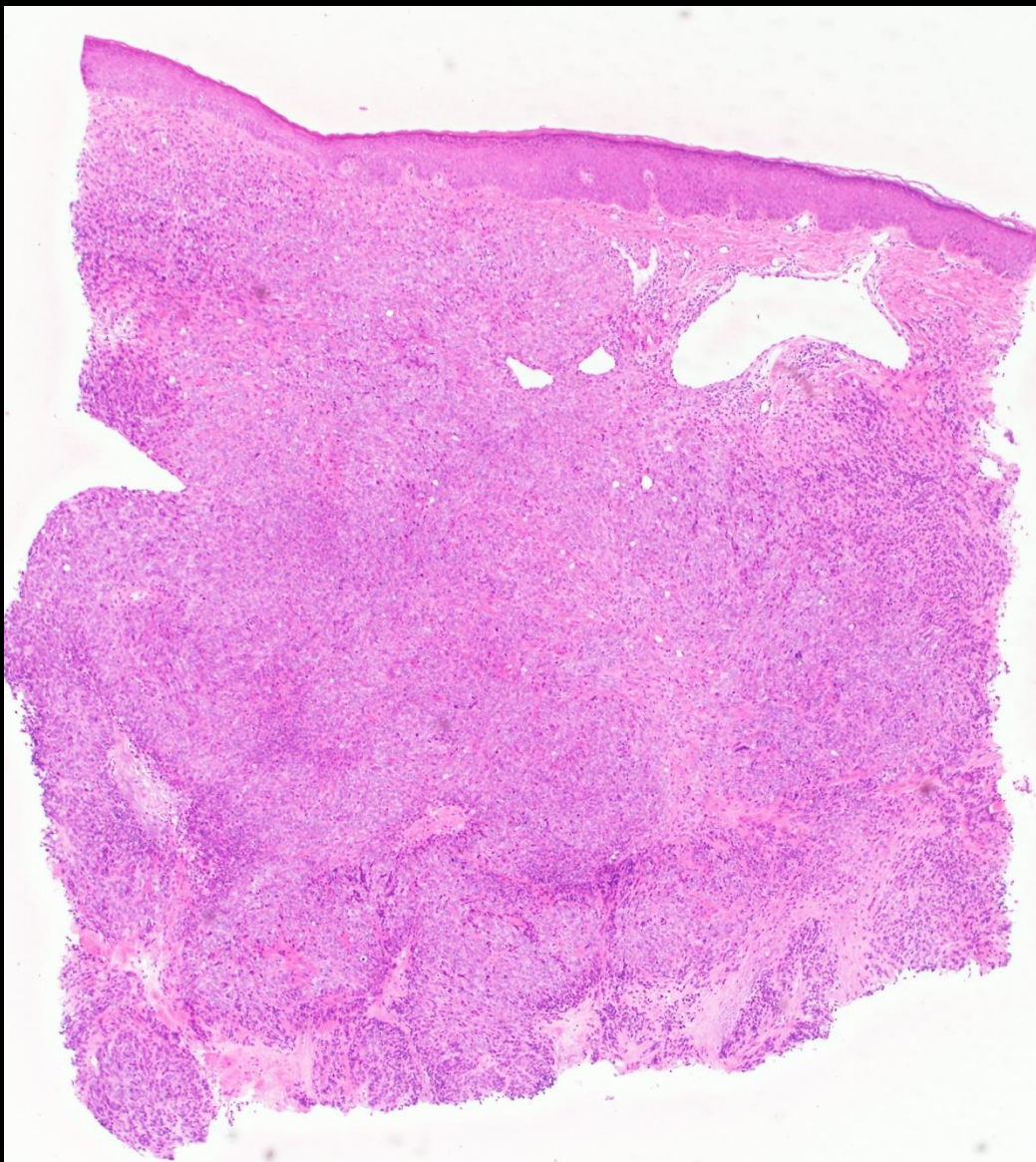
前額部の紅色の光沢を  
もった浸潤性に触れる病変



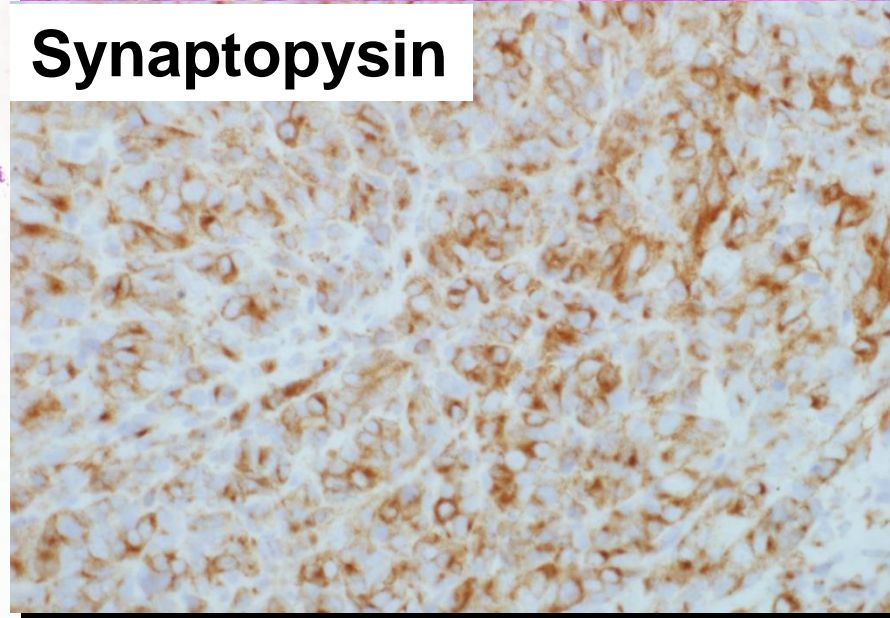
術後の頭頂部



# 最初の皮膚生検組織



**Synaptophysin**



# 免疫染色結果(生檢時)

## 陽性

- Synaptophysin
- S100

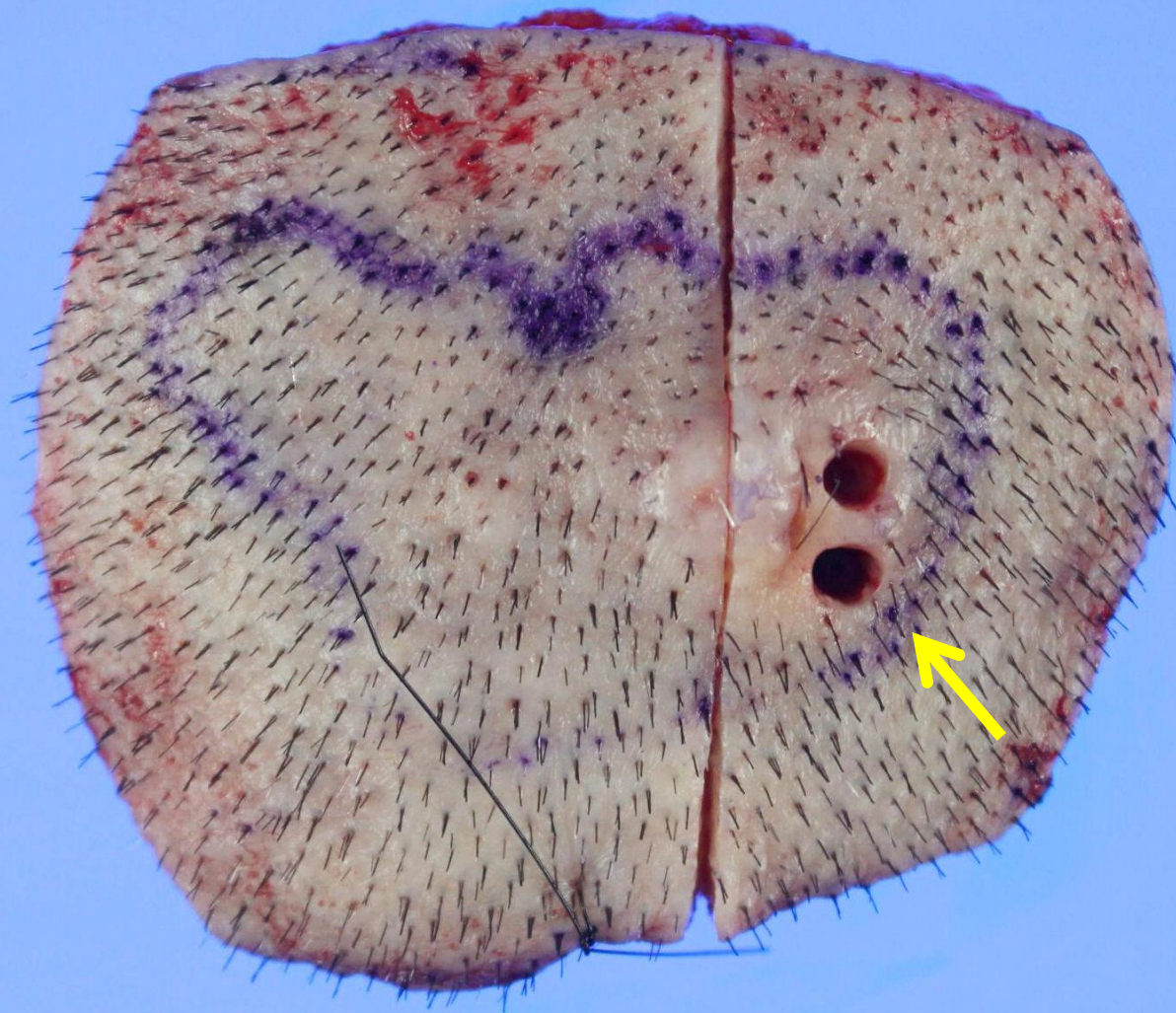
## 陰性

- AE1/AE3
- CK20
- TTF-1
- ChromograninA
- Neurofilament
- LCA
- CD68
- CD34

# 皮膚生検病理診断

Neuroendocrine carcinoma

Suspicious of Merkel cell carcinoma

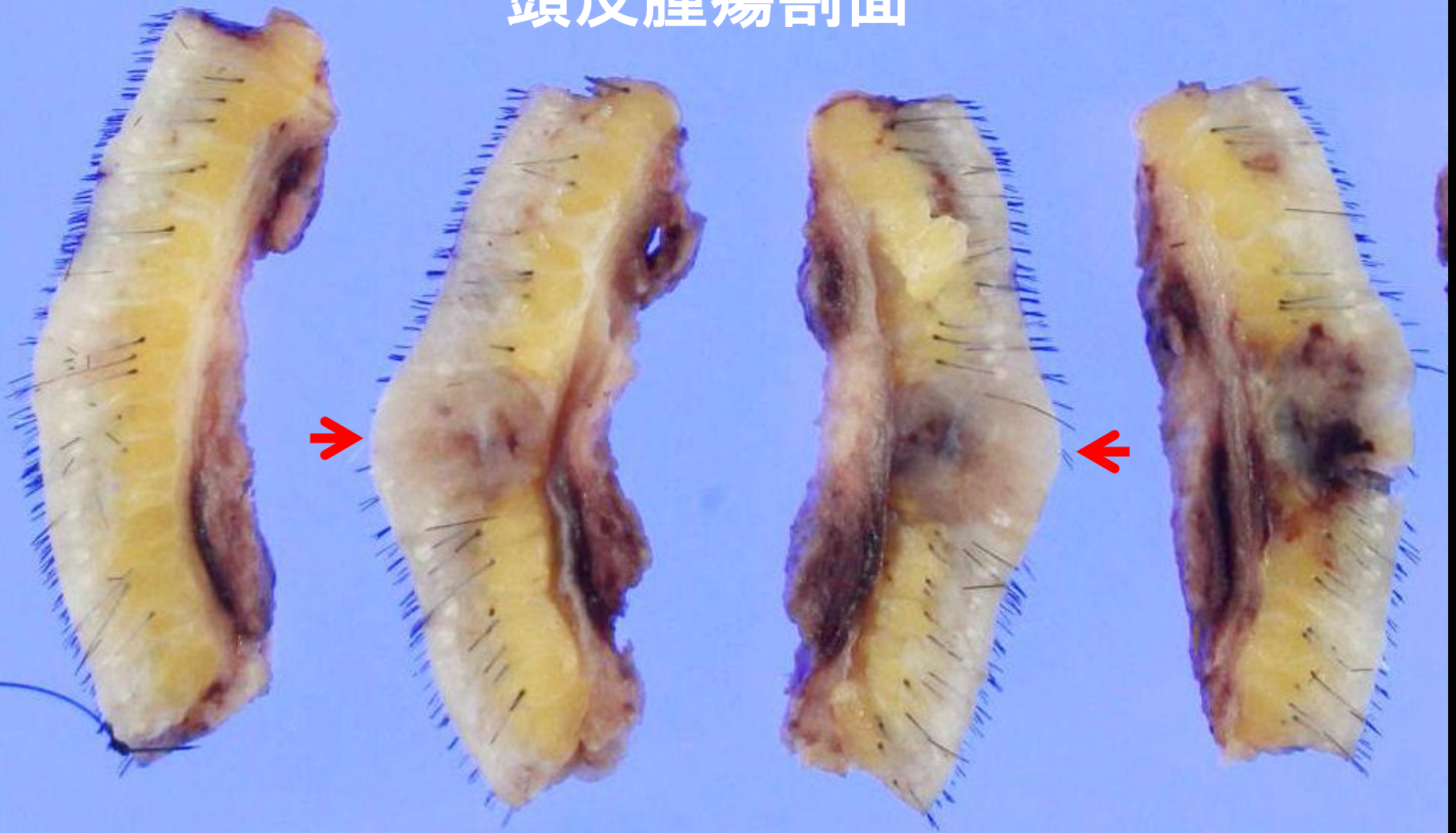


頭皮腫瘍切除標本(生検後)

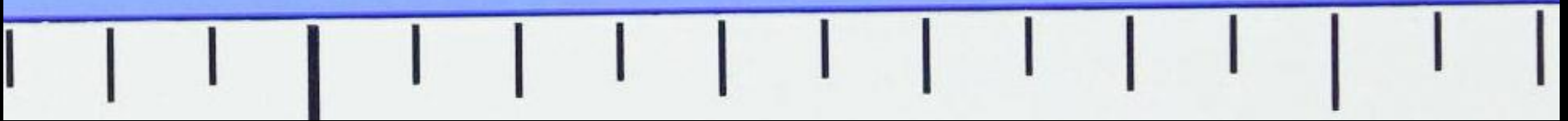


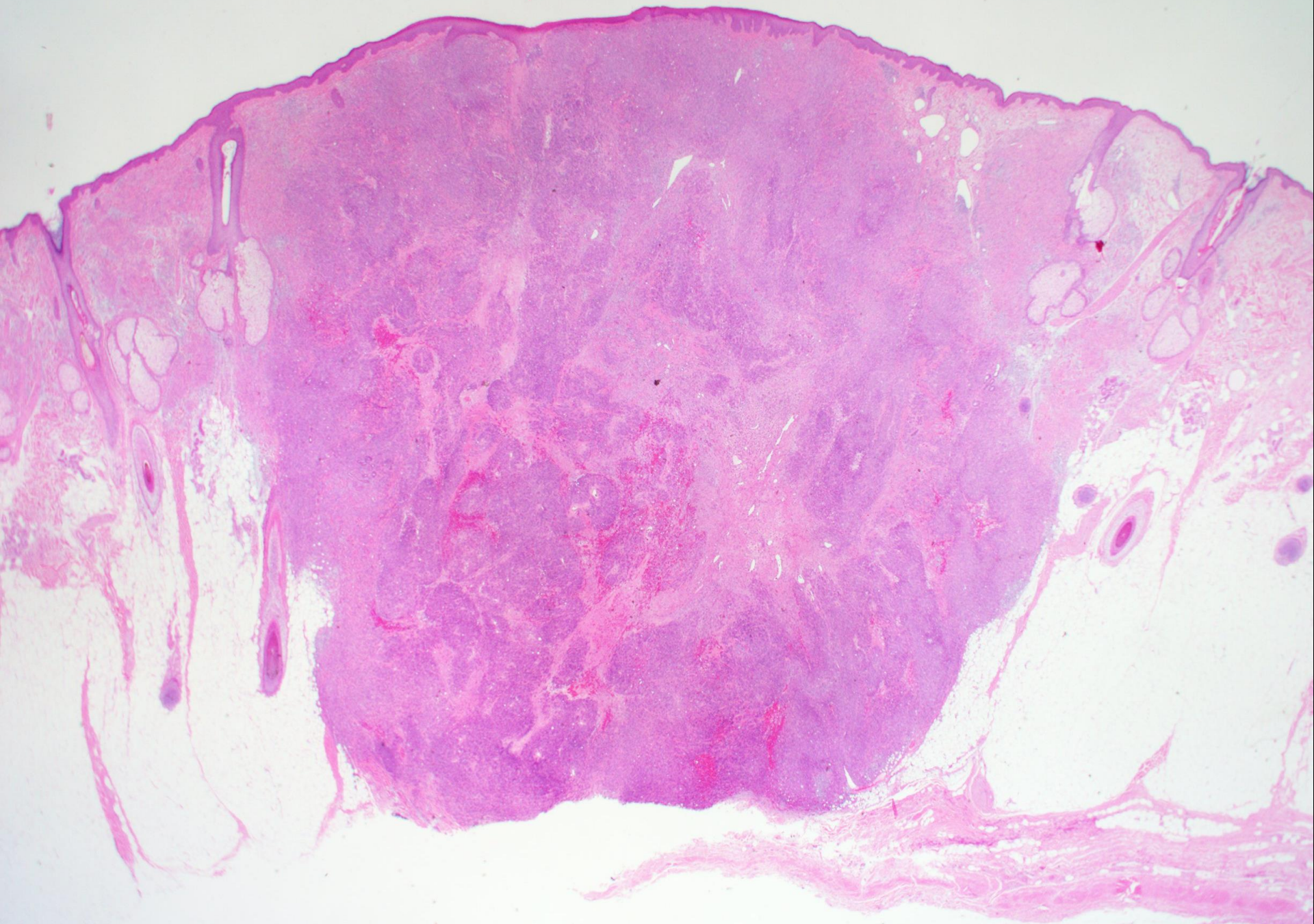


# 頭皮腫瘍剖面

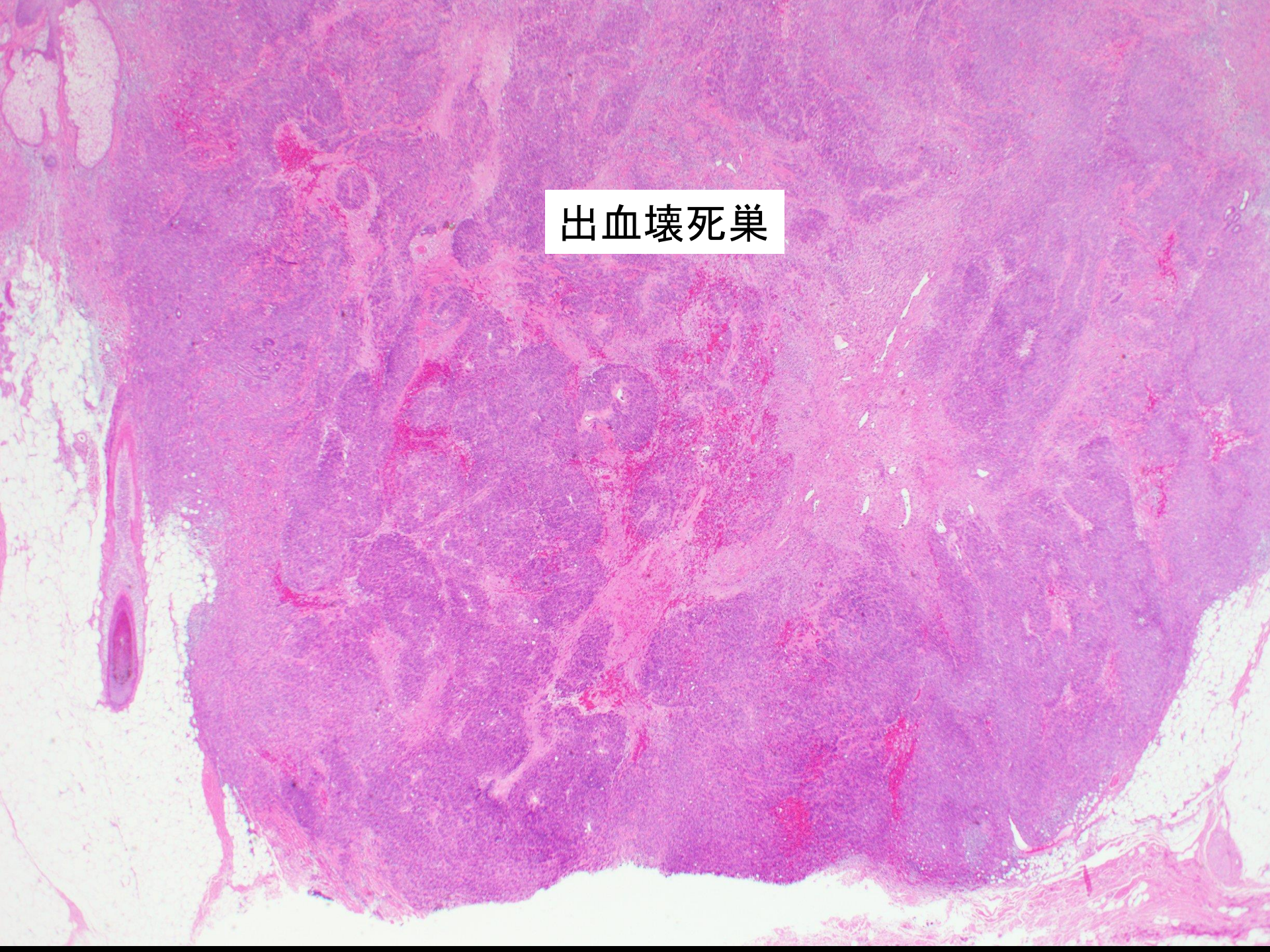


大きさ 15x10mm

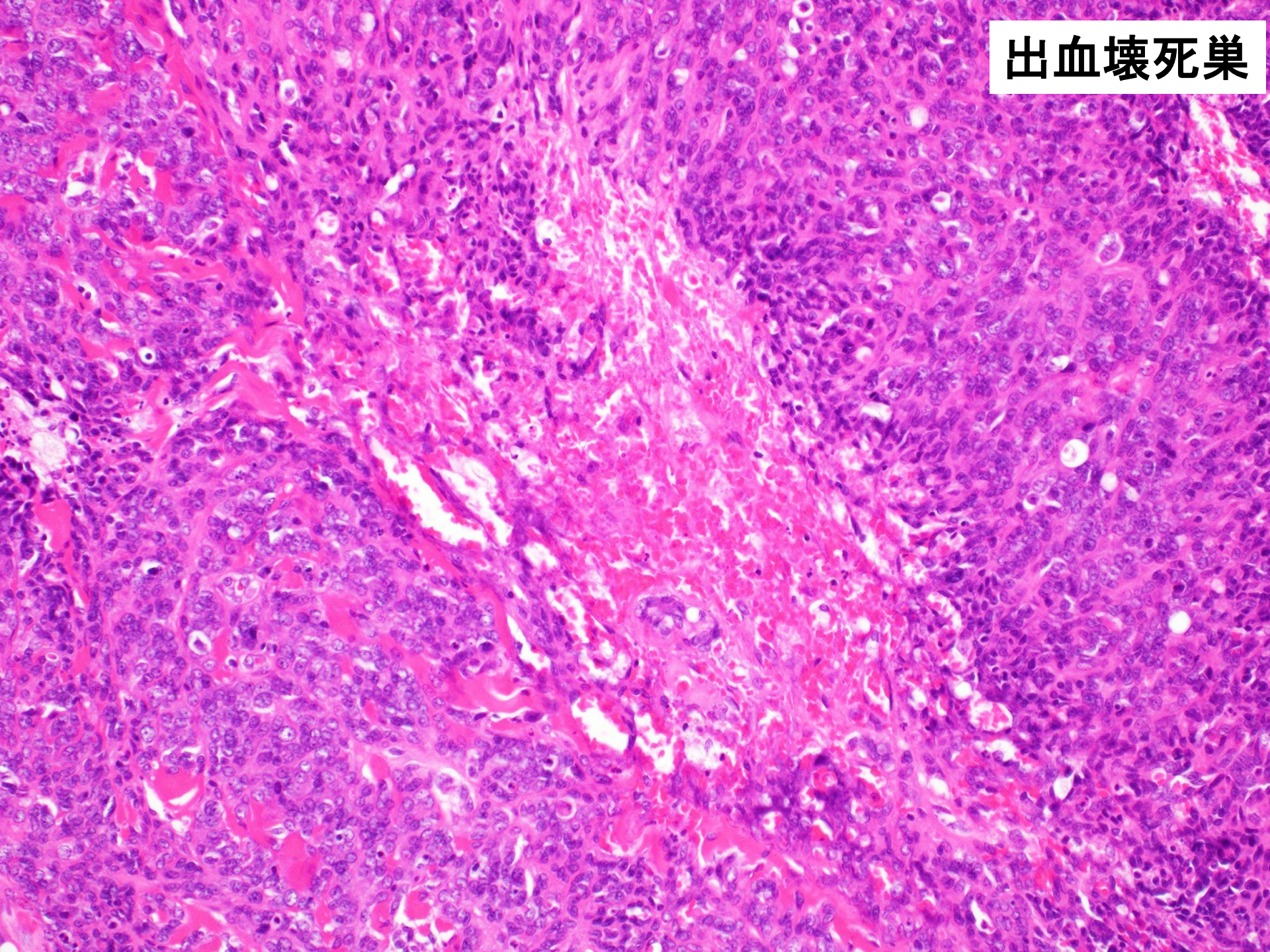


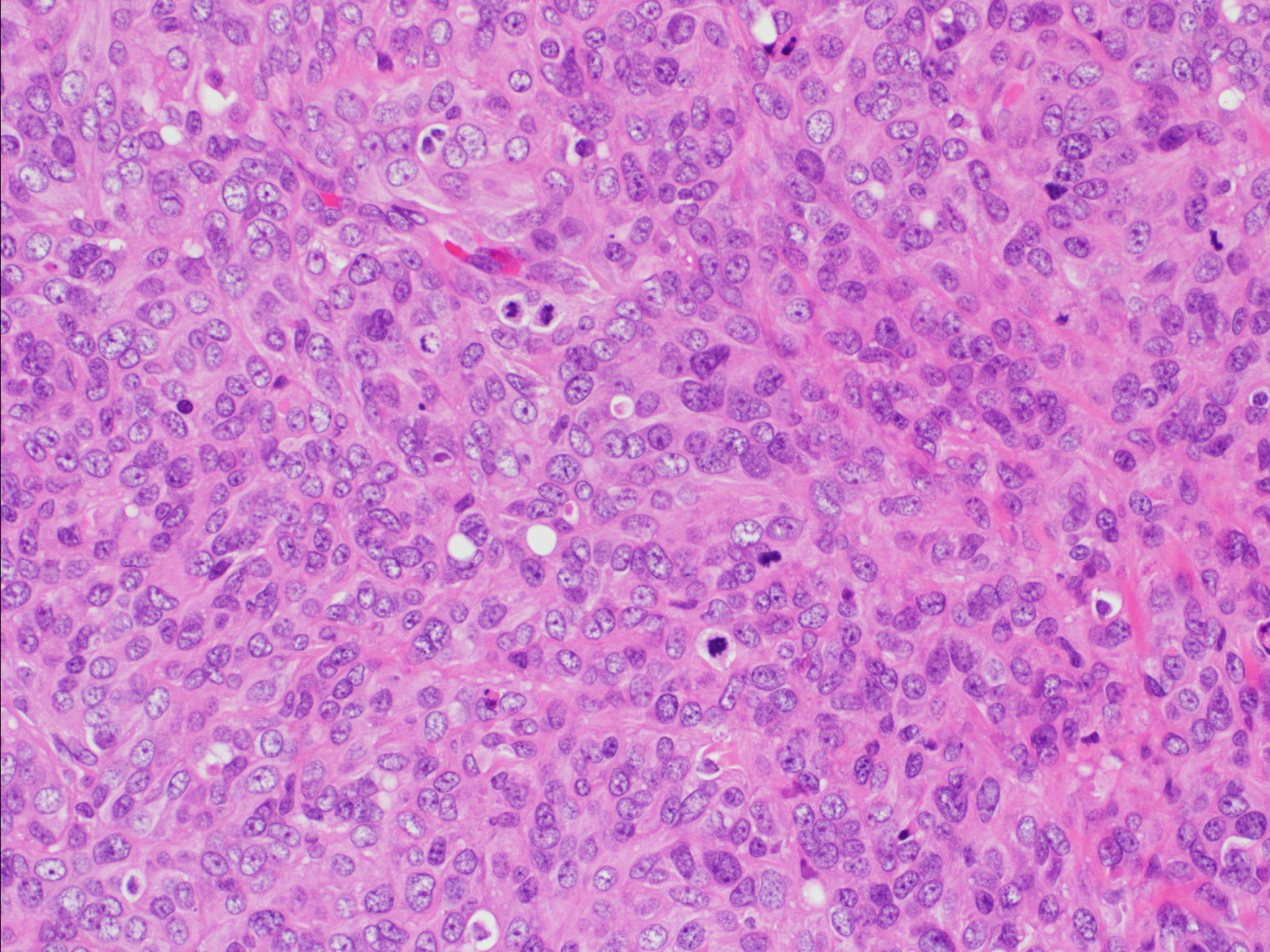


出血壞死巢

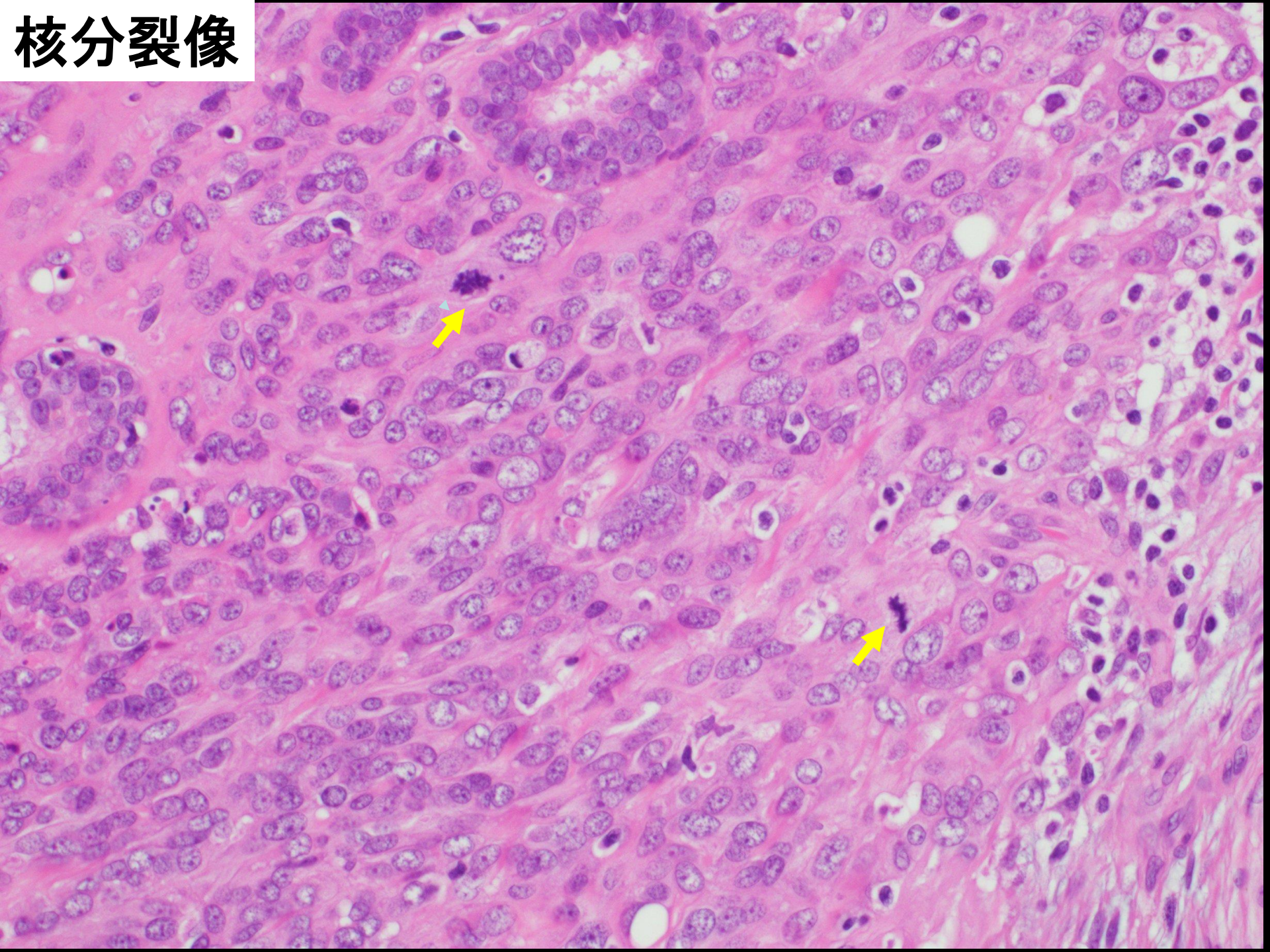


出血壞死巢

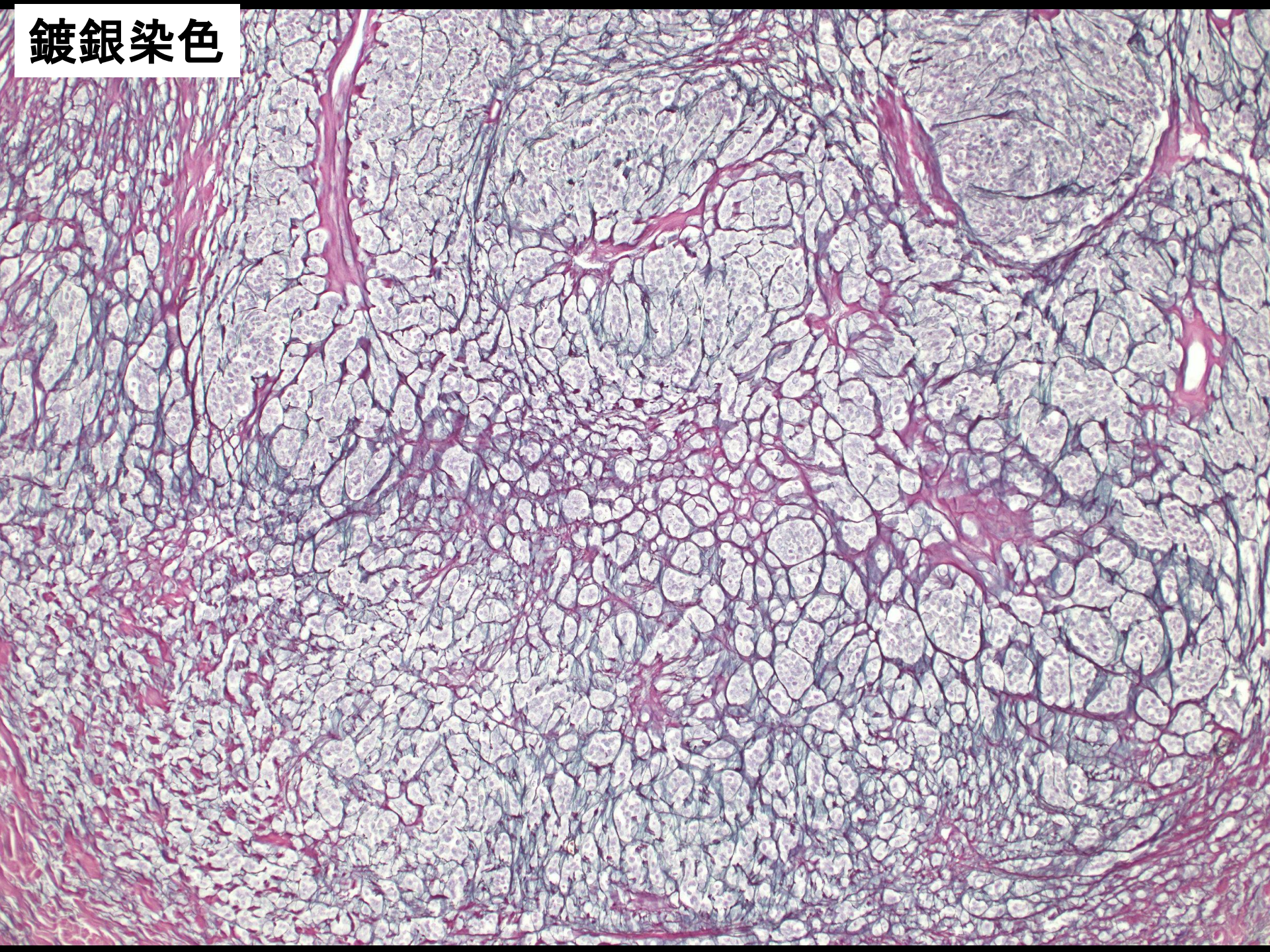




# 核分裂像

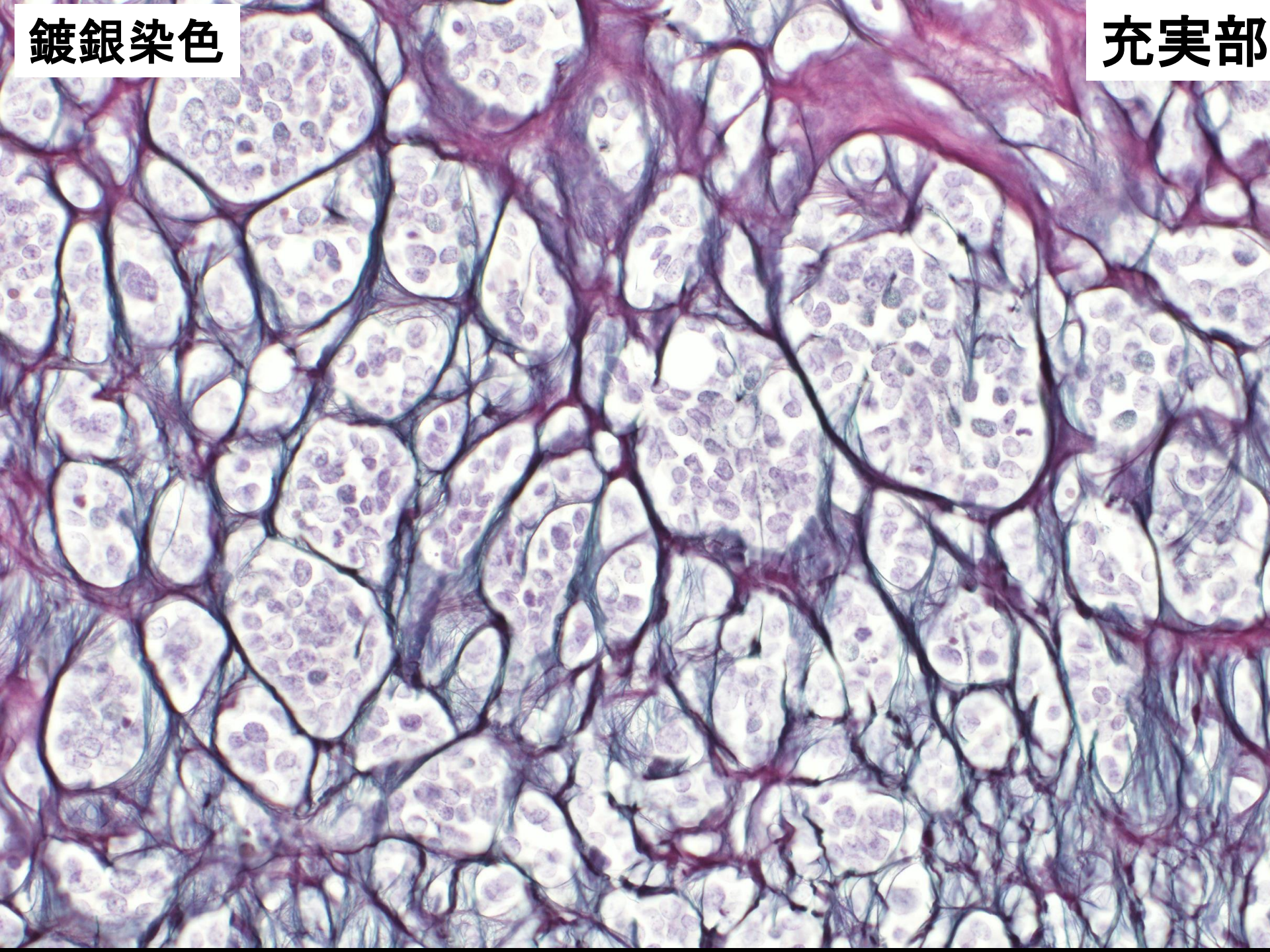


# 鍍銀染色



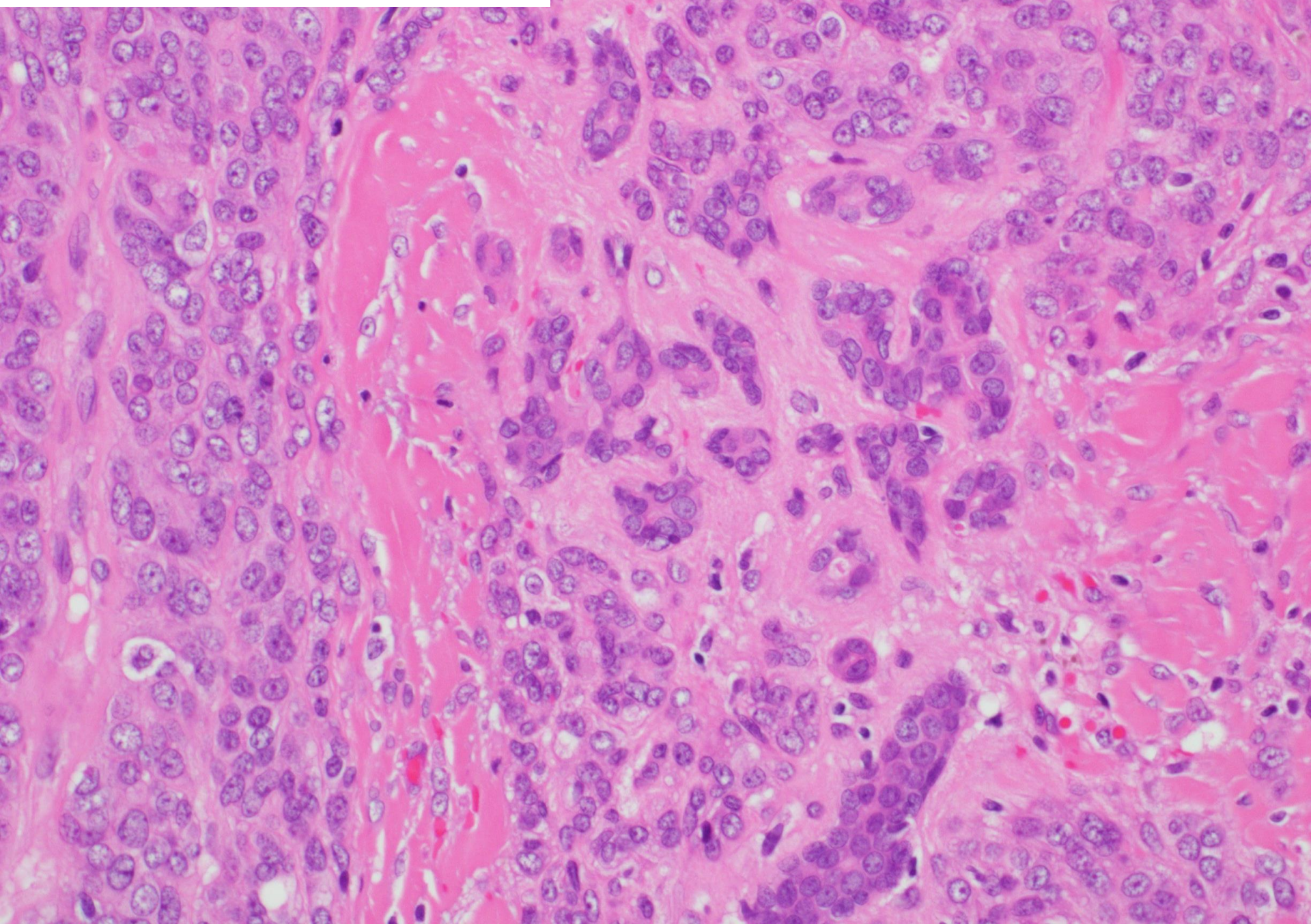
鍍銀染色

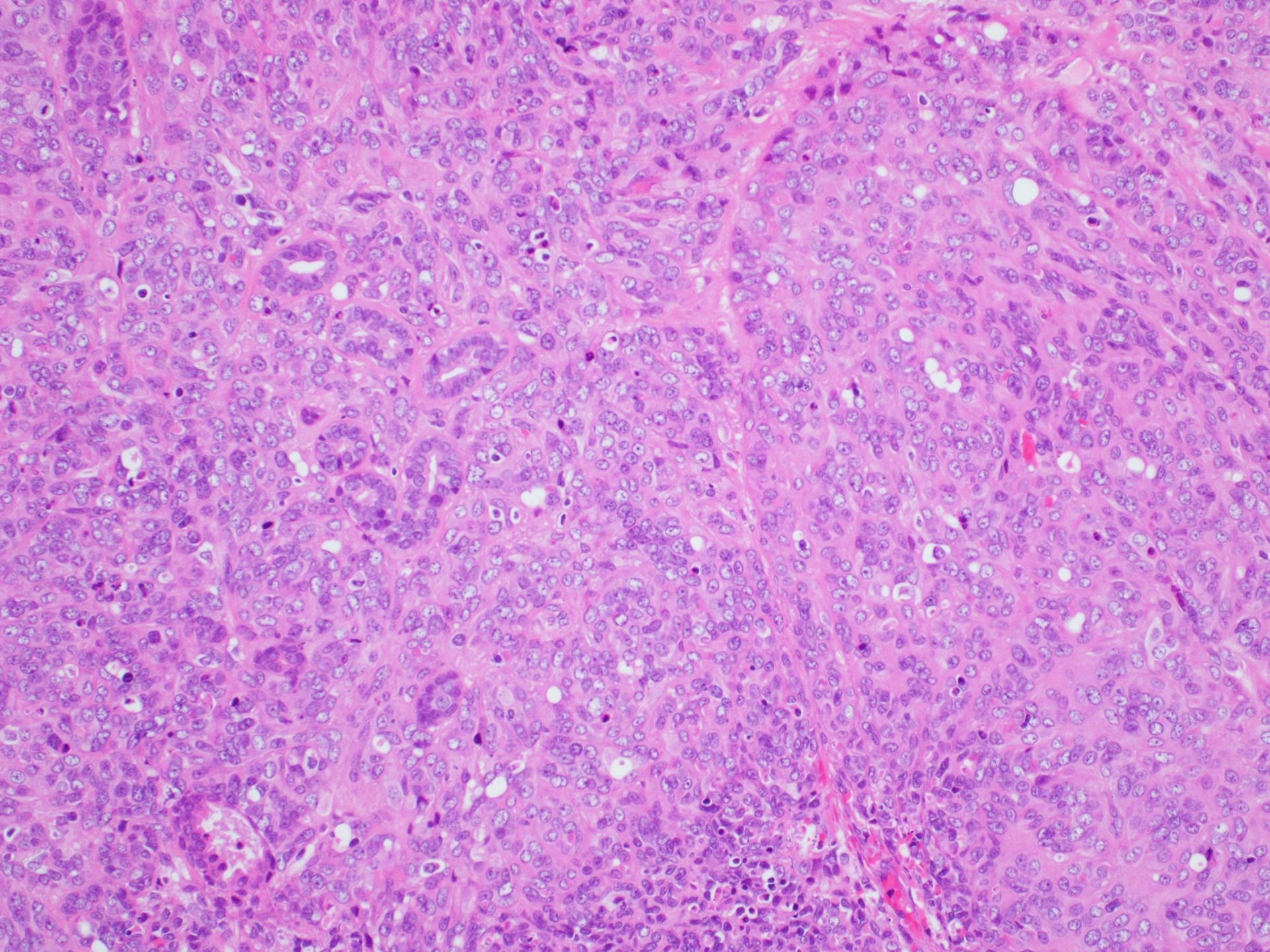
充実部



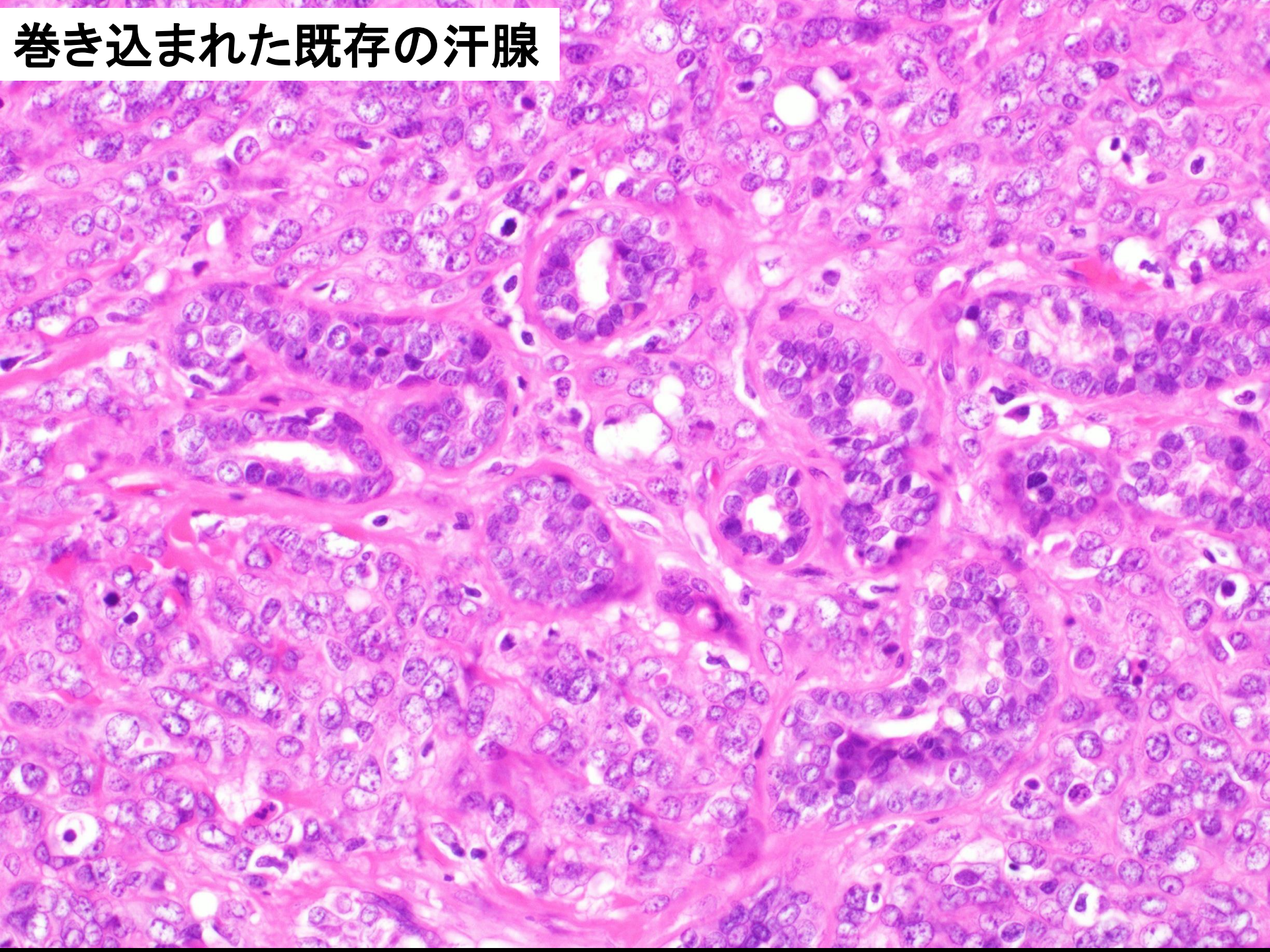


一部では腺管様構造の形成

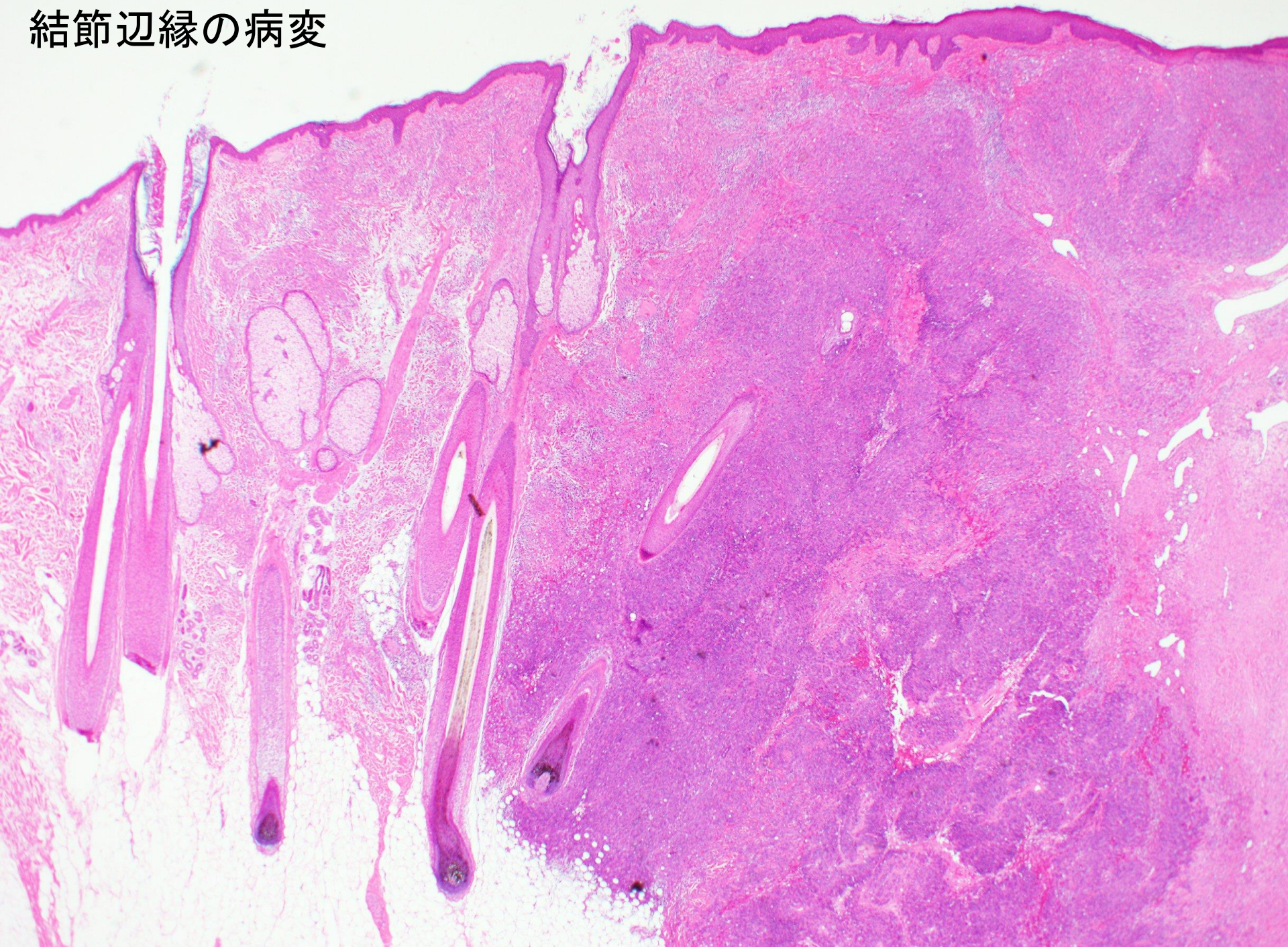




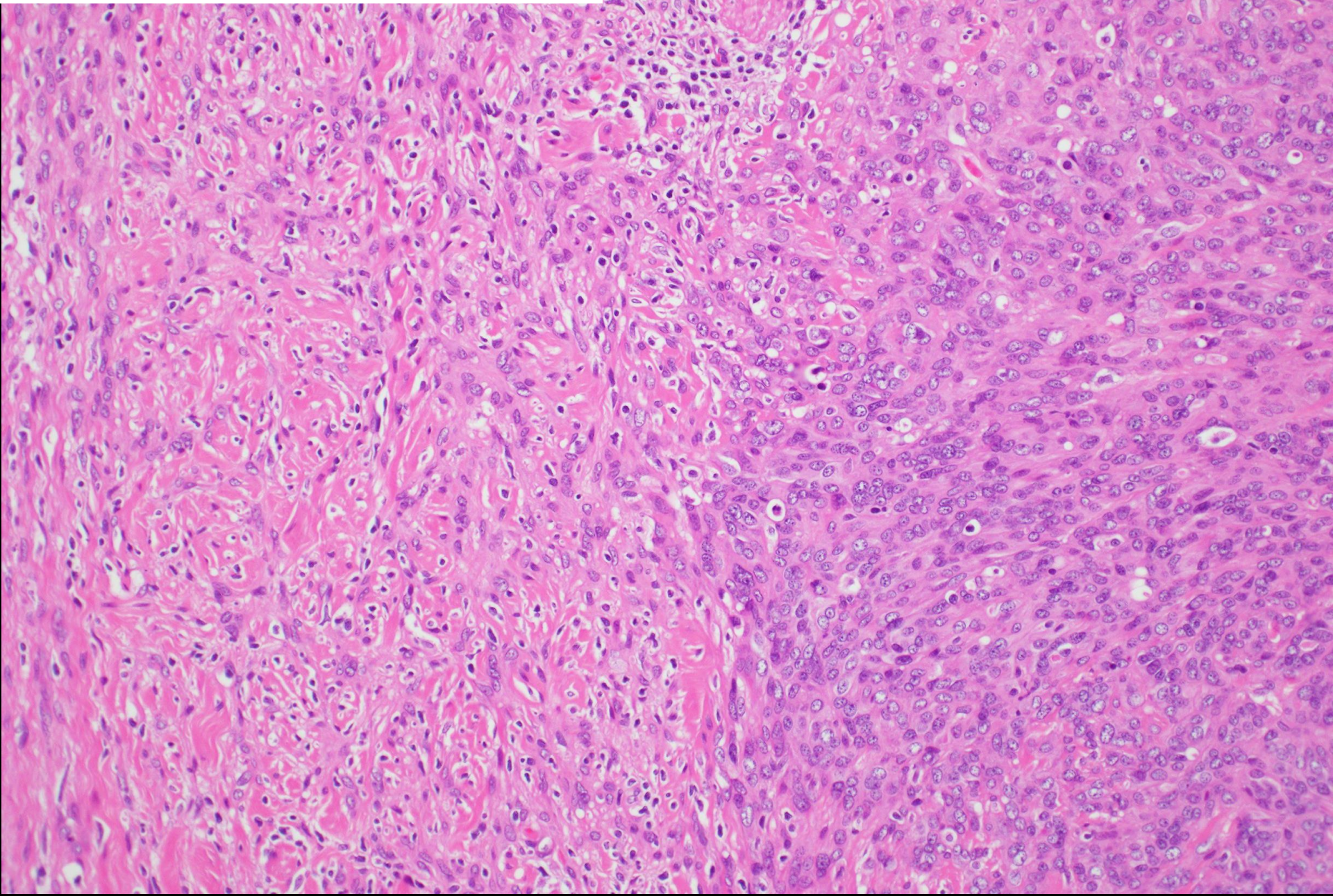
# 巻き込まれた既存の汗腺



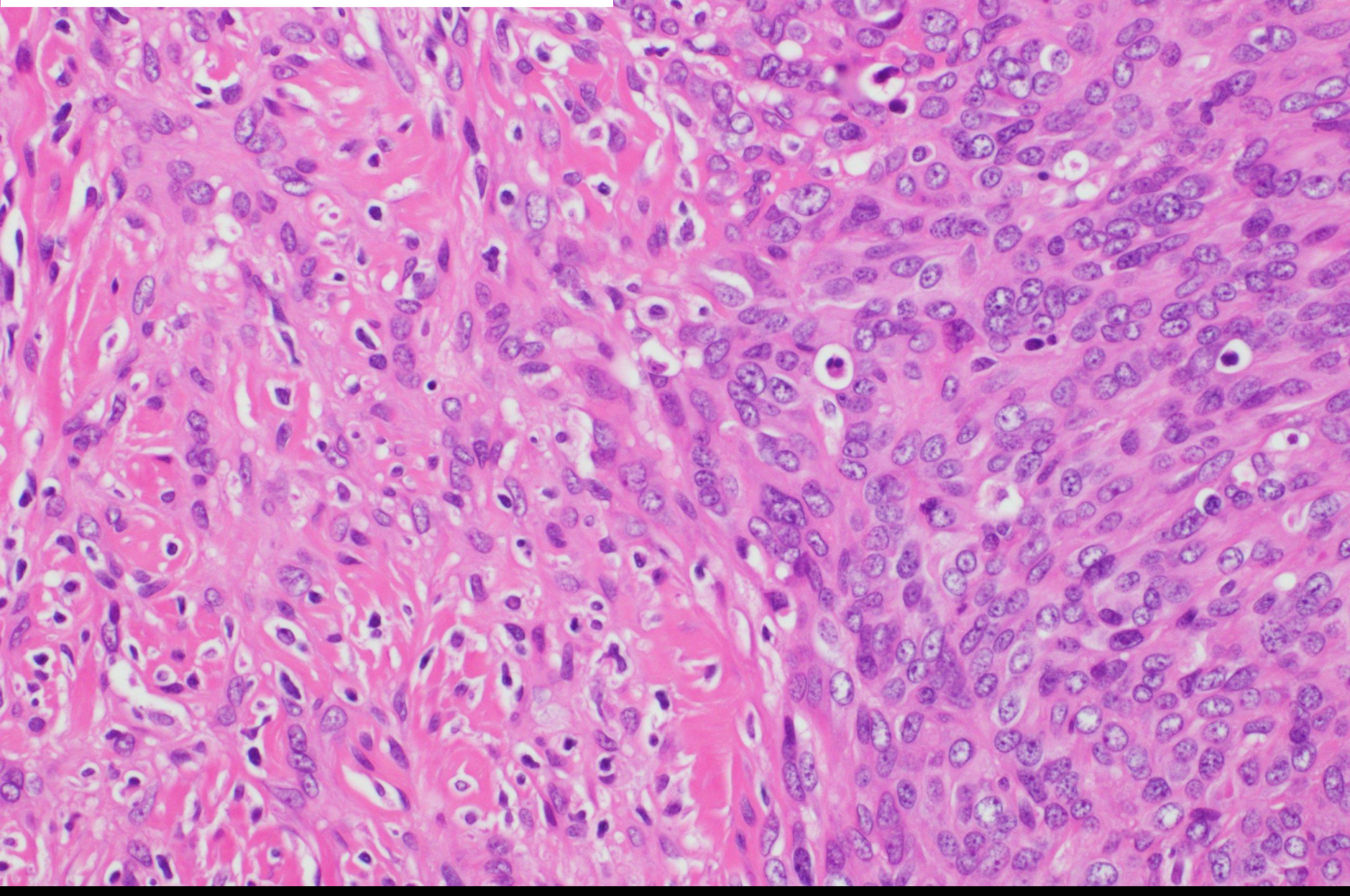
# 結節辺縁の病変



円形腫瘍細胞から紡錘形細胞  
への移行像

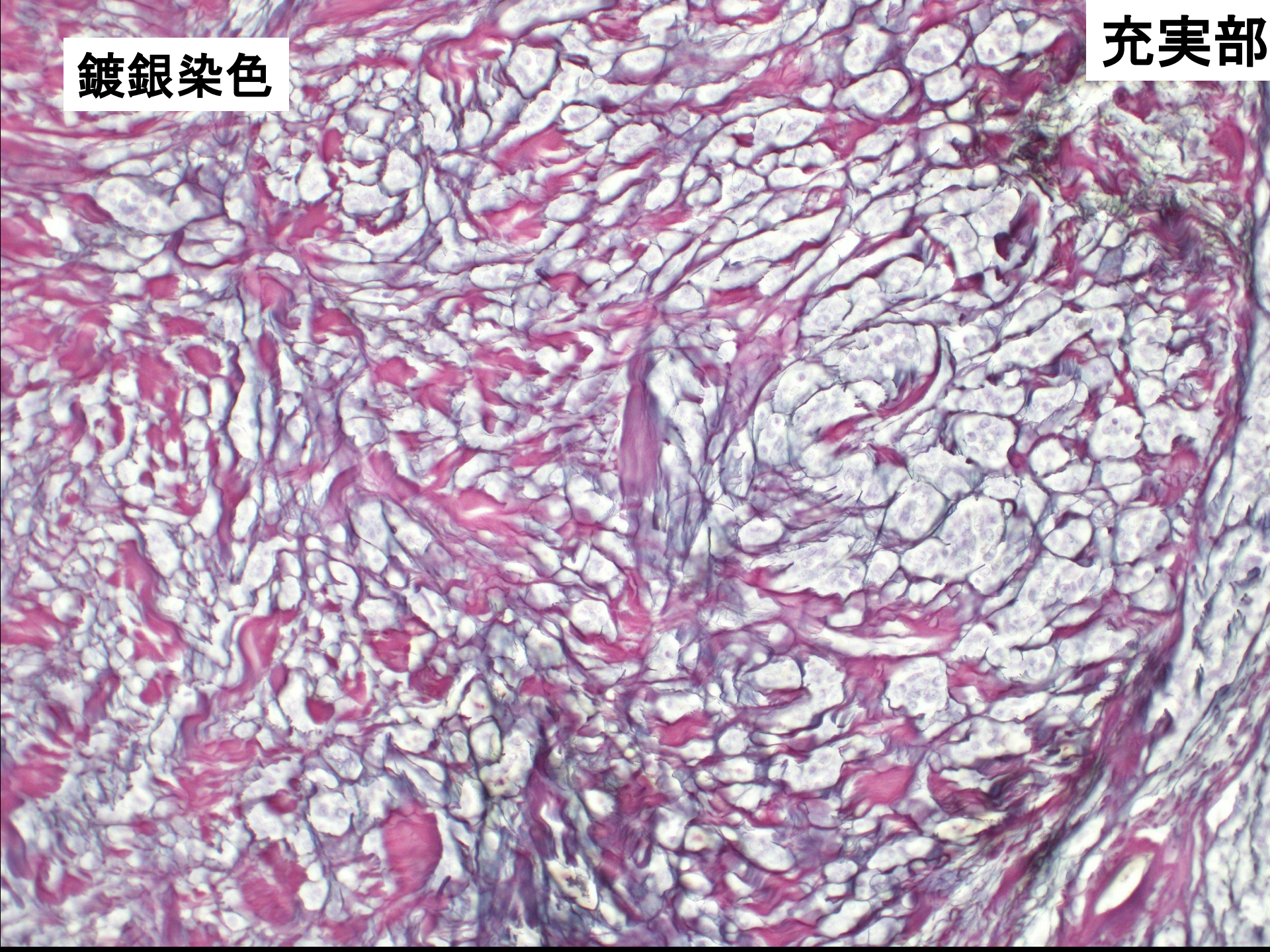


# 円形腫瘍細胞から紡錘形細胞 への移行像

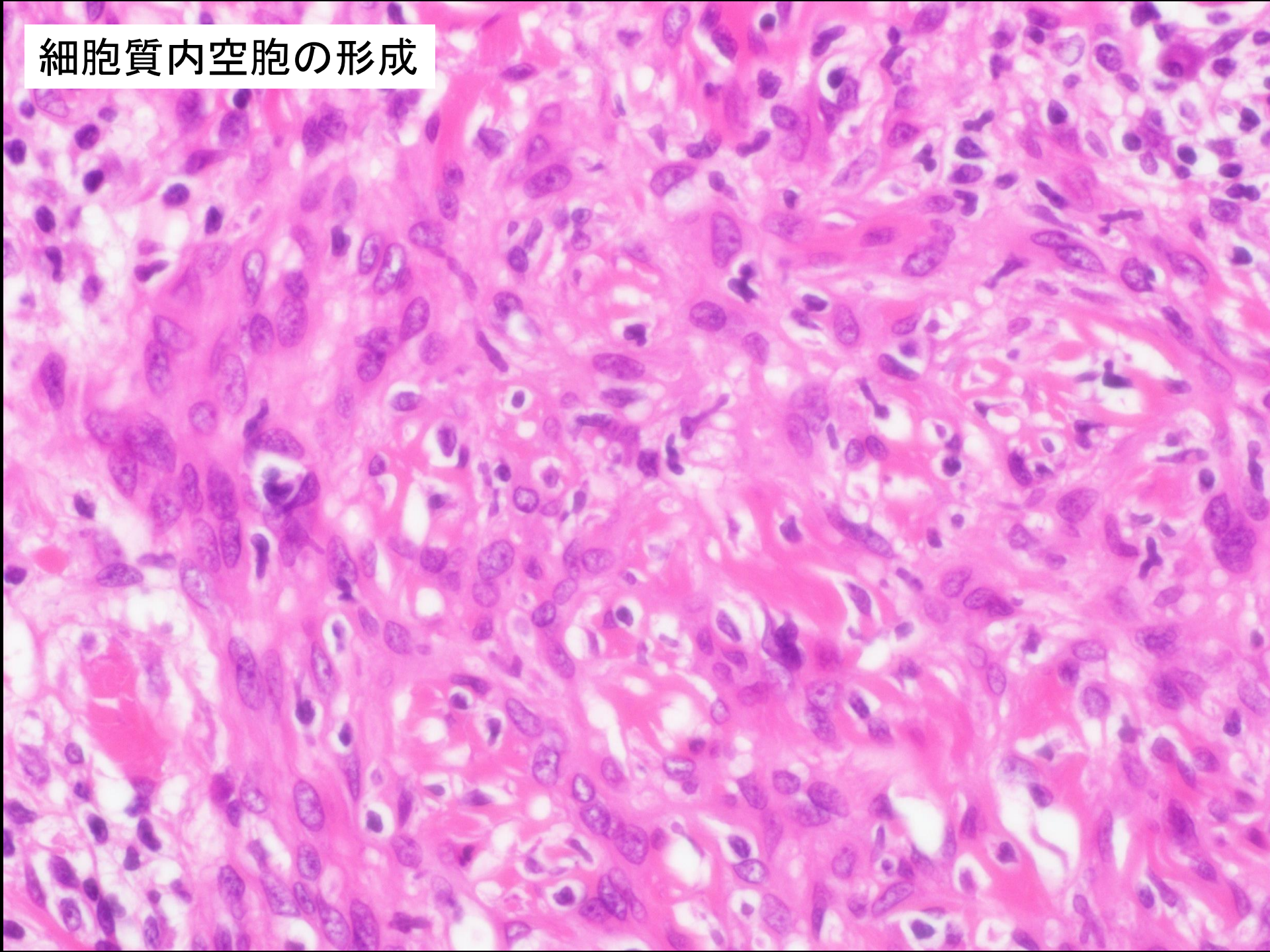


鍍銀染色

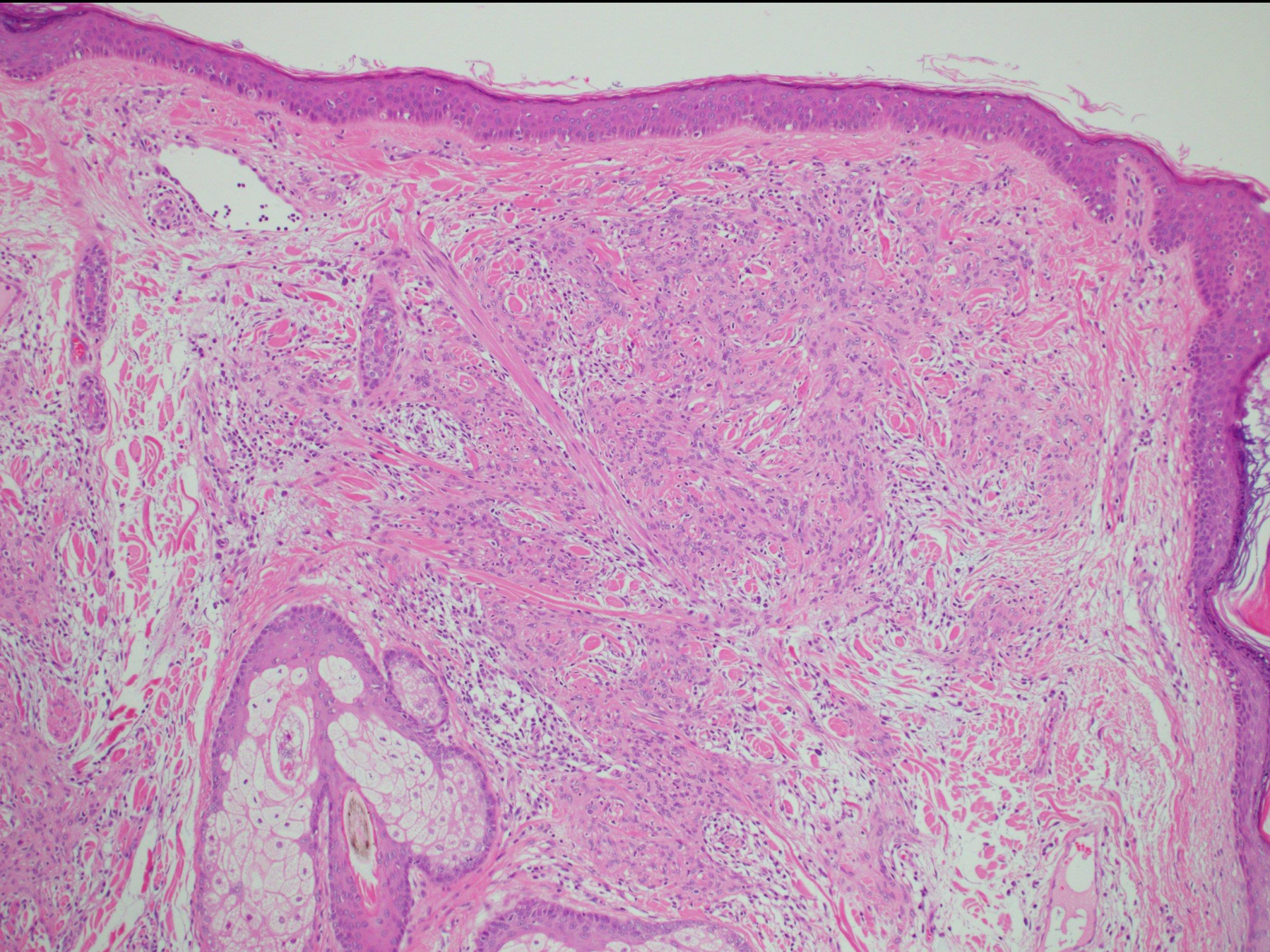
充実部



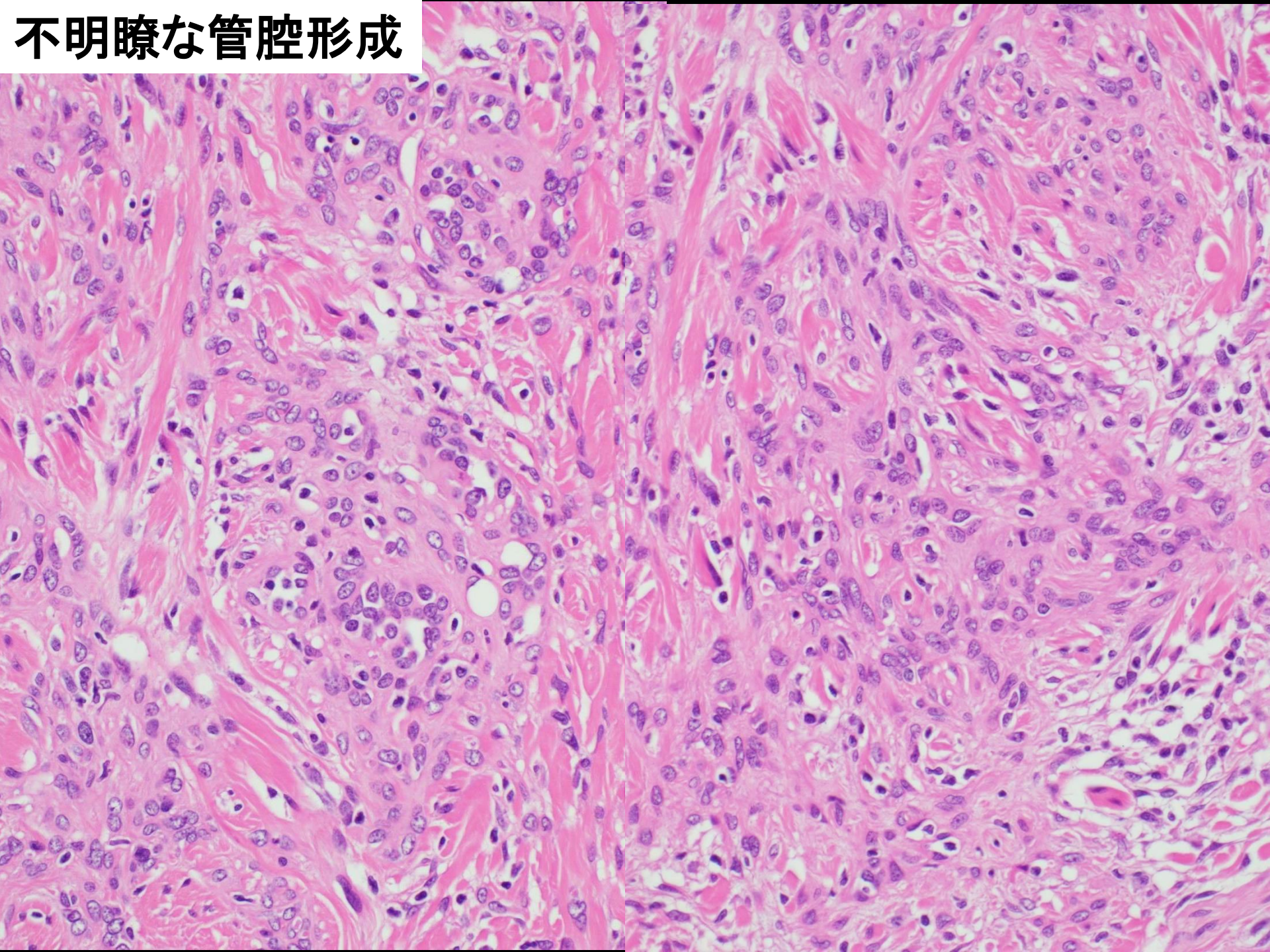
# 細胞質内空胞の形成



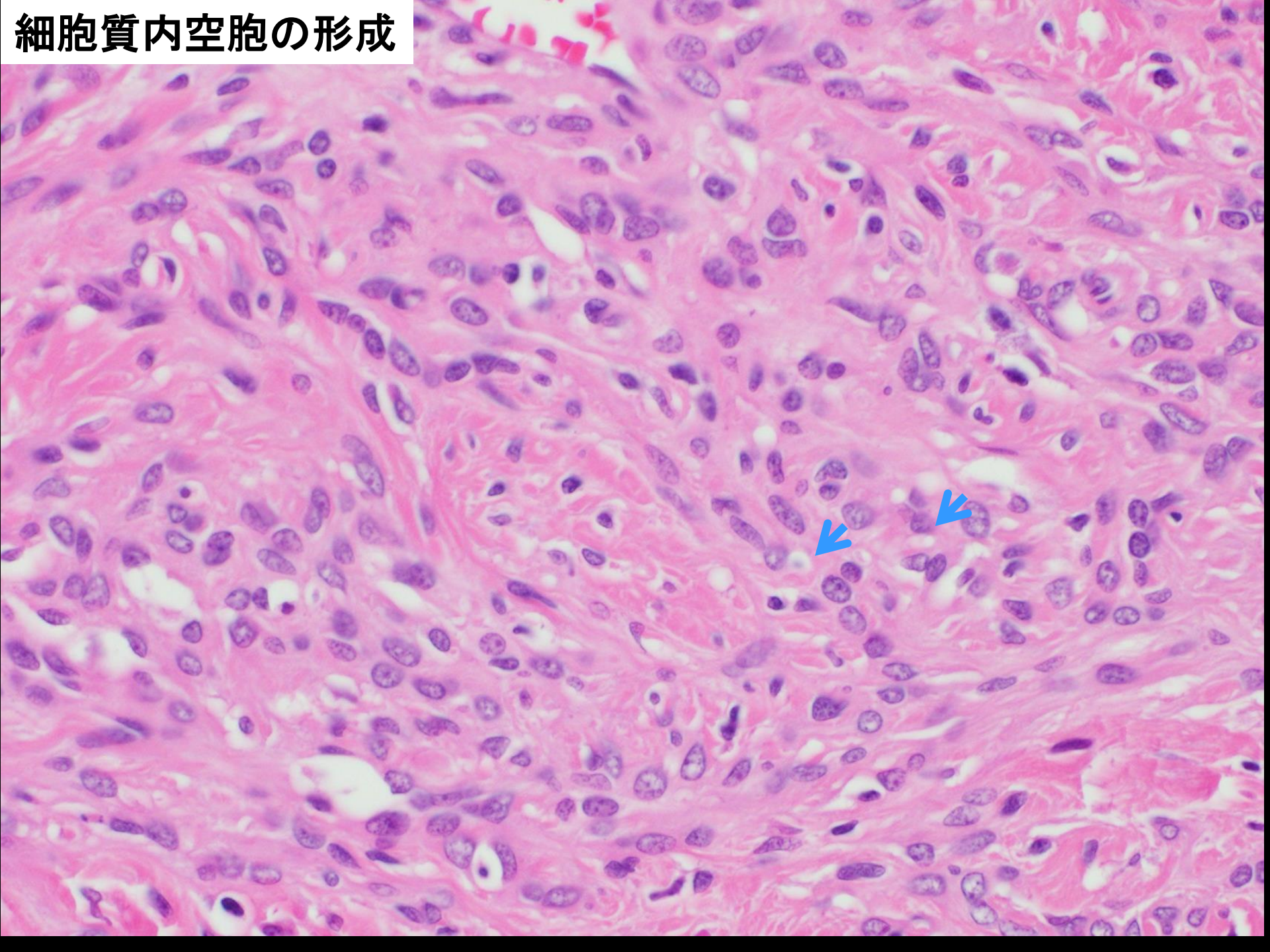




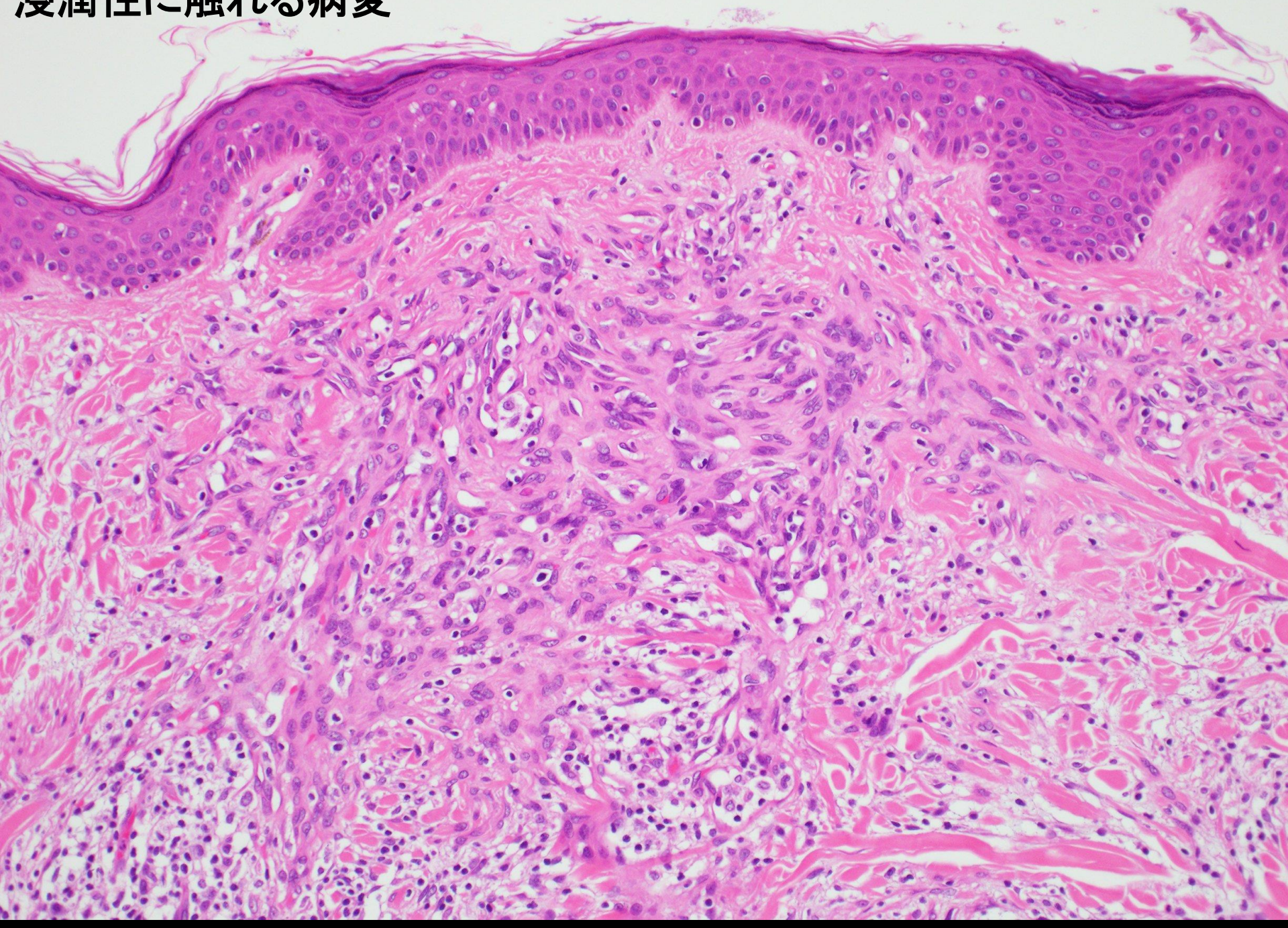
# 不明瞭な管腔形成



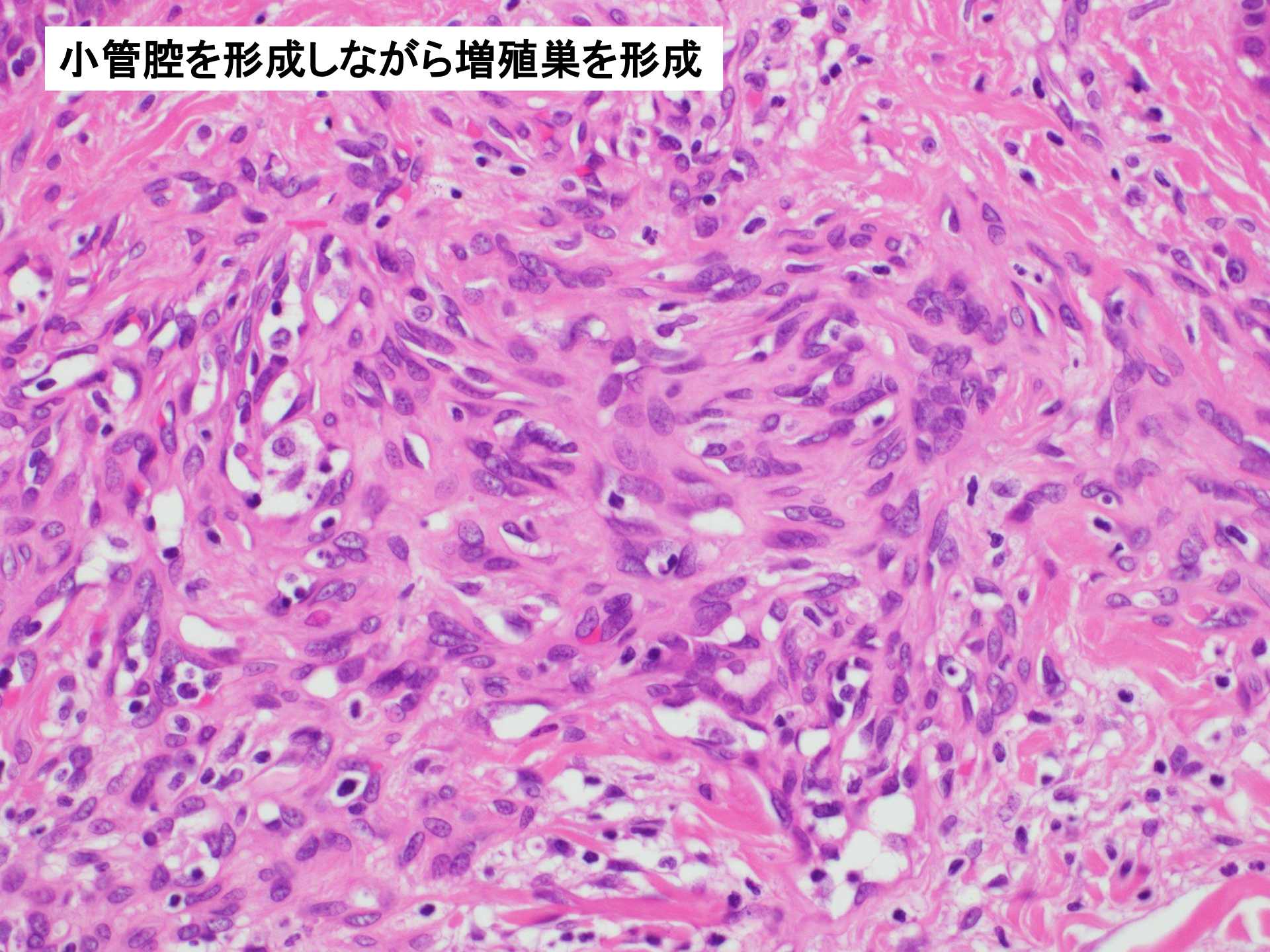
# 細胞質内空胞の形成



# 浸潤性に触れる病変



小管腔を形成しながら増殖巣を形成



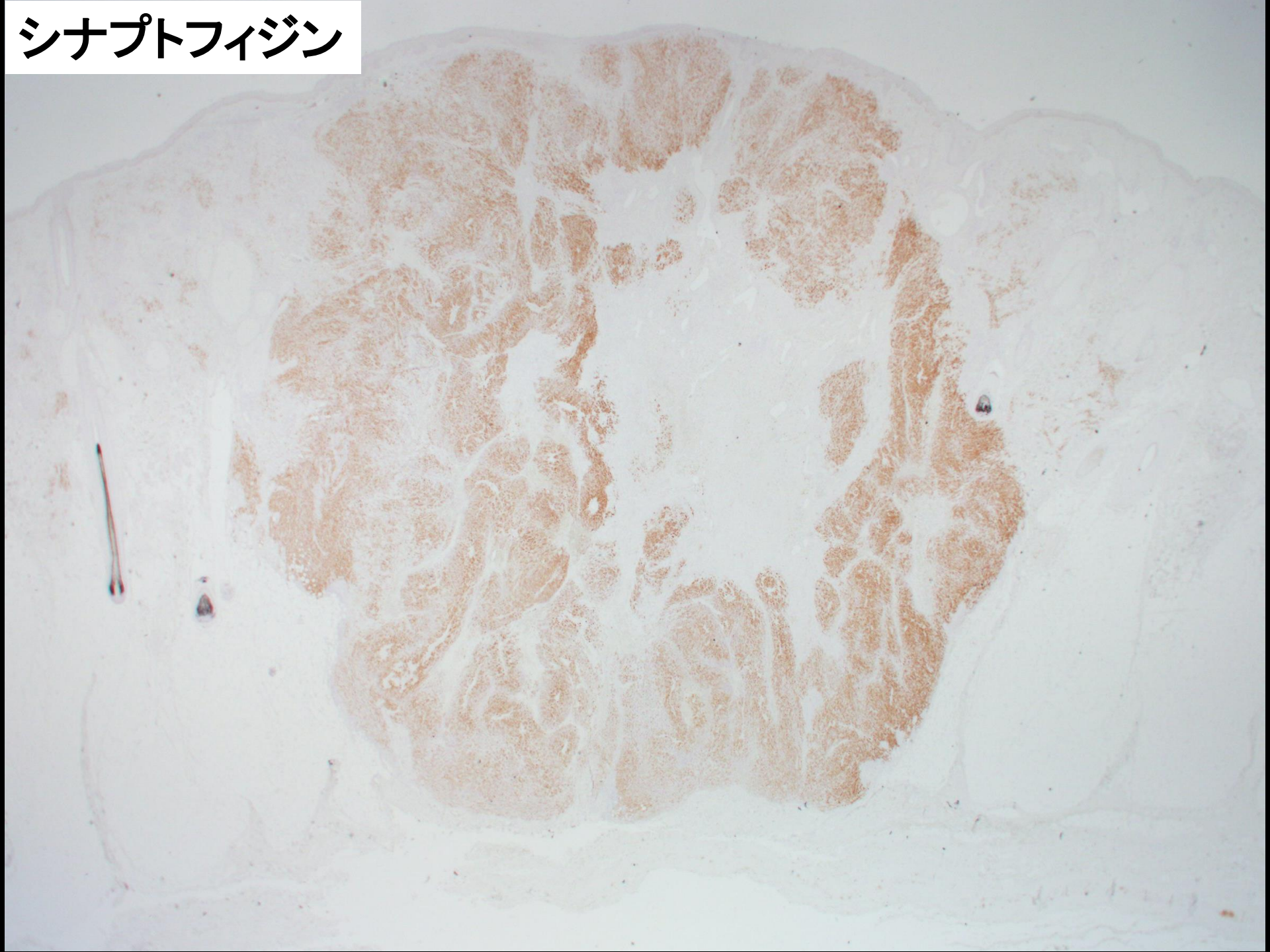
## この腫瘍の特徴

- 病変の中心部に未熟な円形細胞から成る  
結節性病変が存在
- 辺縁には連続して紡錘形細胞へ移行して増殖
- 紡錘形細胞による未熟な管腔形成
- 紡錘形細胞の胞体には細胞質内空胞を形成
- 辺縁にはスキップ病変もあり

## 鑑別診断

- **Angiosarcoma**
- **Hemangioendothelioma**
- **Merkel cell carcinoma**
- **Metastatic neuroendocrine carcinoma**
- **Malignant melanoma**
- **Epithelioid sarcoma**
- **Epithelioid peripheral nerve sheath tumor**

# シナプトフィジン

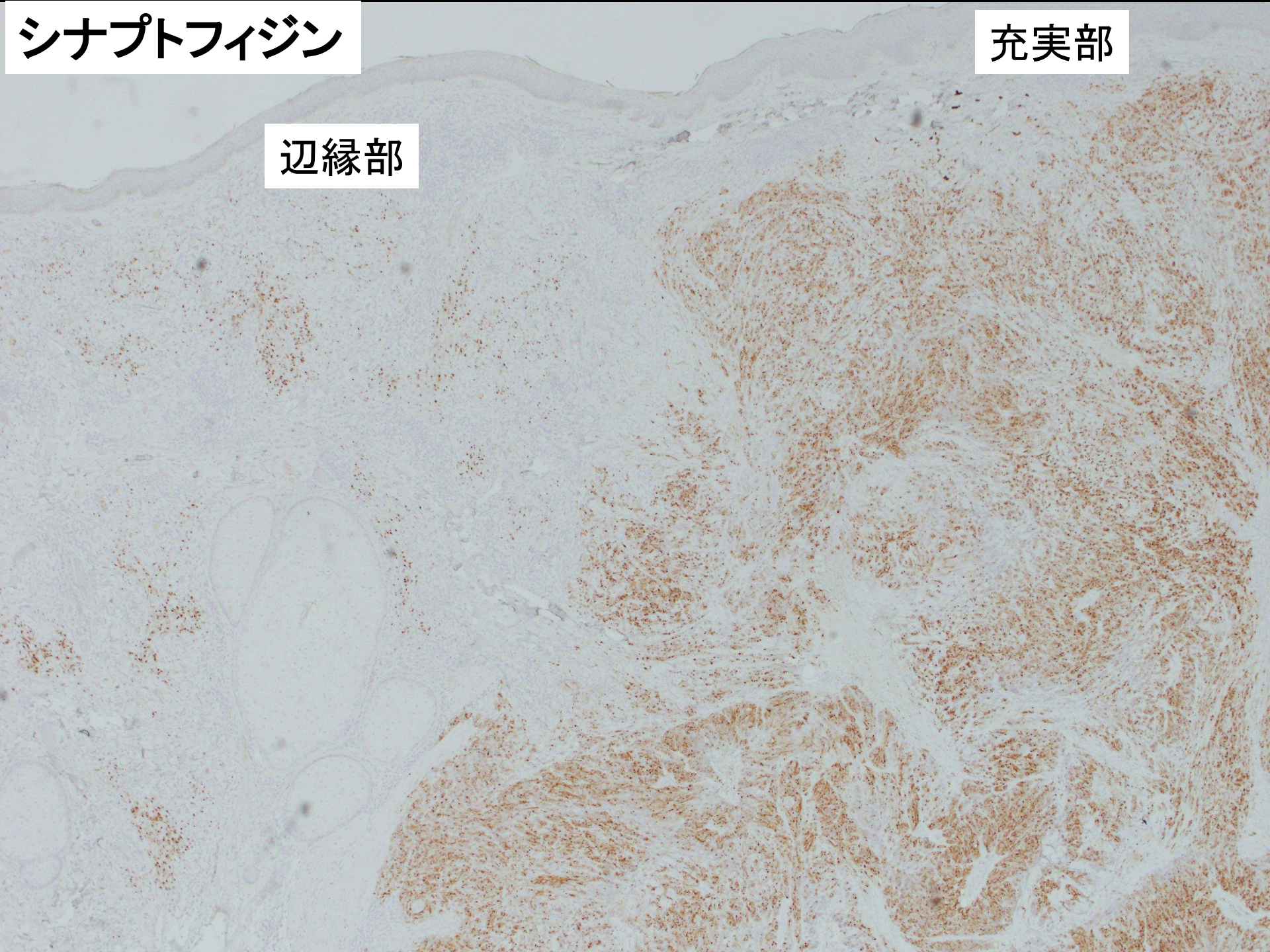




シナプトフィジン

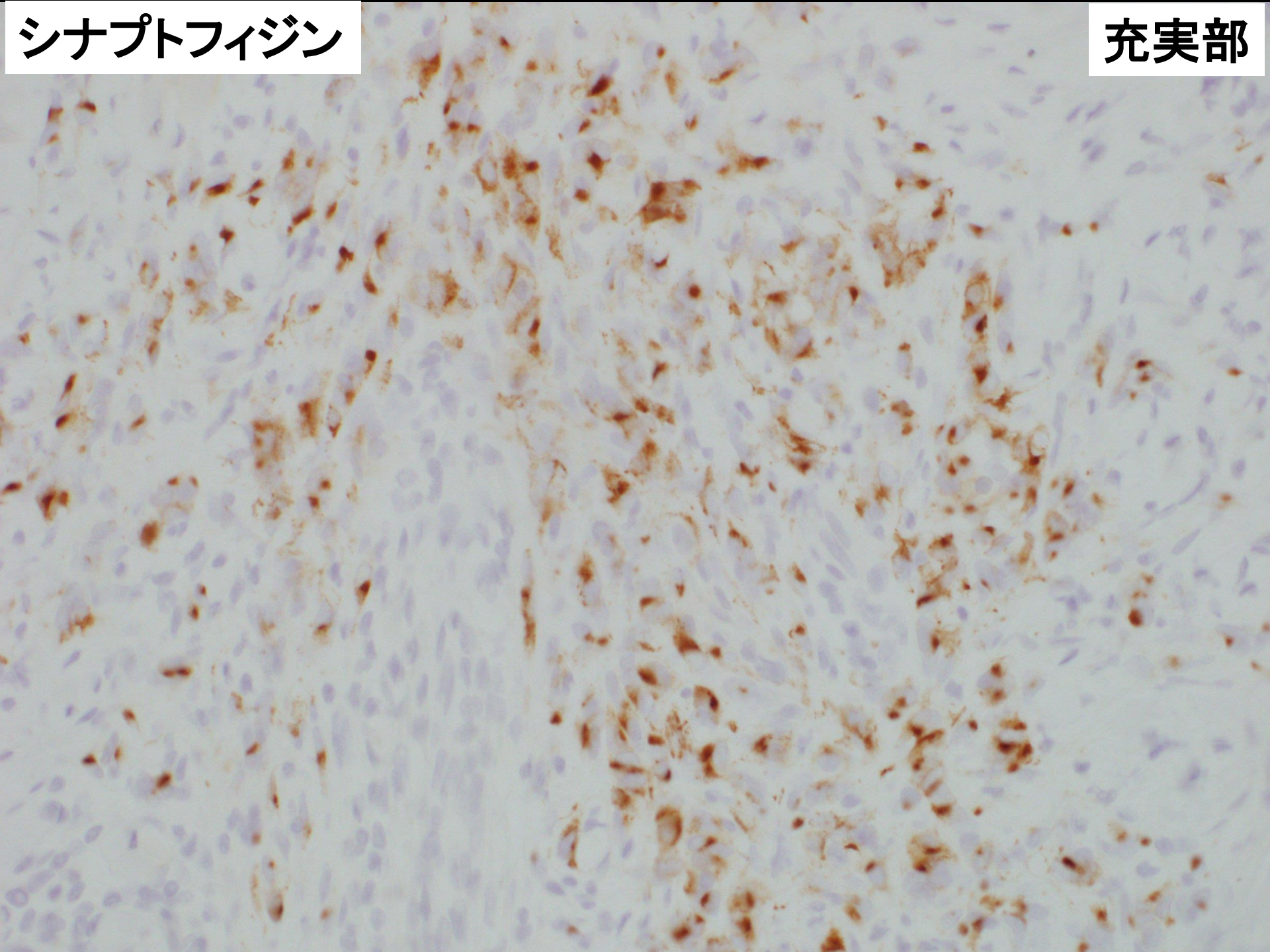
充実部

辺縁部



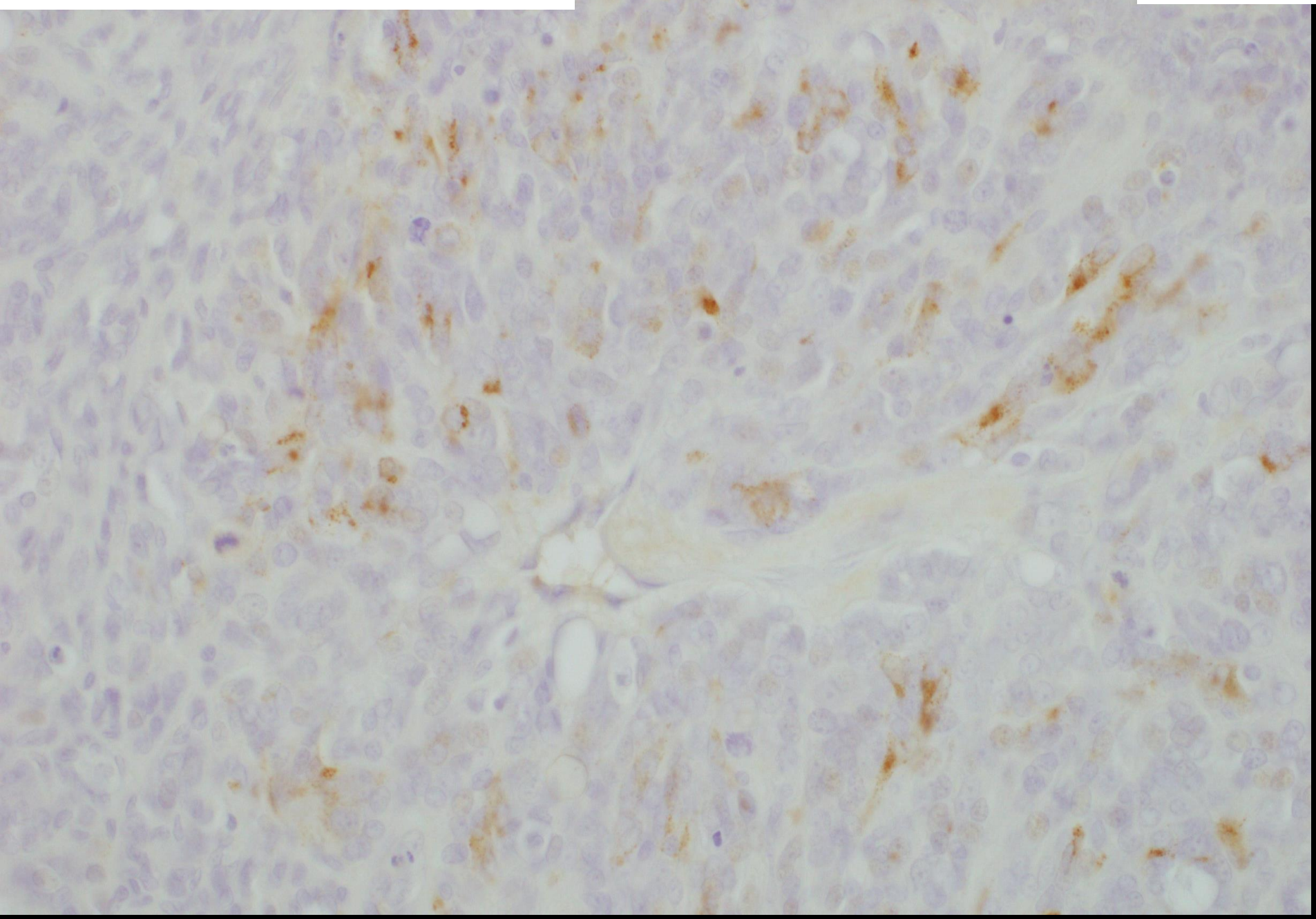
シナプトフィジン

充実部

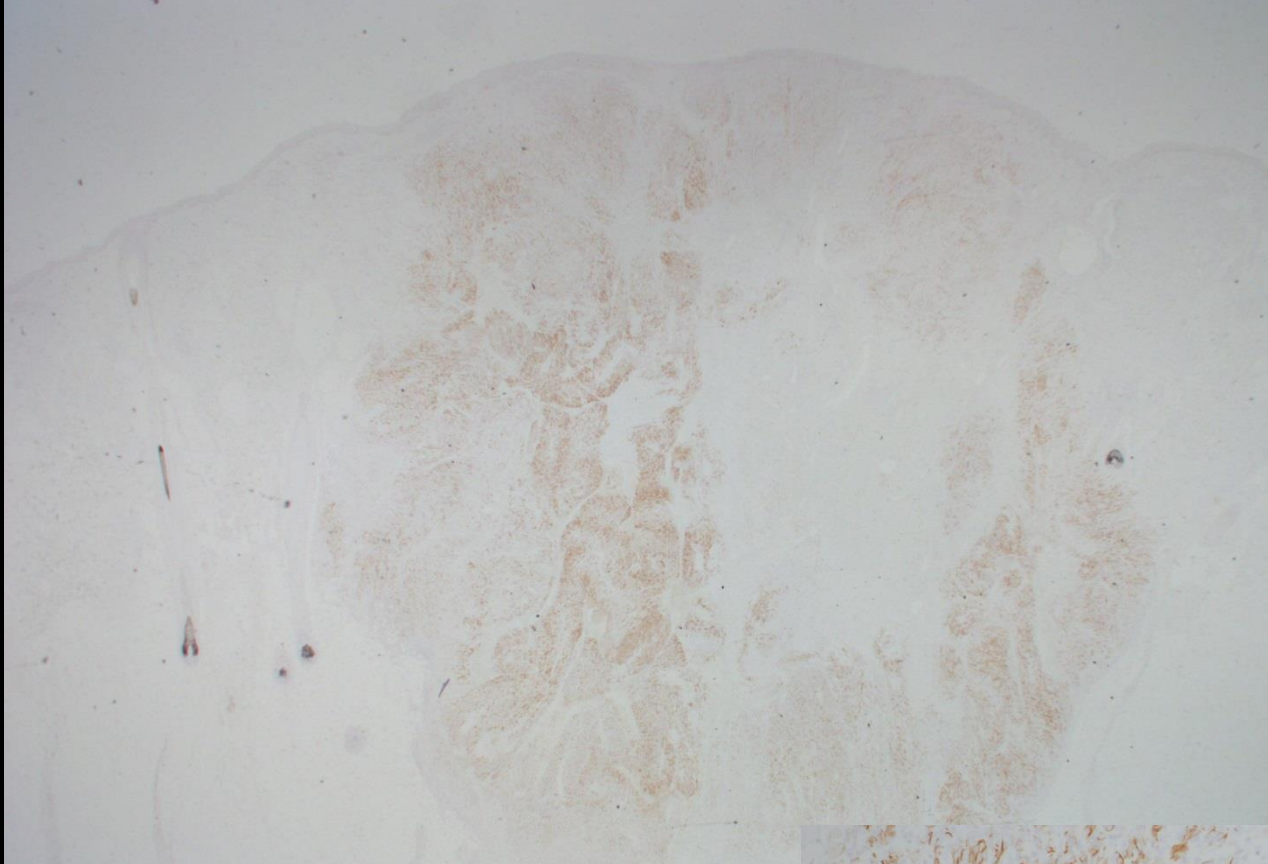


クロモグラニン A focal

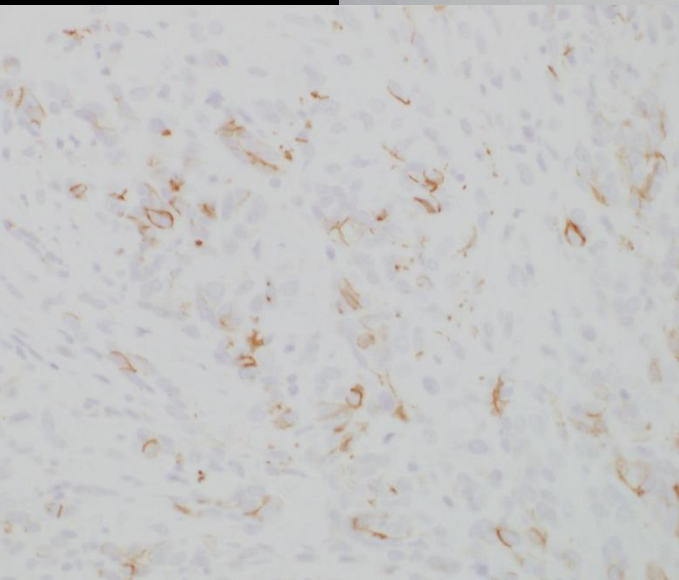
充実部



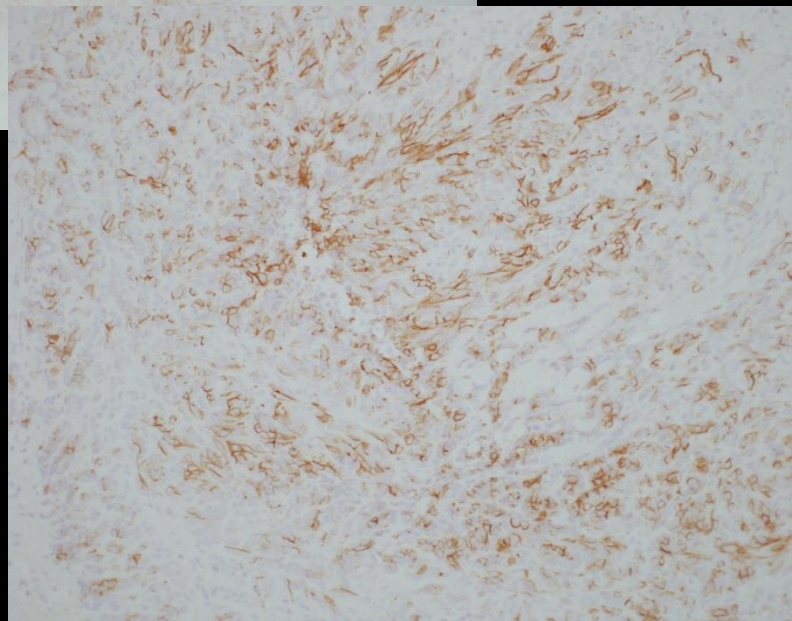
**CD56**



**辺縁部**

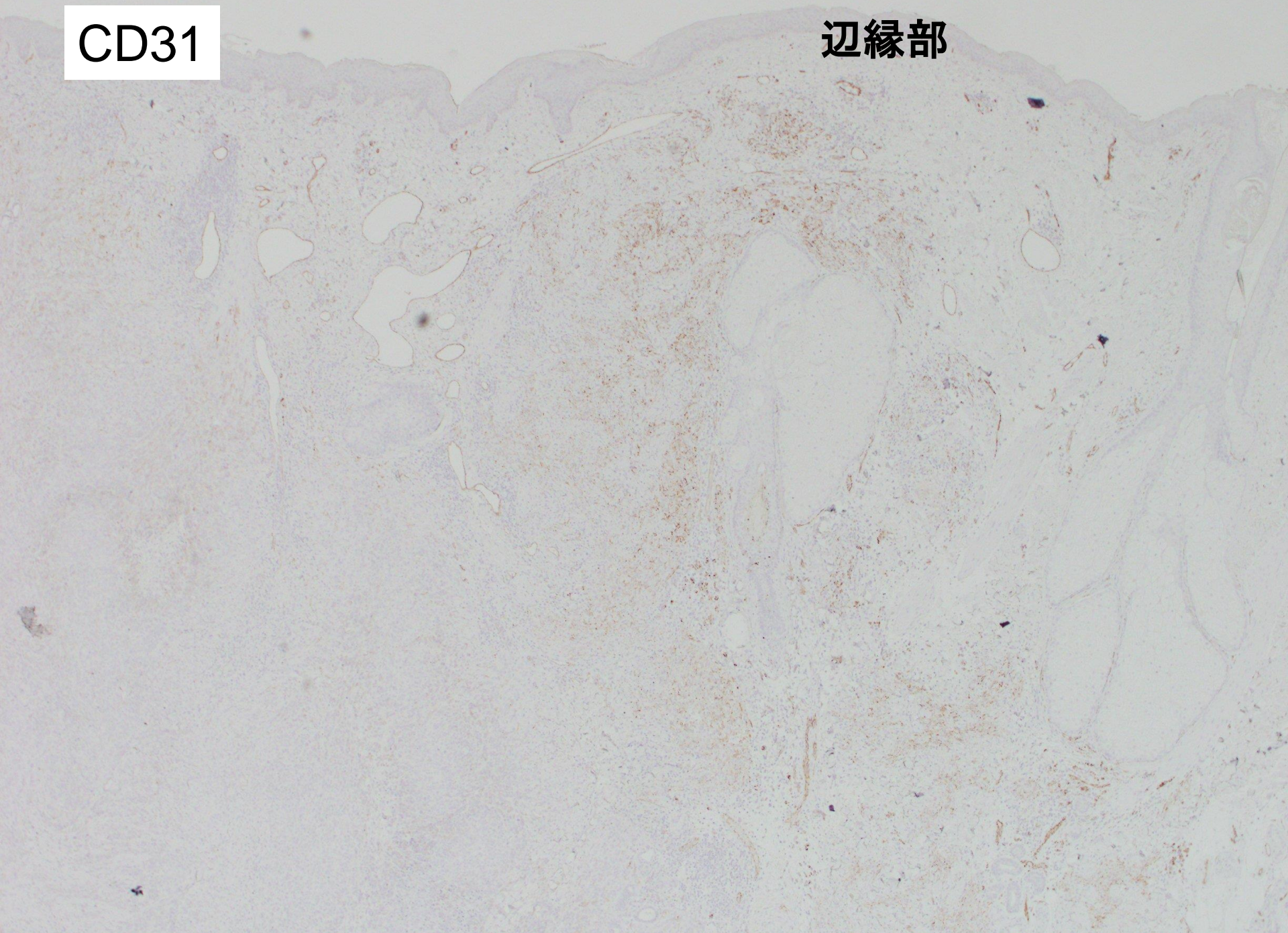


**充実部**

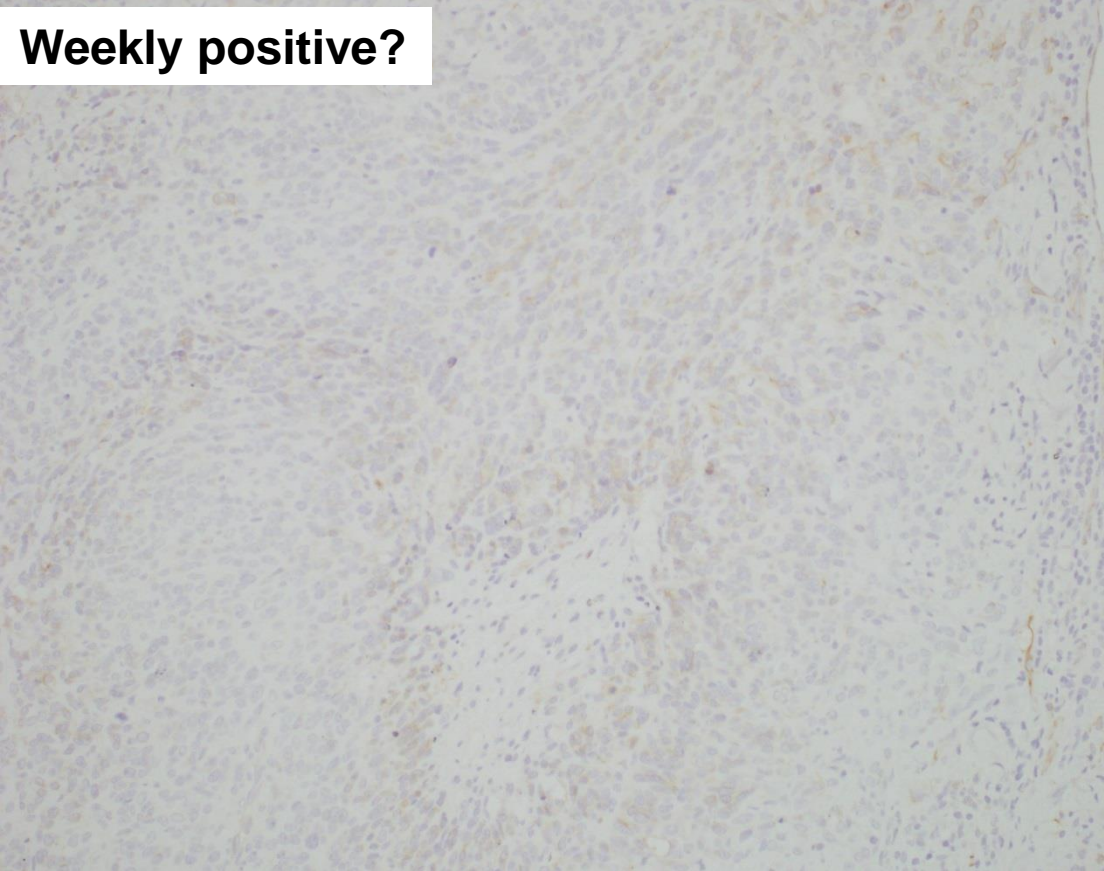


CD31

辺縁部



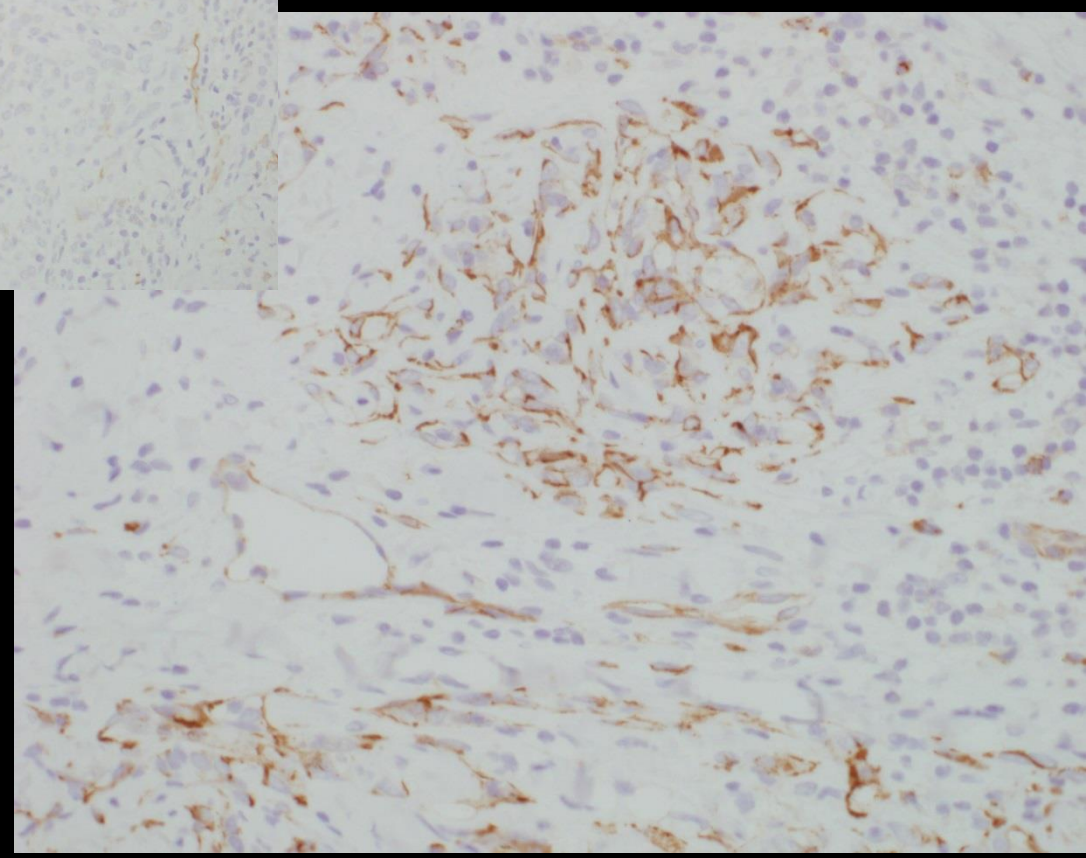
Weekly positive?



CD31

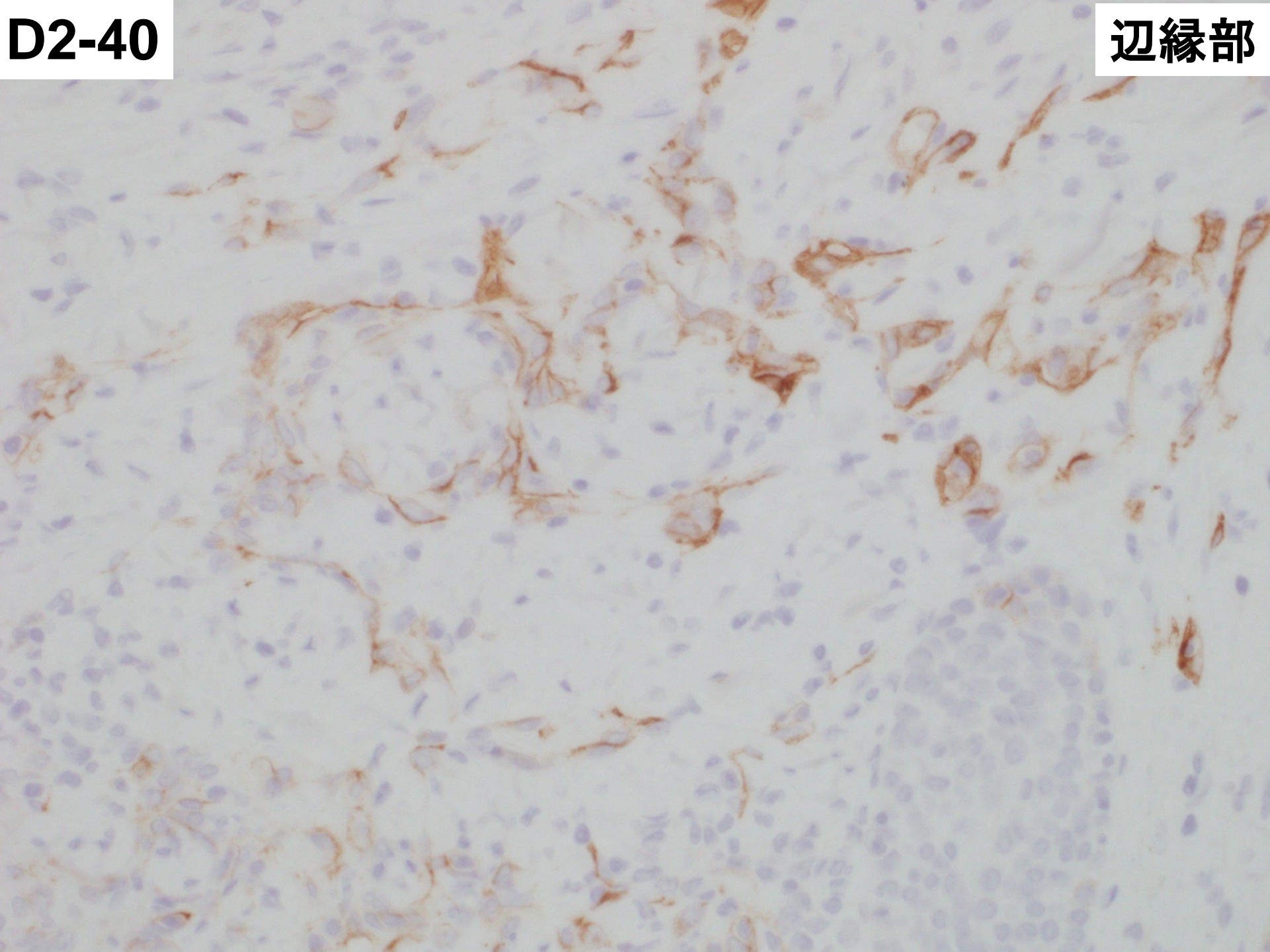
辺縁部

充実部



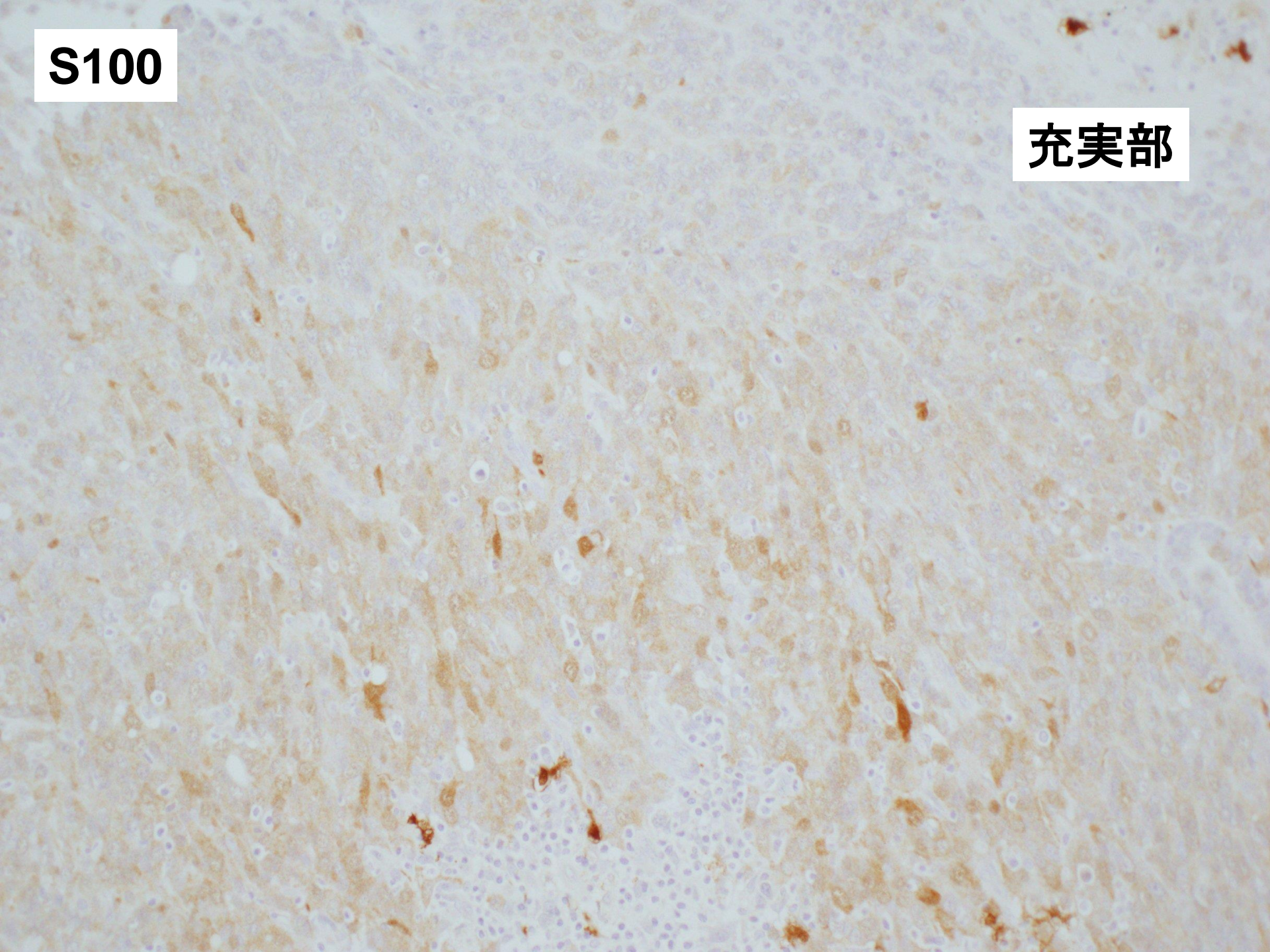
D2-40

辺縁部



**S100**

**充実部**

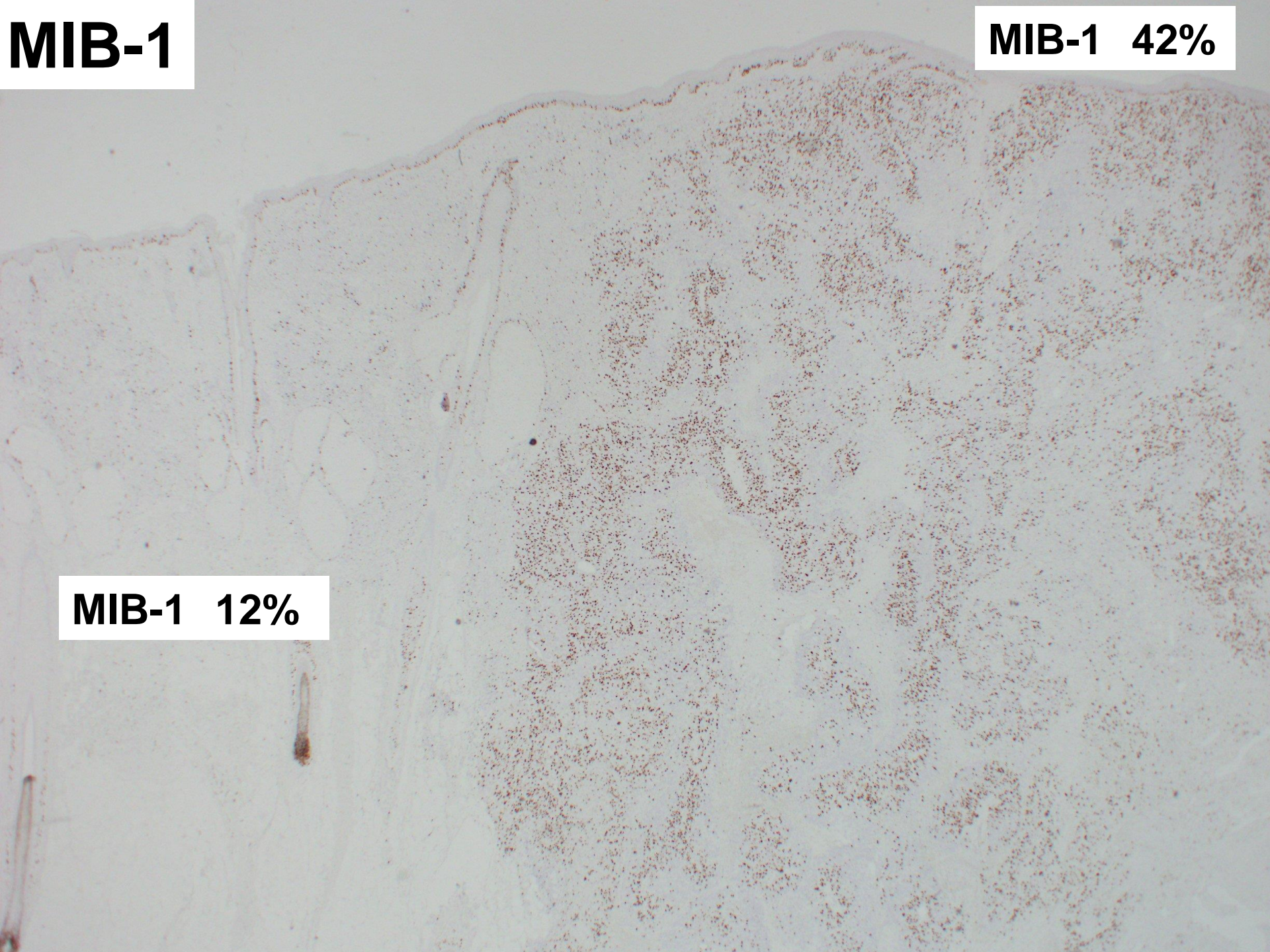




**MIB-1**

**MIB-1 42%**

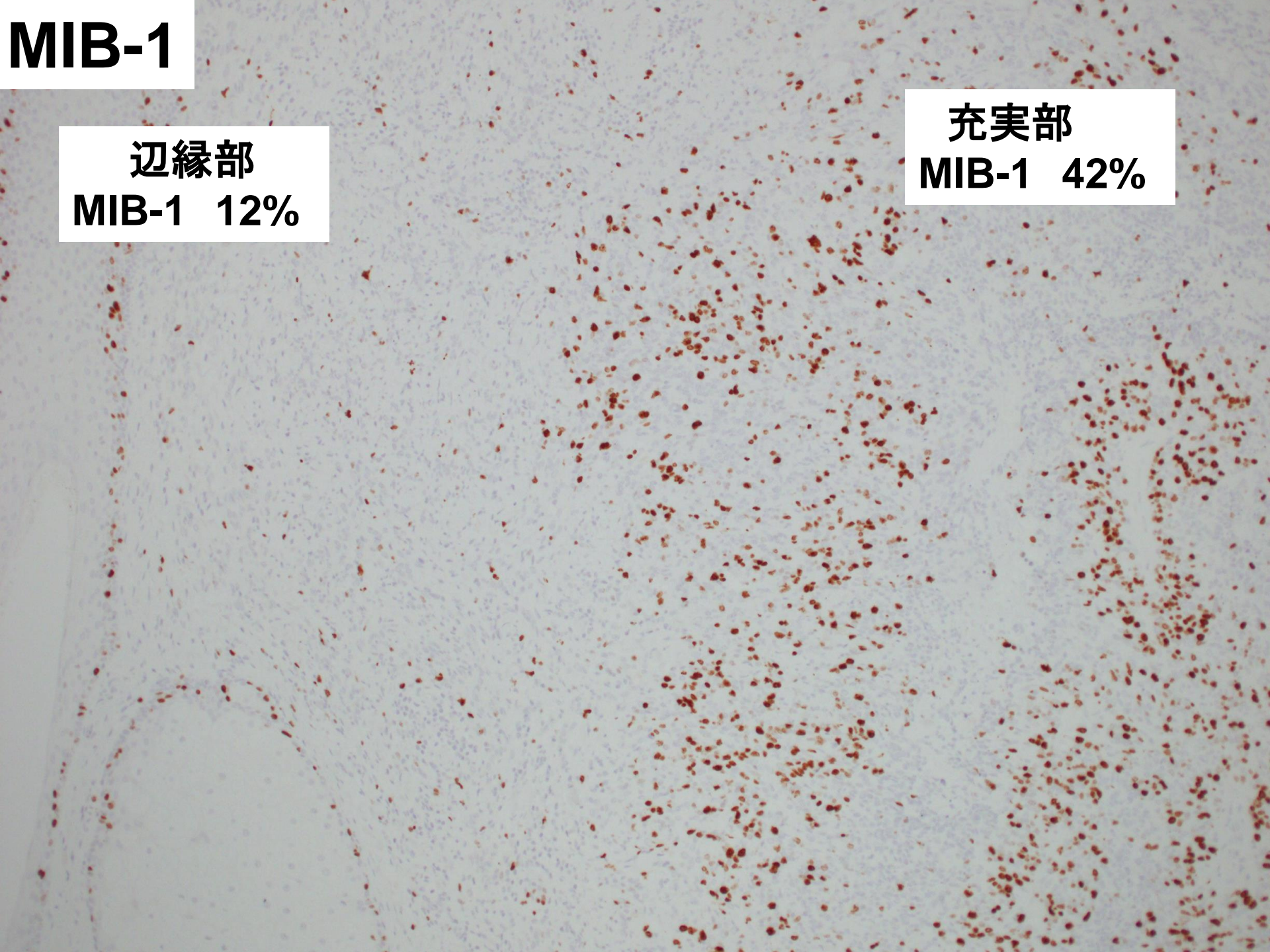
**MIB-1 12%**



# MIB-1

辺縁部  
MIB-1 12%

充実部  
MIB-1 42%



# 免疫染色結果(切除標本)

## 円形細胞成分

陽性

- Synaptophysin
- CD56
- ChromograninA f
- CD31 f w
- Edg-1 f
- S100
- MIB-1 42%

陰性

- CD34
- D2-40
- Factor VIII
- AE1/AE3
- EMA
- CK20
- CAM5.2
- TTF-1
- $\alpha$ -SMA
- NF
- HHF-3
- HMB-45

## 紡錘形細胞成分

陽性

- Synaptophysin
- CD56 f
- ChromograninA f
- CD31
- D2-40
- Edg-1
- MIB-1 12%

陰性

- CD34
- Factor VIII
- AE1/AE3
- EMA
- CK20
- CAM5.2
- TTF-1
- S100
- $\alpha$ -SMA
- NF
- HHF-35
- HMB45

# Aberrant expression of neuroendocrine markers in angiosarcoma: a potential diagnostic pitfall<sup>☆</sup>



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Henry D. Tazelaar MD<sup>c</sup>, Andrew L. Folpe MD<sup>d,\*</sup>

Human Pathology(2014), 45, 1618-1624

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<sup>b</sup>Department of Anatomic Pathology, Hospital AC Camargo, Sao Paulo, SP, Brazil

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Received 14 February 2014; revised 20 March 2014; accepted 26 March 2014

- ・ 3例の神経内分泌マーカー陽性の血管肉腫の検討
- ・ 腎原発の肺転移例(48y F)と2例の頸部原発症例(29y F, 51y F)
- ・ 3例共に少なくとも部分的に Solid lesion を有する
- ・ IHC: CD31、FLI1, ERG は3例とも陽性
- ・ 神経内分泌マーカー陽性の血管肉腫は診断の pit fallとなりうる
- ・ 注意深い形態観察と内皮への分化を示す免疫検査が必要
- ・ Aggressive clinical behaviorが示唆される。

**Table** Immunohistochemical results

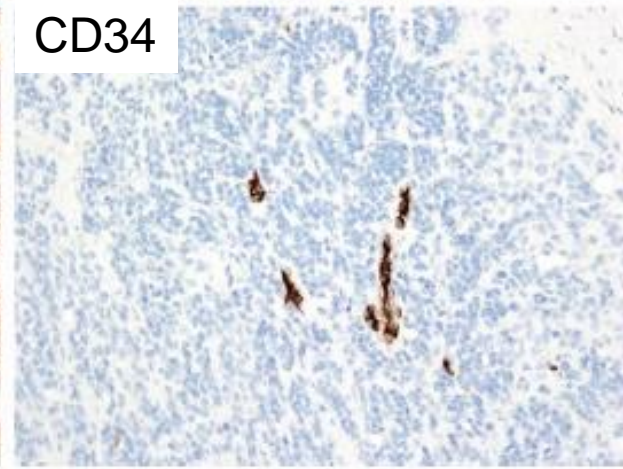
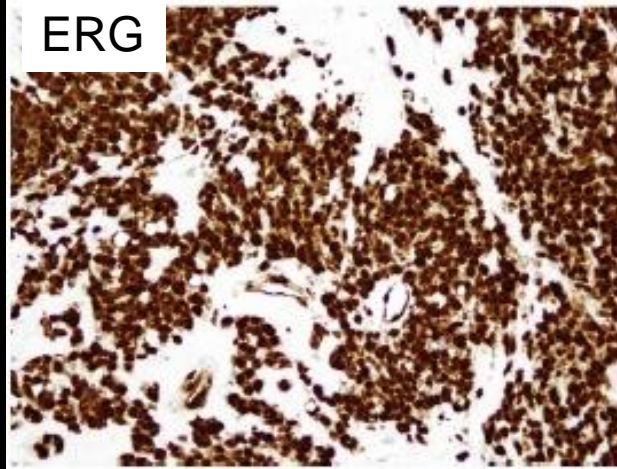
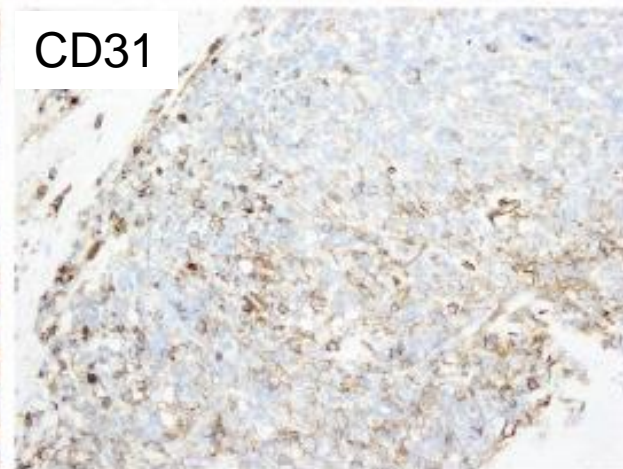
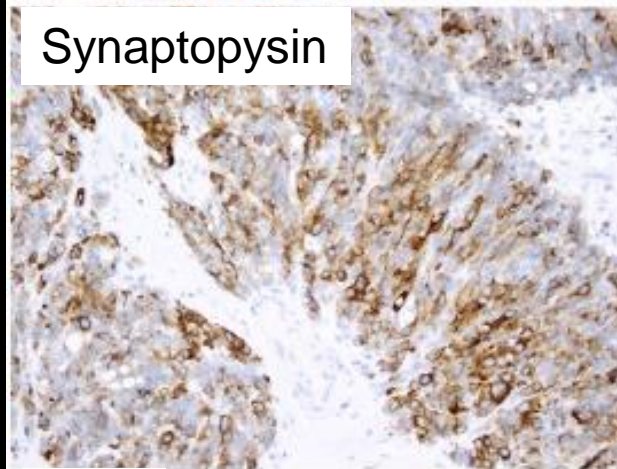
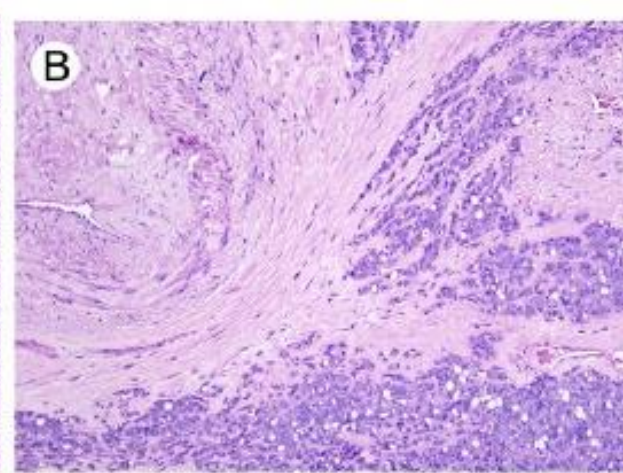
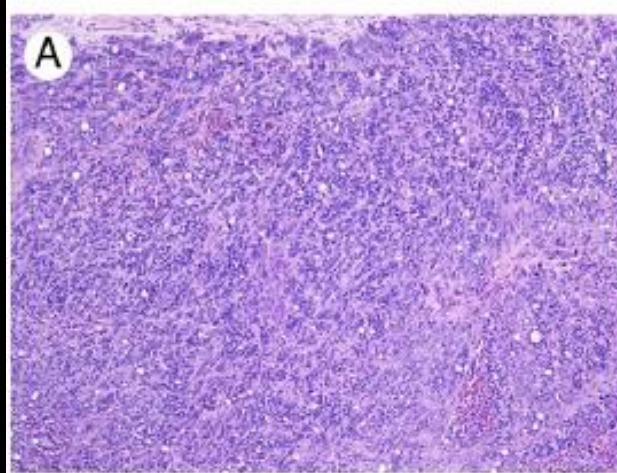
Antigen	Case 1	Case 2	Case 3
Synaptophysin	Positive in >75% of cells <sup>a</sup>	Positive in 5%-10% of cells	Positive in >75% of cells
Chromogranin A	Negative	Positive in >75% of cells <sup>b</sup>	Negative
CD31	Positive in >75% of cells	Positive in >75% of cells <sup>b</sup>	Positive in >75% of cells
CD34	Negative	Negative	Negative
FLII	Positive in >75% of cells	Positive in >75% of cells	Positive in >75% of cells
ERG	Not tested	Not tested	Positive in >75% of cells
Cytokeratins	Negative	Negative	Positive in 25%-50% of cells

<sup>a</sup> Case 1 was positive for synaptophysin by immunohistochemistry performed at 2 outside institutions and by testing at our own institution.

<sup>b</sup> Case 2 was positive for chromogranin A by immunohistochemistry performed at the outside institution, by our own institution at the time of initial evaluation, and on repeat testing at the present time.

**Human Pathology  
(2014), 45, 1618-1624**

# 病例3



# Composite hemangioendothelioma with neuroendocrine marker expression: an aggressive variant

Modern Pathology(2017) 30, 1589-1602

Kyle D Perry<sup>1</sup>, Alyaa Al-lbraheemi<sup>2</sup>, Brian P Rubin<sup>3</sup>, Jin Jen<sup>1,4</sup>, Hongzheng Ren<sup>1</sup>, Jin Sung Jang<sup>4</sup>, Asha Nair<sup>1</sup>, Jaime Davila<sup>4</sup>, Stefan Pambuccian<sup>5</sup>, Andrew Horvai<sup>6</sup>, William Sukov<sup>1</sup>, Henry D Tazelaar<sup>7</sup> and Andrew L Folpe<sup>1</sup>

- **神経内分泌マーカー陽性の11例のComposite HE**
- M:F=6:5、9-55y(median47y)
- wrist, ankle, scalp, hip, and foot) and periaortic tissues, C5 vertebra, pulmonary vein, and liver
- **Solid/epithelioid, nested, and retiform morphology**
- CD31 (10/10), FLI-1 (10/10), ERG (9/9), CD34 (5/10), D2-40 (7/10), Synaptophysin (11/11), chromogranin A (1/11), CD56 (5/11), keratin (0/11),
- local recurrence in one and metastatic spread in four individuals (bone, lung, liver, and brain). One person died of disease
- **Aggressive clinical behavior**

# Composite hemangioendothelioma with neuroendocrine marker expression: an aggressive variant

Kyle D Perry<sup>1</sup>, Alyaa Al-lbraheemi<sup>2</sup>, Brian P Rubin<sup>3</sup>, Jin Jen<sup>1,4</sup>, Hongzheng Ren<sup>1</sup>, Jin Sung Jang<sup>4</sup>, Asha Nair<sup>1</sup>, Jaime Davila<sup>4</sup>, Stefan Pambuccian<sup>5</sup>, Andrew Horvai<sup>6</sup>, William Sukov<sup>1</sup>, Henry D Tazelaar<sup>7</sup> and Andrew L Folpe<sup>1</sup>

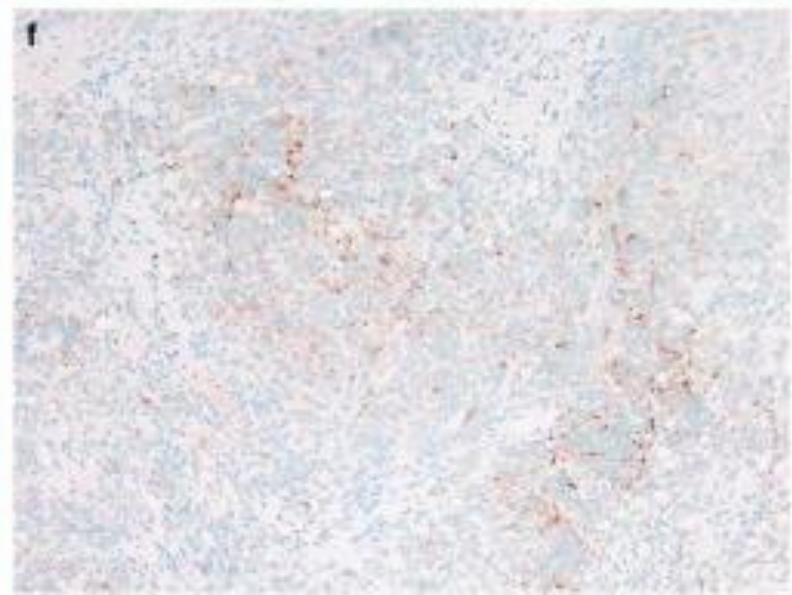
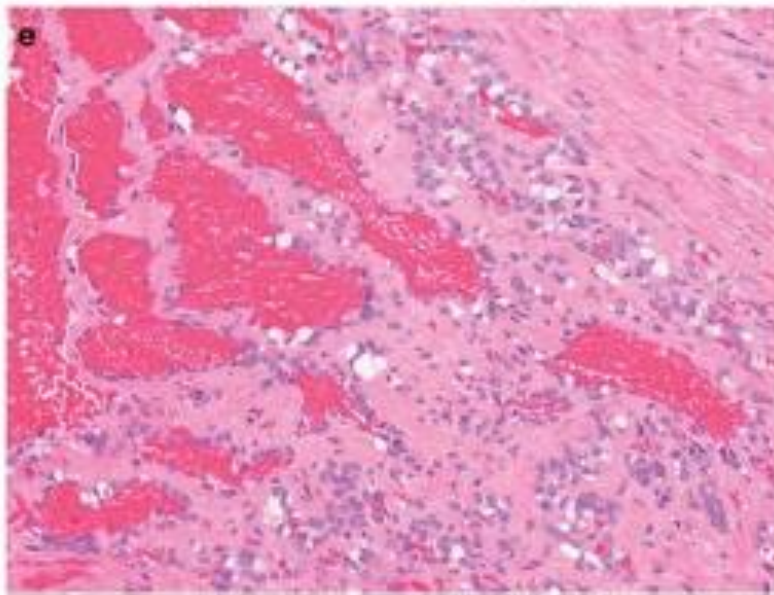
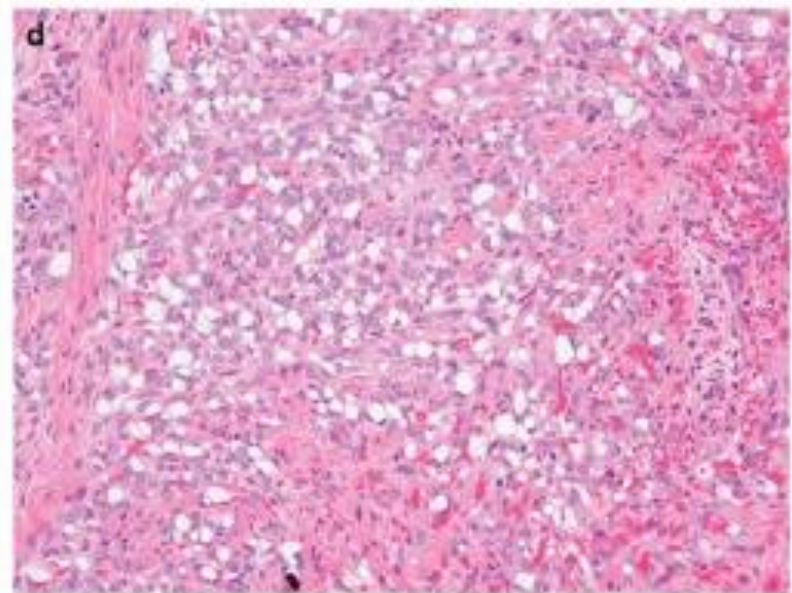
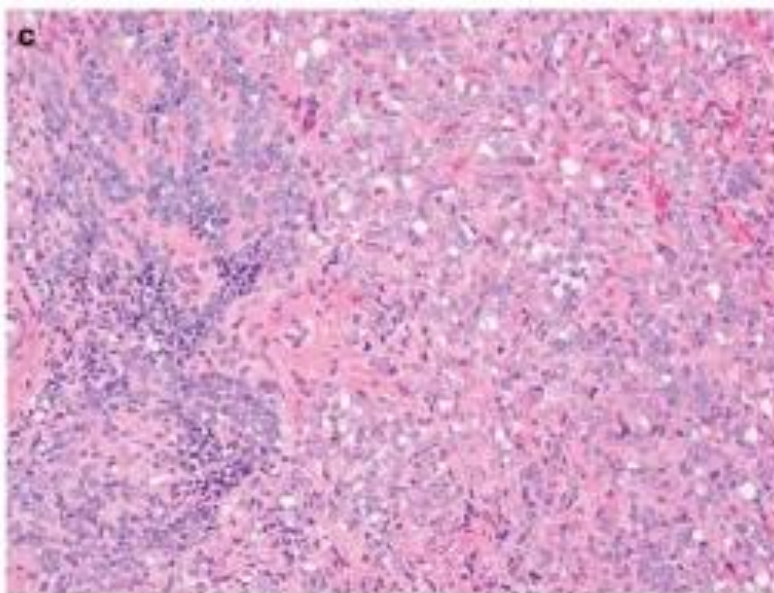
<sup>1</sup>Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA; <sup>2</sup>Department of Pathology, Boston Children's Hospital, Boston, MA, USA; <sup>3</sup>Robert J Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA; <sup>4</sup>Genome Analysis Core, Medical Genome Facility, Center for Individualized Medicine, Mayo Clinic, Rochester, MN, USA; <sup>5</sup>Department of Pathology, Loyola University Medical Center, Maywood, IL, USA; <sup>6</sup>Department of Pathology, University of California San Francisco, San Francisco, CA, USA and <sup>7</sup>Department of Laboratory Medicine and Pathology, Mayo Clinic, Scottsdale, AZ, USA

**Table 1** Clinicopathological, immunohistochemical, and genetic results

Case	Sex	Age (years)	Site	Size (cm)	LR	Met	Status	CD31	ERG	FLI-1	CD34	D2-40	SYN	CGA	CD56	CK	CAMTA1	Genetics
1	M	47	Wrist	7.7	Yes	Liver/lung/humerus	DOD	+	+	+	-	-	+	-	+	-	-	ND
2	F	40	Right ankle	N/A	Yes	-	AWOD	+	+	+	+	-	+	-	-	-	-	ND
3	F	36	Periaortic	2.1	-	Sacrum	AWD	+	+	+	-	+	+	-	+	-	-	PTBP1-MAML2
4	F	40	Vertebral	N/A	-	Lung	AWD	+	+	+	-	+	+	-	-	-	-	ND
5	M	27	Pulmonary vein	N/A	-	Brain	AWD	+	+	+	-	-	+	+	+	-	-	EPC1-PHC2
6	F	14	Ear	3.0	-	-	N/A	+	+	+	+	+	+	-	+	-	-	ND
7	F	55	Superficial hip	0.4	-	-	AWOD	+	+	+	-	+	+	-	-	-	-	ND
8	M	55	Liver	6.0	-	-	AWOD	ND	ND	ND	ND	ND	+	-	-	-	-	ND
9	M	15	Foot	1.2	-	-	AWOD	+	ND	+	+	+	+	-	-	-	-	ND
10	F	50	Cheek	9.5	-	-	N/A	+	+	+	+	+	+	-	+	-	-	ND
11	M	9	Index finger	N/A	-	-	N/A	+	+	+	+	+	+	-	-	-	-	ND

Abbreviations: AWD, alive with disease; AWOD, alive without disease; DOD: dead of disease; LR: local recurrence; Met: metastases; N/A: not available; ND: not done.





**Figure 5** This composite hemangioendothelioma with neuroendocrine marker expression arose in association with a long-standing vascular malformation of the cheek (Case 10) (a). Dilated vascular channels lined by hobnailed cells, adjacent to solid masses of epithelioid endothelial cells (b). The retiform vascular channels in this tumor were often compressed, forming branching structures composed of a solid proliferation of darkly staining hobnail endothelial cells (c). The epithelioid areas showing striking intracytoplasmic vacuolization, as seen in other epithelioid endothelial cell tumors (d). Hemangioma-like structures lined by hobnail endothelial cells were also present (e). Synaptophysin was positive (f).

# 病理診断

**Scale, resection:**

**Angiosarcoma with aberrant  
expression of neuroendocrine marker**

# コンサルテーション結果

九州大学大学院 医学部研究科

形態機能病理 小田 義直教授

Skin, scalp (resection): Angiosarcoma, compatible

We reviewed this case and considered above diagnosis.

Section shows a proliferation of atypical epithelioid tumor cells having oval to polygonal-shaped and vesicular nuclei, eosinophilic cytoplasm and prominent nucleoli, arranged in haphazard patterns. Mitotic figures are frequently seen.

Immunohistochemically, the tumor cells are positive for CD31 (focal) and ERG, but negative for AE1/AE3, CD34, D2-40, FOSB and MPO. SMARCB1/INI1 immunoexpression is preserved.

The feature is compatible with angiosarcoma.

We appreciate you for consulting us.

# Angiosarcoma の aberrant expression marker

- Cytokeratin
- CD30
- CD117(c-Kit)
- Neuroendocrine marker  
(特にSynaptophysin)

# Cutaneous angiosarcoma

- 定 義: 血管、リンパ管の内皮細胞の形質を発現する悪性腫瘍
- 病因分類:
  - 1) 特発性血管肉腫
  - 2) リンパ浮腫性血管肉腫
  - 3) 放射線照射後血管肉腫
- 臨 床: 高齢者の男性に多く、頭蓋や顔面に好発  
皮膚症状: 不明瞭な暗赤紫紅斑、血疱、易出血性隆起性局面、小結節など。しばしば多結節性で潰瘍形成  
血管肉腫の特徴: 衛生的進展巣を形成(局所転移巣)

- 皮膚円形腫瘍で、神経内分泌マーカー (Synaptophysin) が陽性の場合には血管肉腫も鑑別診断に入れる必要がある
- 神経内分泌マーカー陽性の血管肉腫は低分化型(Solid type, epithelioid type) の成分を有し、Aggressive clinical behaviorを示す傾向がある

**TAKE HOME MESSAGE**