Reporting and staging of testicular germ cell tumors. The International Society of Urological Pathology (ISUP) testicular cancer consultation conference recommendations.

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Abstract

The International Society of Urological Pathology held a conference devoted to issues in testicular and penile pathology in Boston in March 2015, which included a presentation and discussion led by the testis microscopic features working group. This conference focused on controversies related to staging and reporting of testicular tumors and was preceded by an online survey of International Society of Urological Pathology members. The survey results were used to initiate discussions, but decisions were made by expert consensus rather than voting. A number of recommendations emerged from the conference, including that lymphovascular invasion should always be reported and no distinction need be made between lymphatic or blood invasion. If lymphovascular invasion is equivocal, then it should be regarded as negative to avoid triggering unnecessary therapy. Lymphovascular invasion in the spermatic cord is considered as category pT2, not pT3 unless future studies provide contrary evidence. At the time of gross dissection, a block should be taken just superior to the epididymis to define the base of the spermatic cord and direct invasion of tumor in this block indicates a category of pT3. Pagetoid involvement of the rete testis epithelium must be distinguished from rete testis stromal invasion, with only the latter being prognostically useful. Percentages of different tumor elements in mixed germ cell tumors should be reported. Although consensus was reached on many issues, there are still areas of practice that need further evidence on which to base firm recommendations.

Introduction

Testicular germ cell tumors have an overall excellent prognosis with modern therapy, however, there are subgroups of patients, for whom the outlook is not universally positive and these patients need to be identified, advised on their prognosis and treated appropriately. Post orchidectomy, patient management is determined by a number of factors that may include histological tumor type, pathological T category (table 1), serum tumor markers (β-human chorionic gonadotrophin (β-HCG), alpha-fetoprotein (AFP)) and radiological stage category. Within AJCC Prognostic Stage Group I (testis confined) disease, microscopic assessments of parameters (some of which are reflected in the pT category), may dictate whether the patient receives adjuvant therapy and what prognostic information the patient is given about the likelihood of later disease relapse[1]. In some countries, there is an increasing trend for surveillance in Prognostic Stage Group I disease, for example, non-seminomatous germ cell tumor (NSGCT) without lymphovascular invasion (LVI) and / or a low percent of embryonal carcinoma and seminoma with or without adverse histological features such as rete testis stroma invasion or larger size (>3-4cm).

The microscopic features working group was charged with reviewing the literature and pre-existing guidelines; including those of the College of American Pathologists[2], UK Royal College of Pathologists[3] and Royal College of Pathologists of Australia[4] and subsequently making a presentation at the International Society of Urological Pathology (ISUP) conference on testicular and penile tumors held in Boston in March 2015. Based on this presentation of the evidence and discussion at the conference, recommendations regarding the reporting of various microscopic features were made. This conference differed from previous ISUP meetings, in that it was not a consensus conference, but an expert driven conference. This

reflects the relative rarity of these tumors, for which expertise is concentrated within certain centres and it is the pathologists who see these tumors on a regular basis who need to determine practice in this area. Thus voting was not undertaken as in previous conferences. Prior to the conference, an online pre-meeting survey had been circulated to ISUP members with 241 respondents and the results were used to help inform discussions (table 2). A publication examining expert testicular tumor pathologists' practice was also referred to as evidence[5].

ORCHIDECTOMY SPECIMENS

Histological Subtype

Testicular tumors should be classified according to the World Health Organization (WHO) bluebook. 97% of survey respondents were using WHO 2004[6] to classify germ cell tumors. WHO 2016 was published in early 2016 and this has superseded and replaced the 2004 version and should now be used for tumor classification[7].

Recommendation: Testicular tumors should be reported according to the WHO 2016 classification.

Tumor Elements / Types in Mixed Germ Cell Tumors

The percentage of embryonal carcinoma in a mixed germ cell tumor is predictive for occult metastases, however the literature is difficult to interpret because there are different dichotomous cut offs according to different studies. Many previous studies have found between 50 and 100% embryonal carcinoma component to be predictive of relapse across the literature[8]. Results are also inconsistent with embryonal carcinoma predominance showing no association with metastatic disease in some studies and being associated with

more frequent local extension in others[9,10]. Choriocarcinoma is also reported to be prognostic with pure and mixed forms showing similar aggressive behaviour[11,12]. Absence of yolk sac tumor is another unfavourable prognostic factor[13].

Recommendations:

Percentages of different elements in mixed germ cell tumors should be reported although there are limited data that, with the exception of extent of embryonal carcinoma, they have prognostic significance.

Germ Cell Neoplasia In-Situ (GCNIS)

98% of survey respondents stated that they did routinely report the presence or absence of GCNIS. GCNIS is not a prognostic factor, but it is seen in the great majority of germ cell tumors and therefore its absence should trigger consideration of a non-germ cell tumor, particularly a sex cord-stromal tumor or a metastasis from an extra-testicular primary site, in the proper setting.

Recommendation:

The presence or absence of GCNIS should be reported whenever possible.

Anatomic Extent

Testicular tumors should be classified by anatomic extent using the TNM staging system. 98% of respondents to the survey were using the TNM classification system. The seventh edition was in use at the time of the conference[14]. Although use of the AJCC 7th edition is still acceptable, there is the option currently of using the 8th edition criteria, but on 1st

January 2018, use of the 8th edition[1] will become mandatory. The AJCC 8th edition[1] supplants the earlier version and this is strongly recommended for use.

Recommendation:

Testicular tumors should be classified by anatomic extent of disease using the AJCC TNM 8th edition no later than 1st January 2018.

Rete testis invasion

94% of pre-meeting survey pathologists who practice some urological pathology always report rete testis invasion, but only 79% distinguish between *pagetoid involvement* or *extension* and rete *stroma invasion***.** In contrast, 96% of testicular tumor expert pathologists distinguish between pagetoid involvement and stroma invasion[5]. The fact that expert testicular tumor pathologists make this distinction in a higher rate of cases than all urological pathologists may reflect an increased awareness of its importance. In one study of 148 orchidectomy specimens of NSGCT, rete testis stroma invasion was identified in 52% (72 of 138 evaluable cases) and exclusive pagetoid spread was found in 17% (23 of 138 evaluable cases). The study found significant statistical correlation between direct rete testis stroma invasion and advanced clinical stage at presentation but no such correlation existed between pagetoid spread of neoplastic germ cells into the rete epithelium[9]. Figure 1 illustrates in-situ spread, not genuine invasion, and in many instances this probably represents contiguous spread of Germ Cell Neoplasia In-Situ (GCNIS) rather than intratubular seminoma. Figure 2, in contrast, demonstrates rete testis stroma invasion. There is no evidence to support pagetoid involvement as a prognostic factor, but there is some evidence to support rete testis stroma invasion as a worse prognostic factor,

especially in seminoma, although the literature is not entirely consistent. In one pooled analysis of 4 large cohort studies of seminoma, rete testis invasion conferred a 1.7x increased risk of recurrence, and if the tumor was >4cm in size and rete testis stroma invasion was present, there was a 3.4x increased risk of recurrence[13]. For NSGCT, there is limited evidence of rete testis stroma invasion as an adverse prognostic factor[9]. The literature is confounded by many studies that do not distinguish between pagetoid spread and stroma invasion of the rete testis. Future studies should seek to address this issue and provide high level evidence to determine if rete testis invasion should become part of staging; currently it is not a component of TNM 8th ed[1].

Recommendations:

Involvement of the rete testis should be reported in testicular tumor specimens.

Pagetoid involvement of the rete epithelium should be distinguished from invasion of the rete stroma

Hilar soft tissue invasion

The hilar soft tissue and rete testis together comprise the hilum of the testis. The hilar soft tissue is a zone of adipose tissue and vessels beyond the rete testis, but before the base of the cord is reached and is adjacent to the head of the epididymis (figure 3). Hilar soft tissue invasion, as shown in figure 4, is the most common site of extratesticular extension in both seminomas and NSGCT[15,16]. In a study of 447 orchidectomies, tumor extension into hilar soft tissues was found in 25% (113/447) cases[17]. In 81% of those cases, extratesticular extension into hilar soft tissues occurred via direct invasion of the rete testis due to close anatomic proximity. The study underscores the significance of adequate sampling of the testicular

hilum at the time of gross dissection[17]. Studies on the value of hilar soft tissue invasion as an adverse factor are relatively few and focus on metastasis at presentation rather than later disease relapse. In one study, on multivariate analysis, both rete testis and hilar soft tissue invasion were strong independent predictors of metastasis at presentation[9]. Despite evidence of potential significance as an adverse factor, there has not been up until now clear guidance on how to categorise these cases. Since the hilum lacks tunica vaginalis, in cases with no LVI, this type of hilar spread may represent a potential under staging pitfall. In one study, half of the cases showing hilar extension were regarded as pT1, using the 2010 AJCC TNM staging[17]. In the pre-meeting survey, general urological pathologists were asked how they would stage hilar soft tissue invasion, with the following responses: 48% T1, 25% T2, 27% T3. In a survey by urological pathologists with specialized expertise in testicular pathology, the responses were 40% T1, 36% T2, 24% T3[5]. This is a difficult area due to relatively limited evidence, T1 is likely an under staging, but T3 (recommended by some guidelines) likely over staging. Following discussion at the conference, it was proposed that T2 is an appropriate compromise on category until more definitive evidence becomes available and this is the assigned pT category in the AJCC TNM 8th edition[1].

Recommendation:

The presence of hilar soft tissue invasion should be reported and is reflected as category pT2 in the 8th edition of AJCC TNM [2016]

Epididymis invasion

In the pre meeting survey, pathologists were asked how they would stage epididymis invasion and the results were: 83% T1, 14% T2, 3% T3. At the time of the conference, the 7th

edition of TNM was in use[14]. The responses may have been biased by the wording of the question, in that using TNM7, it would have been pT1 category. It was discussed at the conference, that although evidence is limited, based on expert consensus opinion, epididymis invasion probably represents relatively aggressive disease, being only infrequently seen and usually in the context of an otherwise locally infiltrative tumor (figure 5). Furthermore, as one can usually only see epididymal invasion following hilar soft tissue invasion, and the latter was considered pT2 (as detailed above) it was agreed that pT2 category is an appropriate designation for epididymal invasion and this is the assigned category in the AJCC TNM 8th edition[1].

Recommendation:

The presence of epididymal invasion should be reported and is reflected as category pT2 in the 8th edition of AJCC TNM [2016].

Tunica Vaginalis Invasion

The tunica vaginalis (TV) is composed of two mesothelial layers; an inner (visceral) and outer (parietal) layer (figure 6). Tumor involving the TV confers a pT2 category in the TNM 8th ed. Pathologists have previously been inconsistent as to whether involvement of either layer of the TV would result in a pT category of pT2, or only invasion of the outer TV constitutes pT2. In the pre meeting survey, pathologists were asked how they would stage tumor invading only the inner serosal lining of the testis in the absence of vascular invasion and the results were: 61% T1, 38% T2, 1% T3. In a survey of experts, the results were: 52% T1, 48% T2[5]. It is therefore clear that previously there was no consensus on whether invasion of the inner TV represents pT2 disease. It was noted that this is a rare route of extratesticular extension

(only 2% cases in one study) and therefore of dubious significance[17]. The value of TV invasion as a prognostic factor shows very little support in the literature. No recommendation was made at the conference as to whether involvement of the inner serosal TV is T2, or just the outer TV. However, in the AJCC TNM 8th edition, involvement of the visceral mesothelial layer (inner TV) will be regarded as pT2[1]. To regard the tunica vaginalis as involved, the mesothelial layer must be perforated, which again is a rare finding (figures 7 and 8). As the outer (parietal) TV can usually only be involved if there is direct invasion through the inner layer, involvement of either layer is pT2.

Recommendation:

Tumour involvement of the visceral (inner) tunica vaginalis should be reported and penetration of this mesothelial layer is considered category pT2 in the 8th edition of AJCC TNM (2016).

Spermatic Cord Invasion

Spermatic cord invasion is direct invasion of the cord, with or without LVI, and warrants a pT3 category in the TNM 8th edition. As discussed below, LVI in the cord without stromal invasion is pT2 category. Where the base of the cord is located was discussed at the conference. Tumor extending beyond the hilum to involve the spermatic cord is considered pT3. Just superior to the head of the epididymis (the epididymis is not part of the spermatic cord) a cross section of the base of the cord can be sampled and visualized and if there is direct invasion in this block by tumour, then this is considered pT3. The distinction of the base of the cord from hilar soft tissue is an anatomical one and needs to be identified macroscopically at the time of gross dissection, microscopically, the landmark is difficult to

see. If the tumor microscopically is adjacent to or surrounds the vas deferens, this is also considered to be spermatic cord invasion[1]

The presence of a tumor deposit in the upper cord in the setting of a tumor confined to the testis with vascular invasion was discussed. 76 % of pre meeting survey respondents would have called this scenario T3 with 21% staging this as T2 with a soft tissue deposit and 3% opted for 'other'. There is limited literature on this topic. In the one published abstract, it showed that these foci are strongly associated with vascular invasion[18]. There was no recommendation on how to stage this scenario made at the conference, although it is a relatively uncommon situation. In the AJCC TNM 8th ed, it is considered as pM1 category[1], but clearly there is a lack of data on this issue and it needs further study.

Recommendation:

Direct involvement of the spermatic cord should be reported and this is considered category pT3 whereas a discontinuous tumour deposit in the cord is pM1 (AJCC TNM 8th edition 2016).

Lymphovascular invasion

Almost all pre-meeting survey respondents reported that they always report the presence or absence of blood vessel invasion. The majority of studies show that LVI correlates with the other factors determining pT2 disease (ie tunica vaginalis invasion), metastatic disease at presentation[10,19,20] and / or relapse[21-30]. Most studies do not discriminate between lymphatic and blood vessel invasion. Some studies specifically found that lymphatic and not blood vessel invasion was associated with prognosis[31] and some found that blood vessel and not lymphatic invasion was prognostic[32]. In the pre-meeting survey, 77% of respondents did not distinguish between lymphatic or blood vessel invasion.

Recommendation:

Lymphovascular invasion should be documented in all testicular cancer cases. Distinguishing between lymphatic and blood vessel invasion is not required.

Accurate assessments of the presence or absence of LVI in Prognostic Stage Group I NSGCT is essential as this is one of the few areas of testicular germ cell tumor practice where we have strong evidence that a microscopic feature confers adverse prognosis. Most studies show LVI to be prognostic for NSGCT, but in the few studies looking at seminomas the data are not as clear[33-35]. The potential reasons for the difference between seminoma and NSGCT include that LVI is more common in NSGCT than seminoma, adverse events are more common in NSGCT and the presence of frequent implantation artefact in seminoma makes assessment difficult and error prone. The presence of LVI in Prognostic Stage Group I NSGCT may determine if the patient receives adjuvant chemotherapy. With an increasing trend for more surveillance in seminoma and less clear evidence of benefit for adjuvant therapy, the distinction in seminoma is of lesser importance. It was discussed at the meeting why we do not have a split staging system for seminomas and NSGCT with LVI only factoring in the NSGCT system, but the consensus was that there was insufficient evidence at present to recommend altering the staging system and LVI should continue to be reported in all germ cell tumors regardless of whether they are seminoma or NSGCT. We should continue to drive for high level evidence of LVI as a prognostic factor in seminoma.

The assessment of LVI is often difficult and it was discussed whether routine use of immunohistochemistry (IHC) could improve reproducibility. IHC is not routinely performed as typically the problem is not whether tumor is in a vessel or not, but whether it is artifactually displaced tumor or genuine.

Recommendation:

Immunohistochemical markers may be used as adjuncts to determine the presence of lymphovascular invasion however their usage is not mandatory.

LVI assessment is often difficult and it was discussed whether if the assessment is made by a central laboratory pathologist who regularly sees high volumes of germ cell tumor cases, this could increase reproducibility. In one study 27% cases on review at a central pathology laboratory were reclassified as LVI and 19% were reclassified as no LVI and only the central pathology LVI correlated with node metastases[36].

Pitfalls in identifying LVI include histiocytes in cord vessels, and proper sampling since the best places to look for genuine LVI are at the periphery of the tumor and in the tunica albuginea (figures 9-11). LVI tends to be over diagnosed in seminoma due to implantation artefact in the adjacent non-tumoral parenchyma. Features thought to be representative of true LVI are shown in table 3 and representative images of genuine and non-genuine LVI are shown in figures 12-15. LVI can be intra-parenchymal, in the cord or in the tunica; all count as pT2. In the pre-meeting survey, pathologists were asked what stage they would assign to LVI in the cord (distant to the tumor) and with no cord stromal invasion. 78% considered this category T2 and 22% T3. Although no publications specifically have studied this issue to date, LVI in cord vessels is currently regarded as pT2 disease and not pT3 (which is reserved for direct invasion into the cord).

60% of pathologists in the pre-meeting survey did not report the type of tumor involved in LVI in mixed NSGCT and no recommendation was made on this. There is no evidence on this issue.

Recommendations:

If LVI is equivocal, one should regard the LVI status as negative to avoid unnecessary adjuvant chemotherapy in pT1 disease.

LVI in the cord is pT2 category and not pT3 (which is reserved for direct invasion into the cord).

RETROPERITONEAL LYMPH NODE DISSECTION (RPLND)

The careful microscopic analysis and reporting of retroperitoneal lymph node dissections is important for prognostic and therapeutic reasons. There are 3 main features to observe – residual, viable, non-teratomatous germ cell tumor, teratoma and scar/necrosis. These findings may be alone or in combination. The presence of any amount of viable non-teratomatous germ cell tumor is an adverse prognostic factor and may mandate additional systemic therapy. Scars/necrosis and teratoma on its own regardless of the level of immaturity or degree of cytologic atypia have a favourable prognosis[37]. If however, the teratoma is associated with a non-germ cell somatic malignancy, the outcome is generally adverse[38]. Additionally, in the rare situation where a cystic trophoblastic tumor has been identified, this is associated with a favourable prognosis[39].

The prognostic significance of the number of positive lymph nodes (LNs), fraction of positive LNs and the presence of extranodal extension is unclear from the literature currently available[40, 41].

Recommendations:

1. The retroperitoneal lymph node dissection report should clearly identify the presence or absence of viable non-teratomatous germ cell tumor and scar/necrosis.

2. The number of positive lymph nodes, fraction of positive lymph nodes and the presence of extranodal extension should be reported recognizing that the prognostic significance of these observations is unclear.

DIAGNOSTIC AND PREDICTIVE BIOMARKERS

Predictive Markers, Immunohistochemistry and i(12p) testing by fluorescence in situ hybridization (FISH)

The use of immunohistochemistry is not discussed in this paper as there is an excellent ISUP published summary[42]. The indications for i(12p) testing by FISH or other appropriate molecular assay are distinction of pre-pubertal type teratomas versus malignant teratomas in a post-pubertal male and in some cases to determine in an extra-testicular site whether a carcinoma or sarcoma is a somatic type malignancy arising in a malignant germ cell tumor. Post-pubertal type teratoma often has an isochromosome of the short arm of chromosome 12 – i(12p) or other forms of 12p amplification on FISH testing, but these determinations should prove negative in pre-pubertal type teratoma, pre-pubertal type yolk sac tumor and spermatocytic tumor. Spermatocytic tumor instead shows gains of chromosome 9 and less frequent gains of chromosomes 1 and 20 with partial loss of chromosome 22[43]. i(12p) status may be diagnostically helpful in select cases where these tumors need to be confirmed or ruled out. There are no predictive or prognostic markers in testicular germ cell tumors that are applicable in routine clinical practice.

Recommendation:

i(12p) may be a useful additional diagnostic tool in certain scenarios.

Summary

This paper provides clarity on several difficult areas of testicular tumor practice and identifies areas which remain unclear and require further study.

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Figure Legends

Figure 1

Pagetoid involvement or extension into the rete testis epithelium of germ cell neoplasia in-situ (GCNIS)/seminoma cells.

Figure 2

Rete testis stroma invasion by seminoma

Figure 3

A low power view of normal testicular hilum. Note the close anatomical proximity of the intratesticular component of the rete testis and highly vascular extratesticular connective tissue, referred to as hilar soft tissue.

Figure 4

Seminoma invading into hilar fat.

Figure 5

Invasion of the epididymis by embyronal carcinoma.

Figure 6

Shows the 2 mesothelial layers of the tunica vaginalis; the inner (visceral) layer lies immediately on top of the tunica albuginea and there is also an outer (parietal) layer.

Figure 7

In figure 7, although seminoma cells are bulging the inner (visceral) tunica vaginalis, there is no perforation of the mesothelial layer and this would therefore not be considered tunica vaginalis involvement.

Figure 8

In figure 8, by contrast with figure 7, there is perforation of the mesothelial layer and this would be considered tunica vaginalis involvement.

Figure 9

A pitfall in identifying LVI in cord vessels is the presence of intravascular histiocytes. If this cannot be resolved on morphology alone, then IHC, such as a CD68 stain for histiocytes can be undertaken for confirmation (small insert).

Figure 10

Atypical histiocytes may be present within vessels and the case may require IHC to definitively exclude tumor cells (atypical histiocyte arrowed).

Figure 11

Cohesive atypical cells adherent to the wall in cord vessels, typical of true LVI by seminoma. This was confirmed by nuclear OCT3/4 positive staining on IHC (small insert).

Figure 12

An examples of genuine lymphovascular invasion. There is seminoma invading into the wall of a blood vessel. Tumor is adherent to the wall and thus genuine.

Figure 13

An example of genuine lymphovascular invasion. Embryonal carcinoma is present within fibrinous thrombus and thus is genuine lymphovascular invasion.

Figure 14

An example of implantation artefact ie non genuine lymphovascular invasion. The implantation artefact by seminoma is severe and tumor is dispersed all over the tissue section.

Figure 15

An example of implantation artefact ie non genuine lymphovascular invasion. The smear artefact is less marked than figure 14, but there are implanted cells on the tunica vaginalis surface, which is a helpful guide that the discohesive cells within the blood vessel (arrowed) are also an artefact.

Table legends

Table 1: The AJCC TNM 8th edition staging system for testicular tumors

Table 2: Results of pre-meeting survey questions and meeting recommendations

Table 3: Morphological features of true lymphovascular invasion

Table 1 AJCC TNM 8th ed[1]

Pathological T (pT)

pTx primary tumor cannot be assessed
pT0 No evidence of primary tumor
pTis Germ Cell Neoplasia In-Situ
pT1 Tumor limited to testis (including rete testis invasion) without lymphovascular invasion

- pT1a Tumor smaller than 3cm in size*
- pT1b Tumor 3cm or larger in size*

pT2 Tumor limited to testis (including rete testis invasion) with lymphovascular invasion
OR
Tumor invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of tunica albuginea with or without lymphovascular invasion.

pT3 Tumor invades spermatic cord with or without lymphovascular invasion.

pT4 Tumor invades scrotum with or without lymphovascular invasion

*Subclassification of pT1 only applies to pure seminomas. NSGCT and mixed germ cell tumors are excluded

Pathological N (pN)

pNx Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis with a lymph node mass 2cm or smaller in greatest dimension and less than or equal to five nodes positive, none larger than 2cm in greatest dimension.
pN2 Metastasis with a lymph node mass larger than 2cm but not larger than 5cm in greatest dimension: or more than five nodes positive, none larger than 5cm: or evidence of extranodal extension of tumor
pN3 Metastasis with a lymph node mass larger than 5cm in greatest dimension

Definition of distant metastasis (M)

M0 No distant metastasis
M1 Distant metastasis

- M1a Non-retroperitoneal nodal or pulmonary metastases
- M1b Non-pulmonary visceral metastases

Table 2

Results of pre-meeting survey questions and meeting recommendations

Question	Results (%)	Results (absolute numbers)	Recommendations
System used to classify germ cell tumors? WHO 2004 BTTP Earlier WHO BTTP and WHO	 97 <1 <1 2	 226 1 1 4	WHO 2016 should be used to classify germ cell tumours (this was not published at the time of the conference).
Always use the TNM staging classification? Yes No	 95 5	 219 11	Testicular tumors should be classified by anatomic extent of disease using the AJCC TNM 8th edition no later than 1st January 2018.
Routinely report the presence of germ cell neoplasia in-situ (GCNIS) ? Yes No	 98 2	 226 4	Report the presence or absence of GCNIS whenever possible
Always report whether vascular invasion is present or absent? Yes No	 100 0	 227 1	Always report whether lymphovascular invasion (LVI) is present or absent.
Distinguish between lymphatic and blood vessel invasion ? Yes No	 23 77	 54 176	Distinguishing between blood vessel and lymphatic invasion is not required
Report the type of tumor involved in LVI ? Yes No	 40 60	 93 137	No recommendation

Stage of blood vessel invasion in cord – T2 or T3 ? T2 T3	 78 22	 180 50	LVI in the cord is assigned a category of pT2 and not pT3
Always report rete testis invasion ? Yes No	 94 6	 217 15	Always report rete testis invasion
Distinguish between pagetoid and stroma invasion? Yes No	 79 21	 184 48	Pagetoid involvement of the rete epithelium and invasion of the rete stroma must be distinguished
How would you stage hilar fatty tissue invasion adjacent to the epididymis, no LVI? T1 T2 T3	 48 25 27	 108 57 62	The presence of hilar soft tissue invasion should be reported and is reflected as category pT2 in the 8th edition of AJCC TNM [2016]
How would you stage epididymis invasion, no LVI ? T1 T2 T3	 83 14 3	 190 32 7	The presence of epididymal invasion should be reported and is reflected as category pT2 in the 8th edition of AJCC TNM [2016]
How would you stage tumor invading inner serosal lining of testis, not the outer layer, no LVI ? T1 T2 T3	 61 38 1	 139 86 3	No recommendation made at the conference. AJCC TNM 8th ed clarifies that involvement of the visceral mesothelial layer is assigned a category of pT2
How would you stage tumour deposit in the			No recommendation made.

upper cord with separate tumor confined to testis, LVI present? T2 with soft tissue deposit T3 Other	 21 76 3	 49 174 7	In AJCC TNM 8th ed, this is assigned an M1 category.
Do you always report the percentages of different tumor types ? Yes No Only % embryonal Other	 94 4 <1 1	 216 10 1 3	Percentages of different elements in mixed germ cell tumors should be reported although there are limited data that, with the exception of extent of embryonal carcinoma, they have prognostic significance

Table 3

Morphological features of true lymphovascular invasion

•Tumor occupies a lymphovascular structure lined by flattened endothelial cells.

•The cluster may not conform to the exact shape of the vascular lumina.

•Associated fibrinous thrombosis and or mural attachment and re-endothelialization.

•Lack of obvious background artifactual deposition of germ cell tumor cells on the tunical surface.

•Cluster is more cohesive and has a rounded smooth edge.

•Cluster looks markedly different in its architecture from surrounding tumor.

•The LVI may be peripheral or intratumoral, both count as T2

Table legends

Table 1: The AJCC TNM 8th edition staging system for testicular tumors

Table 2: Results of pre-meeting survey questions and meeting recommendations

Table 3: Morphological features of true lymphovascular invasion

Figure 1

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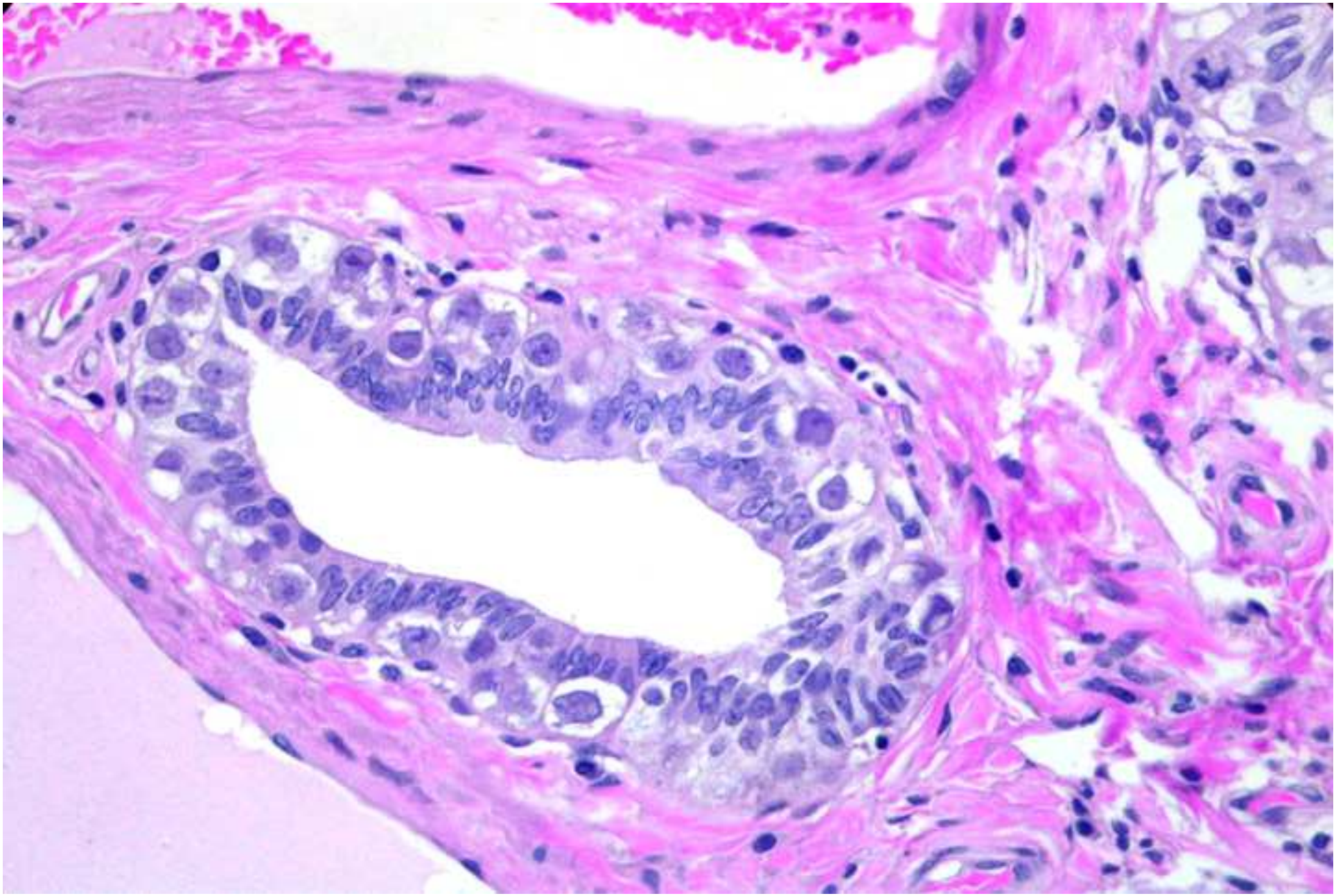

Figure 2

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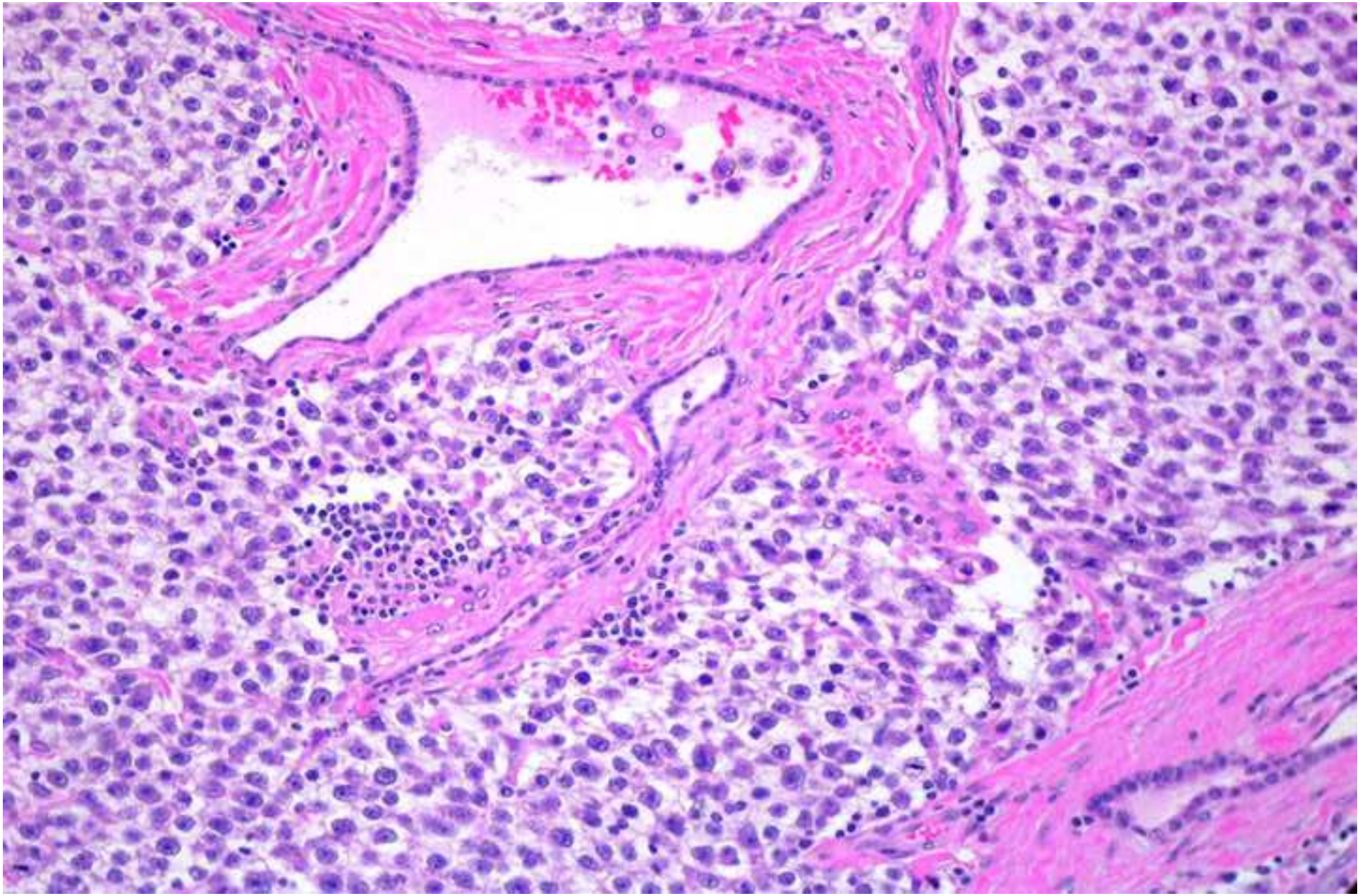

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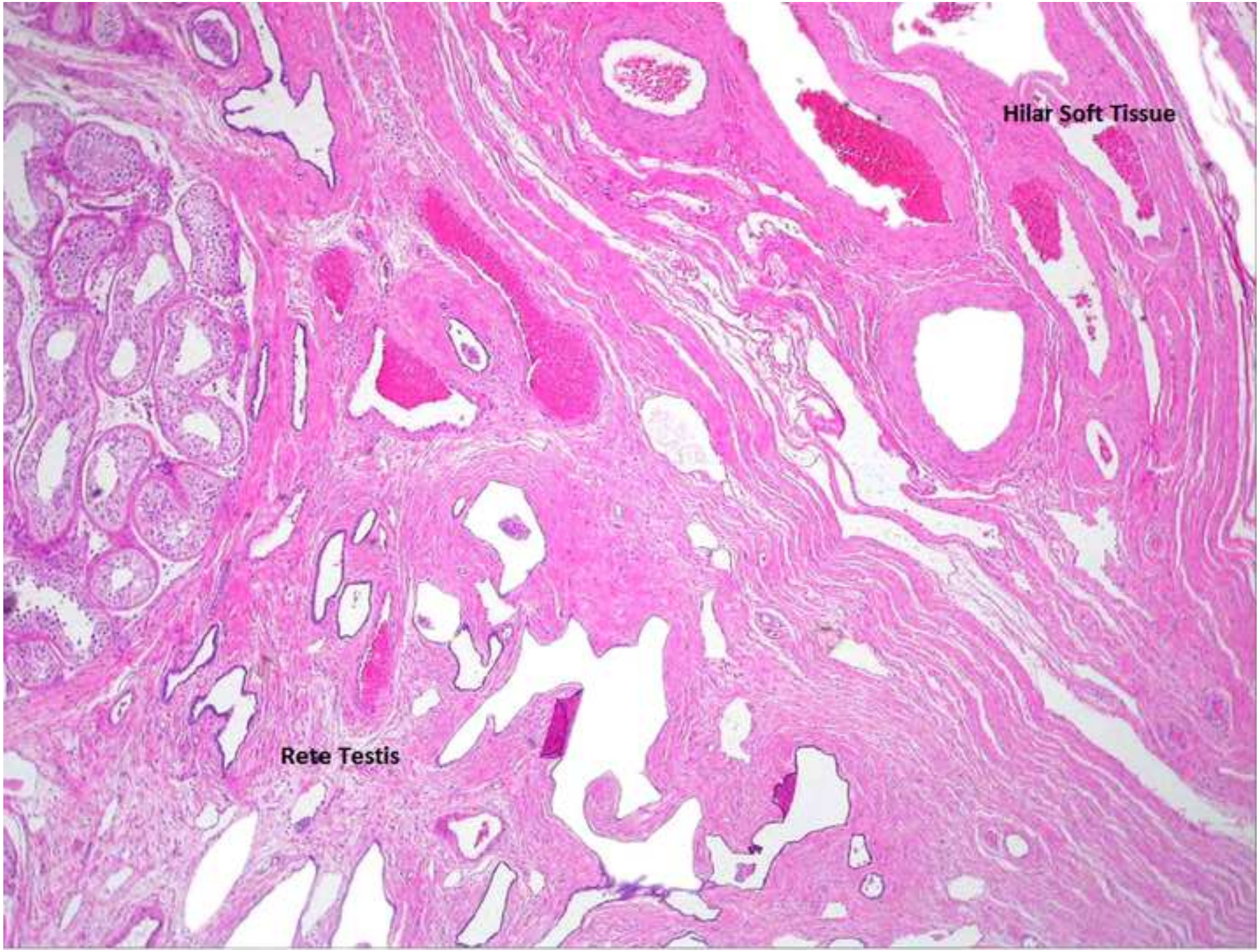

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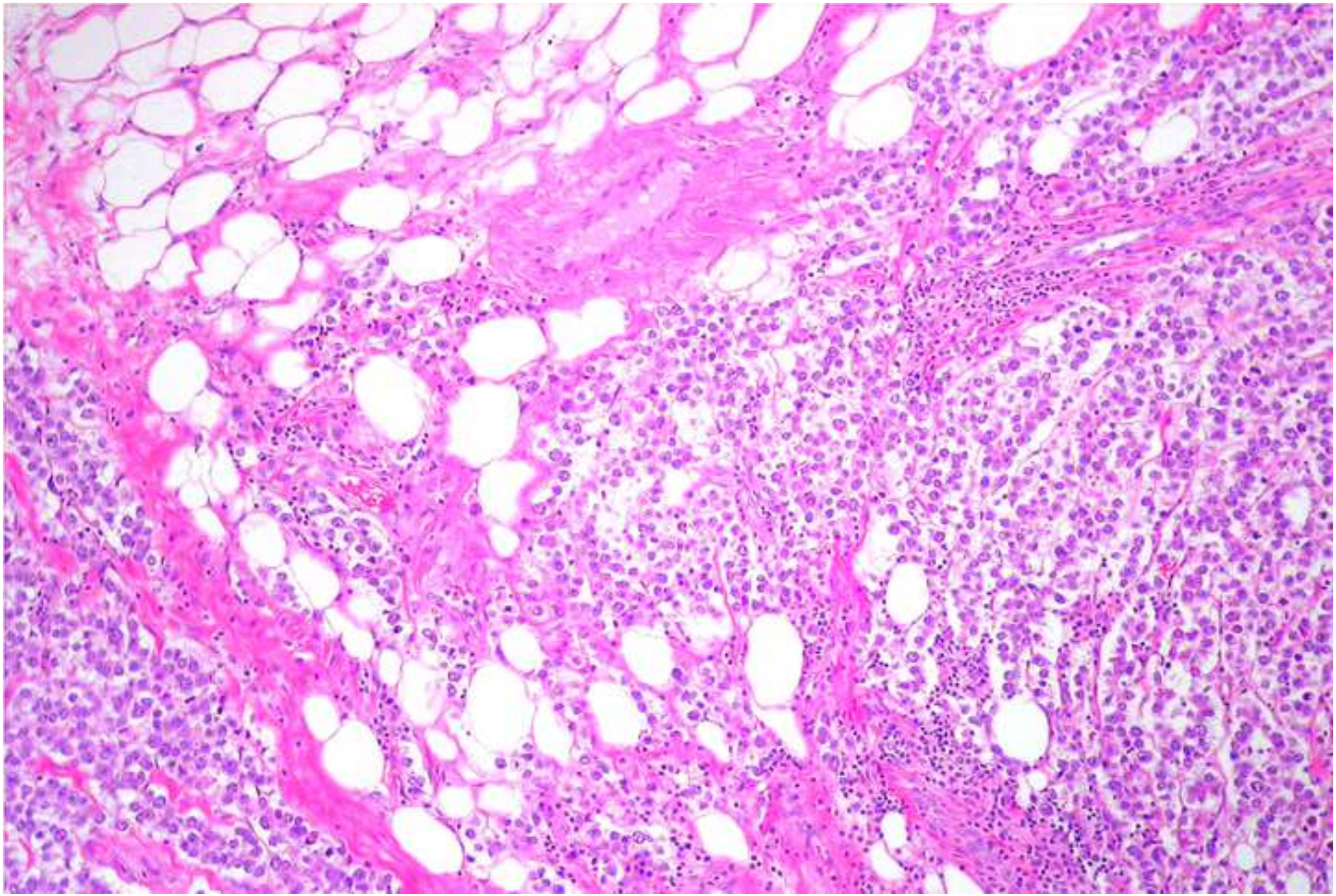

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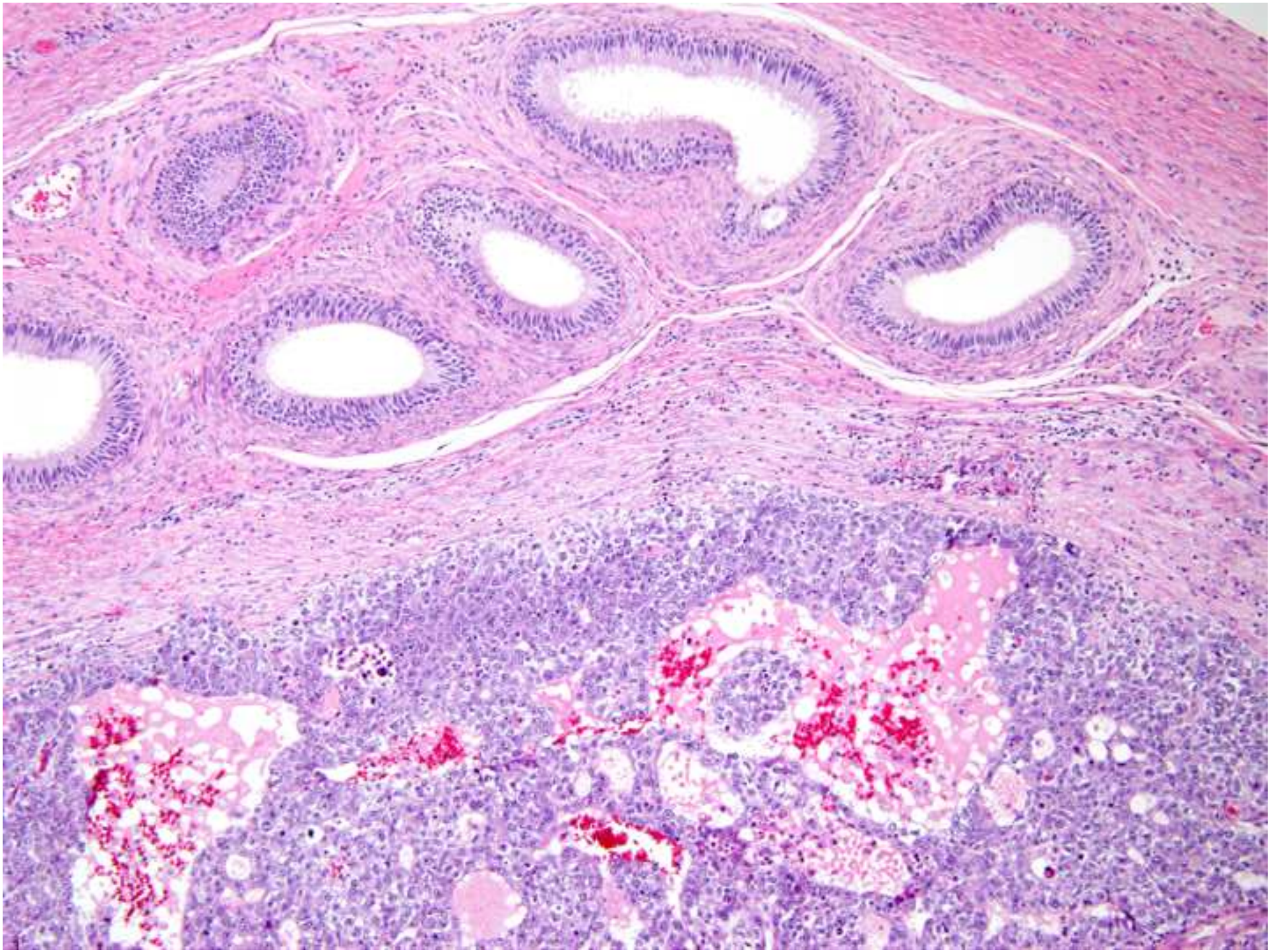

Figure 6

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Figure 7

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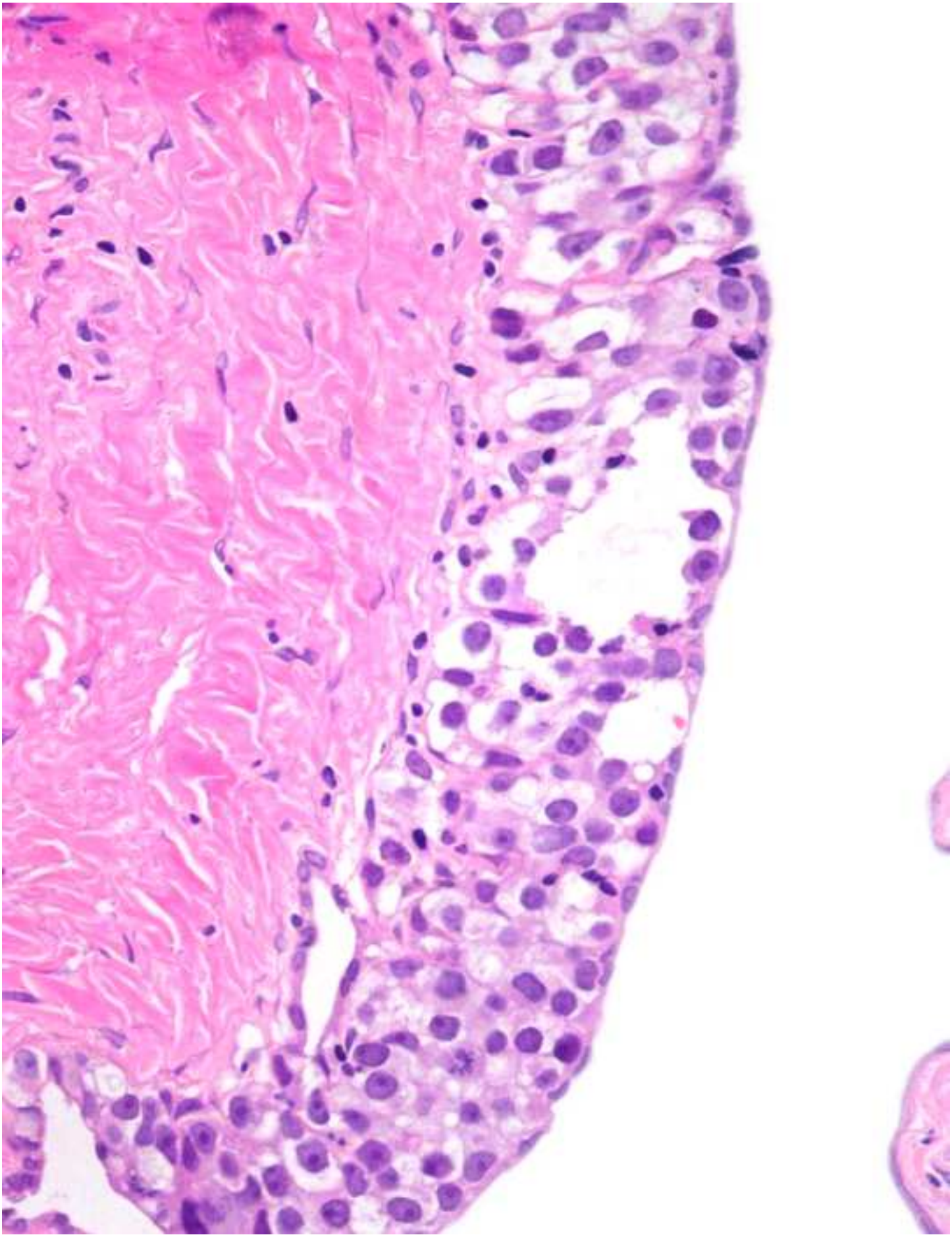

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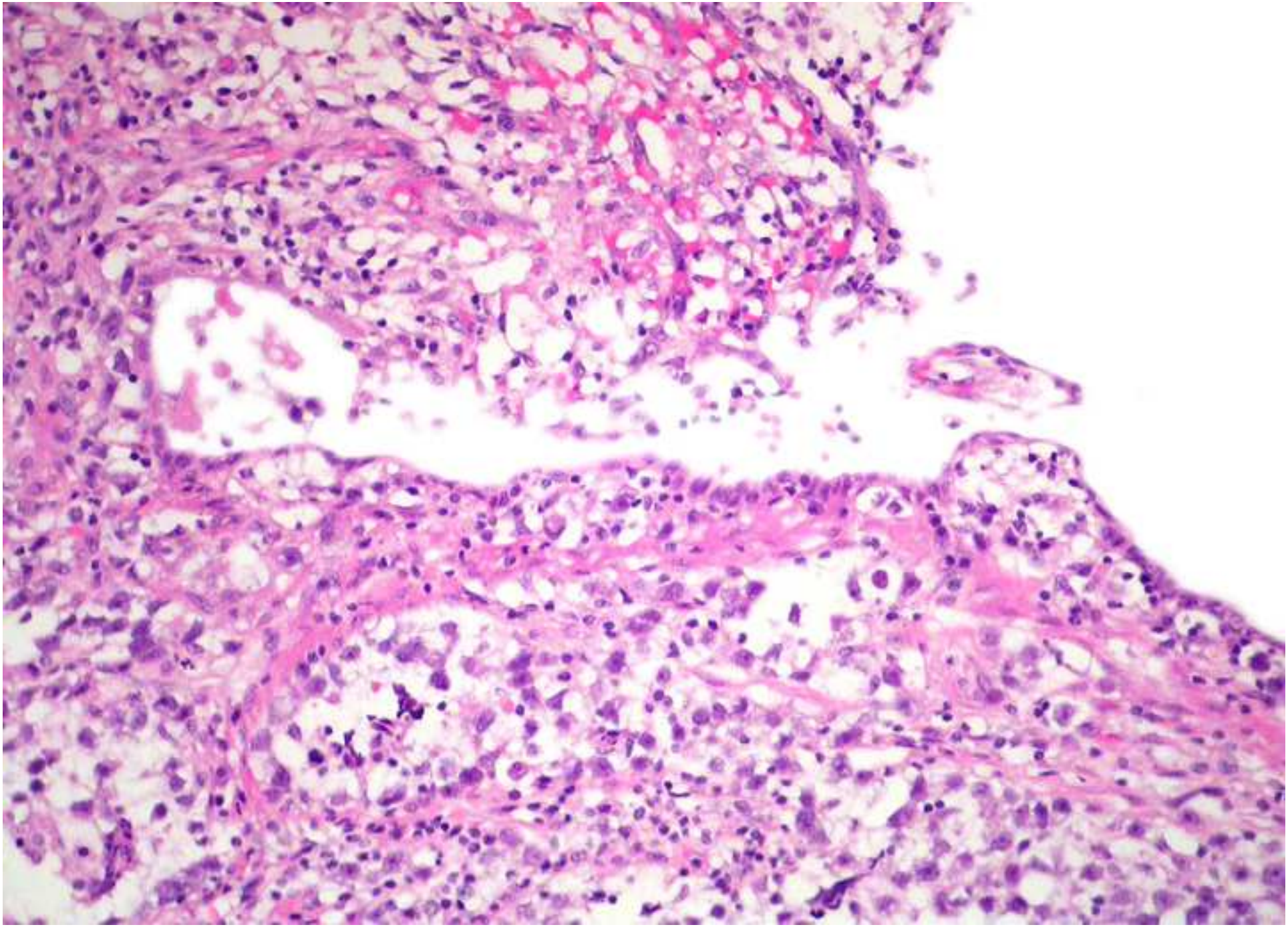

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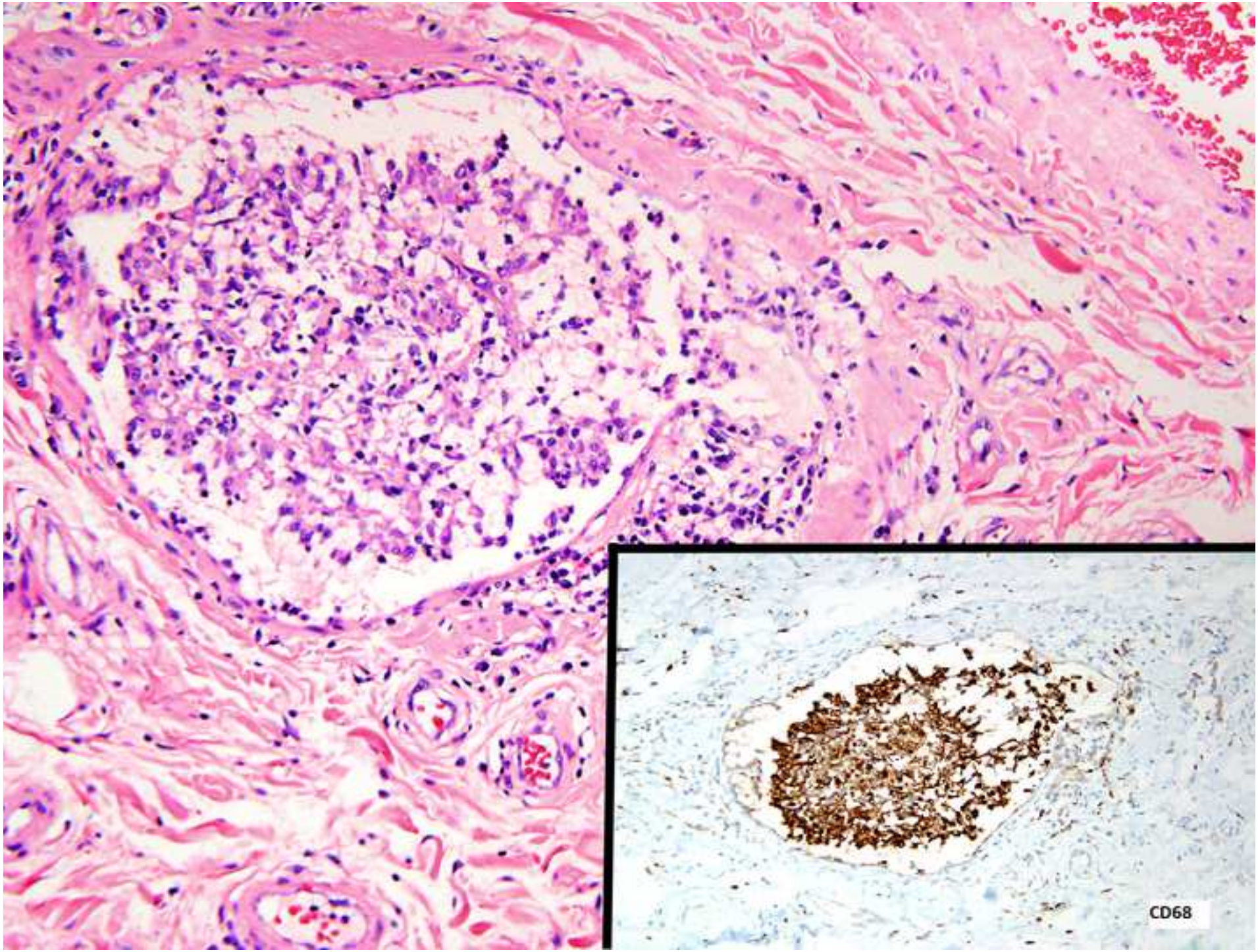

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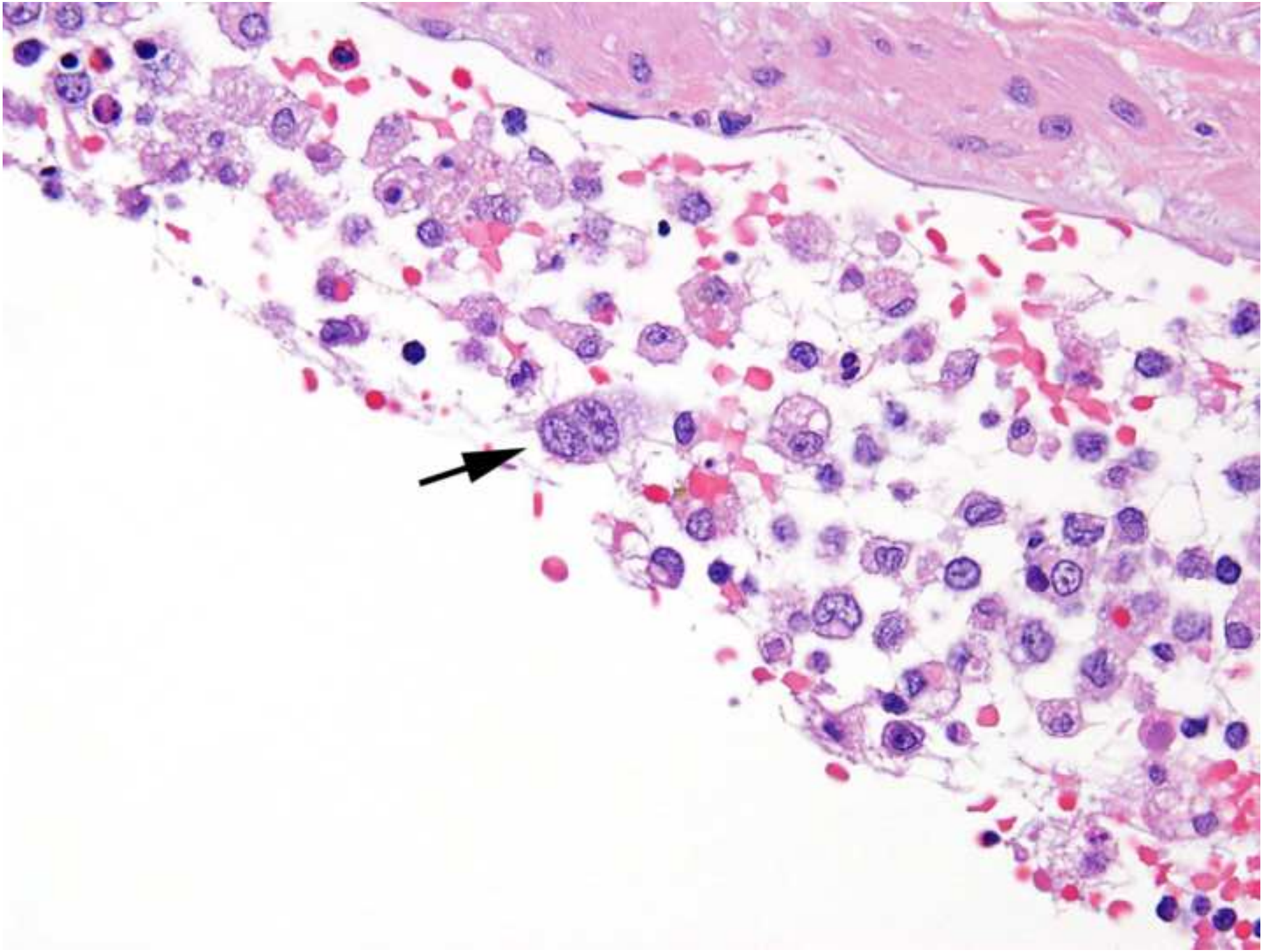

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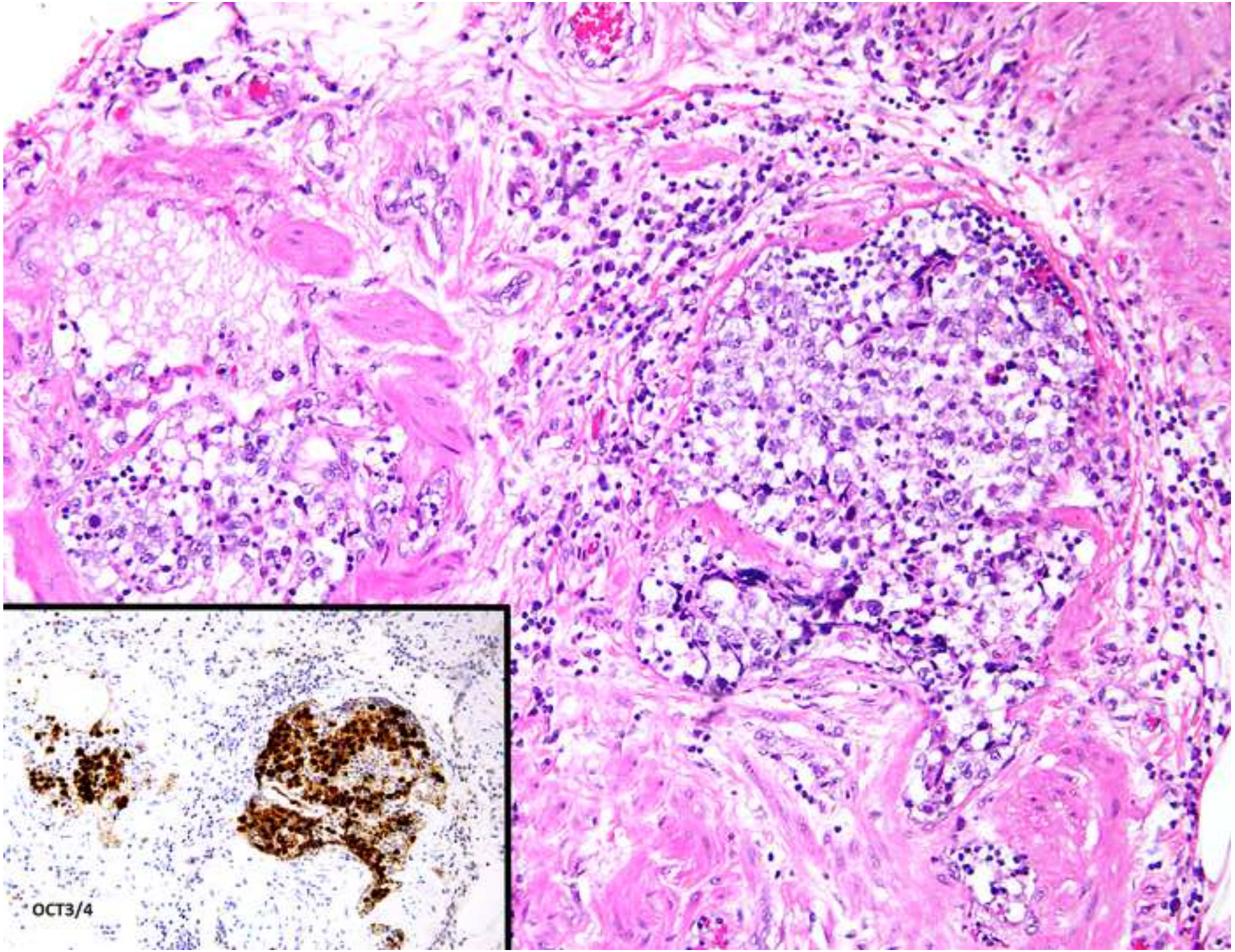

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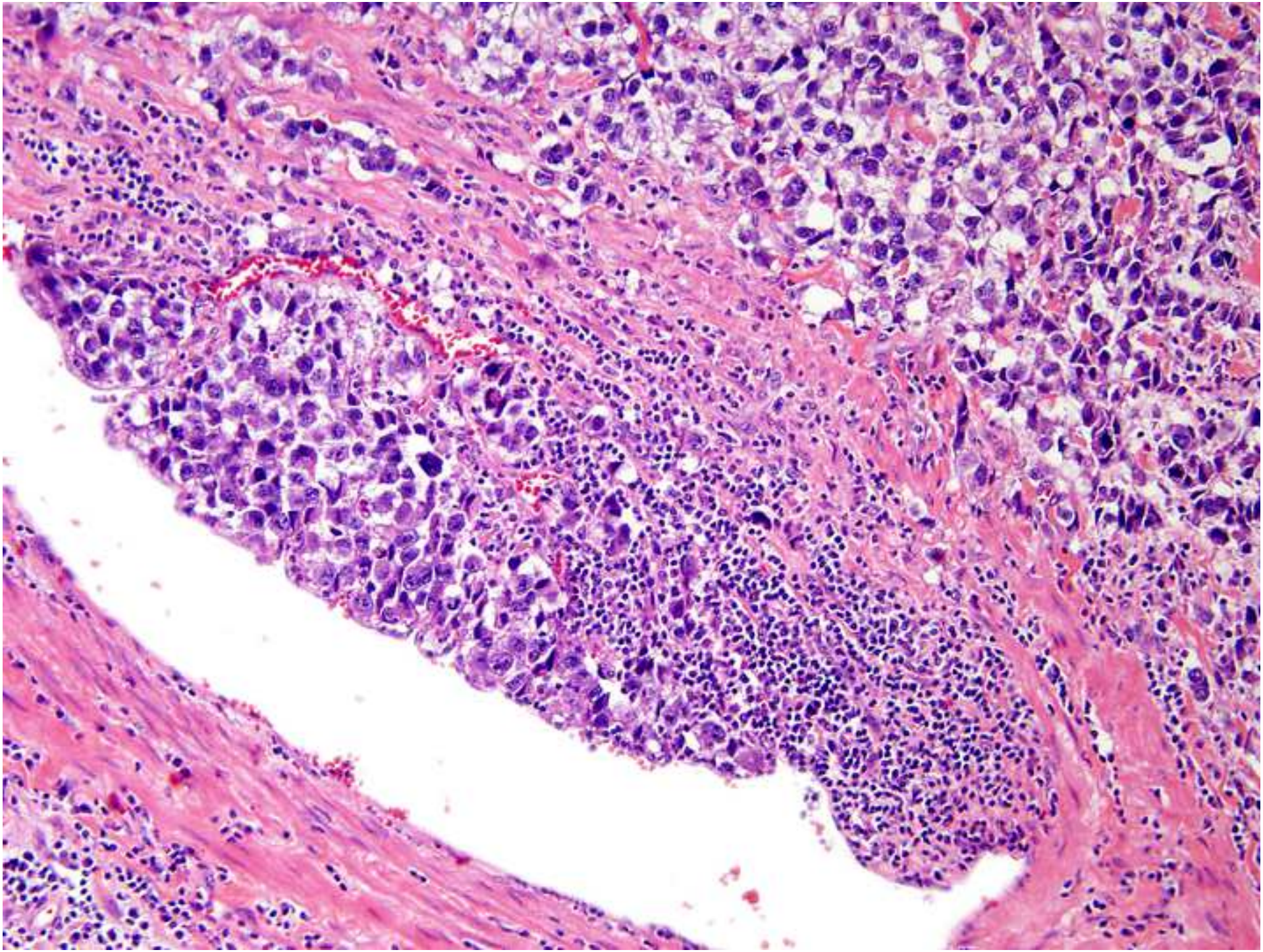

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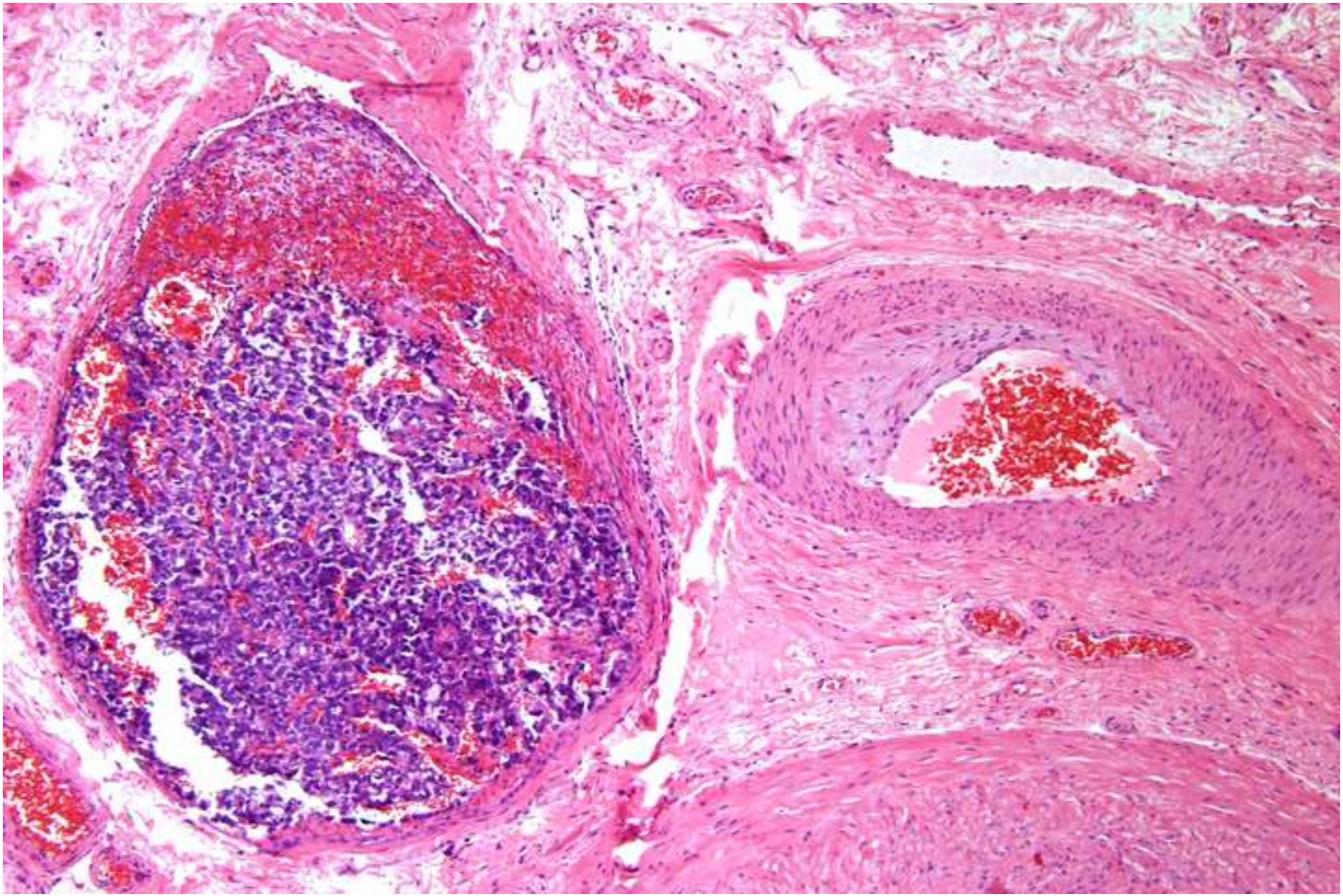

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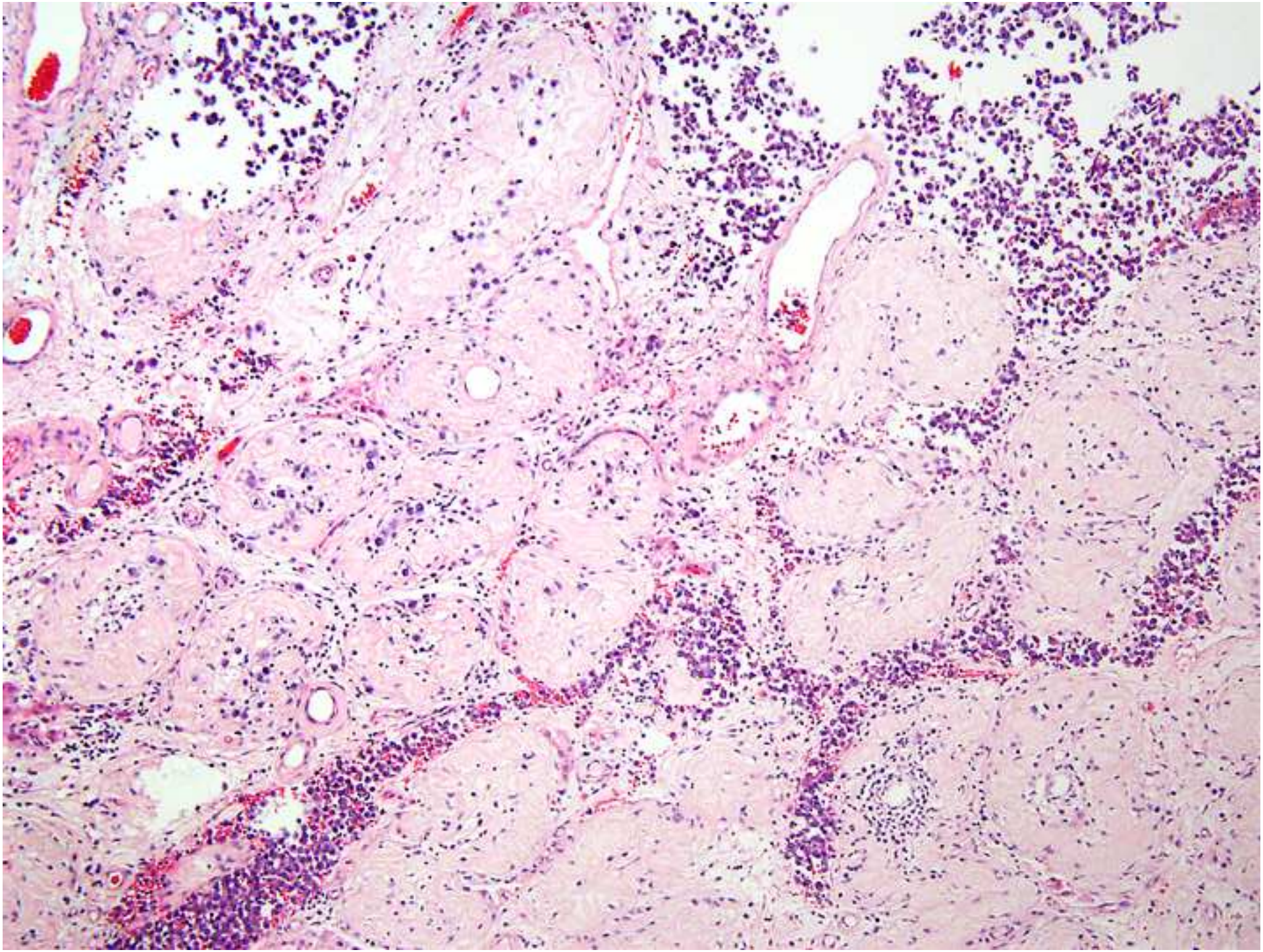

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