

Korea-Taiwan-Japan Joint Meeting for Gynecological Pathology

Mini-lecture

Female Adnexal Tumor of Probable Wolffian Origin (FATWO) in Taiwan: A Small Case Series and Literature Review

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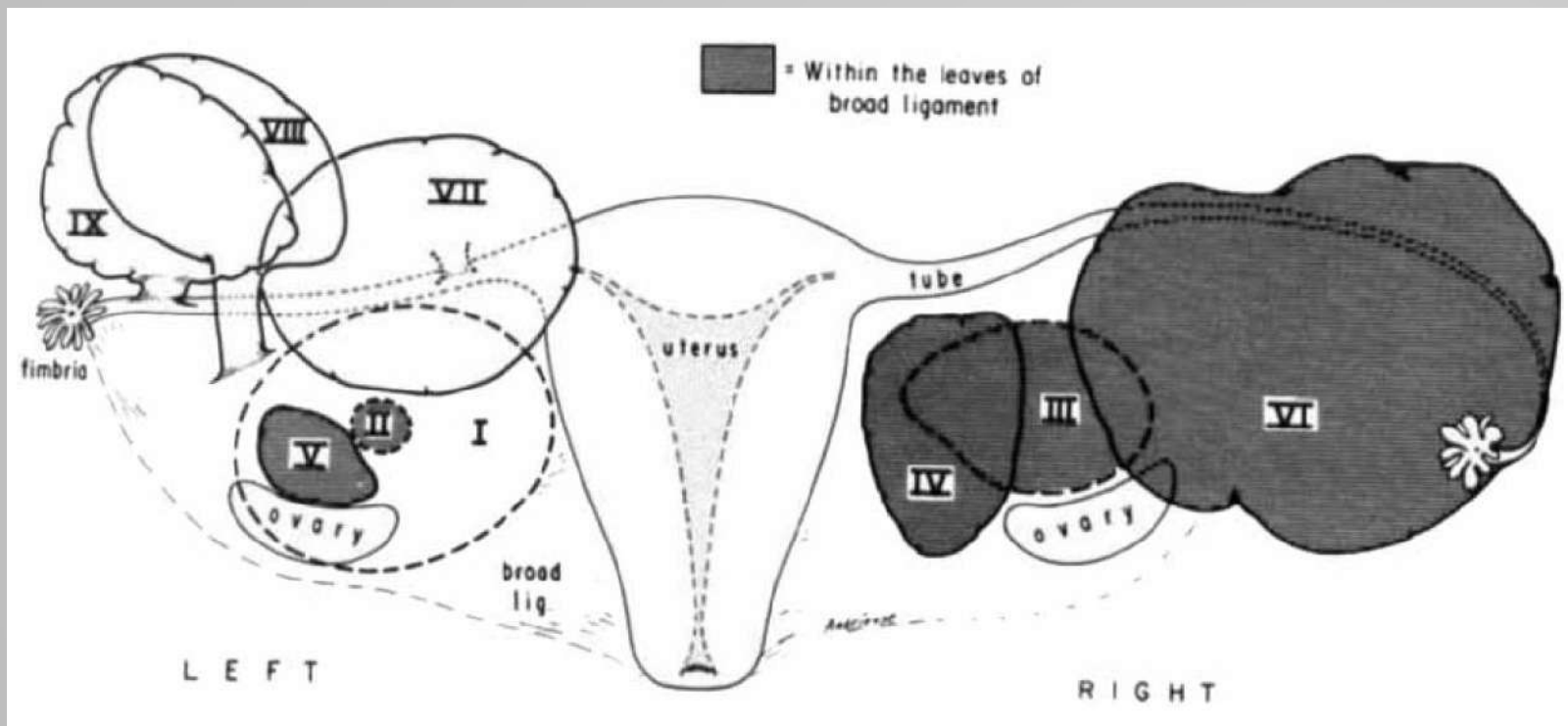
Outlines

- **Introduction & Literature Review**
- **Case Series**
 - Morphology
 - Immunohistochemical profiles
 - Genetic profiles
- **Take Home Message**

Introduction: Female Adnexal Tumor of Probable Wolffian Origin (FATWO)

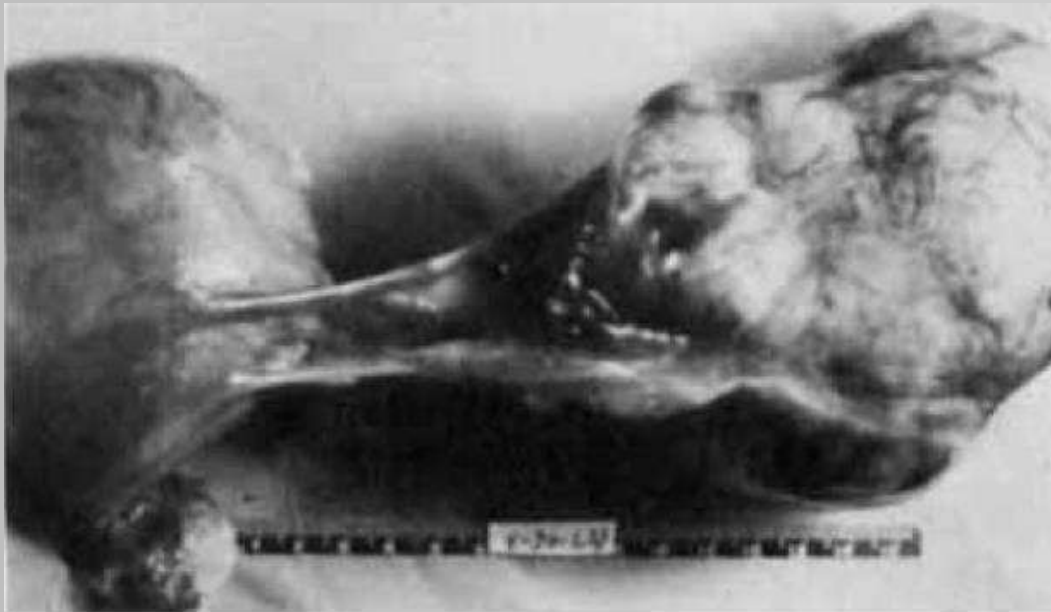
- Rare **extraovarian, extratubal** tumors firstly reported by Kariminejad and Scully in a 9-case series in 1973.
- Currently “an epithelial tumor of Wolffian (mesonephric) origin.”
- Most of the cases are **benign** or **indolent** tumors confined within adnexa.
- Low grade malignant potential or aggressive behaviors in a minor (10%) cases
 - Recurrence / Metastasis

- Often in broad ligament, mesosalpinx, ovarian hilus and pelvis.



Location & Gross Features

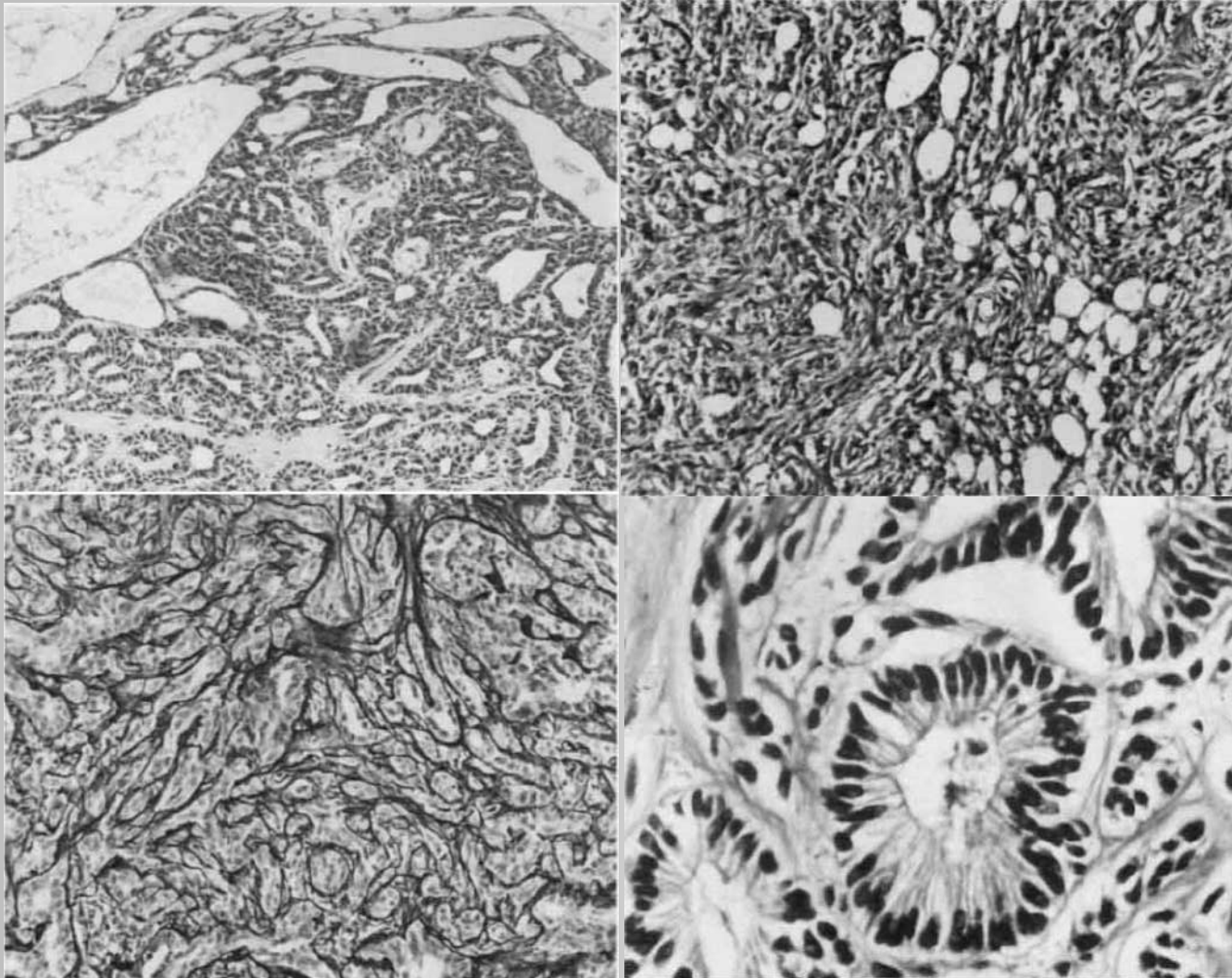
- Often in broad ligament, mesosalpinx, ovarian hilus and pelvis.
- **Encapsulated, solid ovoid masses** with nodular, or lobulated appearance.



Three Pattern in the Original Article

- Solid or diffuse arrangement
- Closely packed, winding, branching, and anastomosing **tubules**
- A **sieve-like pattern** with hollow tubules varying in size and shape with occasional **cyst formation**

Three Pattern in the Original Article



Case Series

Case Series in Taiwan

- An inter-institutional review
- Four cases (1 benign, 3 malignant) retrieved
- All arising from **adnexa** of middle to old age women (50~63 y/o)
- Size varies from <1 cm to 16 cm
- 3 malignant cases
 - Radical surgery and chemotherapy
 - One with local recurrence
 - Follow-up interval: 12~51 months
 - All alive with or without diseases

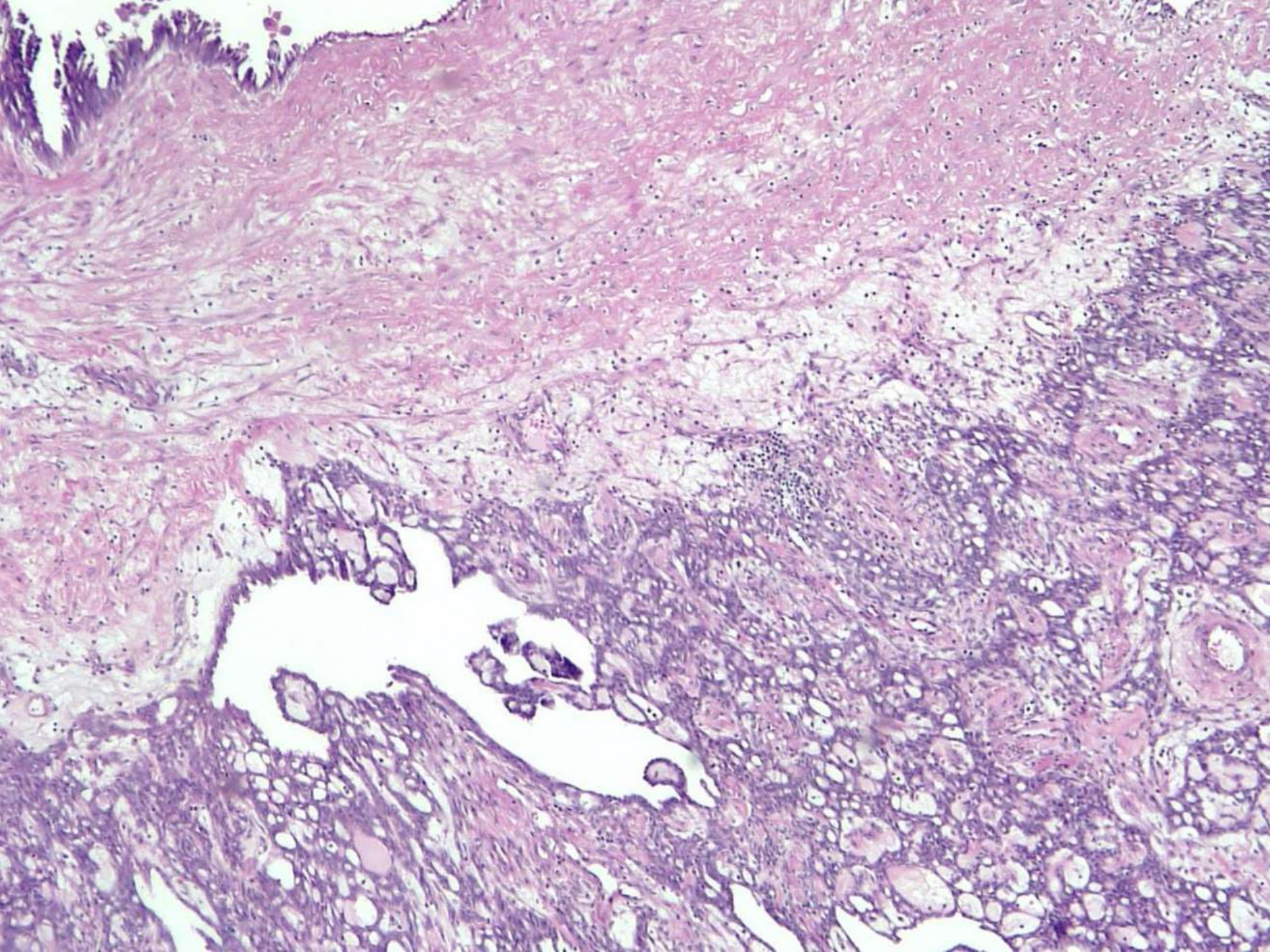
Case Series in Taiwan

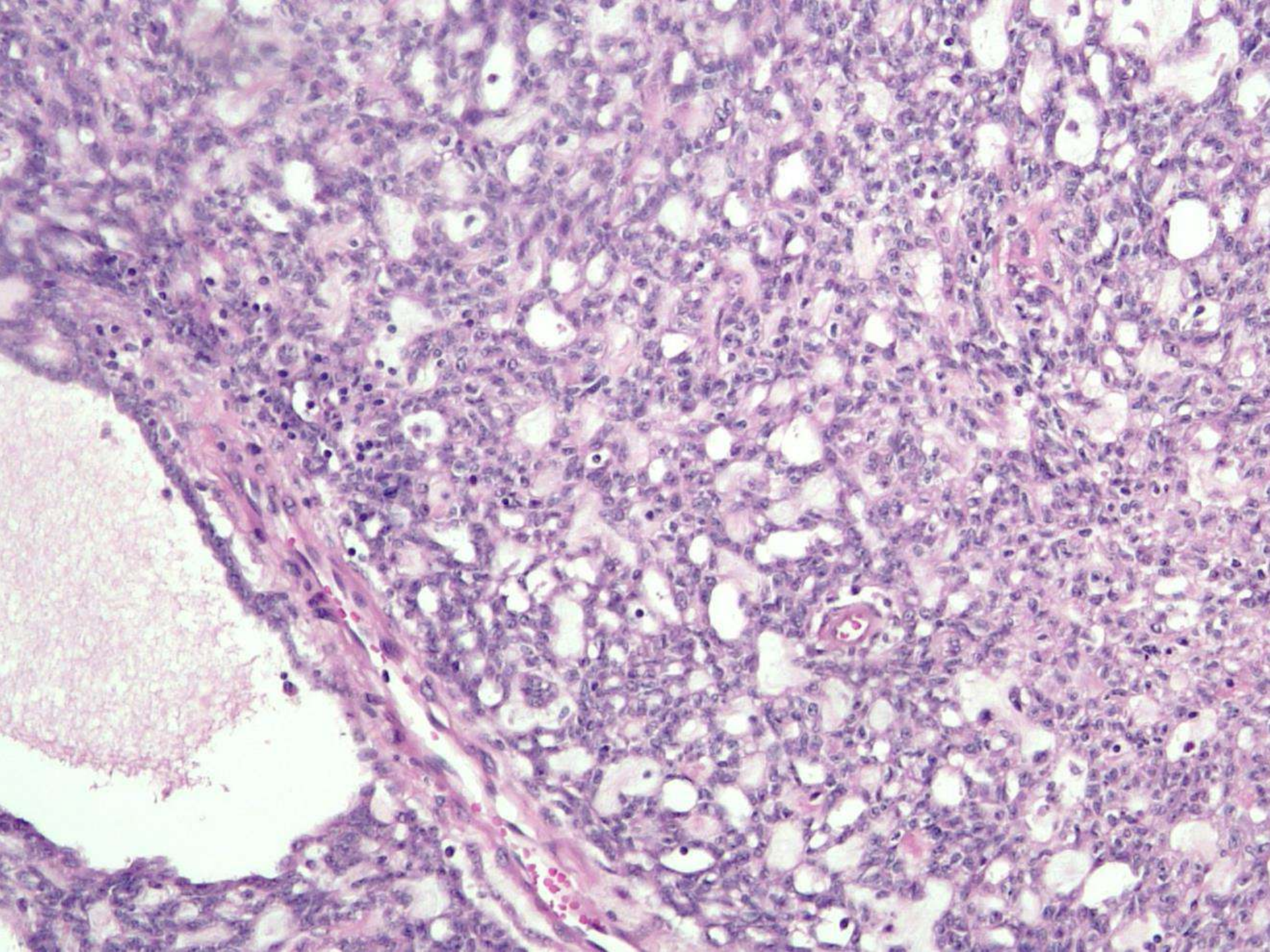
Case	Age	primary site	Surgery	Chemo	Interval of F/U	Current status
1	60	right fallopian tube	salpingo-oophorectomy	N	Loss of F/U	
2	50	right adnexa	Staging surgery	Y	12 months	alive
3	61	left ovary	Staging surgery	Y	42 months	alive
4	63	left ovary	Staging surgery	Y	51 months	alive, recurrence

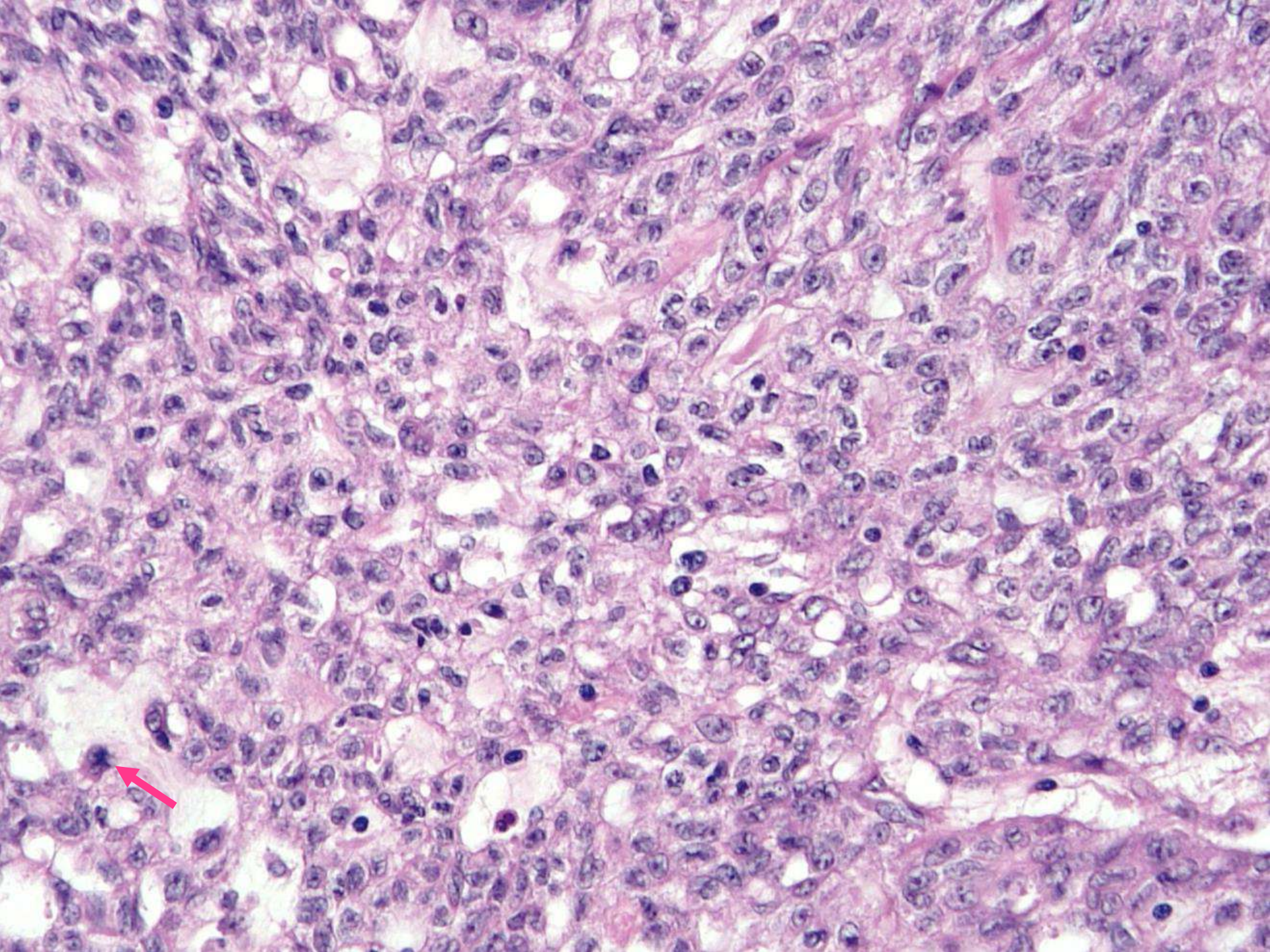
Microscopic finding in four cases

Case 1

Sieve-like pattern

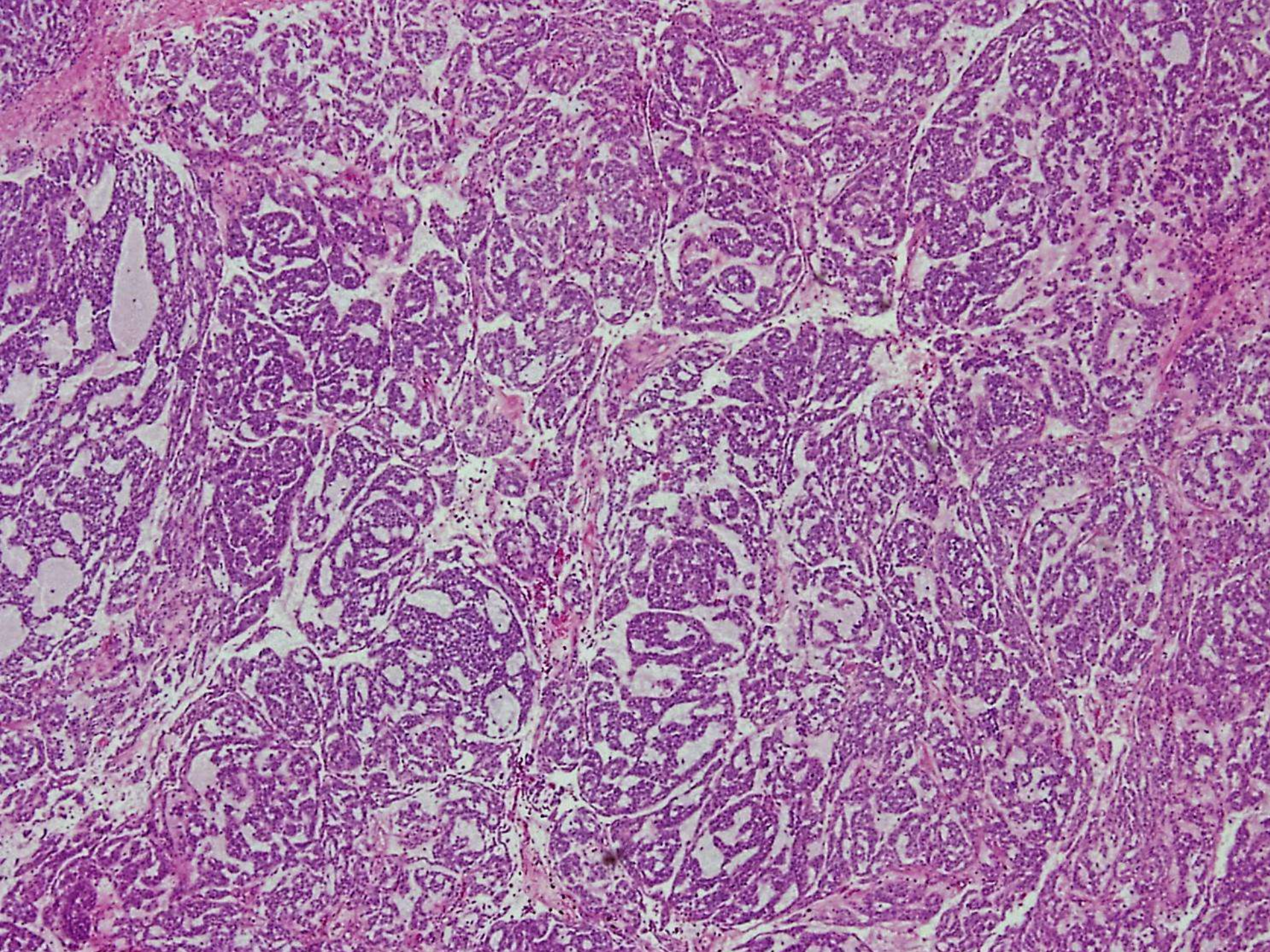


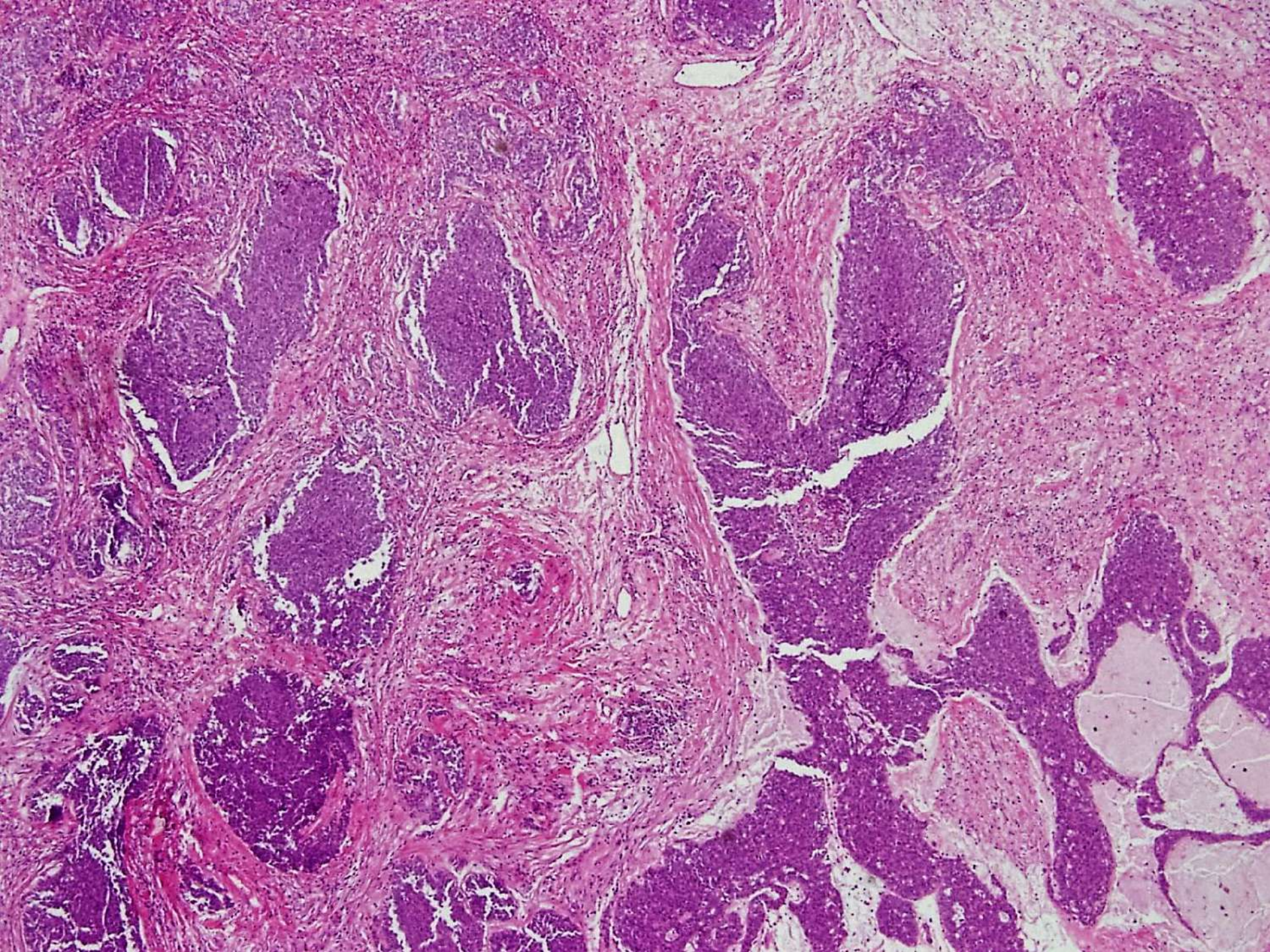


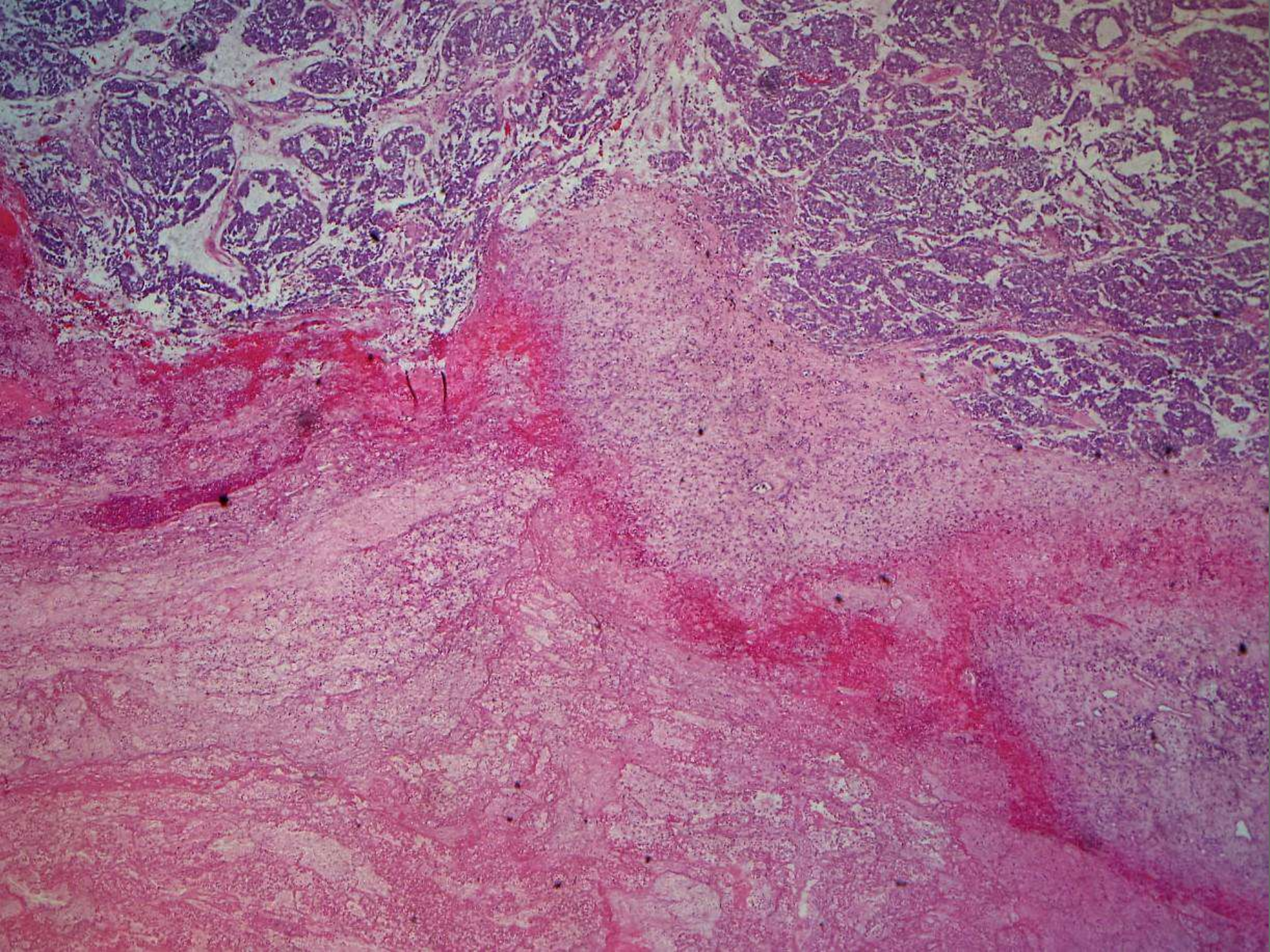


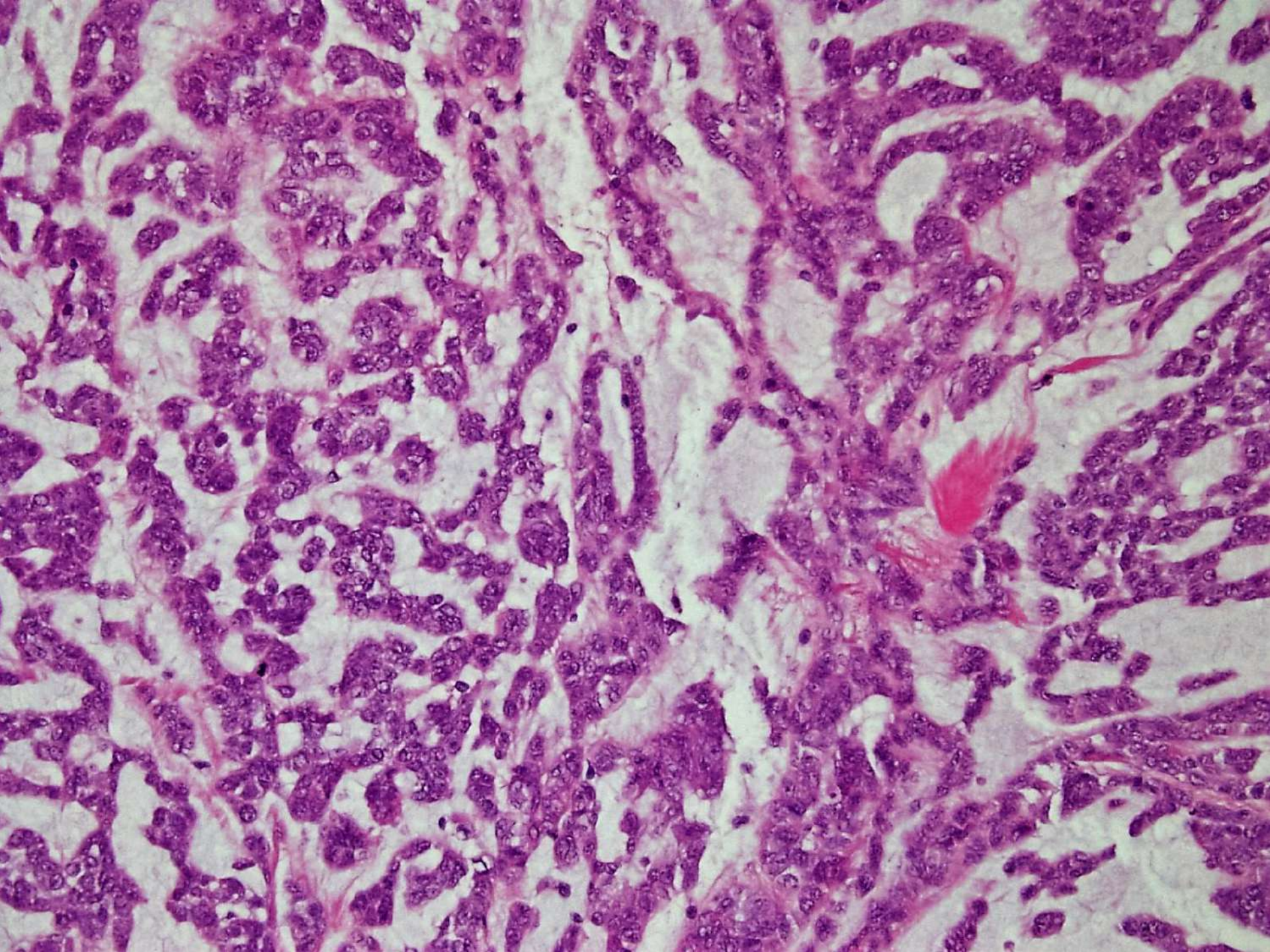
Case 2

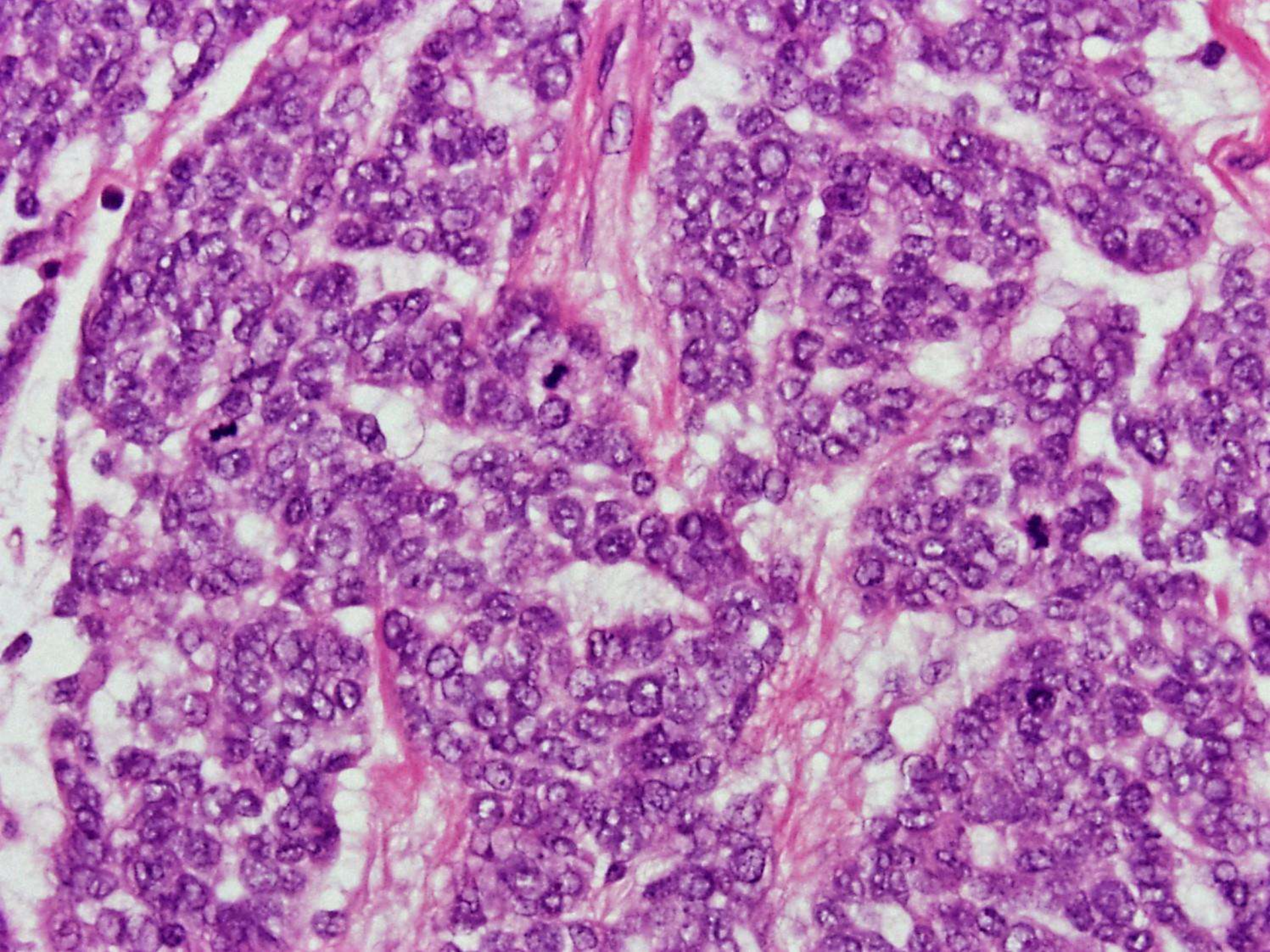
Solid and sieve-like pattern





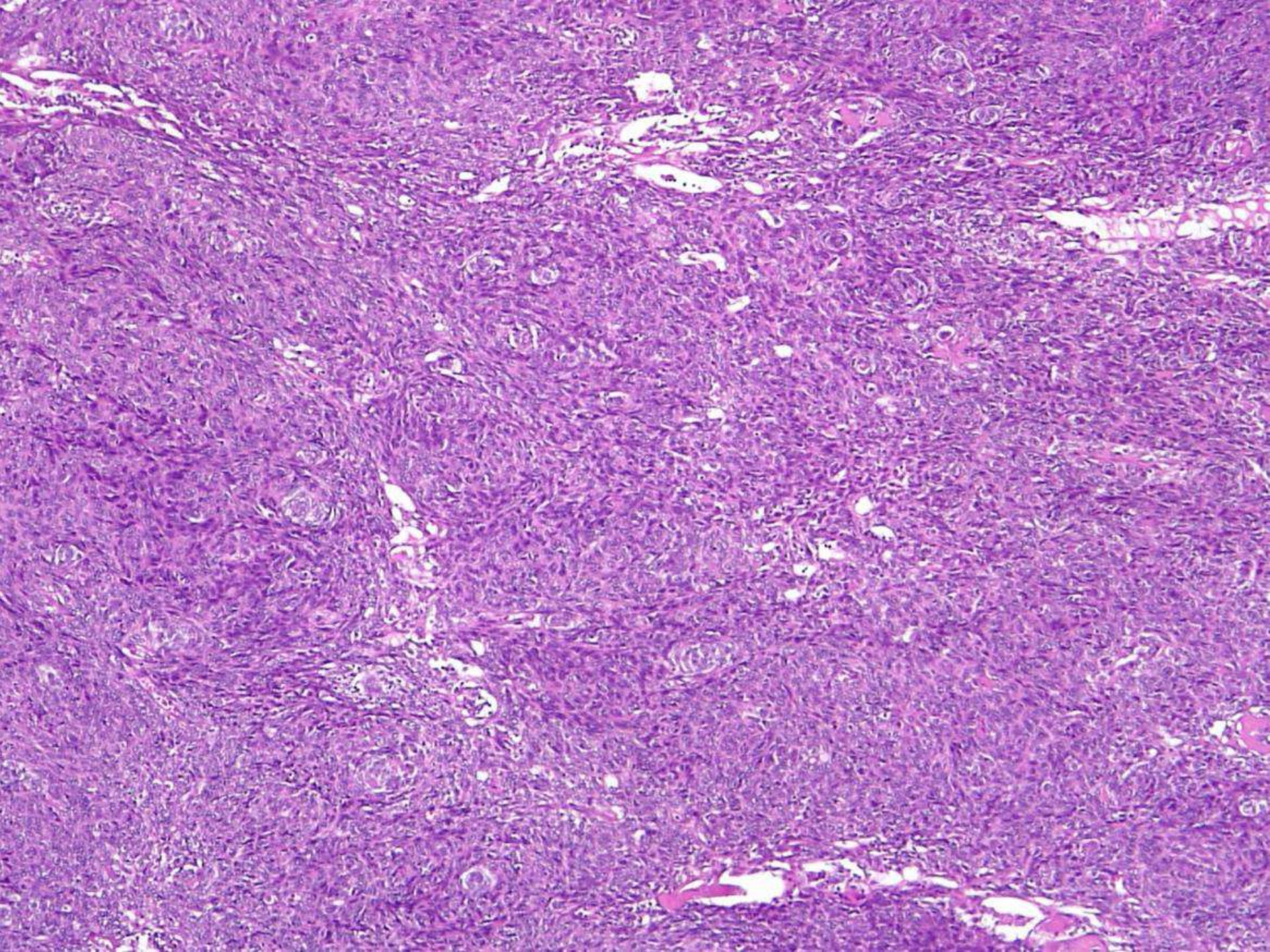


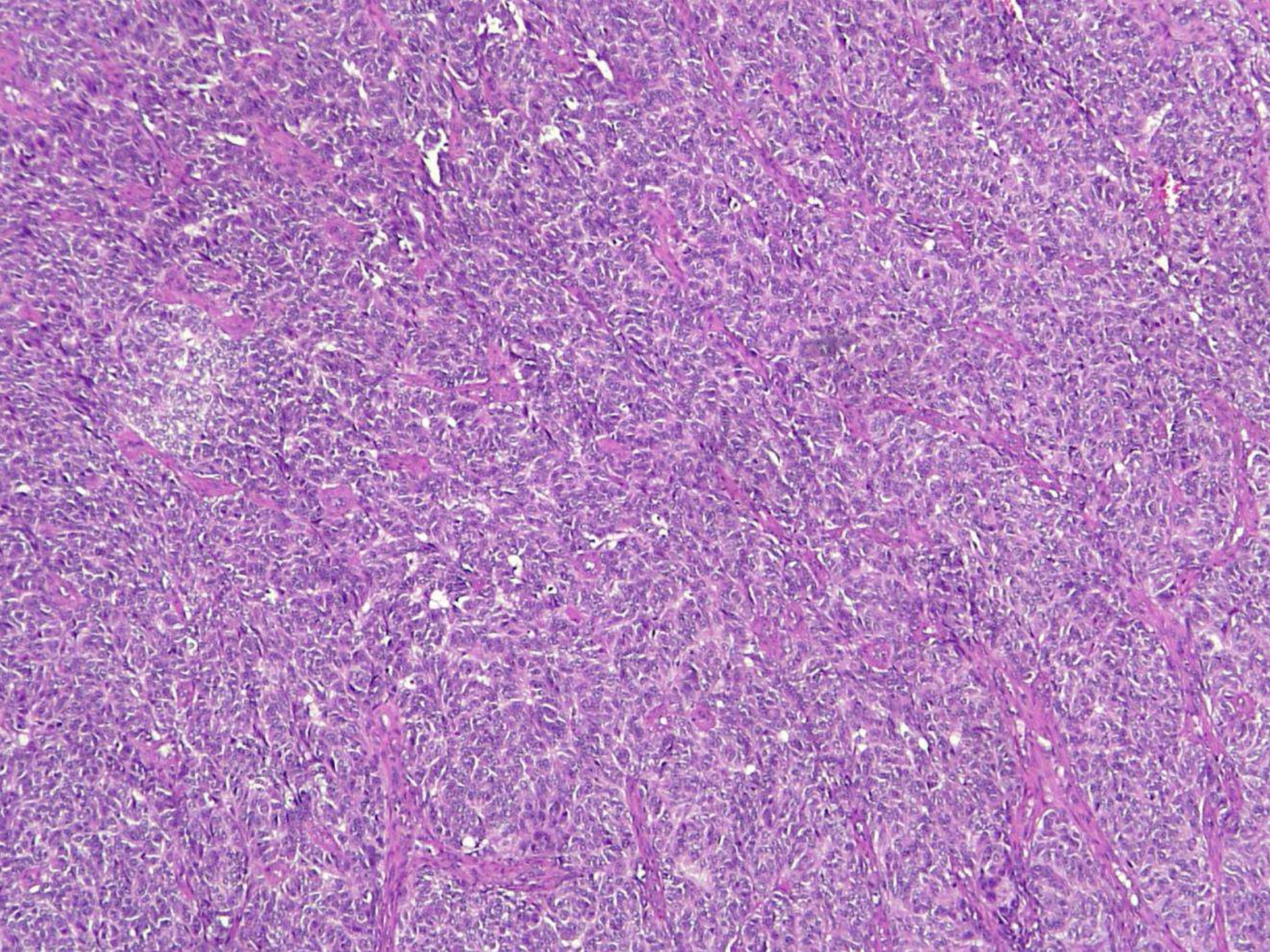


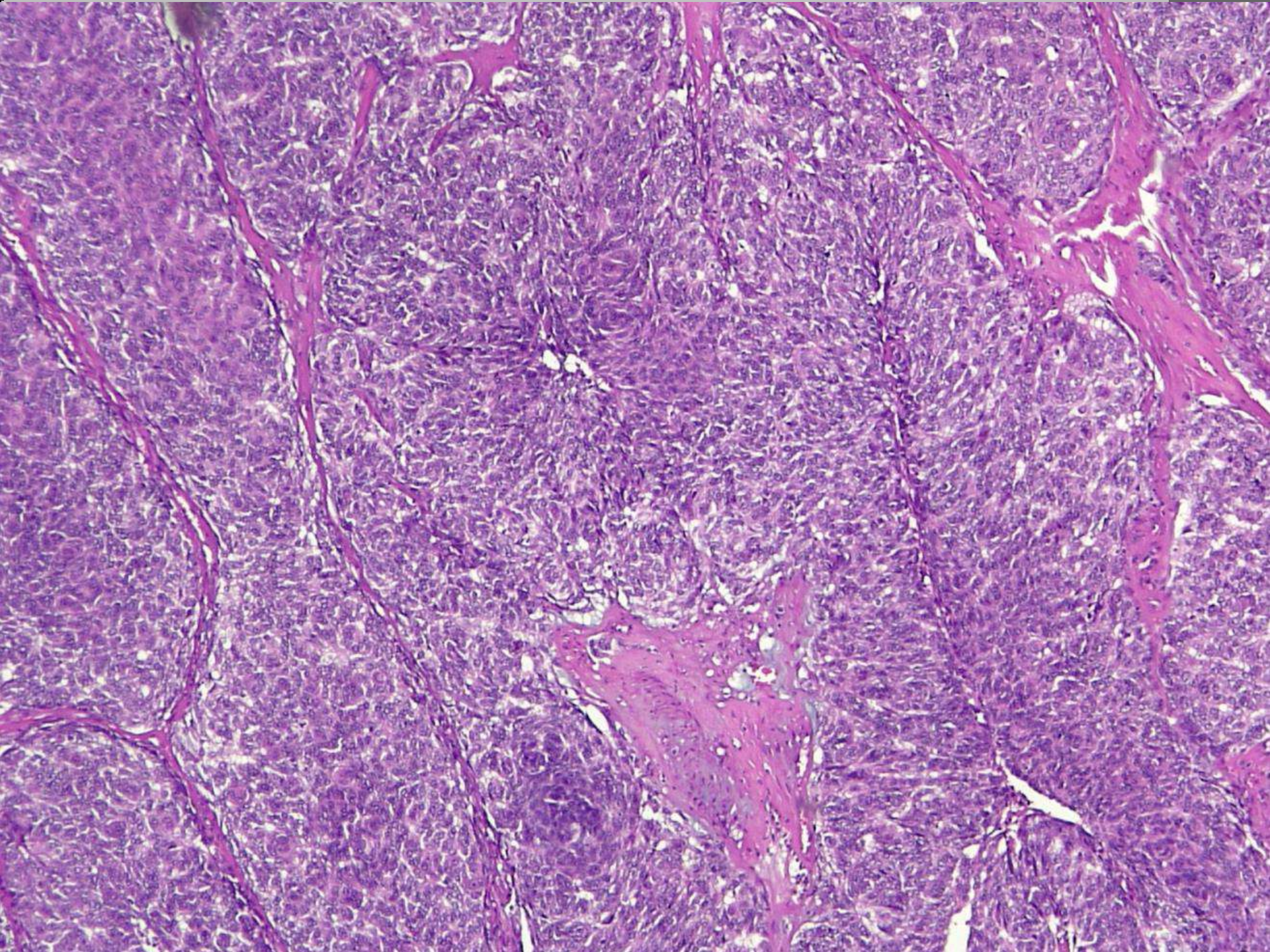


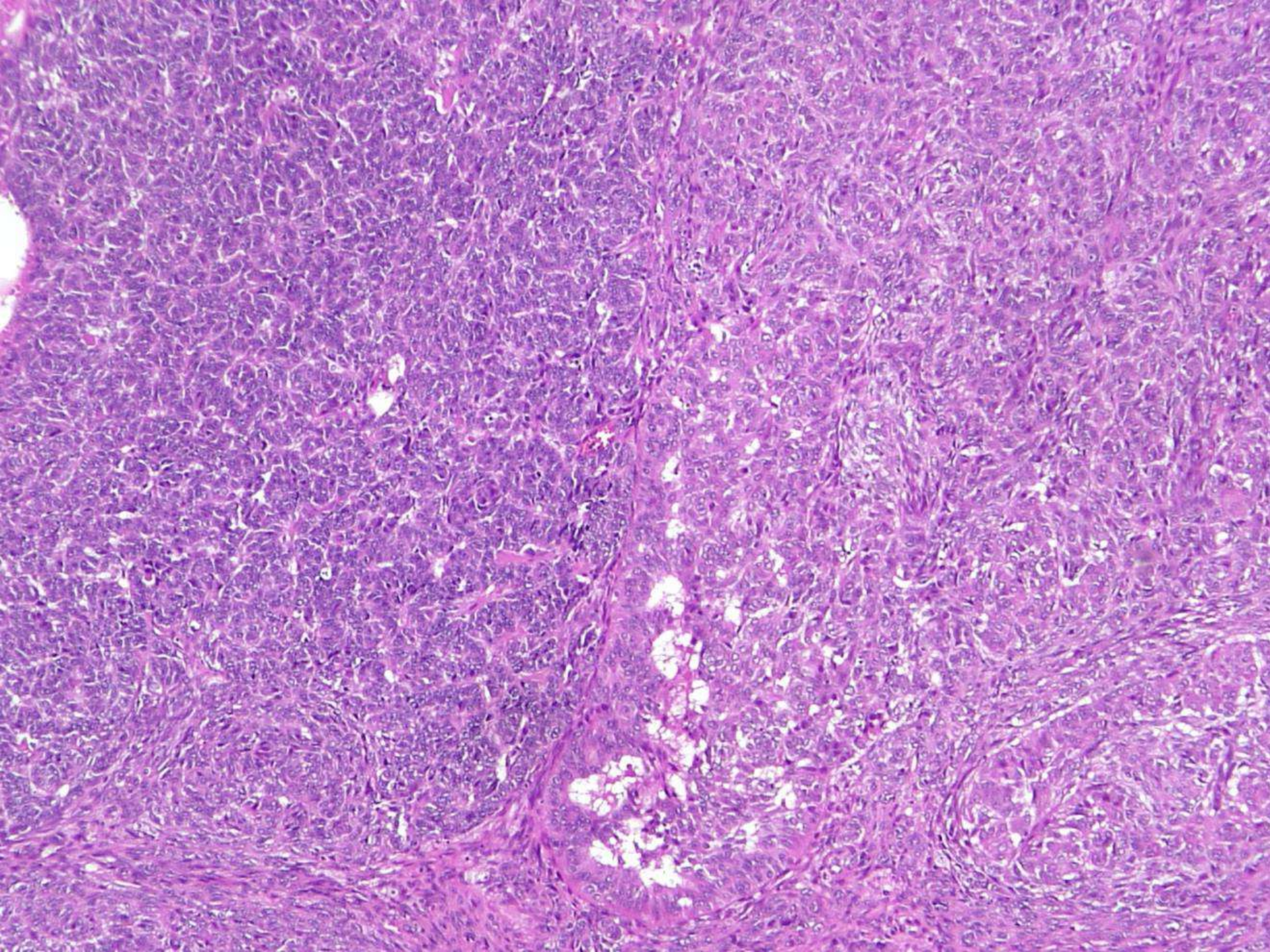
Case 3

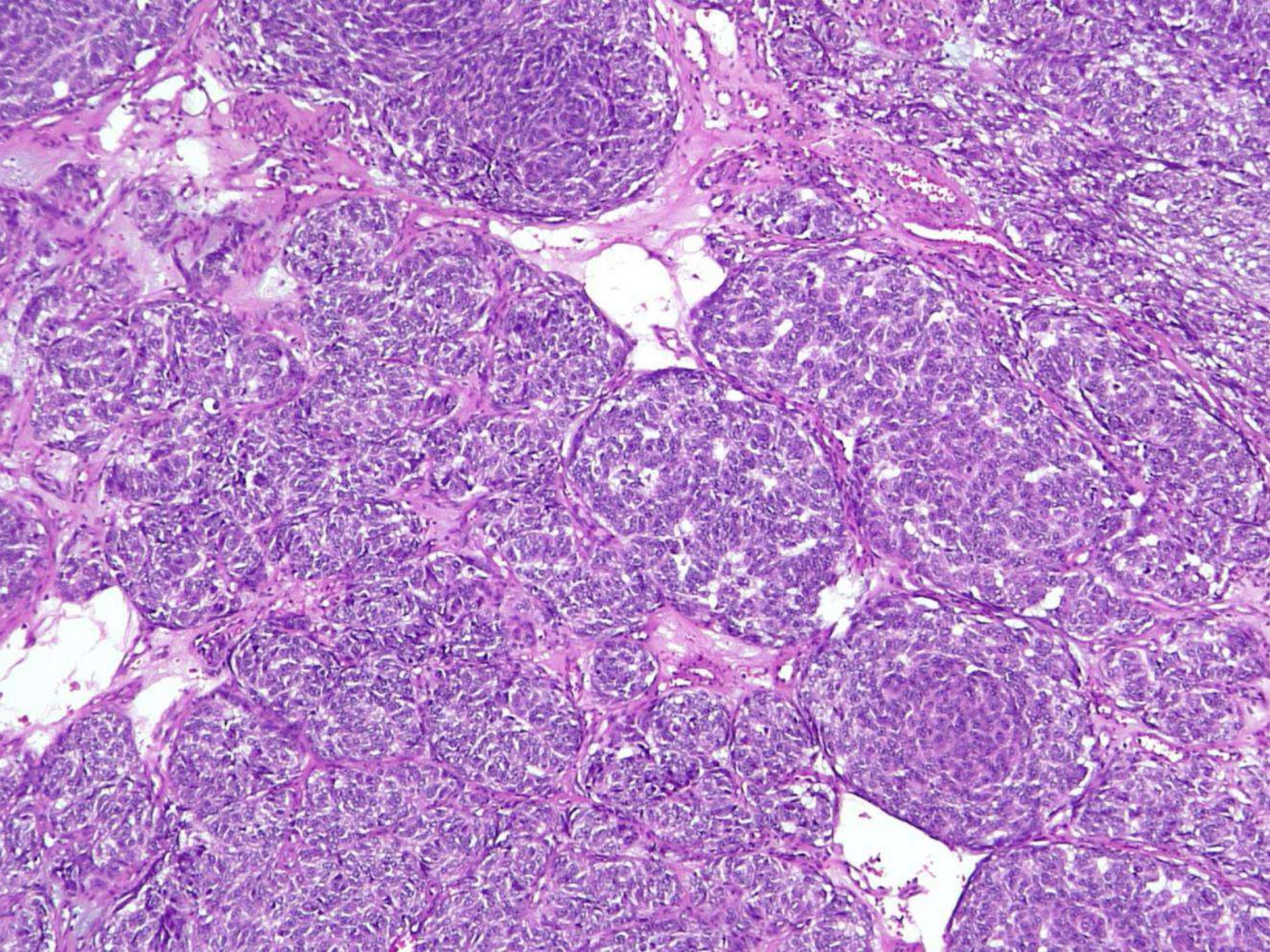
Solid and tubular pattern

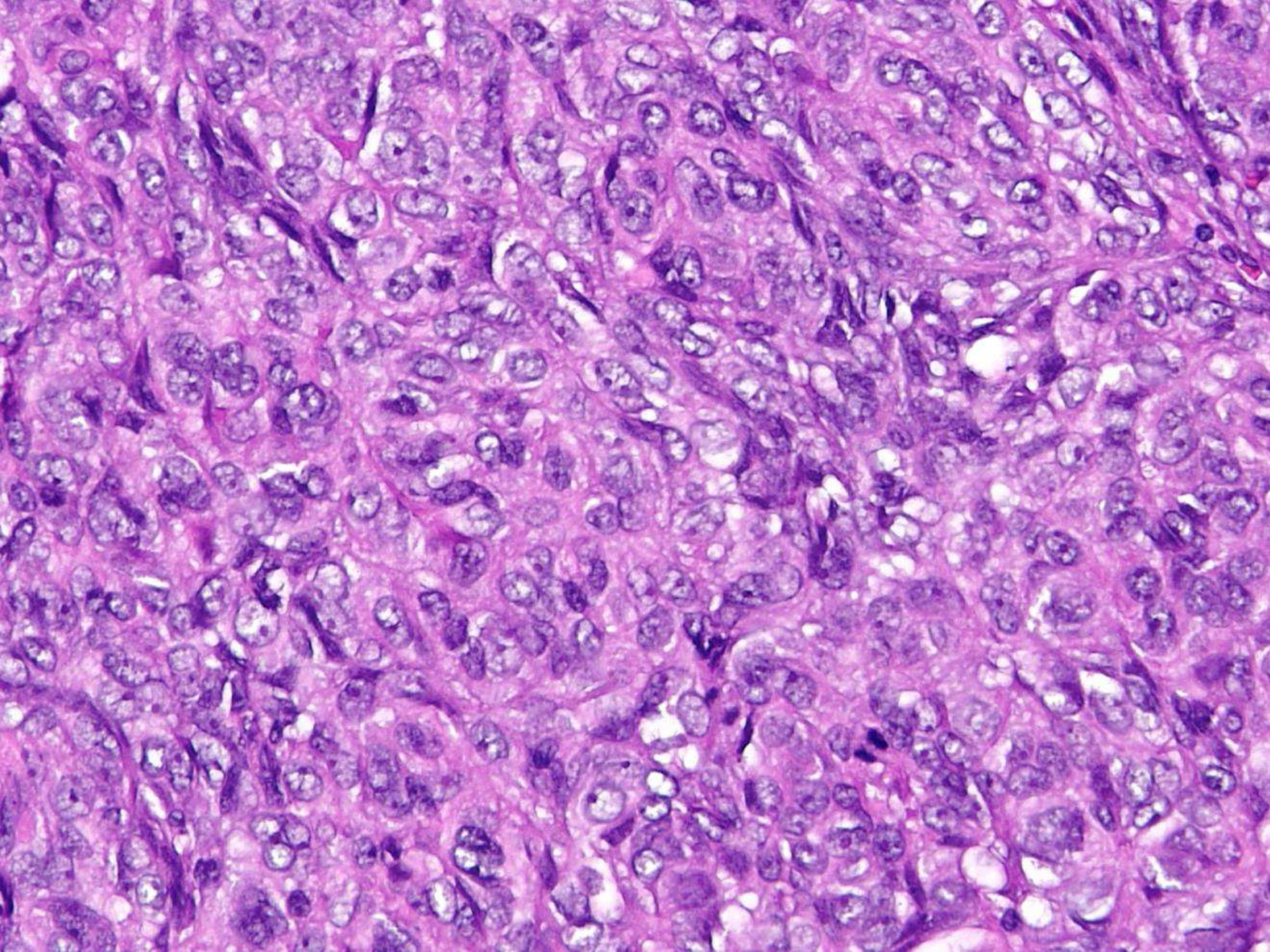






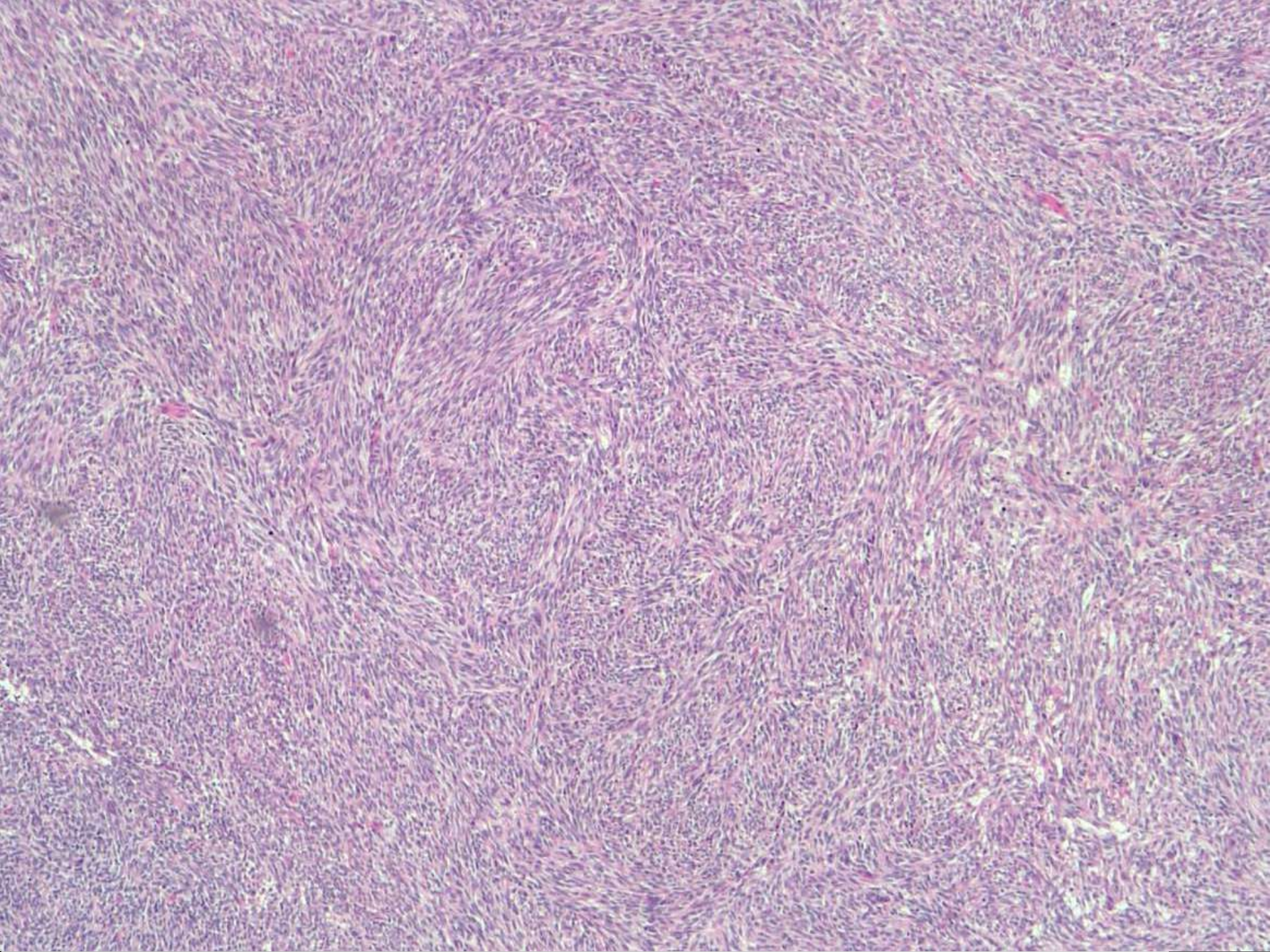


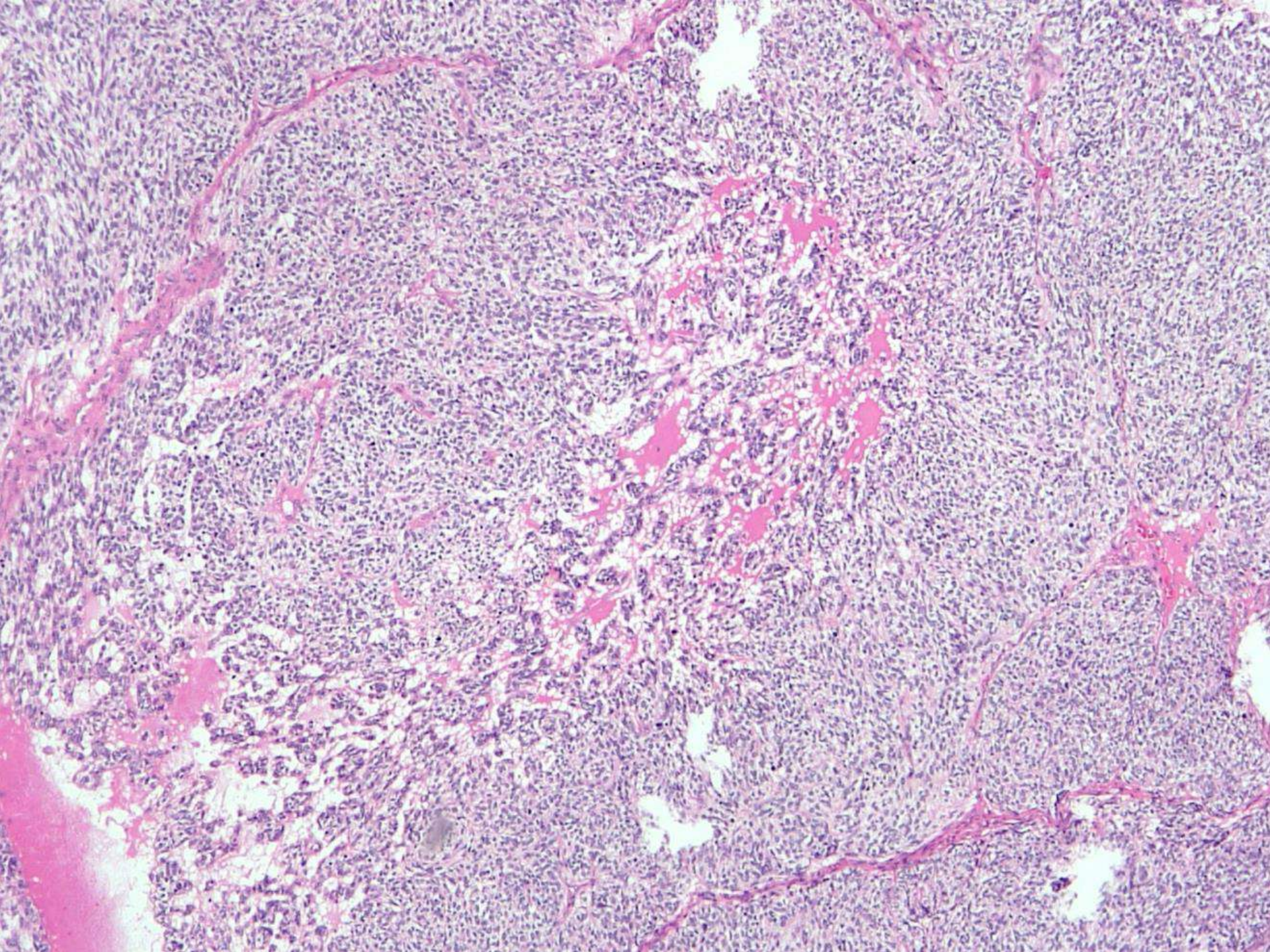


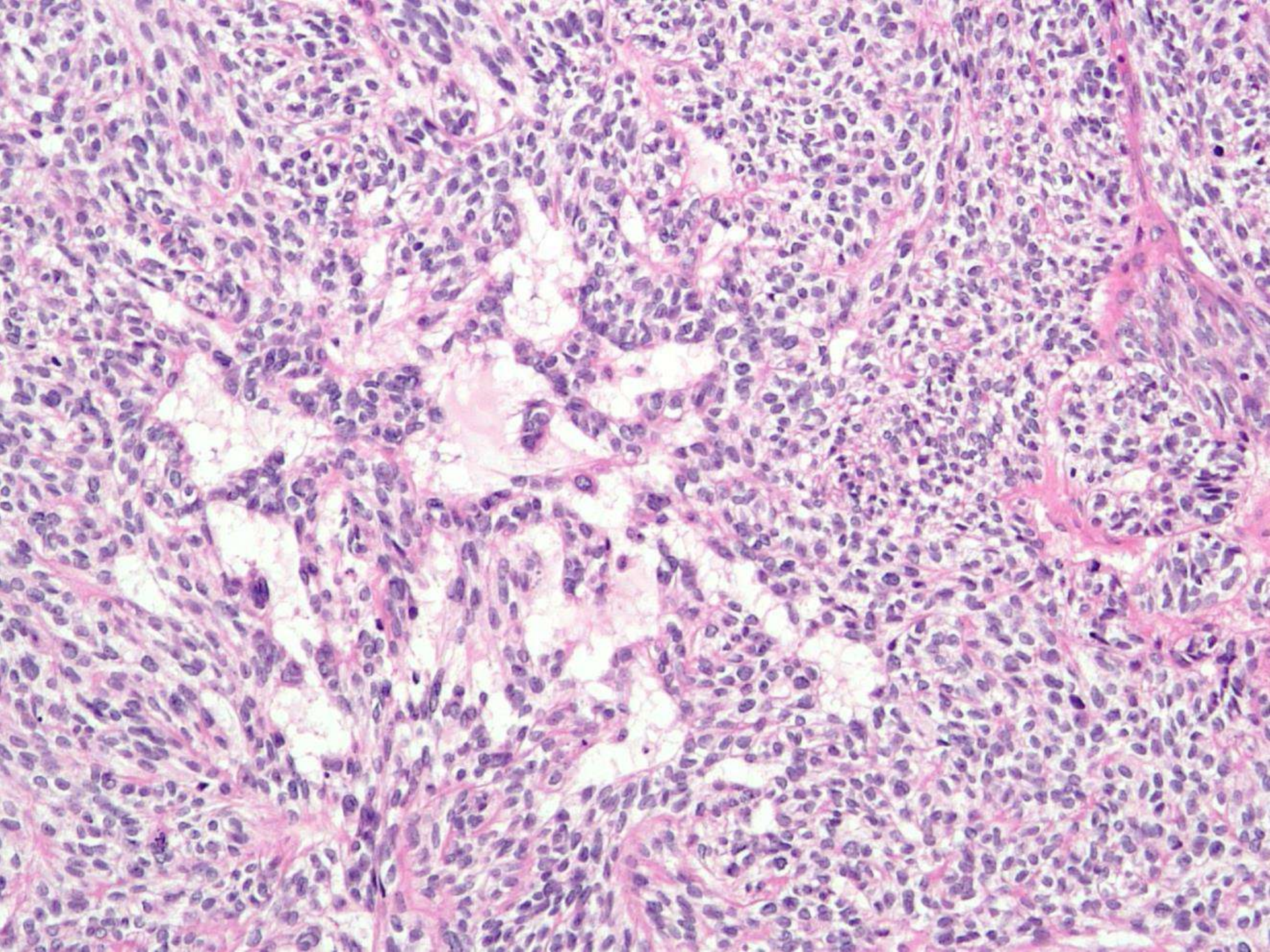


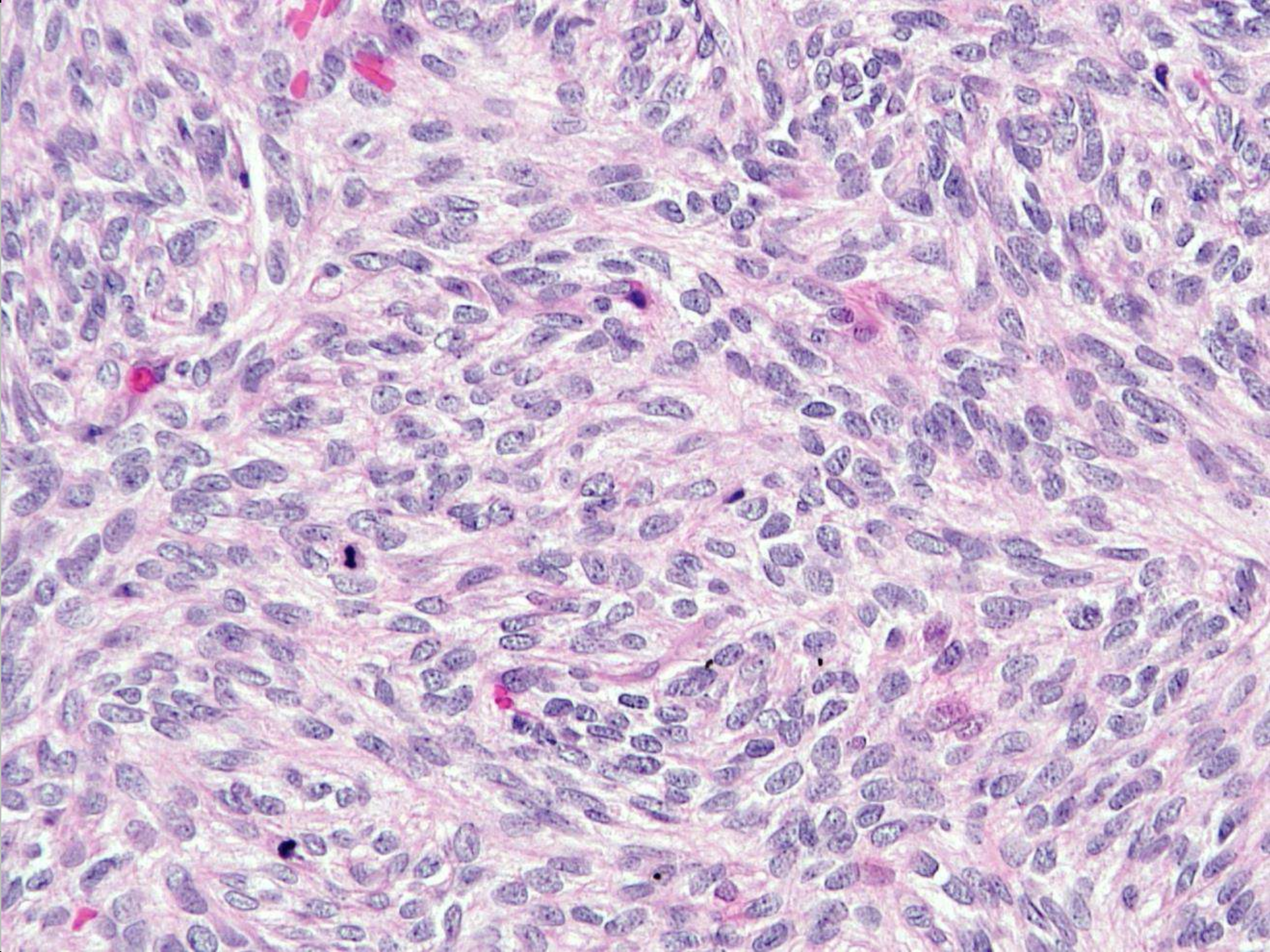
Case 4

Spindle cell morphology









Summary in morphology

- **Sieve-like** and **tubular** pattern are most characteristic.
- Solid or spindle cell morphology would cause difficulty in diagnosis
 - Try to find minor sieve-like or tubular components
- Malignant cases defined by **nuclear atypia, infiltrative growth pattern and frequent mitoses**
 - The nuclear grading is not so “high grade” to fit in typical high grade carcinoma or sarcoma

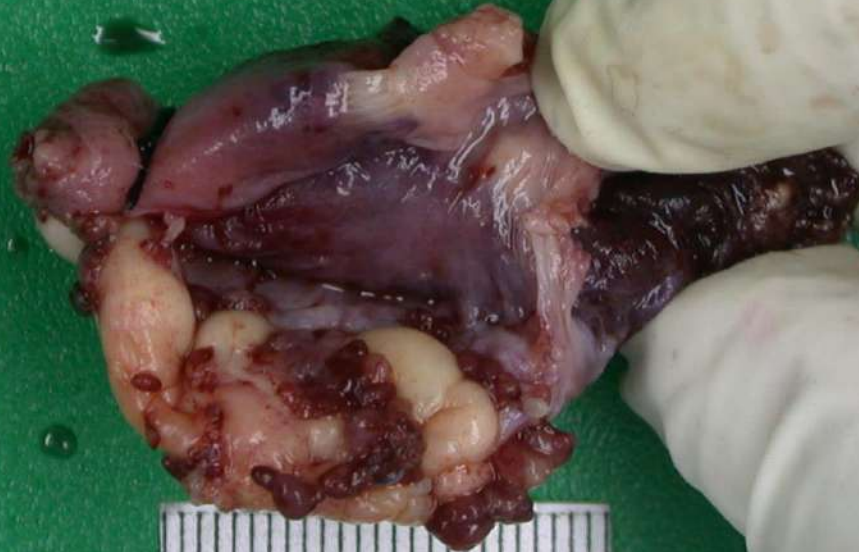
How to Make Differential Diagnosis?

- **Gross examination**
 - Primary site?
 - Ovary? Tube? Others?
- **Microscopic examination**
 - Diffuse pattern
 - Tubular pattern
 - Sieve-like pattern
 - Spindle cell morphology

R't tumor



R't OV+tube



How to Making Differential Diagnosis?

- **Diffuse pattern**

- Un-/Poorly-differentiated carcinoma?
- Neuroendocrine carcinoma?

- **Tubular pattern**

- Endometrioid adenocarcinoma?
- Granulosa cell tumor?
- Sertoli (-leydig) cell tumor?

- **Sieve-like pattern**

- Endometrioid adenocarcinoma?
- Granulosa cell tumor?
- Adenomatoid tumor/Mesothelioma?

- **Spindle cell morphology**

- Adenomatoid tumor/Mesothelioma?
- Fibroma/Thecoma?
- Sarcoma? (Leiomyosarcoma? Endometrial stromal sarcoma?)

Immunohistochemical profiles

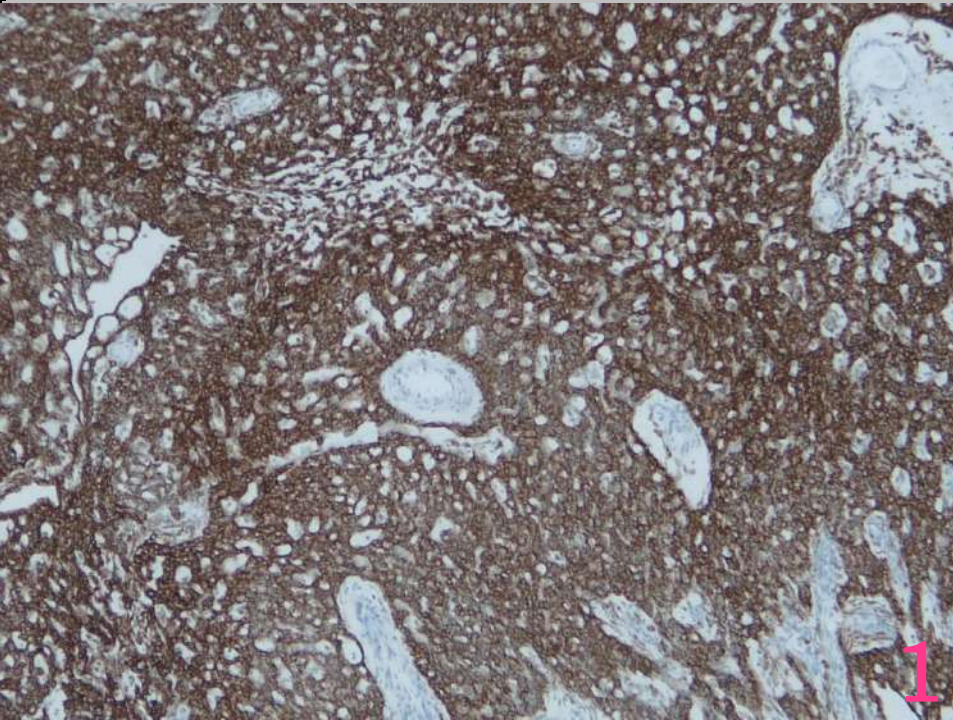
Wolffian Adnexal Tumor, So-Called Female Adnexal Tumor of Probable Wolffian Origin (FATWO):

Immunohistochemical Evidence in Support
of a Wolffian Origin

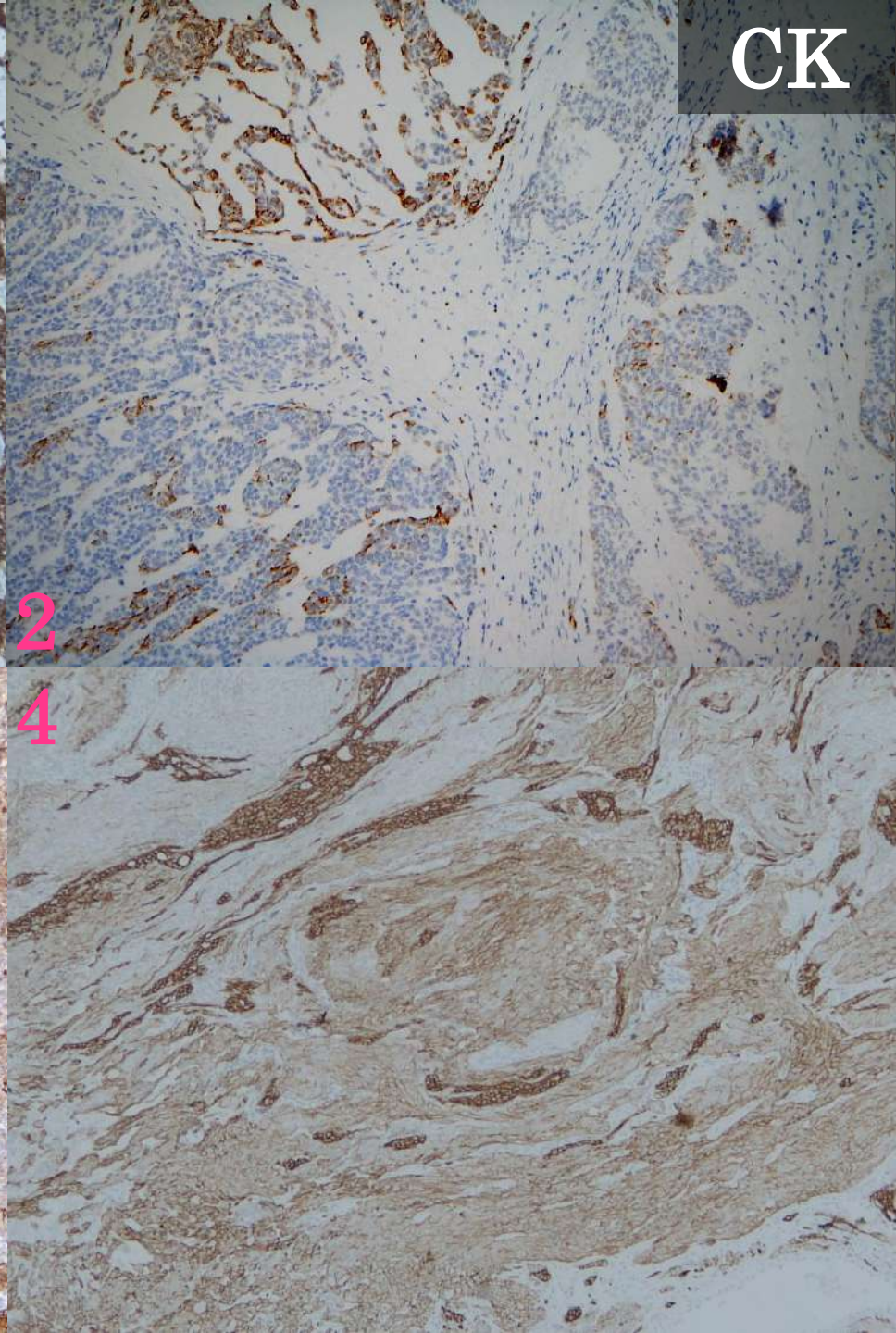
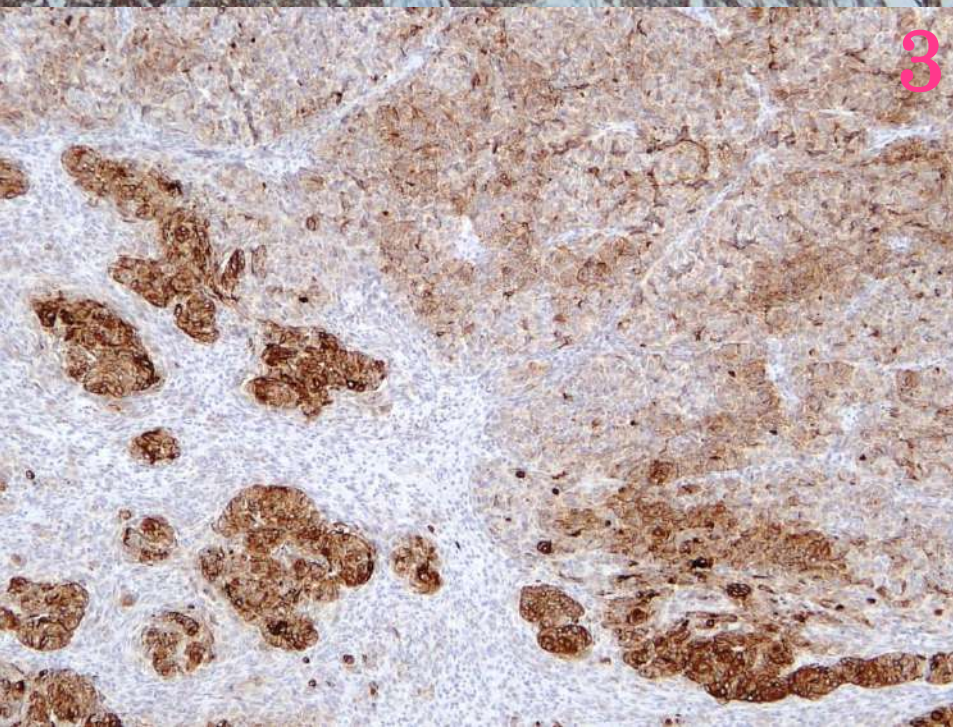
HUMAN PATHOLOGY

Volume 30, No. 7 (July 1999).

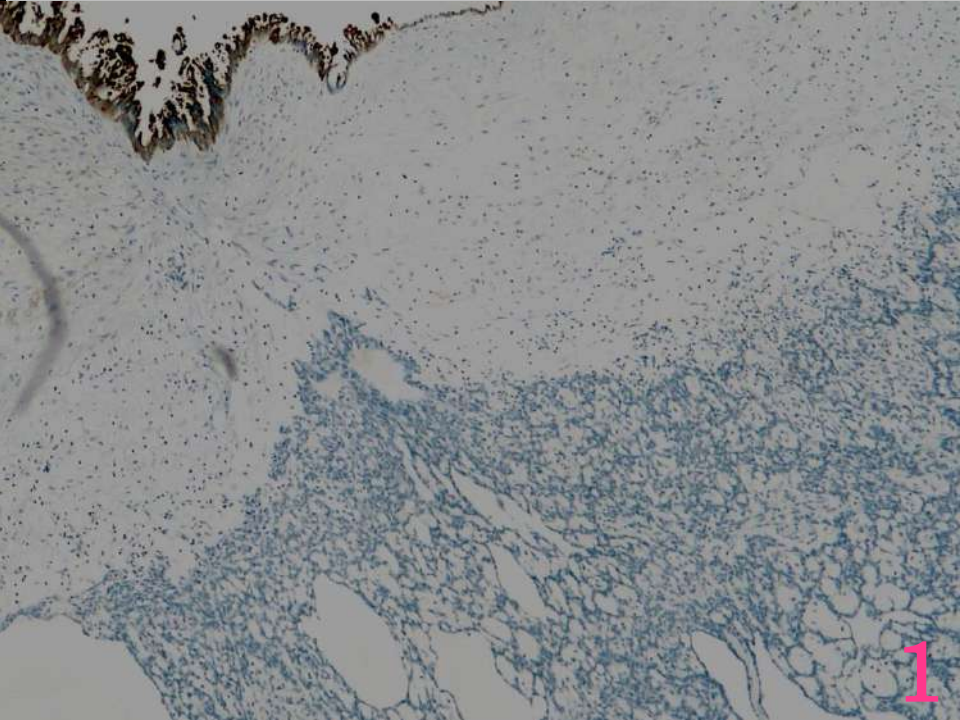
	Wolffian Adnexal Tumor No. Positive (%)	Rete Ovarii No. Positive (%)	Mesonephric Remnants No. Positive (%)
AE1/3, CK1	25 (100)	12 (100)	10 (100)
CAM 5.2	25 (100)	12 (100)	10 (100)
CK7	22 (88), focal	12 (100), focal	10 (100), diffuse
CK20	2 (8), focal	0 (0)	1 (10)
EMA	3 (12), focal	0 (0)	10 (100)
Keratin 903	4 (17)	7 (59), focal	9 (90)
Inhibin	17 (68)	7 (59)	0 (0)
ER	7 (28)	1 (8)	0 (0)
PR	6 (24)	1 (8)	0 (0)
AR	11 (78)	5 (100)	5 (100)
Calretinin	20 (91)	3 (100)	5 (83)
Vimentin	25 (100)	9 (90)	5 (50)
mCEA	0 (0)	0 (0)	0 (0)



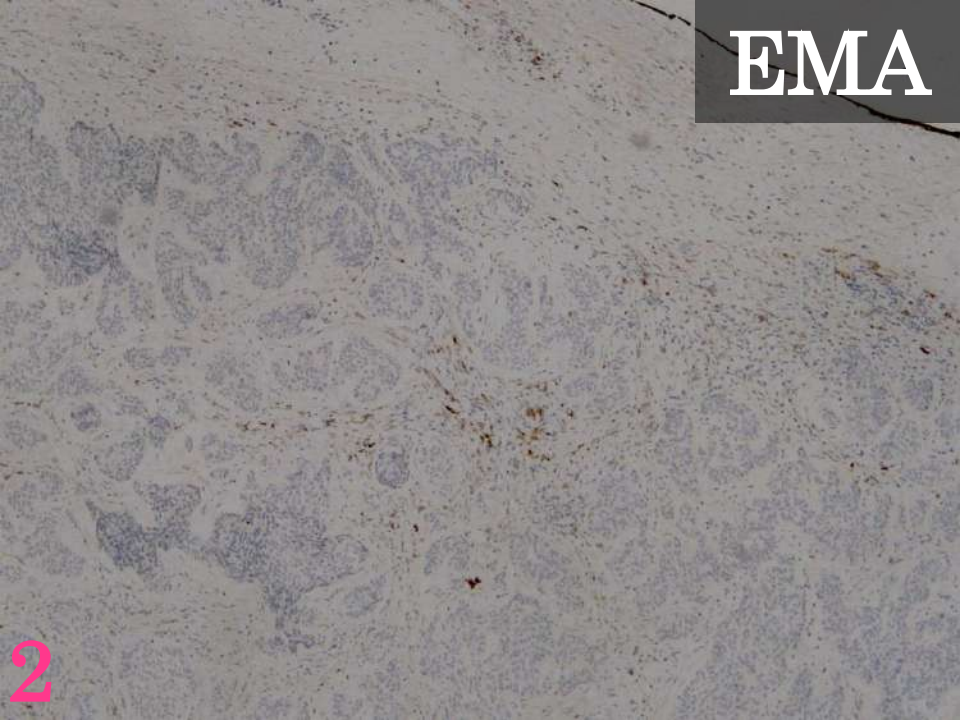
1 2
3 4



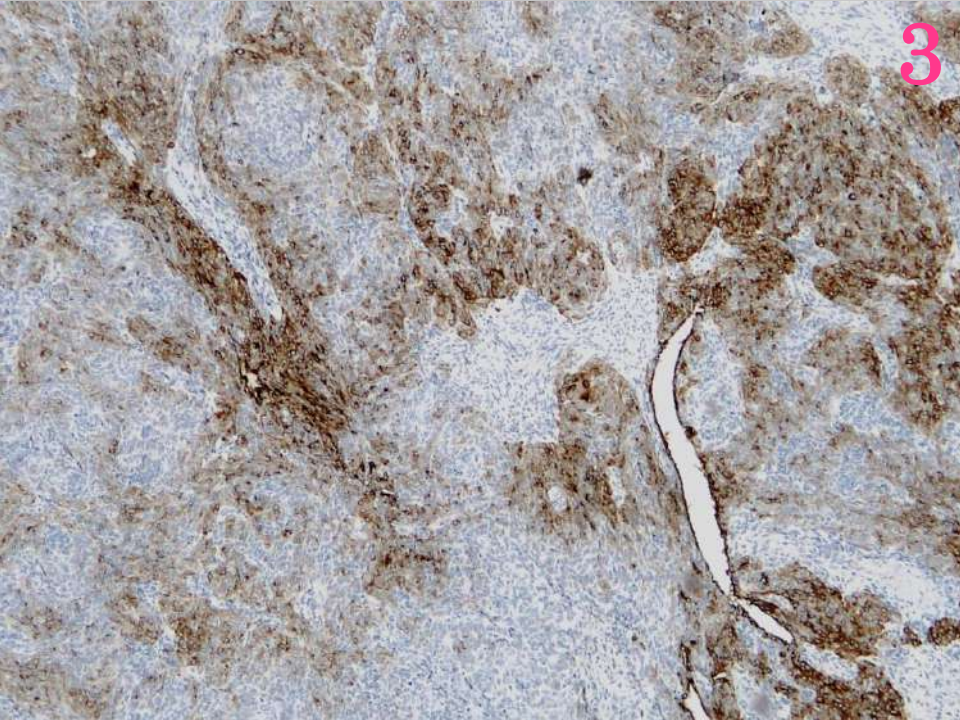
CK



1 2

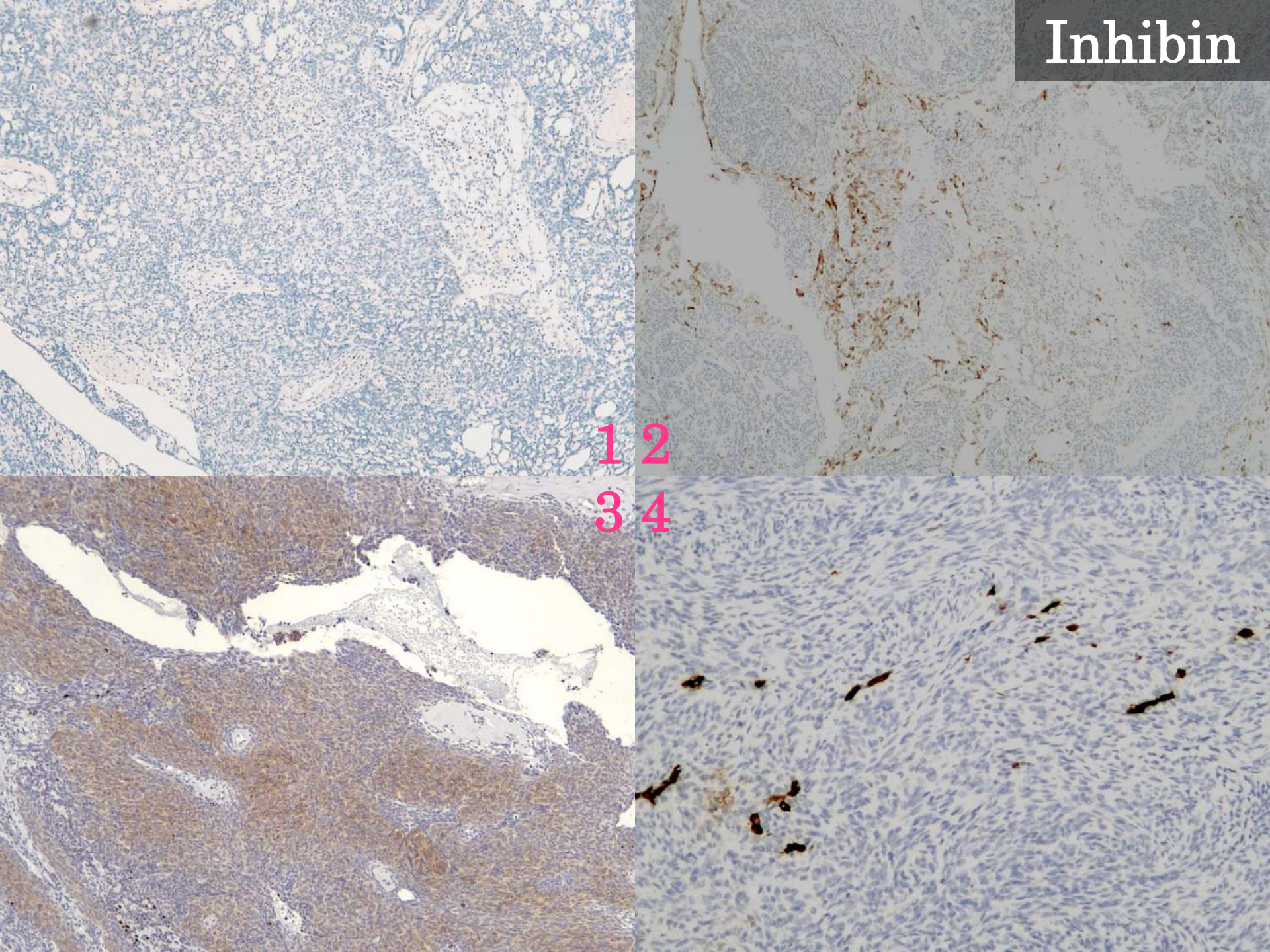


3 4

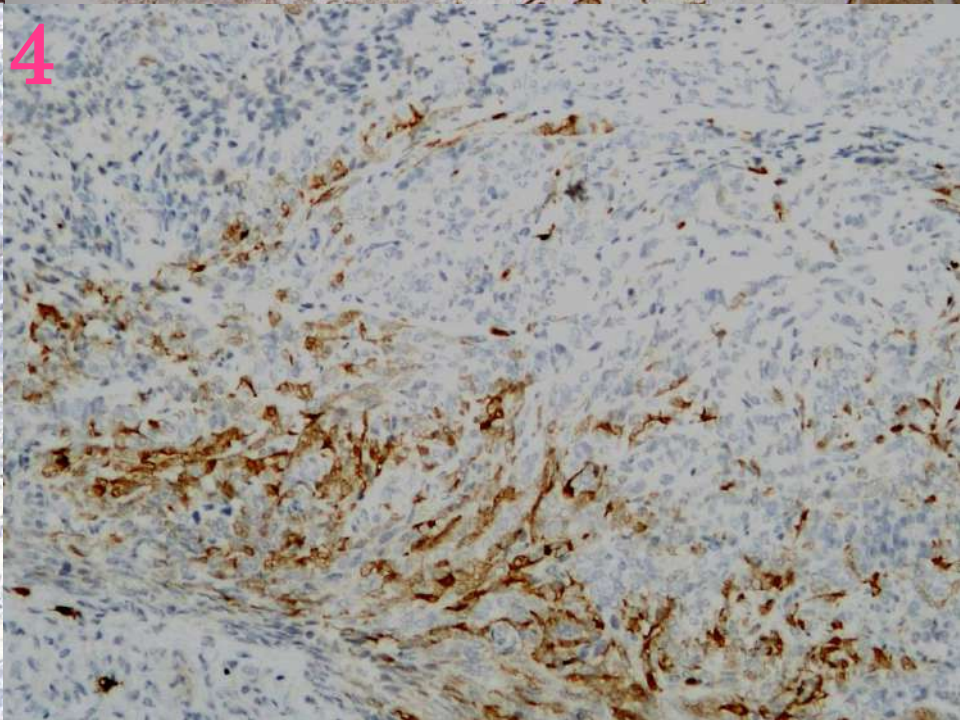
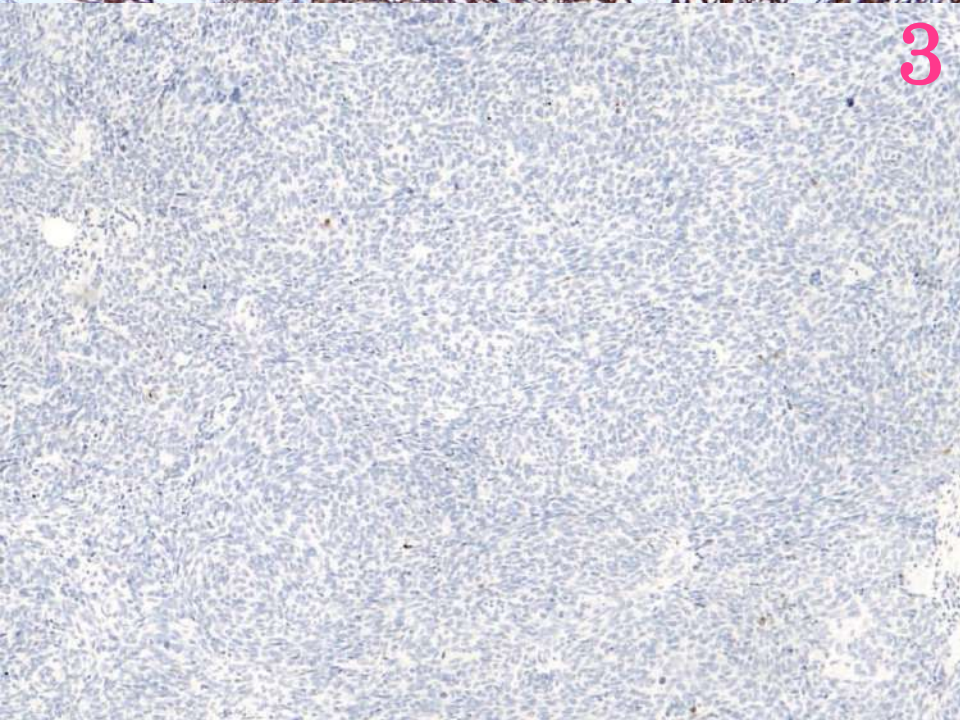
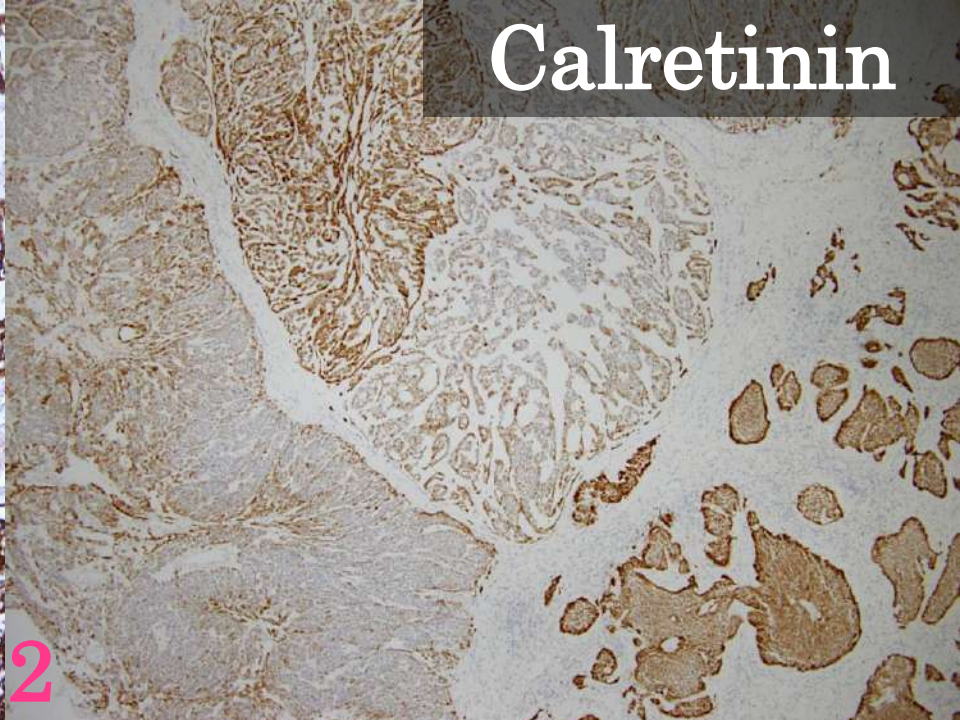
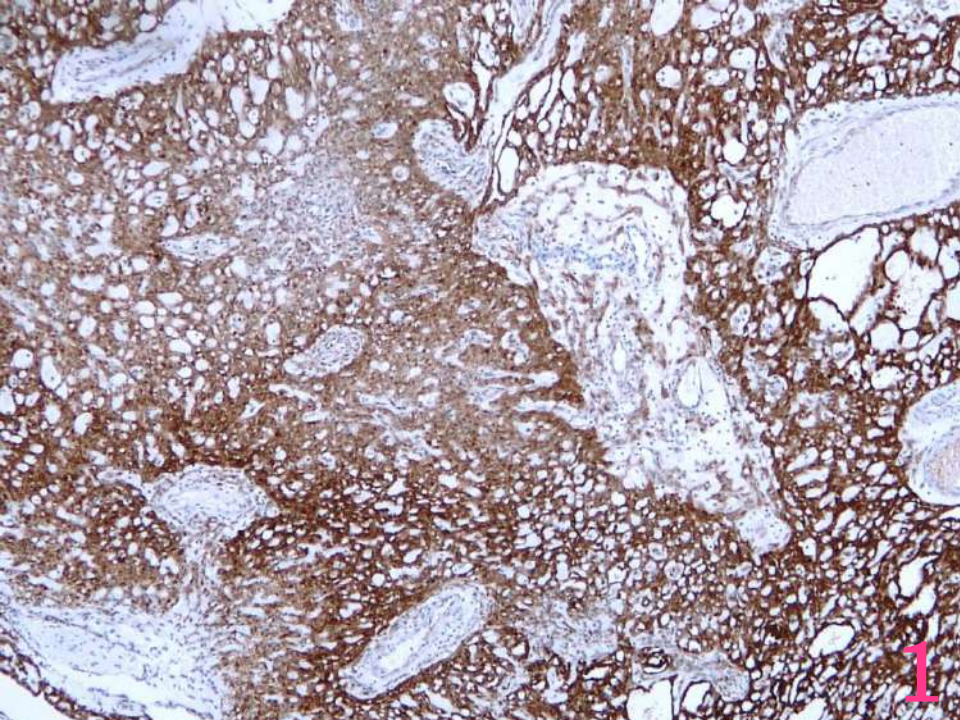


Not performed

Inhibin

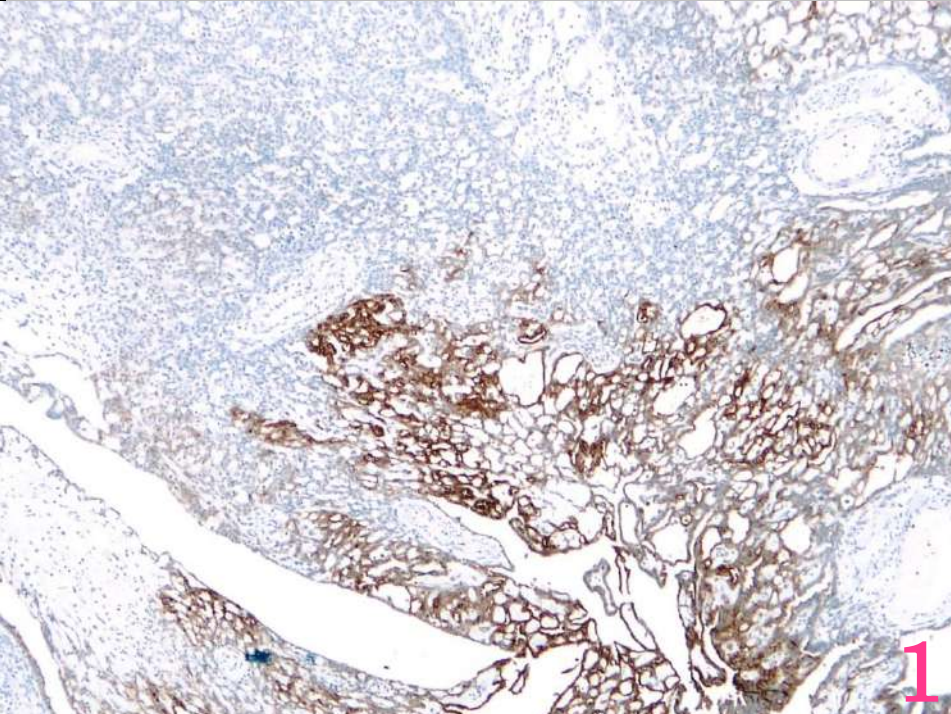


Calretinin

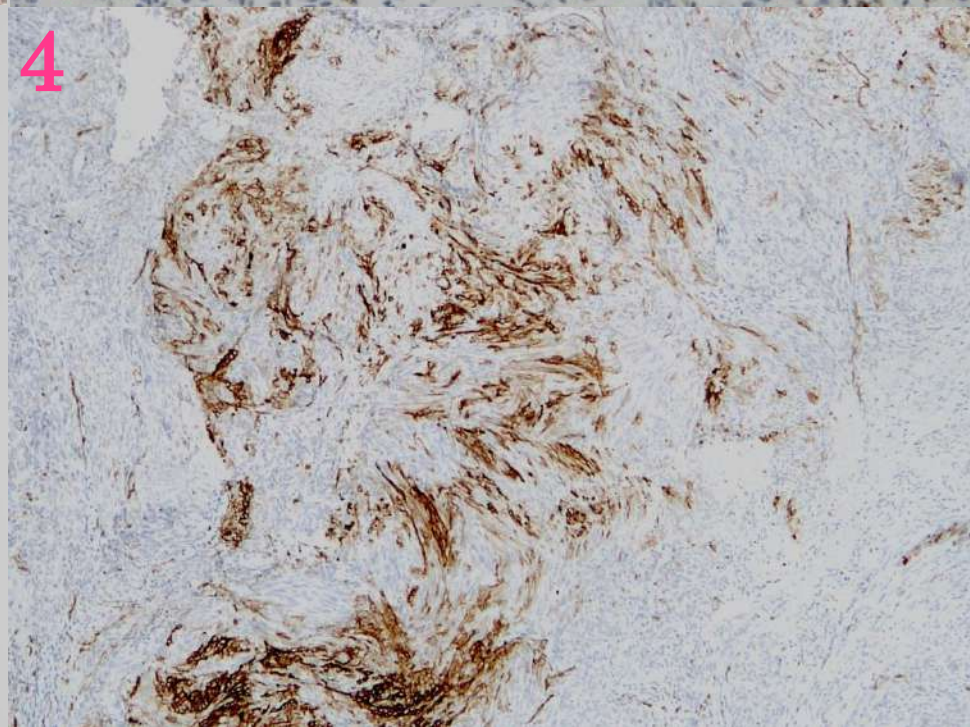
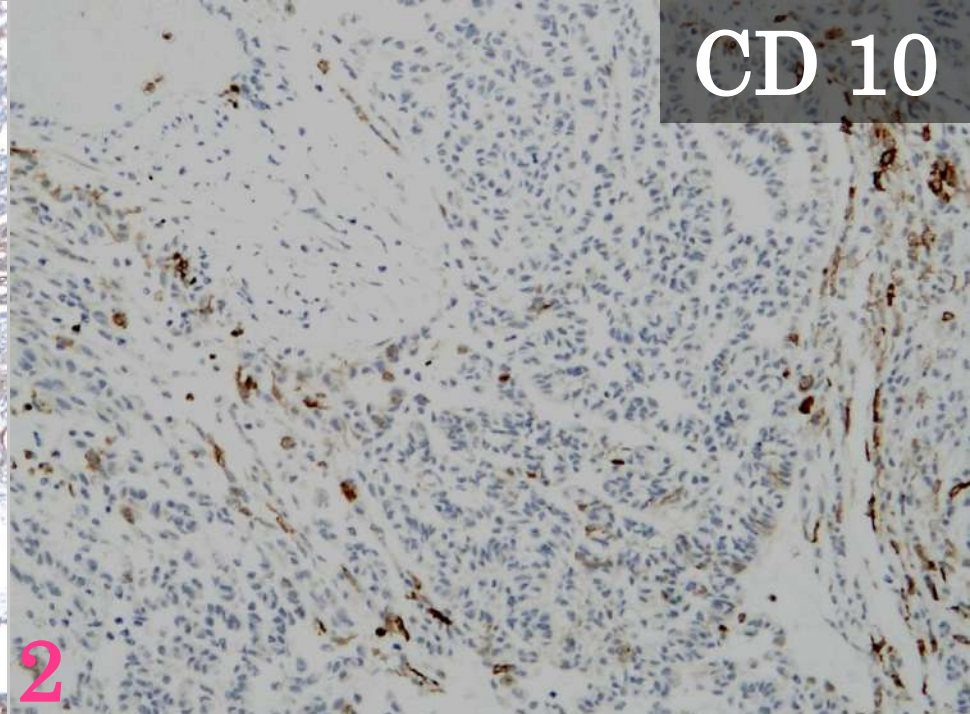


1 2
3 4

CD 10



1 2
3 4



Not available,
also positive

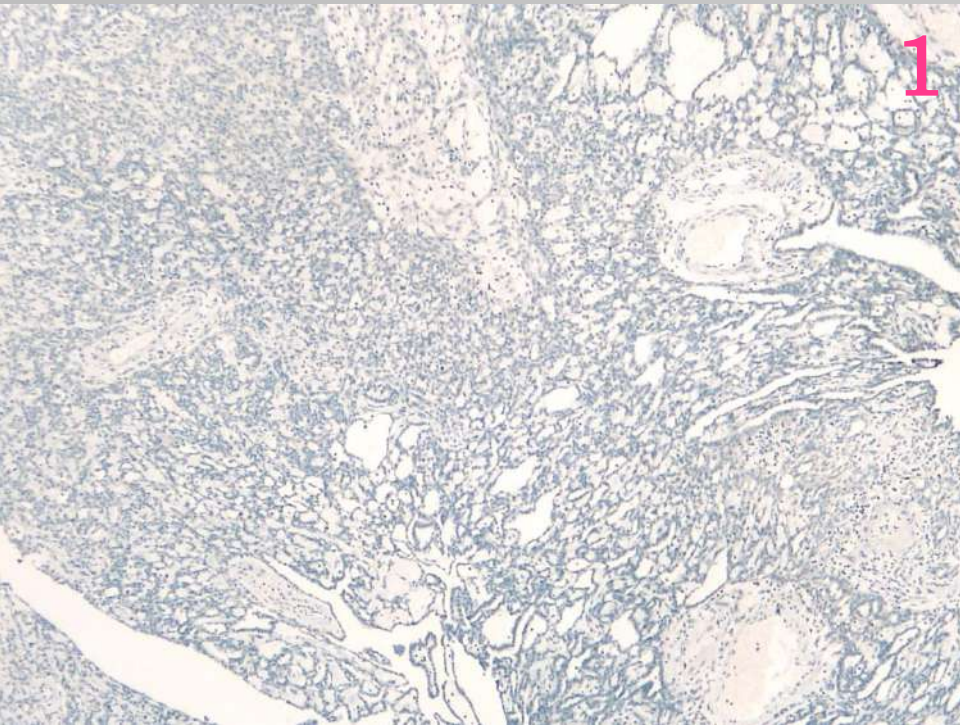
Are General Markers Helpful?

Case	1	2	3	4
CK	+	+	+	+
EMA	-	-	Focal +	/
Inhibin	-	-	Weak +	-
Calretinin	+	+	-	-
CD10	Focal +	Focal +	+	+

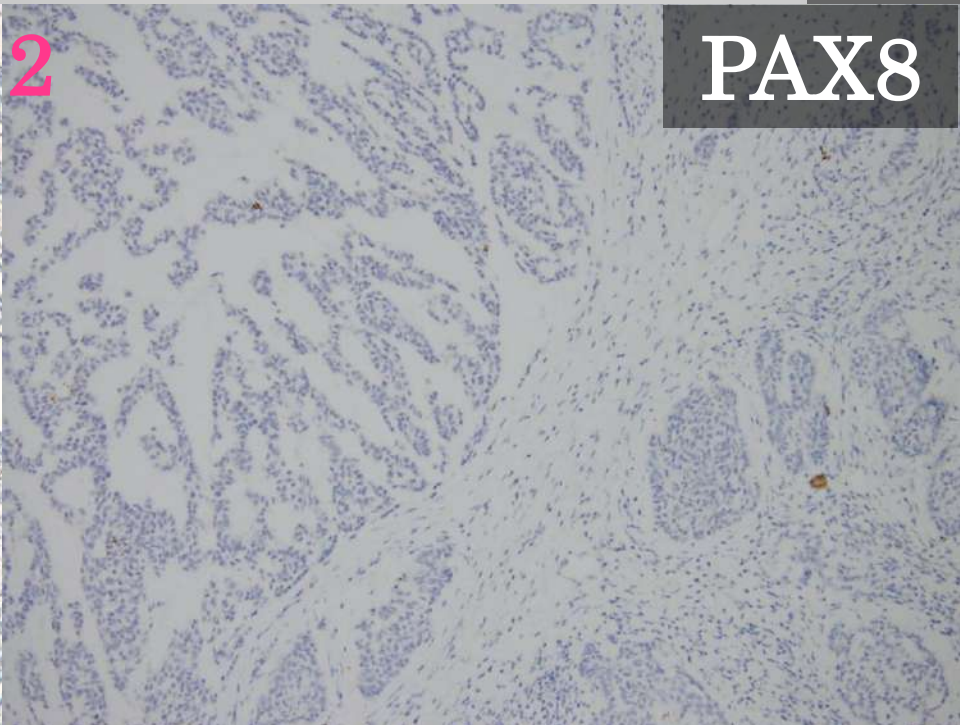
Value of PAX-8 and SF-1 Immunohistochemistry in the Distinction Between Female Adnexal Tumor of Probable Wolffian Origin and its Mimics

Abha Goyal, M.D., Ramya P. Masand, M.D., and Andres A. Roma, M.D.

Int J Gynecol Pathol Vol 35, No. 2 March 2016



1 2



PAX8

Summary in IHC profiles

- **Markers with diffuse expression**
 - Pan-CK / Calretinin / Vimentin
- **Markers with variable expression**
 - Inhibin / Hormonal marker (ER/PR) / CD10
- **Marker for differential diagnosis**
 - Inhibin / Pax-8 / CD10

A Possible Panel

- Pan-CK / Calretinin / Inhibin / CD10 / Pax-8

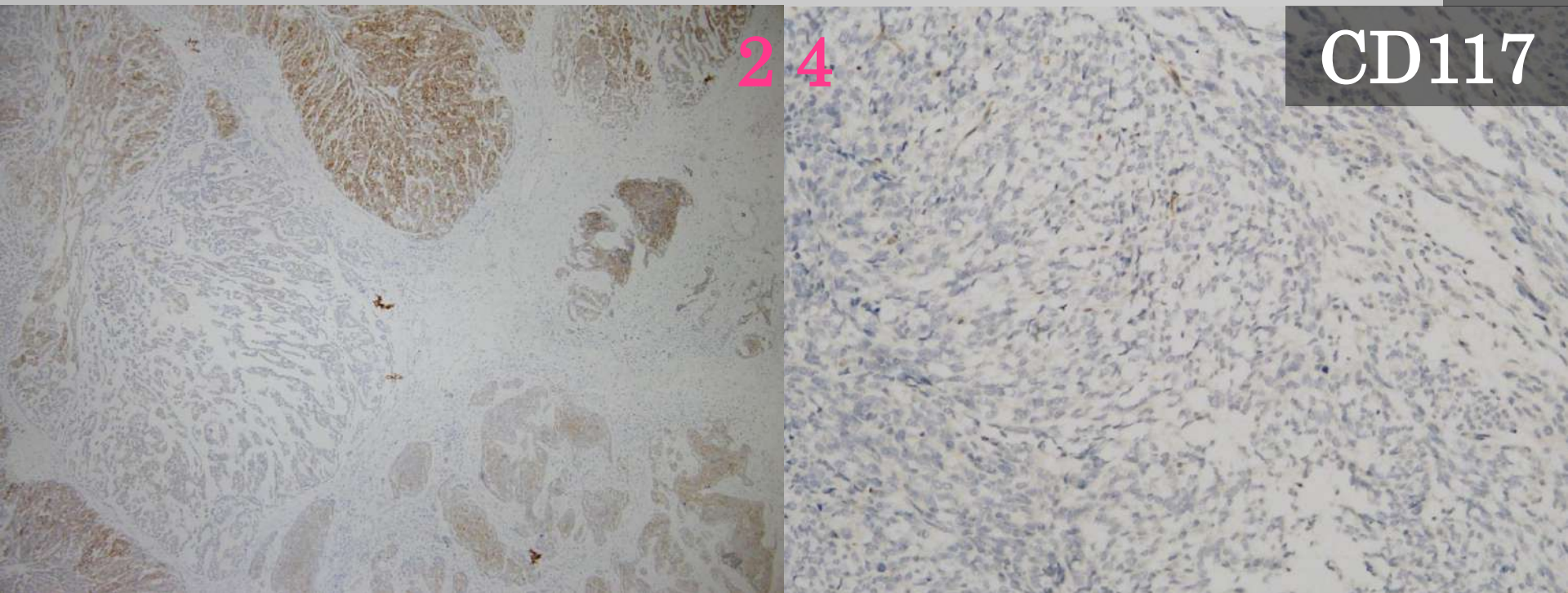
Case Report

Female adnexal tumor of probable wolffian origin: Morphological, immunohistochemical, and ultrastructural study with *c-kit* gene analysis

Oi Harada,¹ Hiroyoshi Ota,² Kimiyo Takagi,³ Hiroyuki Matsuura,⁴ Eiko Hidaka⁵ and Jun Nakayama¹

Departments of ¹Pathology, ²Biomedical Laboratory Sciences and ⁵Laboratory Medicine, Shinshu University School of Medicine, Matsumoto and Departments of ³Obstetrics and Gynecology and ⁴Laboratory Medicine, Iiyama Red Cross Hospital, Iiyama, Japan

Pathology International 2006; 56:95-100



Genetic Profiles

- CD117 (c-kit) expression: not necessarily relating to genetic mutation on c-kit and PDGFR gene (Harada, et al. Pathology International 2006; 56: 95-100)
- NGS analysis revealing FATWO a genetically heterogeneous tumor (Cossu, et al. Int J Gynecol Pathol 2017 (Epub ahead))
 - Three cases, three pathways: CTNNB1 + MET / PIK3CA / BRAF + CDKN2A

TABLE 2. NGS-based results in the cases under investigation

Case	Gene	Protein	Coding	Function	Type	Coverage	Allele Coverage
1	<i>CTNNB1</i>	p.Ser33Cys	c.98C>G	Missense	SNV	1768	C = 1090, G = 678
1	<i>MET</i>	p.Glu168Asp	c.504G>T	Missense	SNV	1986	G = 1020, T = 966
1	<i>KDR</i>	p.Gln472His	c.1416A>T	Missense	SNV	1994	A = 1036, T = 958
2	<i>BRAF</i>	p.Val600Glu	c.1799T>A	Missense	SNV	1495	T = 1324, A = 171
2	<i>CDKN2A</i>	p.Tyr129Ter	c.387C>A	Nonsense	SNV	1999	C = 1241, A = 758
2	<i>TP53</i>	p.Pro72Arg	c.215C>G	Missense	SNV	1361	C = 74, G = 1287
2	<i>KDR</i>	p.Gln472His	c.1416A>T	Missense	SNV	1055	A = 991, T = 64
3	<i>PIK3CA</i>	p.Ile391Met	c.1173A>G	Missense	SNV	1726	A = 723, G = 1003
3	<i>KDR</i>	p.Gln472His	c.1416A>T	Missense	SNV	1994	A = 971, T = 1023

Functionally unknown sequence variants are italicized.

NGS indicates next-generation sequencing; SNV, single-nucleotide variations.

Take Home Message

- FATWOs are rare and possibly misdiagnosed.
 - Identification of characteristic **Sieve-like** and **tubular** pattern would be helpful in diagnosis
- Using an IHC panel would be also helpful
 - **Pan-CK / Calretinin / Inhibin / CD10 / Pax-8**
- Heterogeneity in genetics
- No histological criterion predicting clinical behavior, and no standard treatment medication

Acknowledgement

- Dr. Chiung-Ru Lai (Taipei Veterans General Hospital)
- Dr. Tsui-Lien Mao (National Taiwan University Hospital)
- Dr. Yee-Jee Jan and Dr. Chih-Ying Wu (Taichung Veteran General Hospital)
- Dr. Wan-Lin Shen and Dr. Sheng-Tsung Chang (Chi-Mei Hospital).

Thank you for your
attention