CASO CLÍNICO- PATOLÓGICO

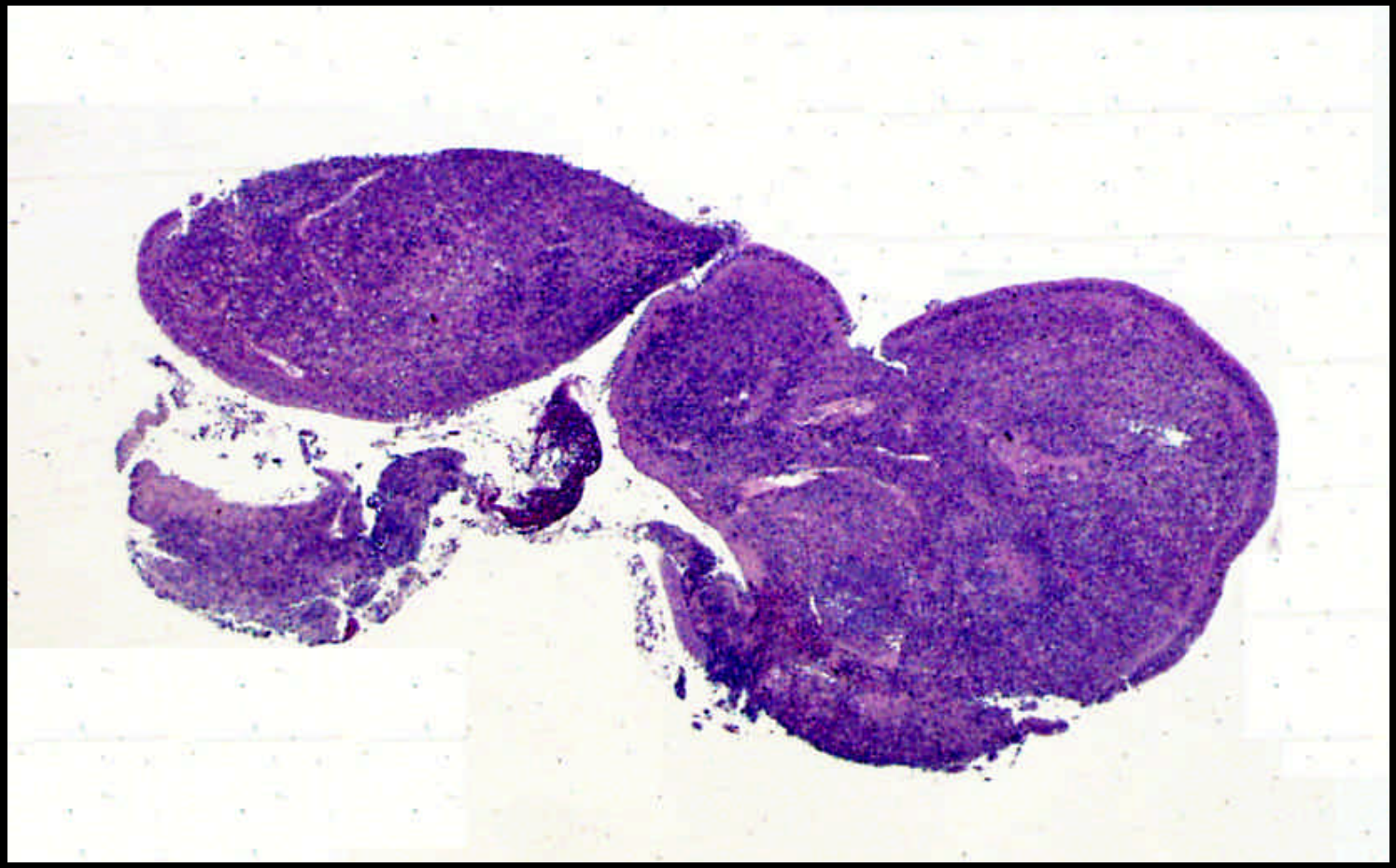
Santiago Montes Moreno, Miguel Ángel Martínez González.
Departamento de AP. H. U. 12 de Octubre, Madrid.

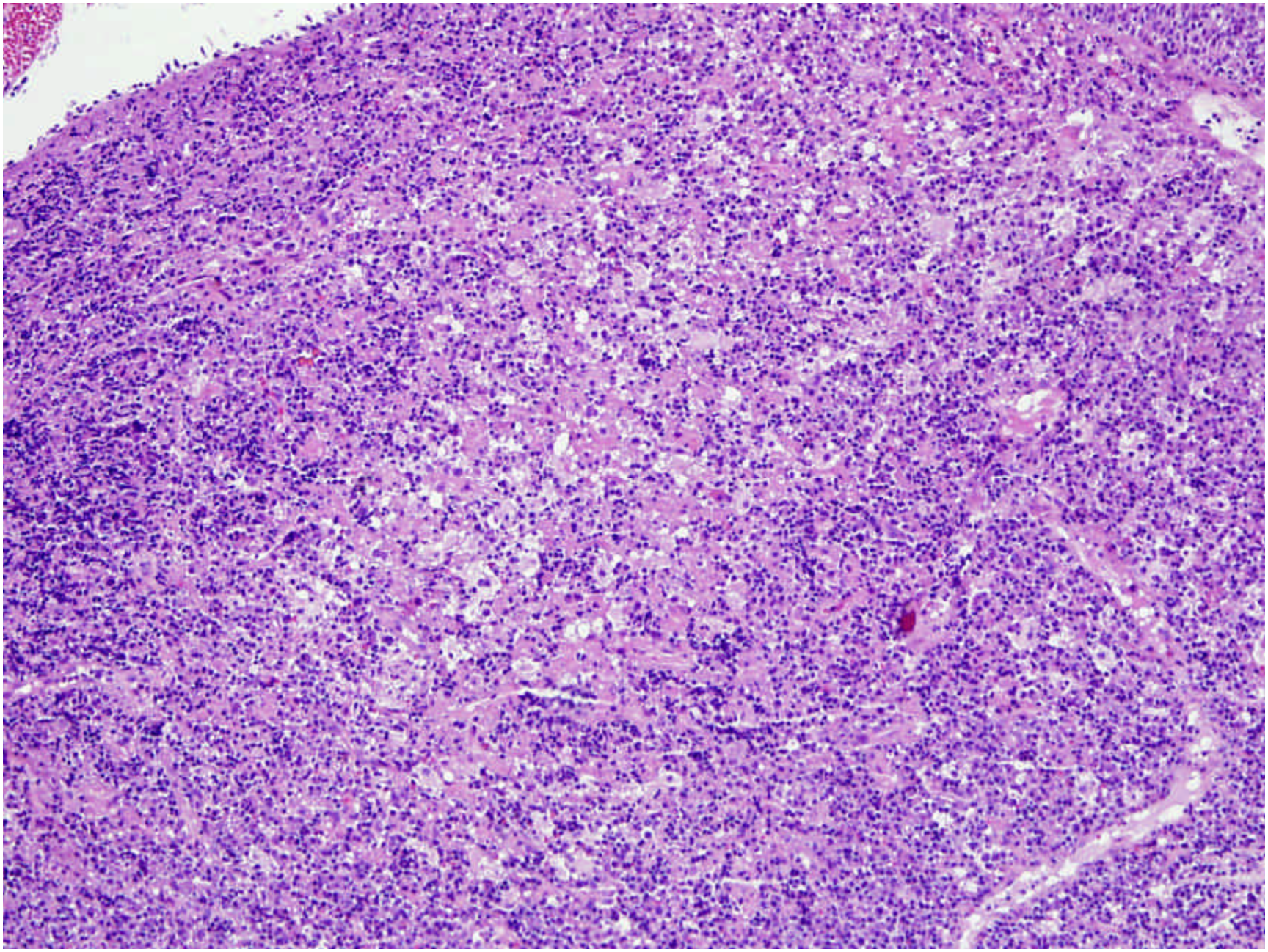
CASO CLÍNICO- PATOLÓGICO

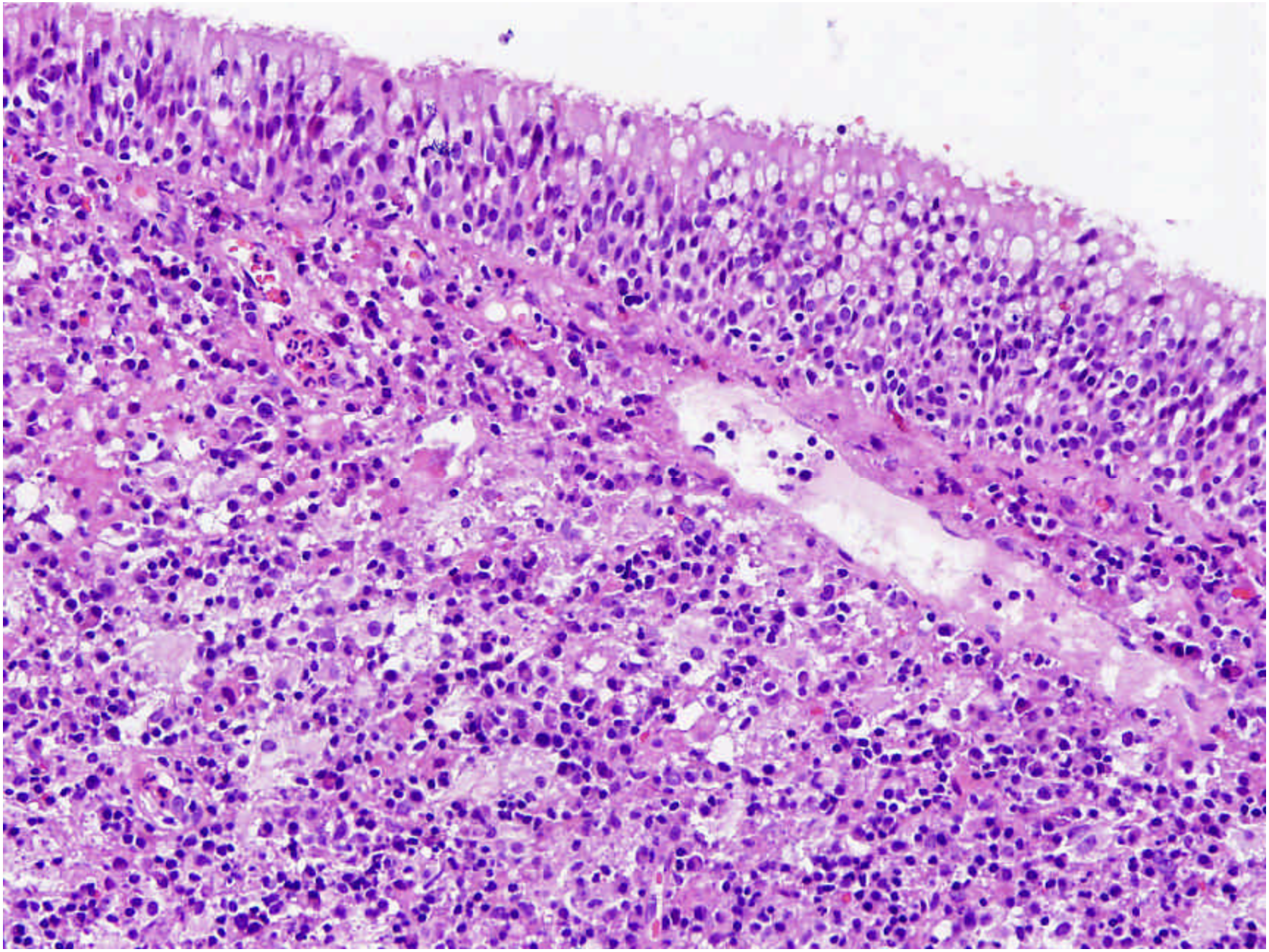
- Mujer de 50 años que desarrolla una clínica de 7 meses de evolución de insuficiencia respiratoria nasal, dolor e hipoacusia con sensación de taponamiento de oído derecho.
- **EF**: Adenopatías cervicales bilaterales y bultoma submandibular derecho no dolorosos.
- **TAC**: Adenopatía yugulodigástrica D, submandibular I y retrofaríngeas D con imágenes sugestivas de necrosis y captación en anillo.

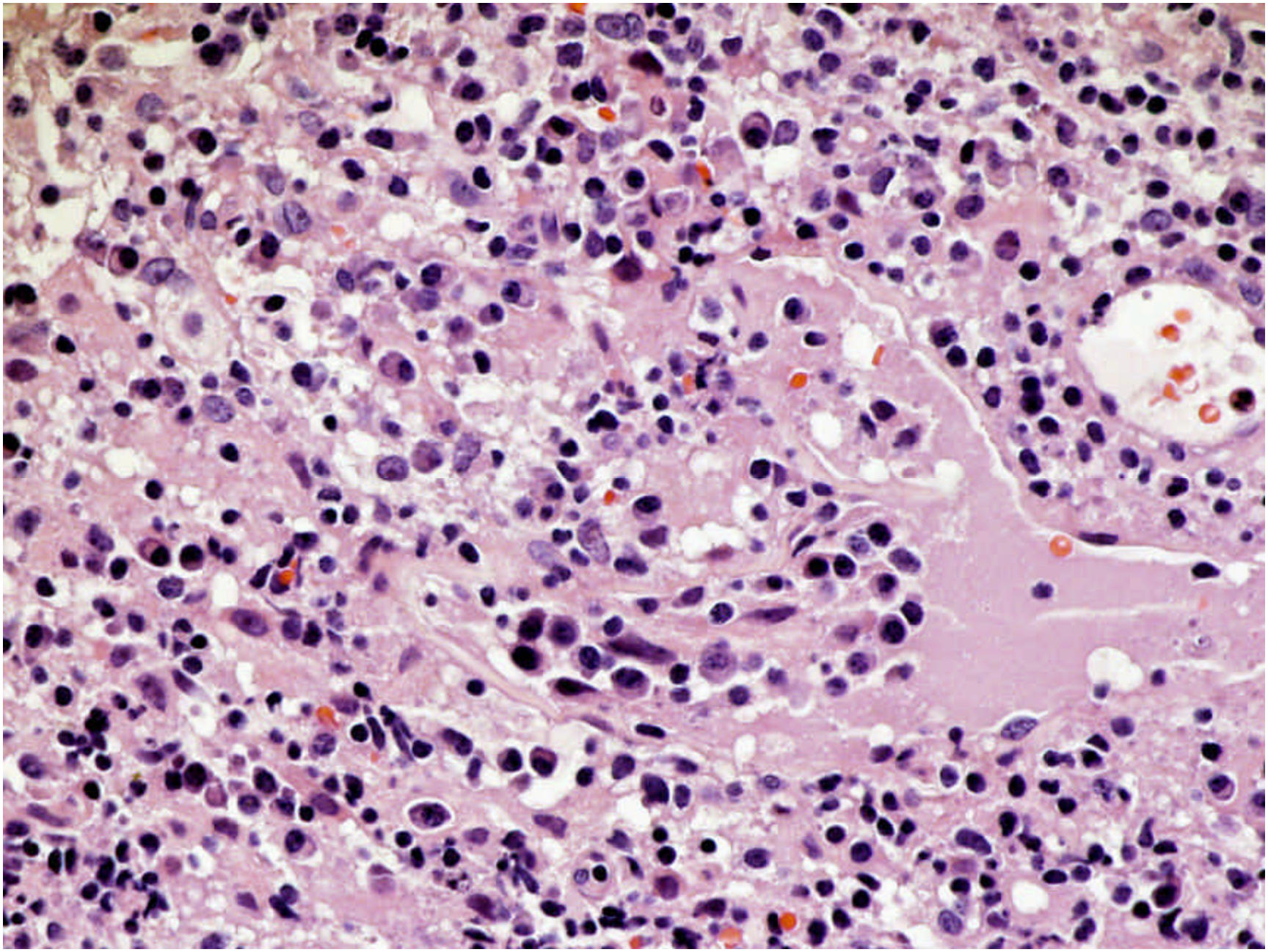
  Tumor en nasofaringe que afecta a rodete tubárico D

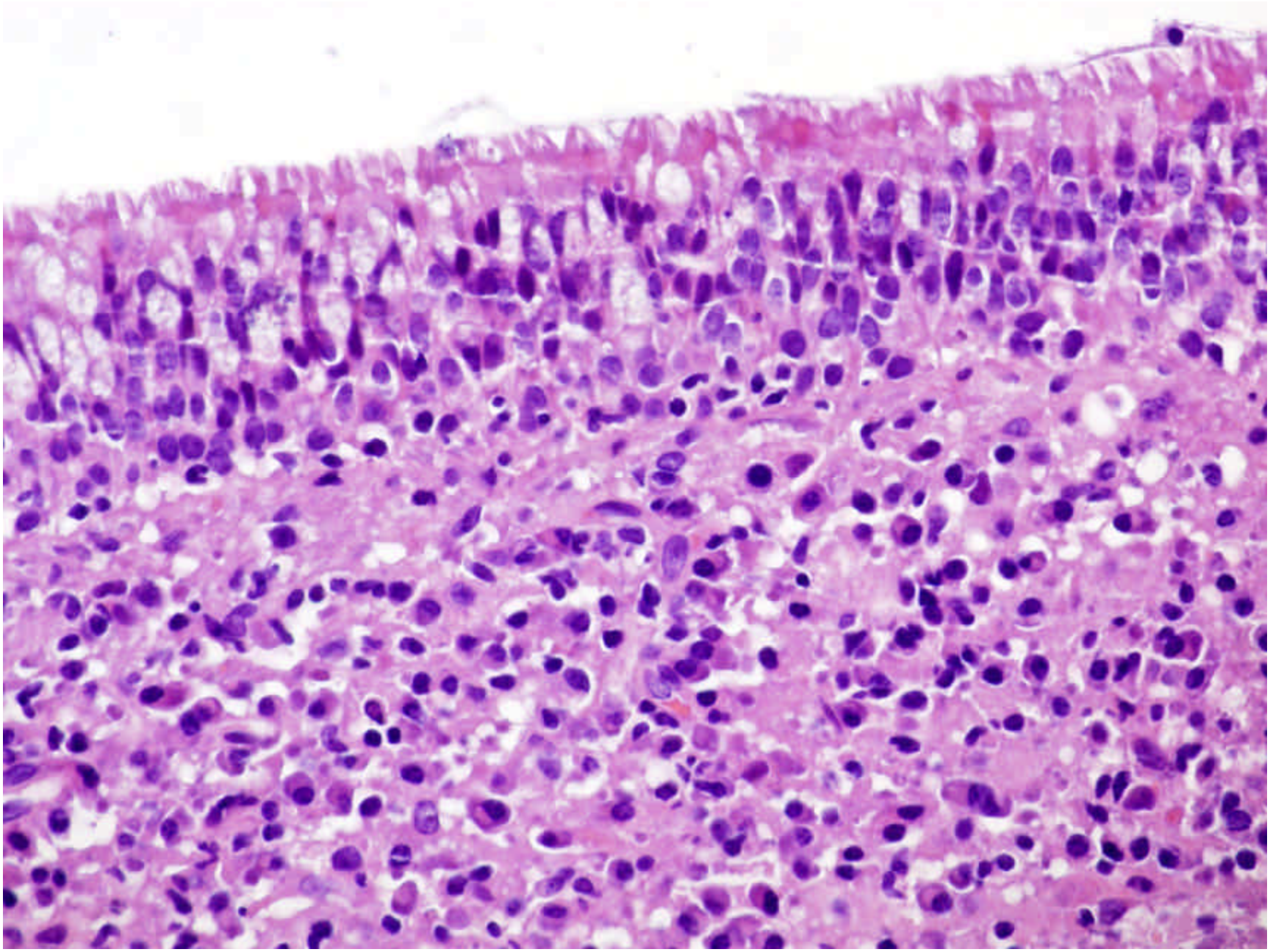
Con la sospecha clínica de proceso linfoproliferativo se realiza biopsia de cavum.

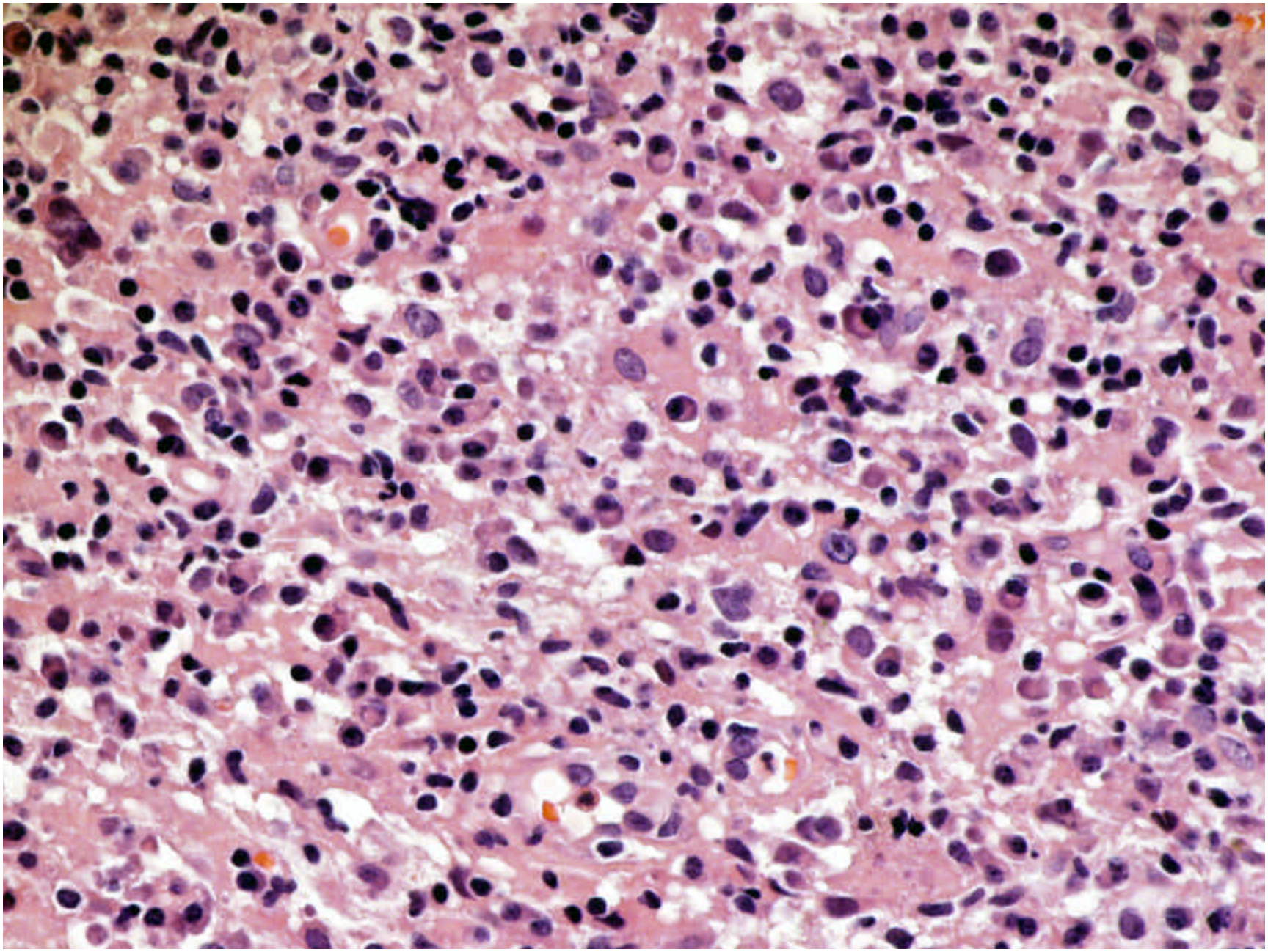


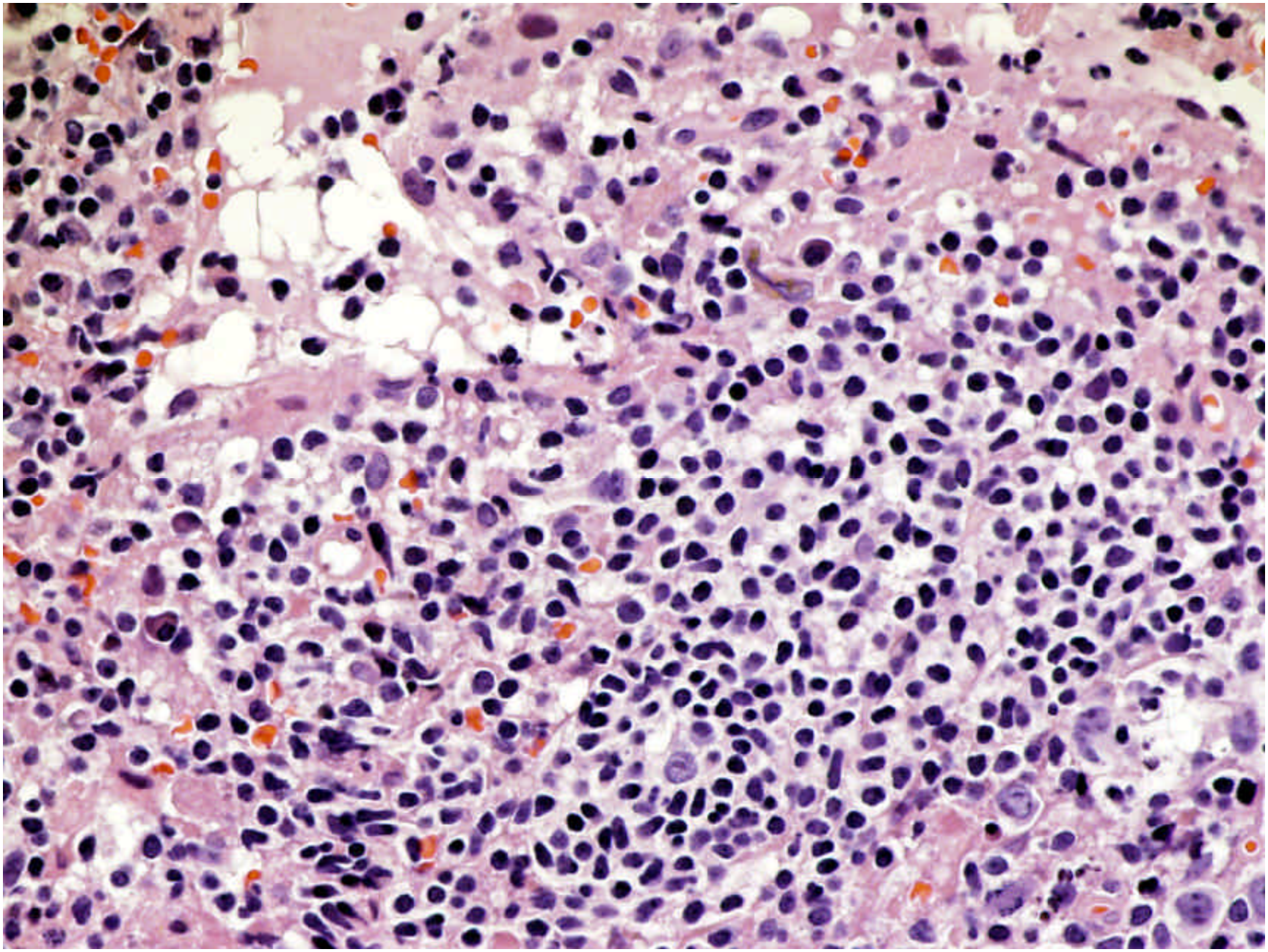


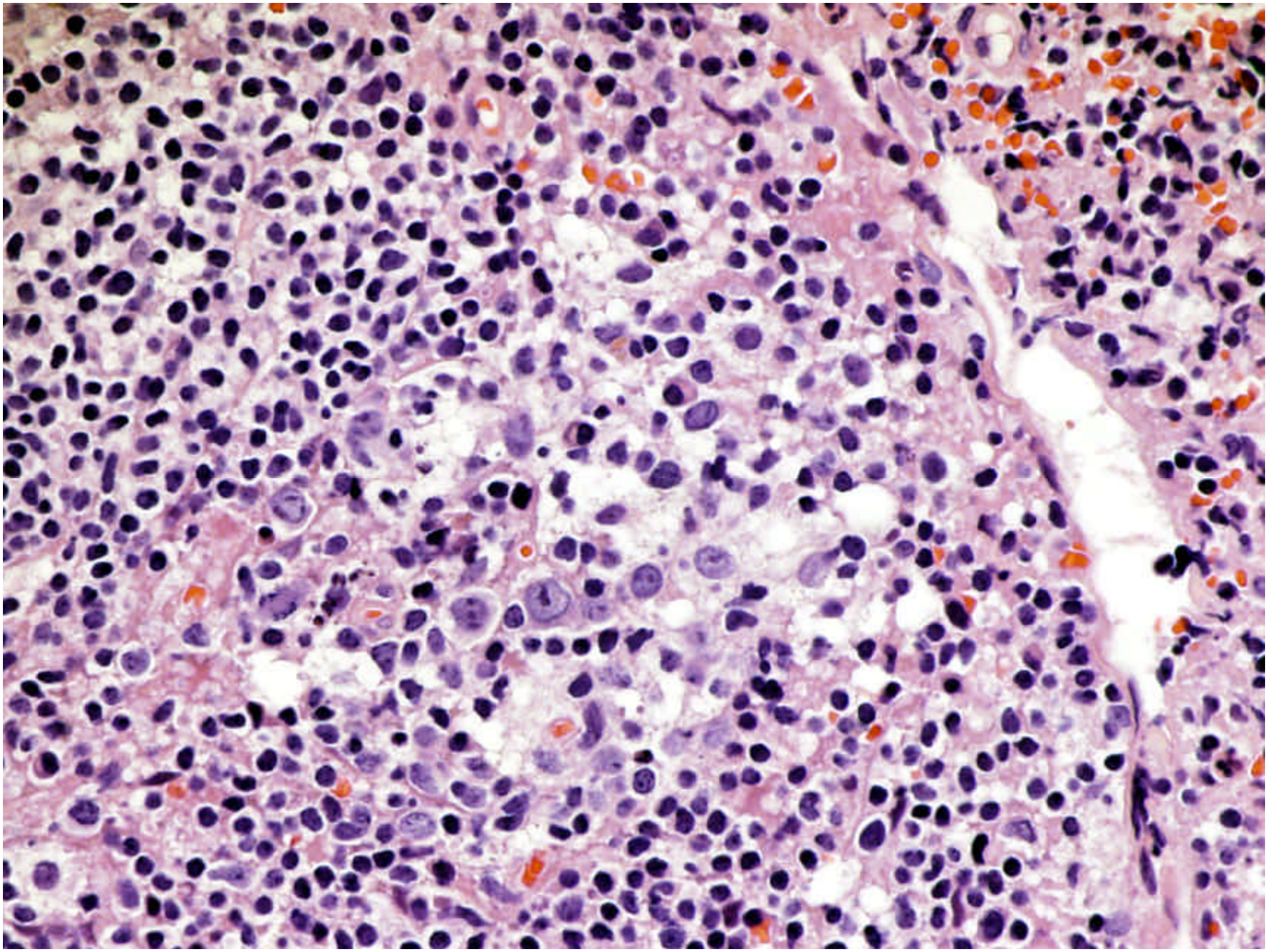




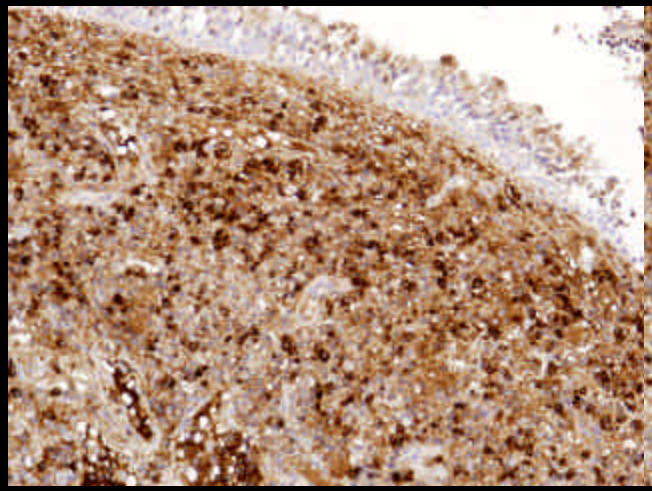








kappa



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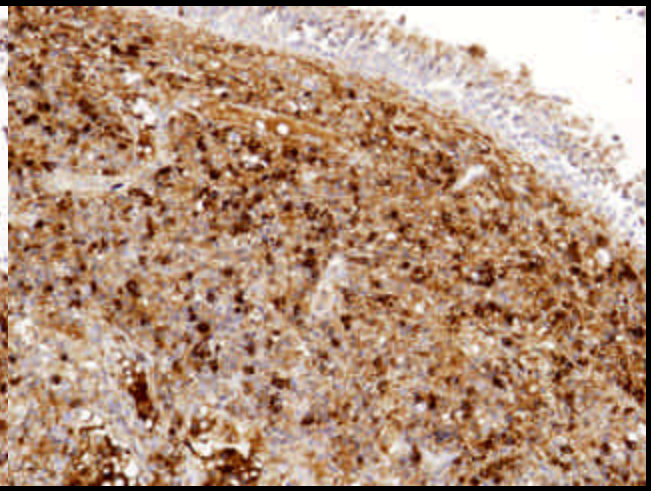
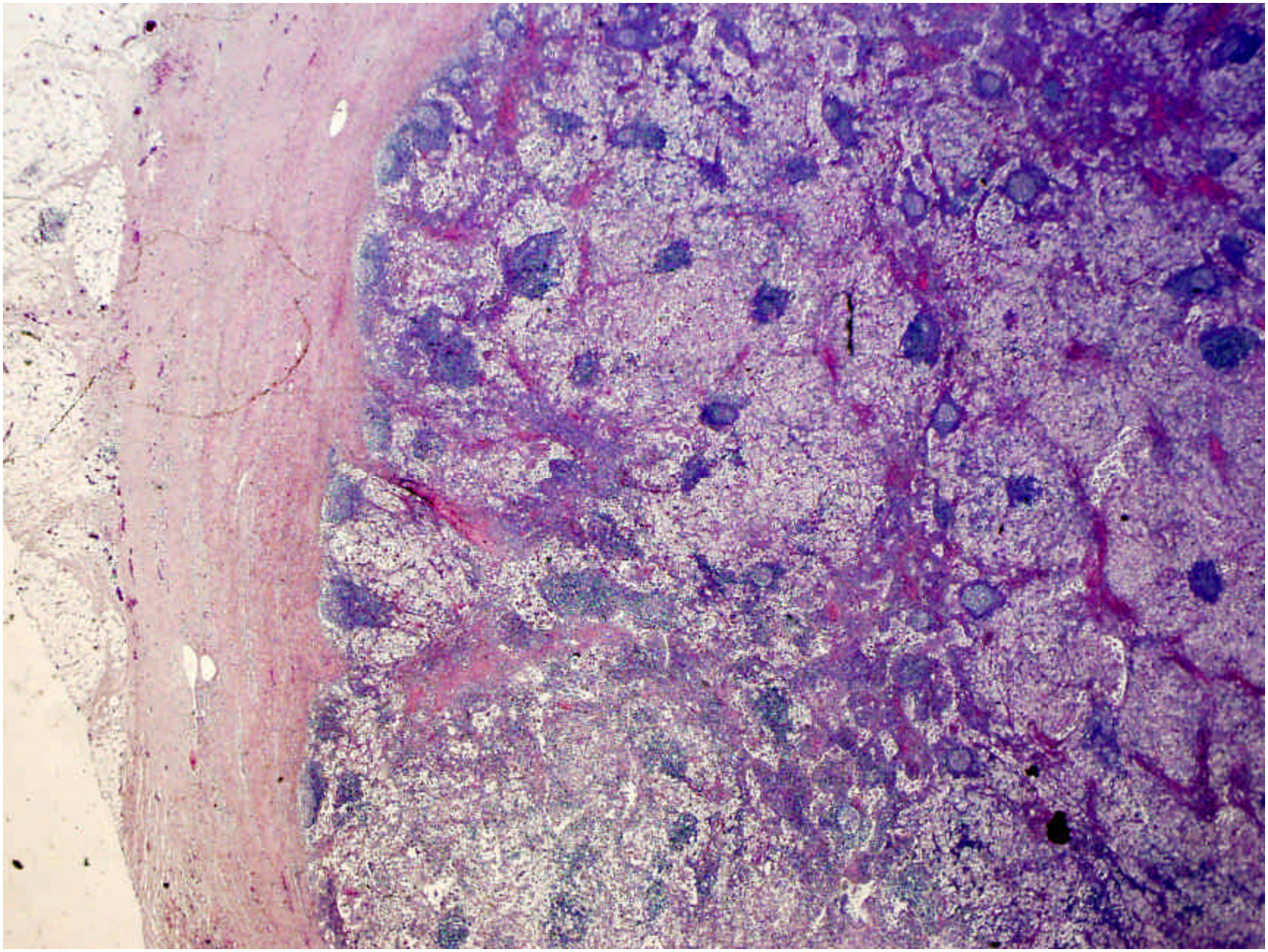
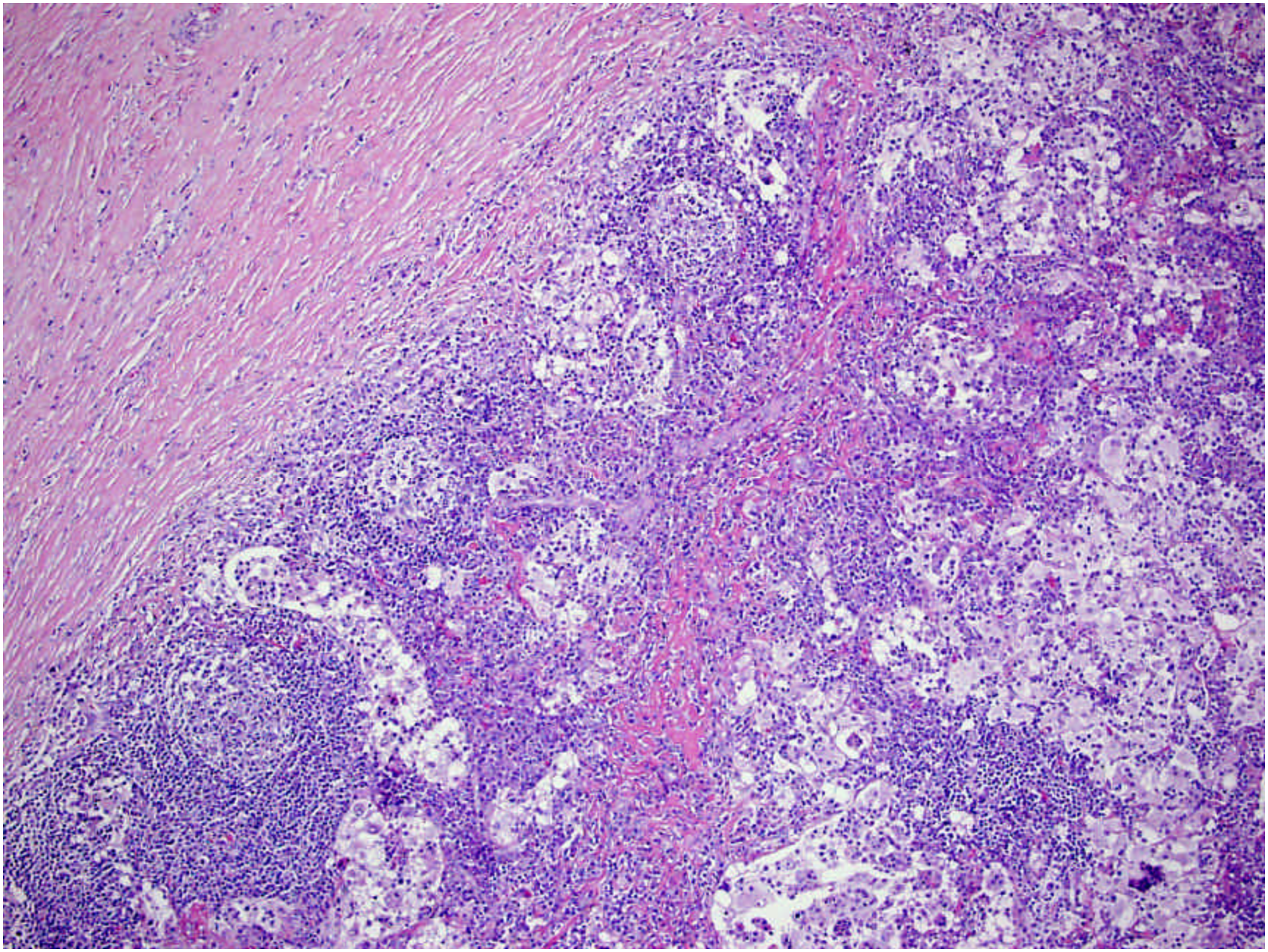
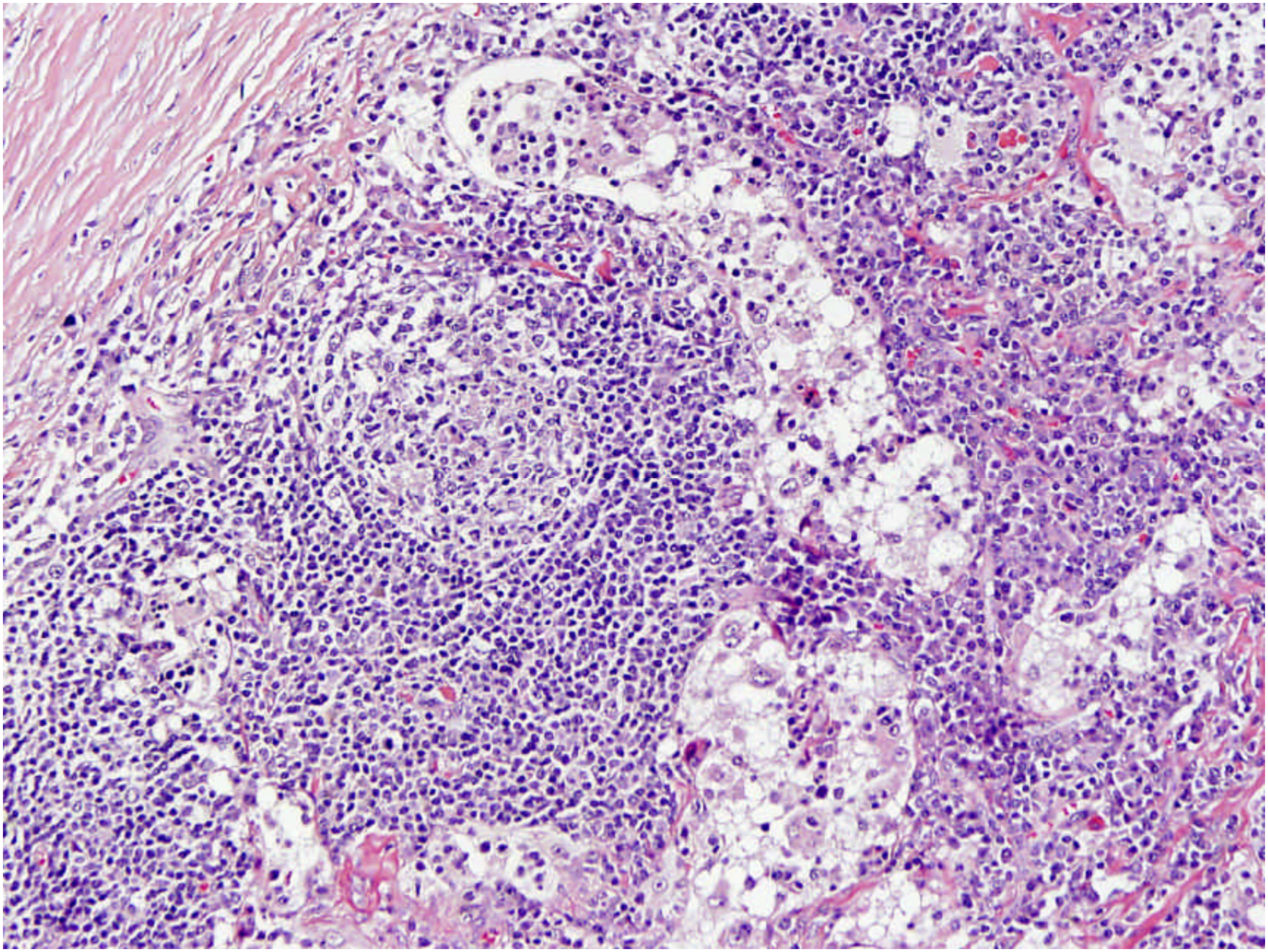
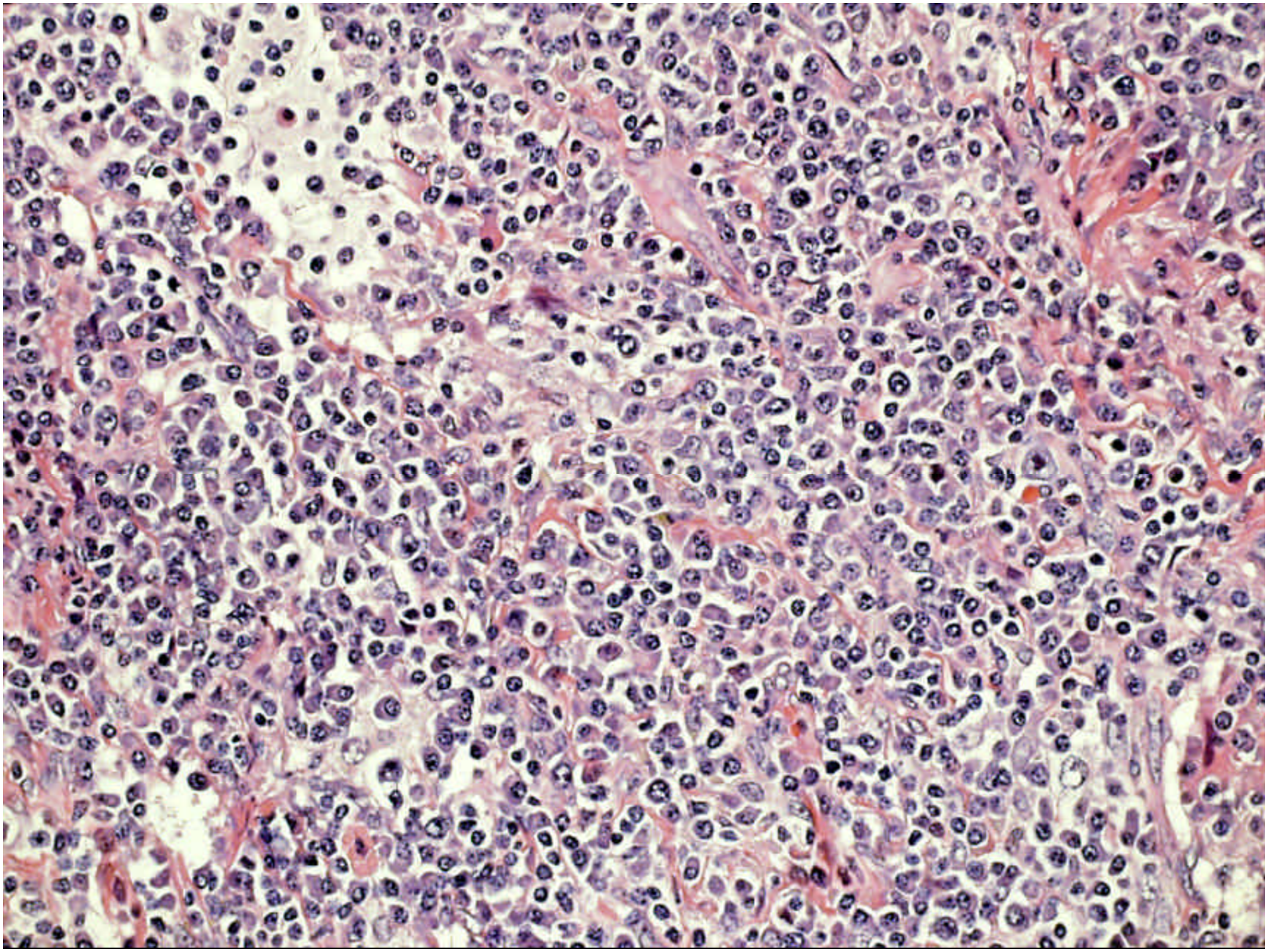


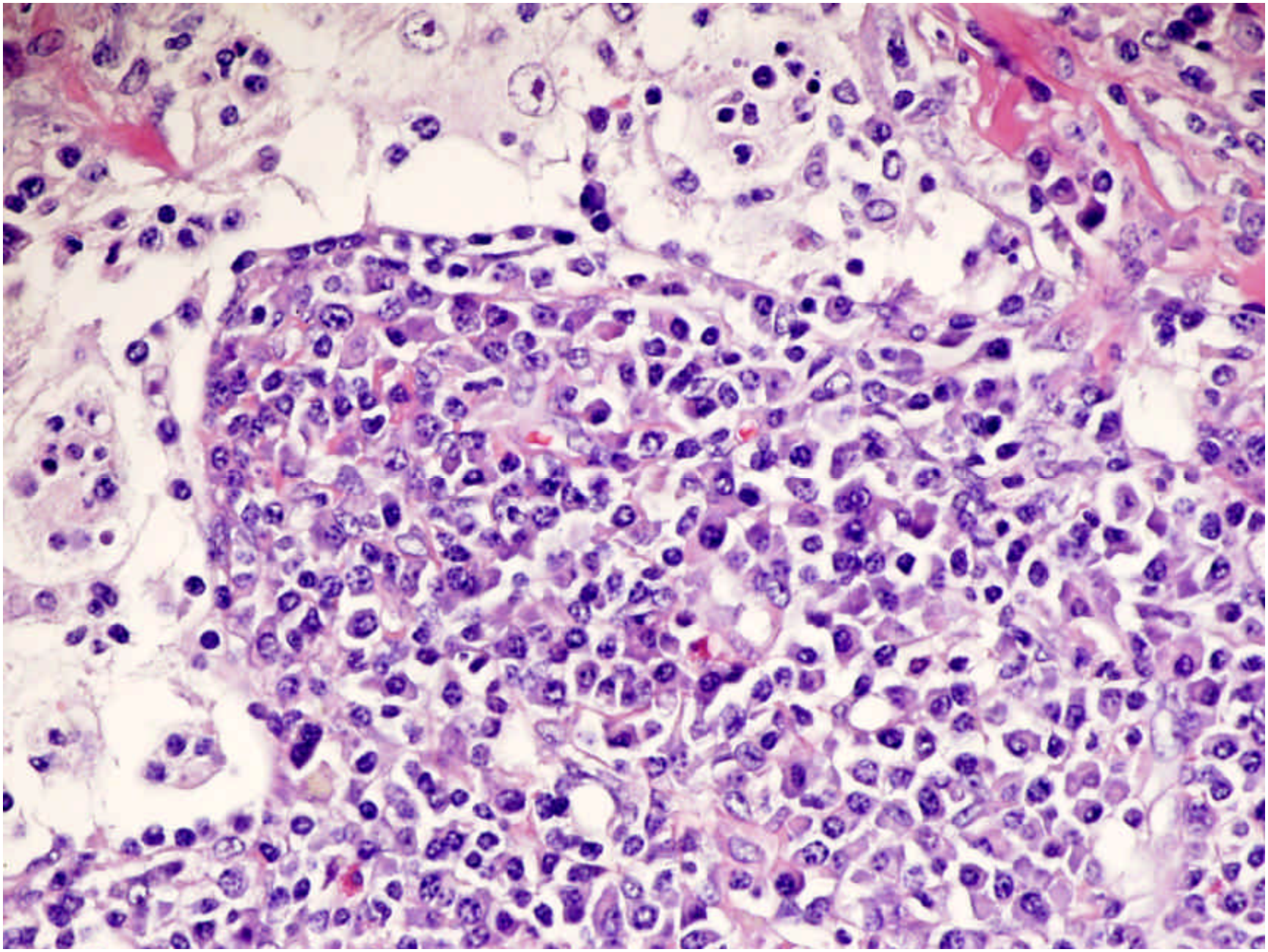
DAP: Mucosa tubárica con infiltrado inflamatorio inespecífico, de probable naturaleza reactiva.

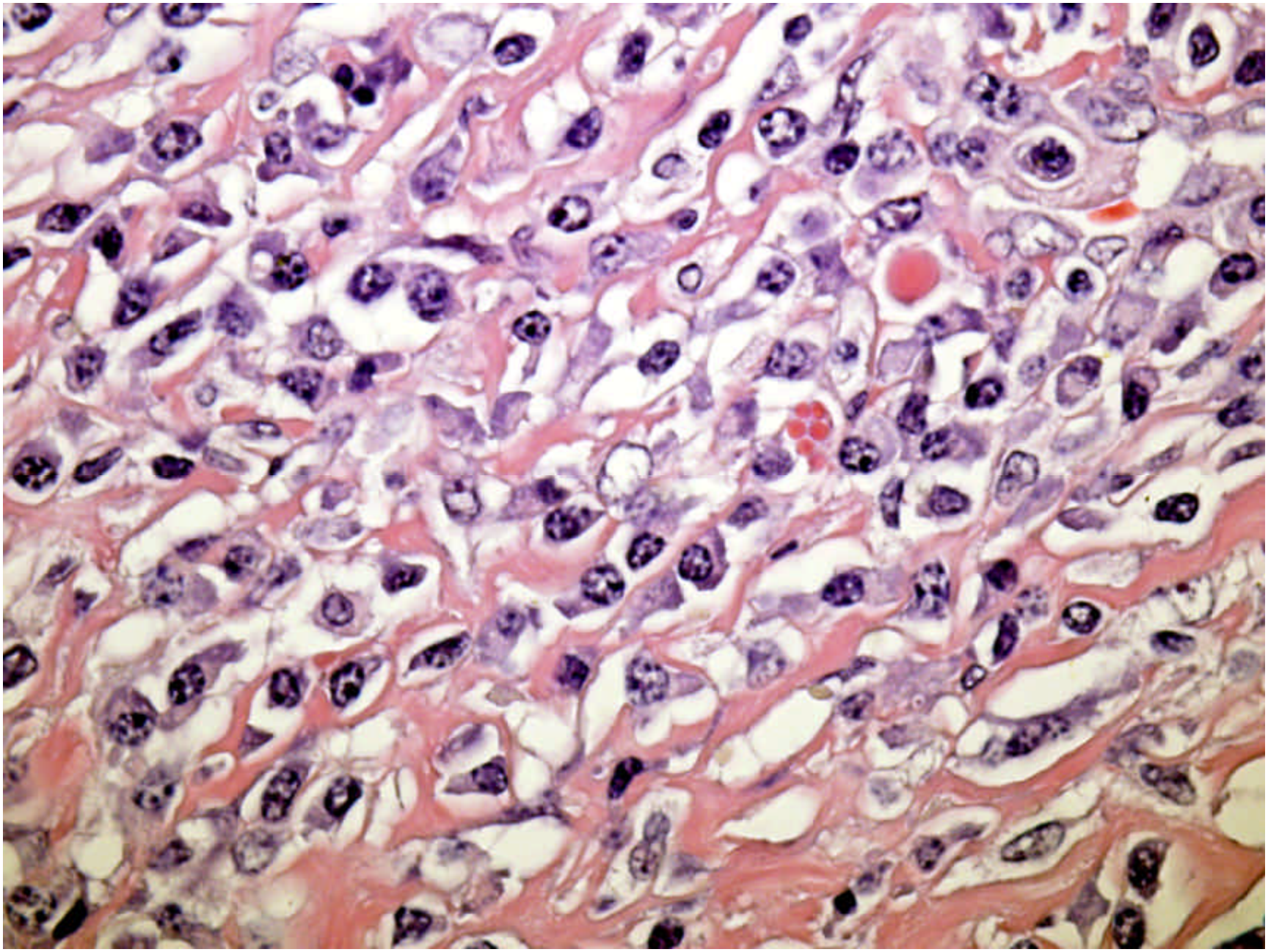


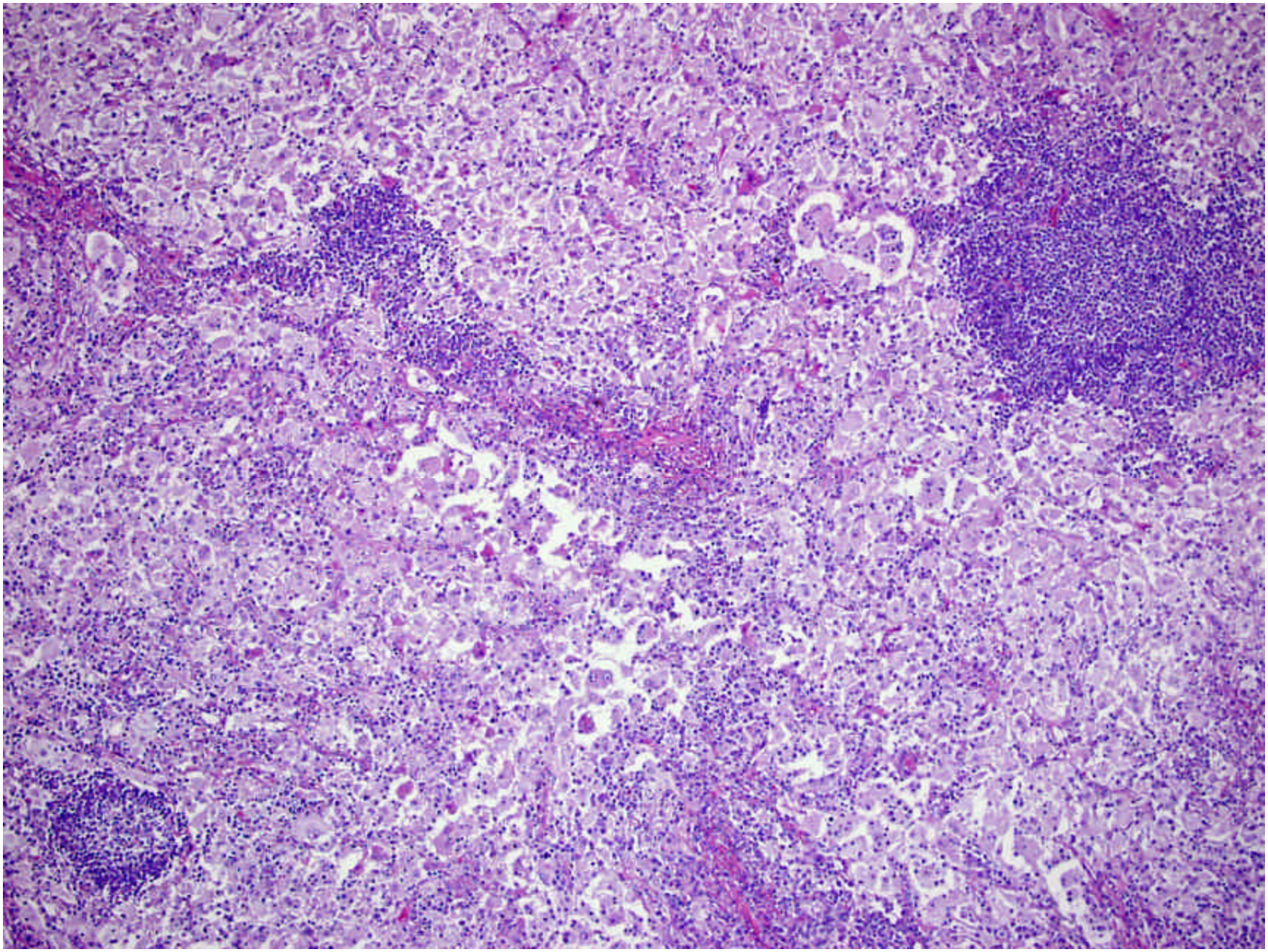


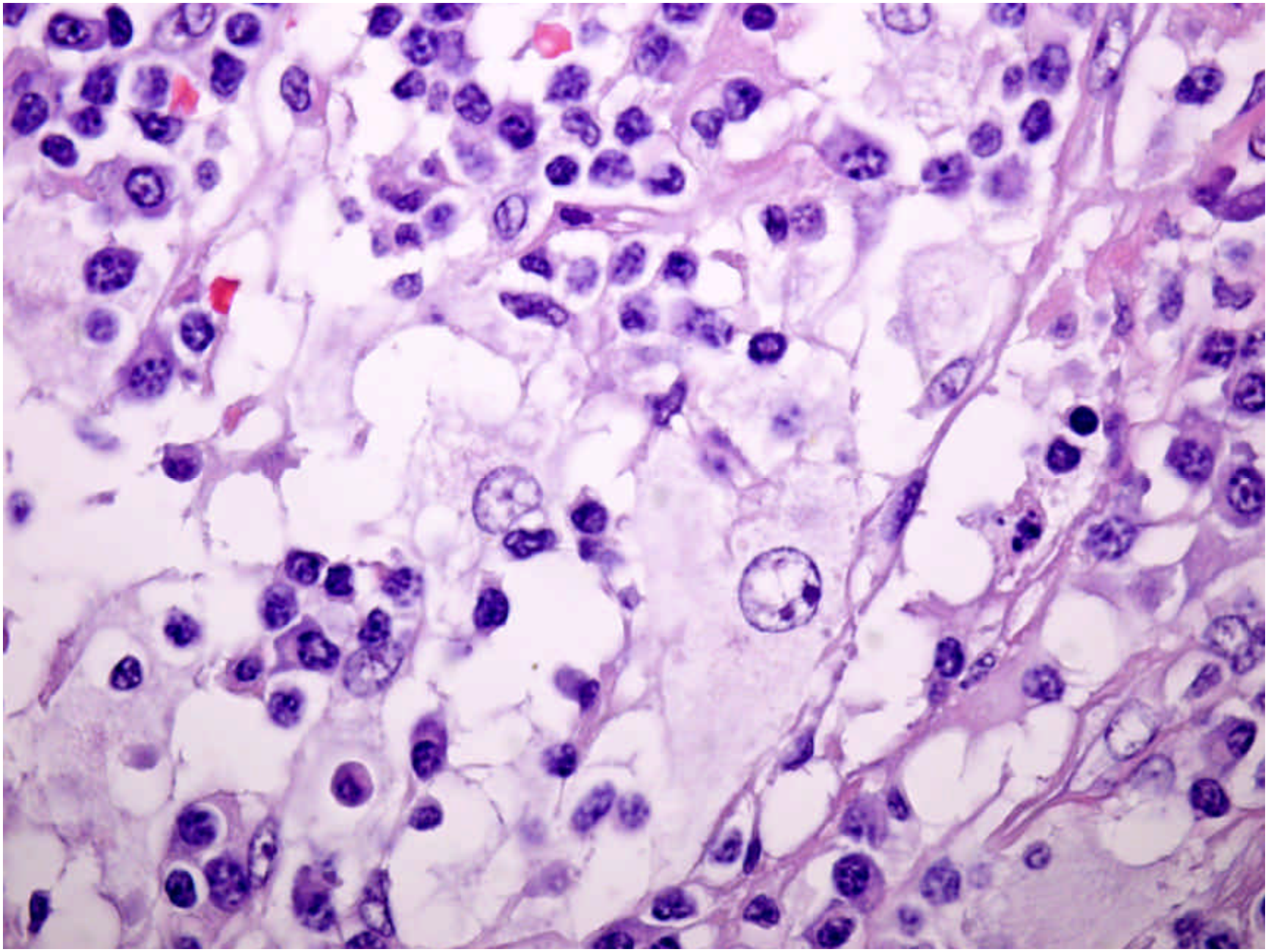


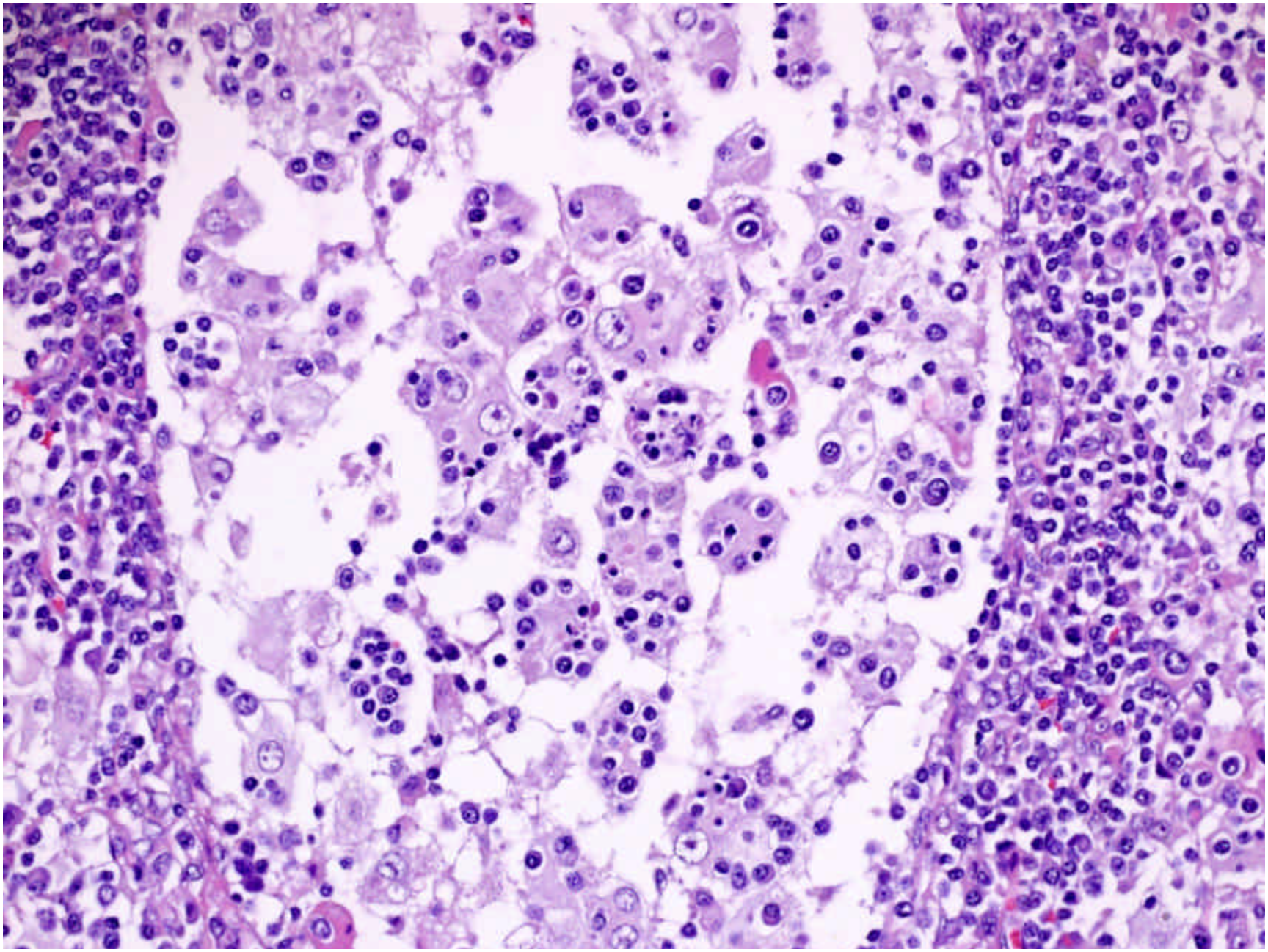


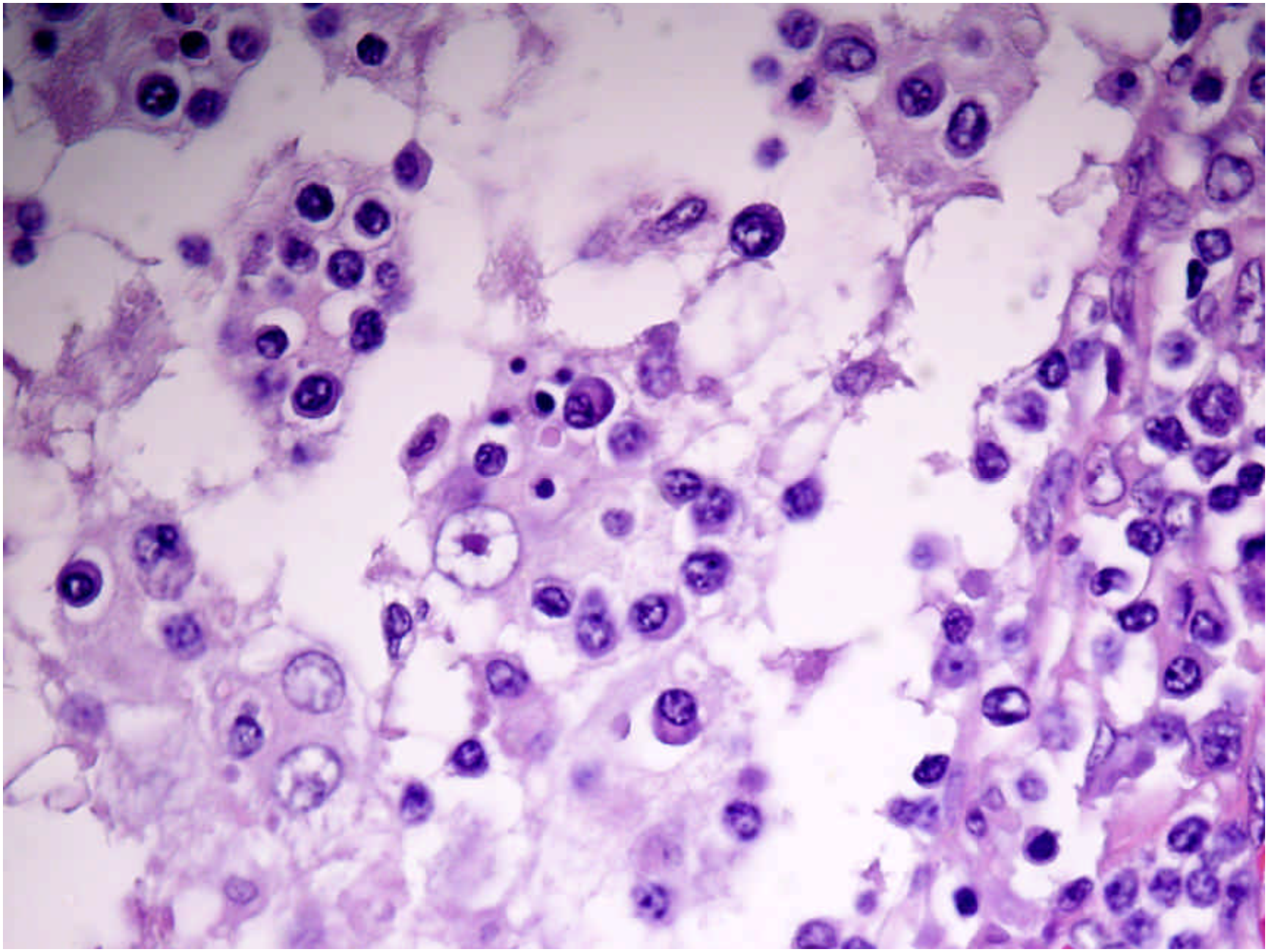


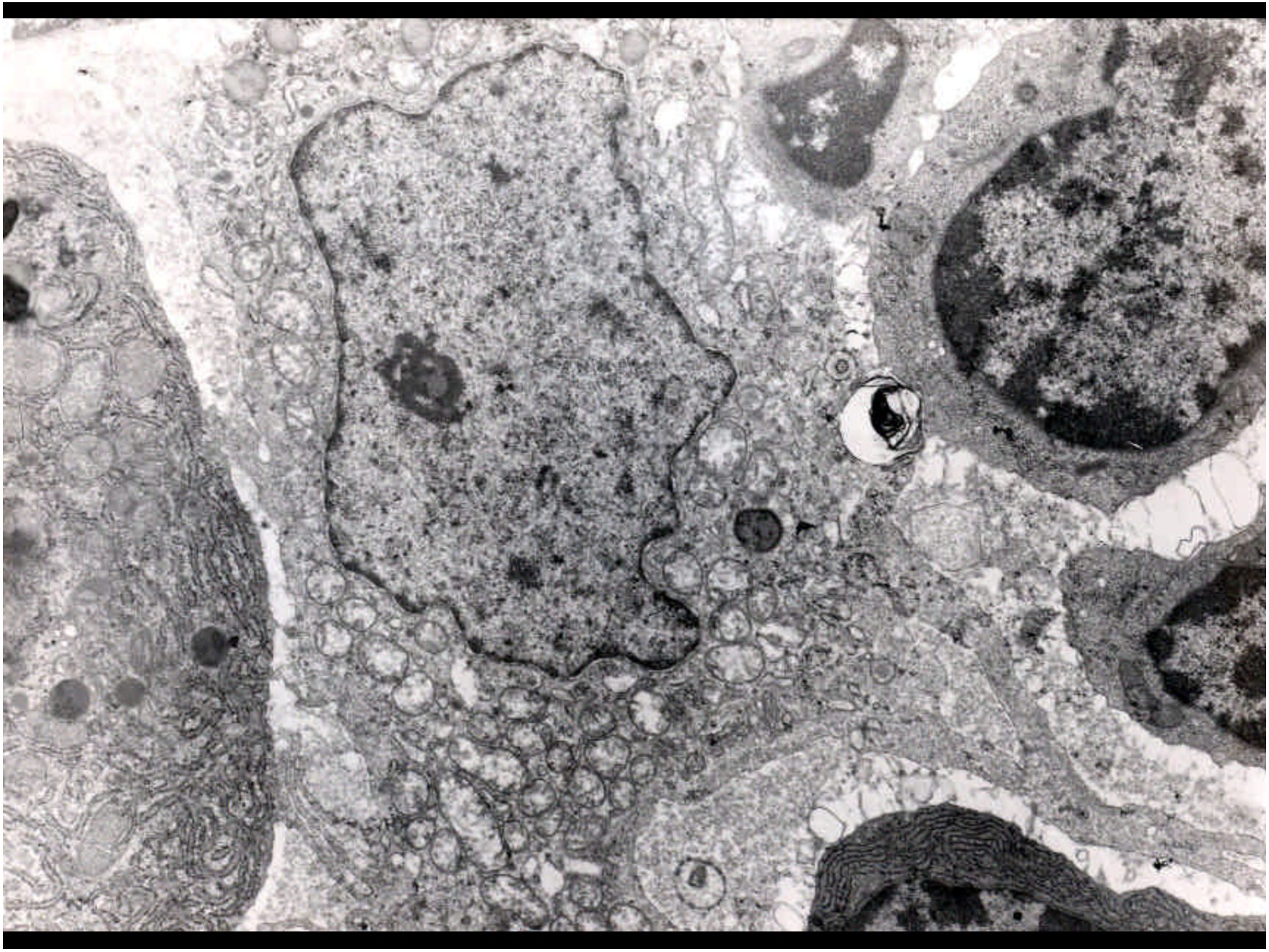


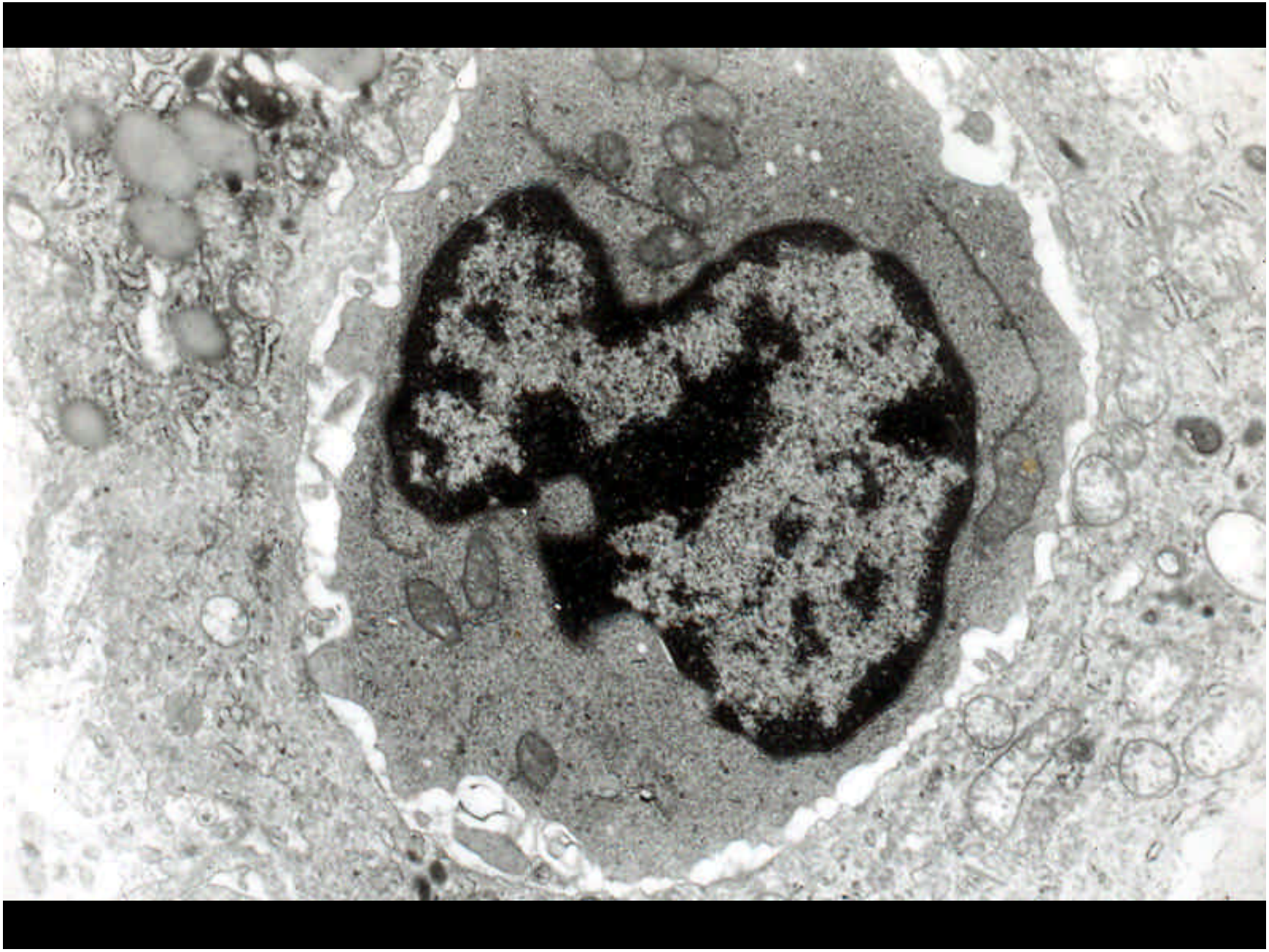


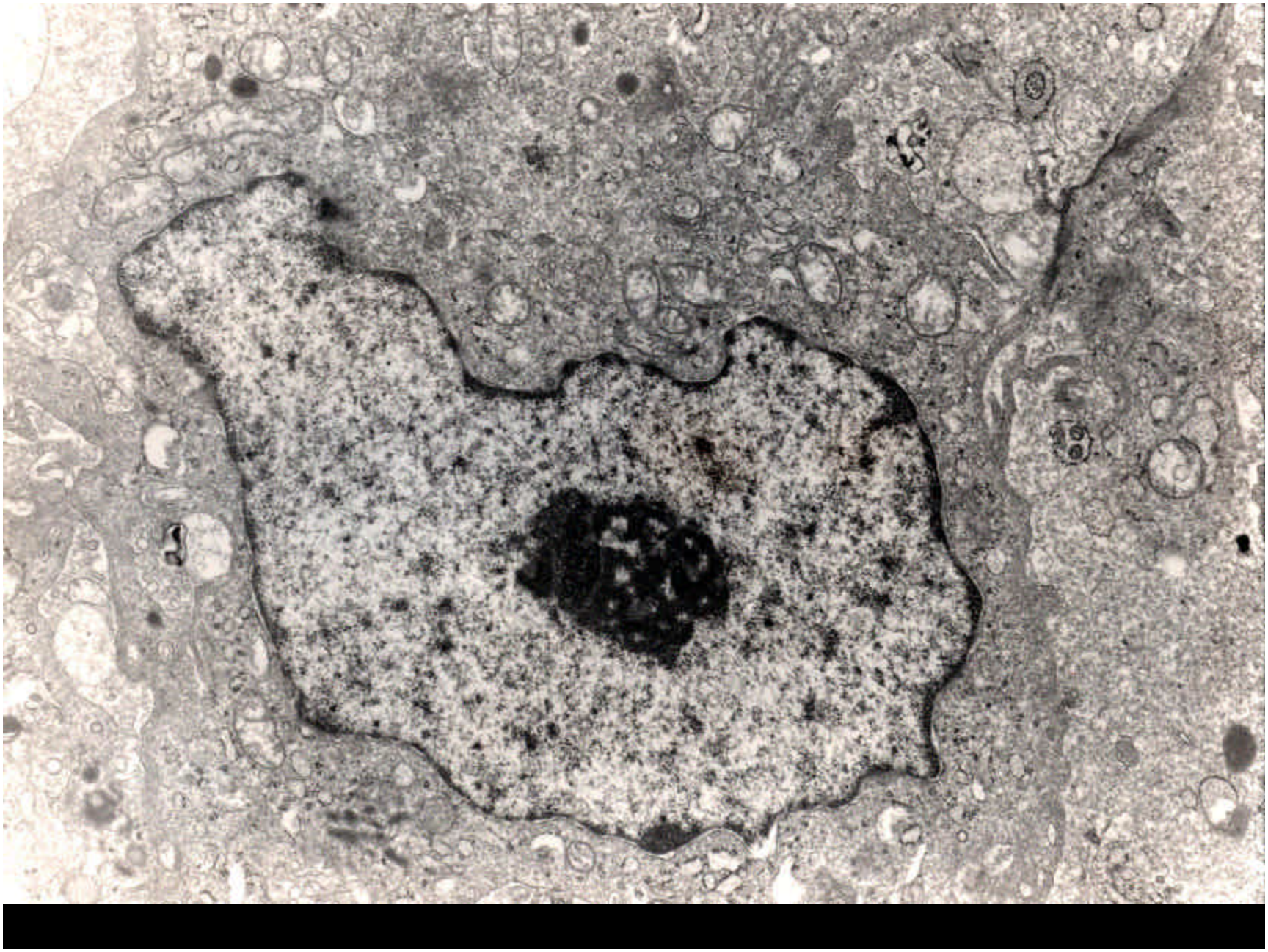


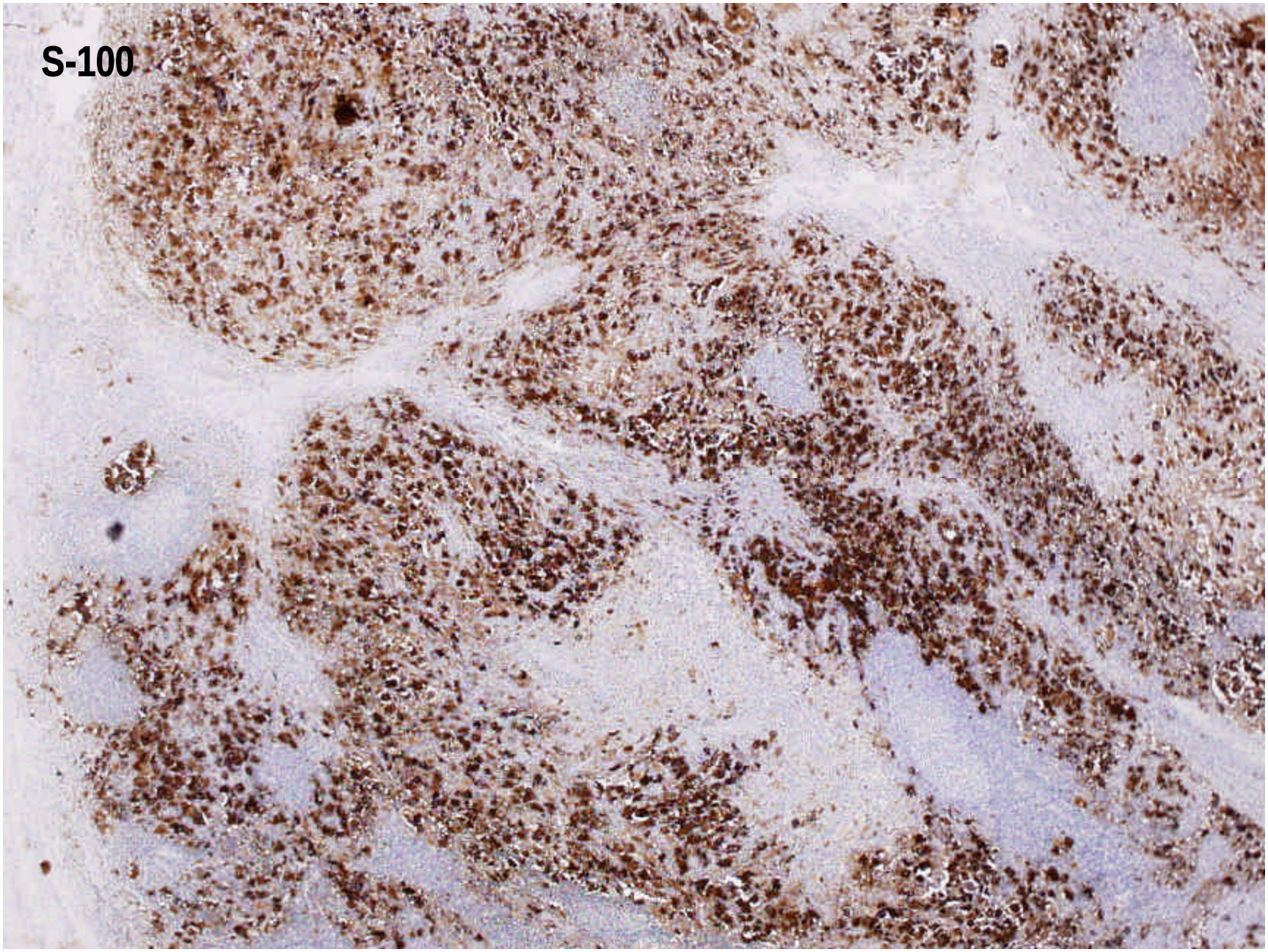


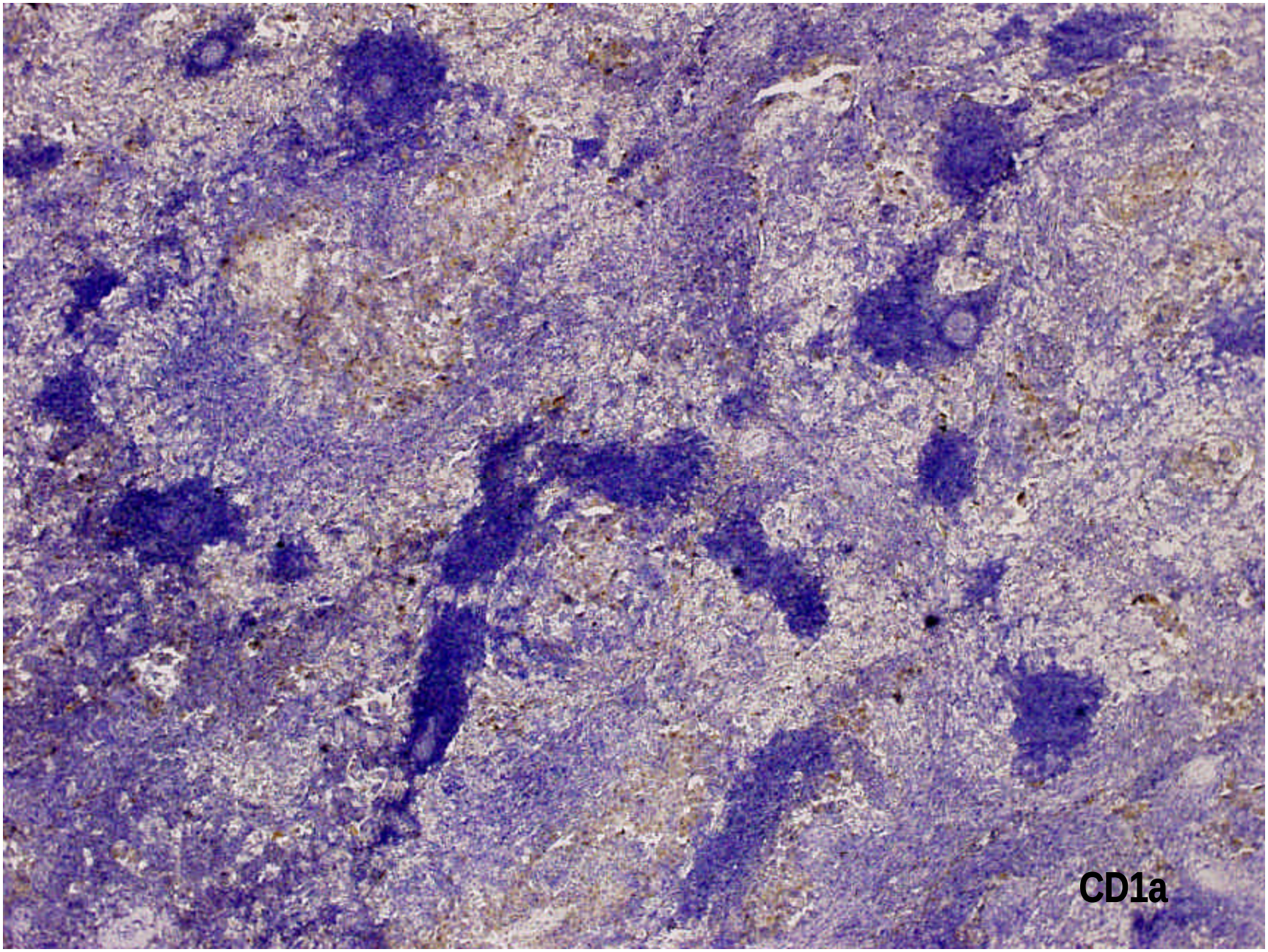




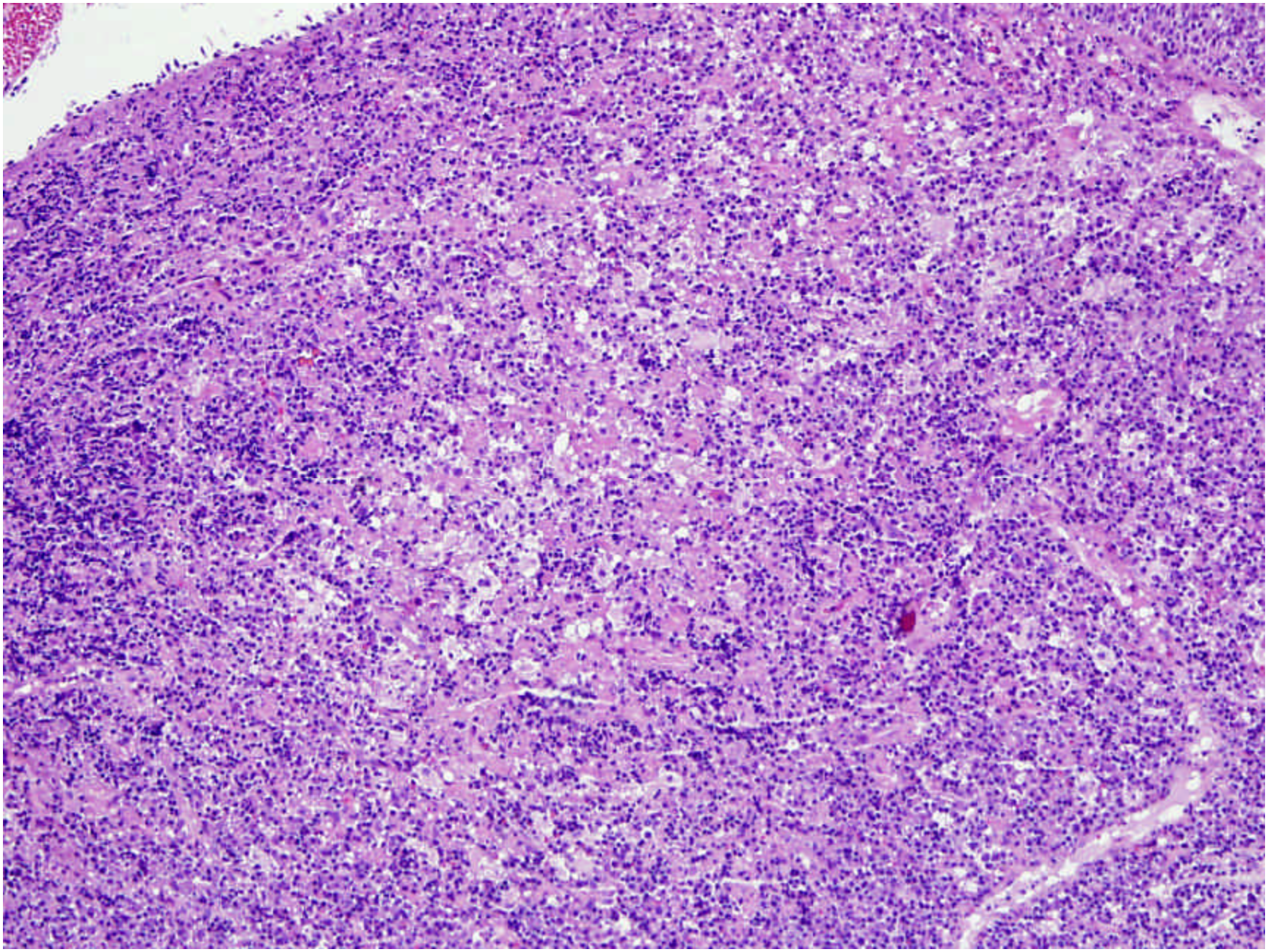





S-100


CD1a

DAP: Ganglio linfático con Enfermedad de Rosai- Dorfman.



Sinus Histiocytosis With Massive Lymphadenopathy

A Newly Recognized Benign Clinicopathological Entity

Juan Rosai, MD, and Ronald F. Dorfman, MRBCh, St. Louis

Four cases of a newly recognized benign disease which in the past has been confused with malignant reticuloendotheliosis are described. It is characterized clinically by massive lymphadenopathy, especially of the cervical region, fever, and leukocytosis, and pathologically by a prominent enlargement of lymph nodes due to dilatation of the subcapsular and medullary sinuses, which may progress to total effacement of the architecture. Most of the cells filling the sinuses are non-neoplastic histiocytes, often containing phagocytosed lymphocytes. The disease runs a benign, albeit prolonged, clinical course. The etiology and pathogenesis are unknown.

RETICULOENDOTHELIOSIS is probably one of the most confusing terms in pathology. It has been used as a generic term embracing both benign and malignant lesions of the reticuloendothelial system,[1-6] especially the group of diseases designated as histiocytosis X (Letterer-Siwe disease, Hand-Schuller-Christian disease, and eosinophilic granuloma,[7-14] and a group of obscure familial diseases[15]). In addition, it has often been employed as a wastebasket for malignant conditions of the hematopoietic system which are not easily classified as one of the conventional malignant lymphomas.

It is the purpose of this paper to report four cases of yet another condition formerly included under the heading of the reticuloendotheliloses, which we believe has clinical and pathologic features distinctive enough to be considered as a separate entity.

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From the Division of Surgical Pathology, Department of Pathology, Barnes Hospital and Washington University School of Medicine, St. Louis.

Reprint requests to Division of Surgical Pathology, Barnes Hospital, Barnes Hospital Plaza, St. Louis 63110 (Dr. Rosai).

Materials and Methods

Four cases which we have designated as sinus histiocytosis comprise the subject of this report. Cases 1 and 2 are from Barnes Hospital. Cases 3 and 4 were previously seen by one of us (R.F.D.) at the South African Institute for Medical Research, Johannesburg, South Africa. Clinical histories and microscopic slides were reviewed, and follow-up information was obtained. The lymph node biopsies had been fixed in formaldehyde solution, embedded in paraffin, and stained with hematoxylin and eosin. Additional stains obtained included Masson's trichrome, Wilder's reticulum, PAS with and without diastase digestion, Gomori's methenamine silver, Grant's, Ziehl-Neelsen, and oil red O stains.

Report of Cases

CASE 1.—A 7-month-old white male infant presented on May 1962 with a painless, firm, slightly mobile mass in the right parotid area of two months duration. Oxytetracycline (Terramycin) hydrochloride had been administered with no effect. The patient had had two recent episodes of "severe cold," treated with penicillin and chloramphenicol (Chloromycetin). The temperature was 101.8 F (38.8 C). There was a hypochromic anemia (hemoglobin level of 7.2 gm. and red blood cell count [RBC] of 3,230,000/cu mm), interpreted on a nutritional basis. The white blood cell count (WBC) was 14,350/cu mm, with 56% segmented neutrophils and 32% lymphocytes. Determination of serum proteins was not made at this time. At operation, a firm, tannish, homogeneous mass involved the parotid gland and was biopsied. An adjacent soft, white, nodular lymph node measuring 1 cm was ex-

SINUS HISTIOCYTOSIS WITH MASSIVE LYMPHADENOPATHY: A PSEUDOLYMPHOMATOUS BENIGN DISORDER

Analysis of 34 Cases

JUAN ROSAI, MD,* AND RONALD F. DORFMAN, MBBCH†

Thirty-four cases of sinus histiocytosis with massive lymphadenopathy (SHML) are analyzed. Most of the cases involved Negro children and were characterized by cervical lymphadenopathy, which was often bilateral, painless, and of massive proportions. Other lymph node groups were sometimes involved. Fever, leukocytosis with neutrophilia, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia were common features. The involved lymph nodes showed pericapsular fibrosis; dilatation of sinuses; presence of numerous intrasinusal histiocytes with abundant clear cytoplasm, occasionally multinucleated, foamy or atypical; and large collections of plasma cells. A striking and constant finding was the presence of many lymphocytes and other hematopoietic cells within the cytoplasm of the sinus histiocytes. The disease characteristically followed a protracted clinical course, with eventual spontaneous regression of the lymphadenopathy and total recovery in most cases. The etiology and pathogenesis are unknown. In this regard, the most likely possibilities include a specific infectious process and a status resulting from an immunologic defect.

IN 1969, WE DESCRIBED FOUR CASES OF A CONDITION we named "sinus histiocytosis with massive lymphadenopathy (SHML)"[23] and made reference to two others previously reported.[7,27] Subsequently, we have had the opportunity to study 30 additional examples. The detailed analysis of these 34 cases establishes conclusively the validity of SHML as

From the Division of Surgical Pathology, Department of Pathology, Washington University School of Medicine and Barnes Hospital, St. Louis, Mo.; and the Division of Surgical Pathology, Department of Pathology, Stanford University Medical Center, Stanford, Calif.

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* Assistant Professor of Pathology, Washington University School of Medicine, St. Louis, Mo.

† Associate Professor of Pathology and Co-Director of the Division of Surgical Pathology, Stanford University Medical Center, Stanford, Calif.

Address for reprints: J. Rosai, MD, Division of Surgical Pathology, Barnes Hospital, Barnes Hospital Plaza, St. Louis, Mo. 63110.

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ERD ganglionar- ERD extraganglionar

ERD en Cabeza y Cuello.

Wenig Bm, Abbondanzo SL, Childers EL, Kapadia SB, Heffner DR. Extranodal sinus histiocytosis with massive lymphadenopathy (Rosai- Dorfman disease) of the head and neck. *Hum Pathol* 1993; 24: 483.

ERD en Cabeza y Cuello. DIAGNÓSTICO DIFERENCIAL:

-Infecciones fúngicas

-Rinoescleroma (células de Mikulicz)

-Sífilis secundaria

-Lepra

-Granulomatosis de Wegener

-Plasmocitosis de Membranas Mucosas

-Linfoma T/NK extranodal de tipo nasal.

-Linfoma de Hodgkin

-Histiocitosis de células de Langerhans

Extranodal Sinus Histiocytosis With Massive Lymphadenopathy (Rosai-Dorfman Disease) of the Head and Neck

BRUCE M. WENIG, MD, SUSAN L. ABBONDANZO, MD, ESTHER L. CHILDERS, DDS, SILLOO B. KAPADIA, MD, AND DENNIS R. HEFFNER, MD

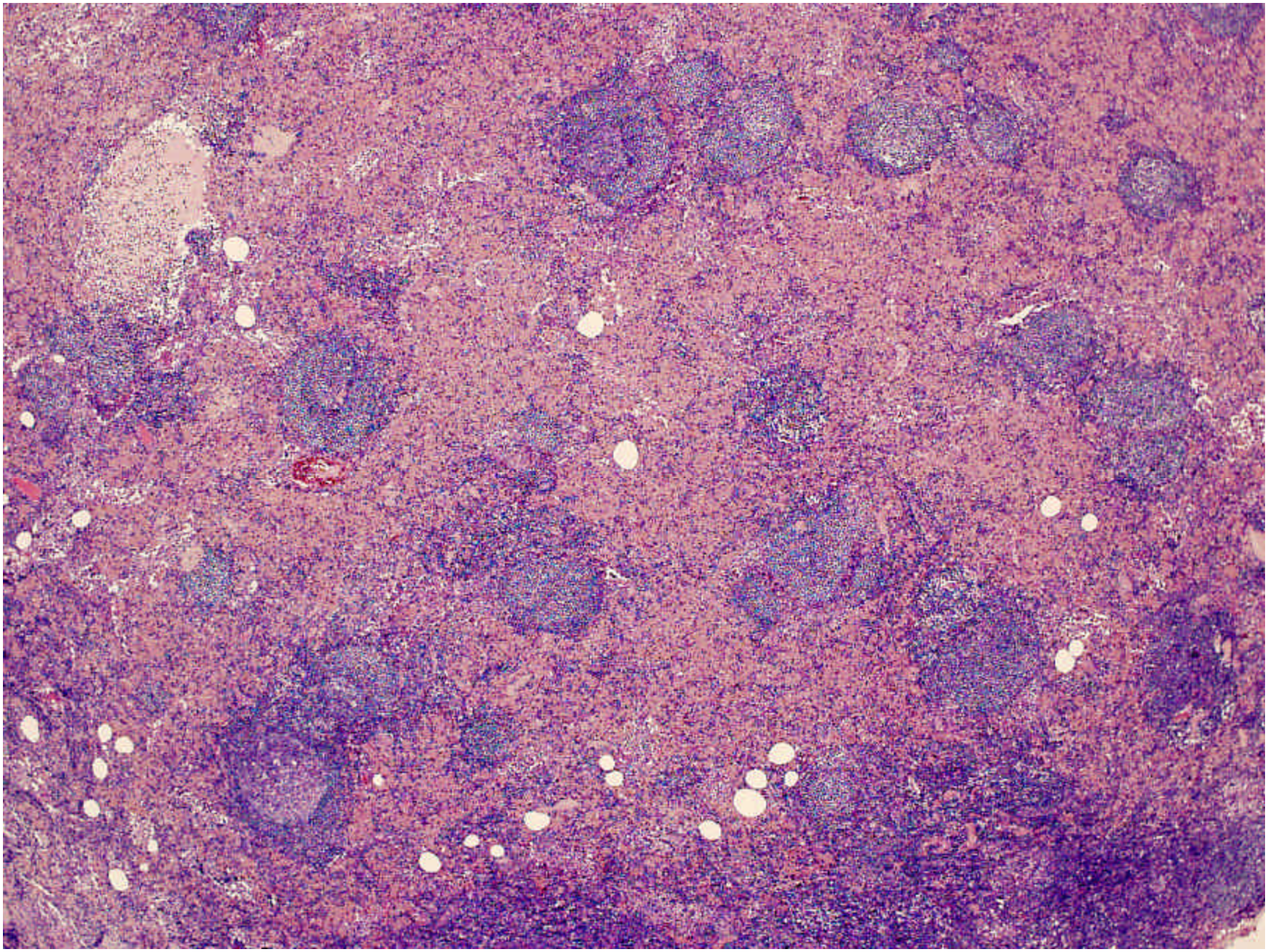
HUMAN PATHOLOGY Volume 24, No. 5 (May 1993)

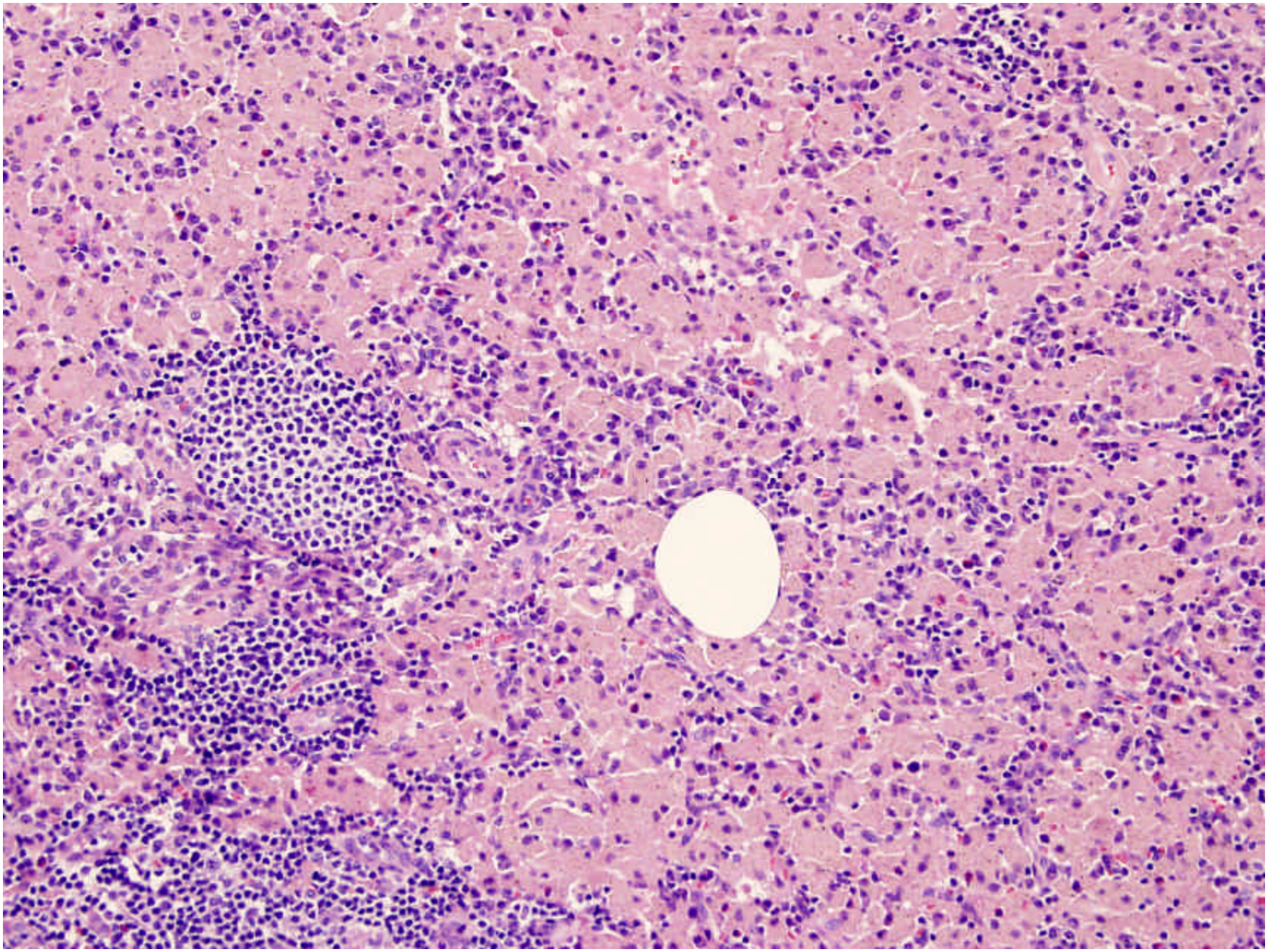
Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymhadenopathy (Rosai- Dorfman disease). Review of the entity. *Semin Diagn Pathol* 1990, 7: 19.

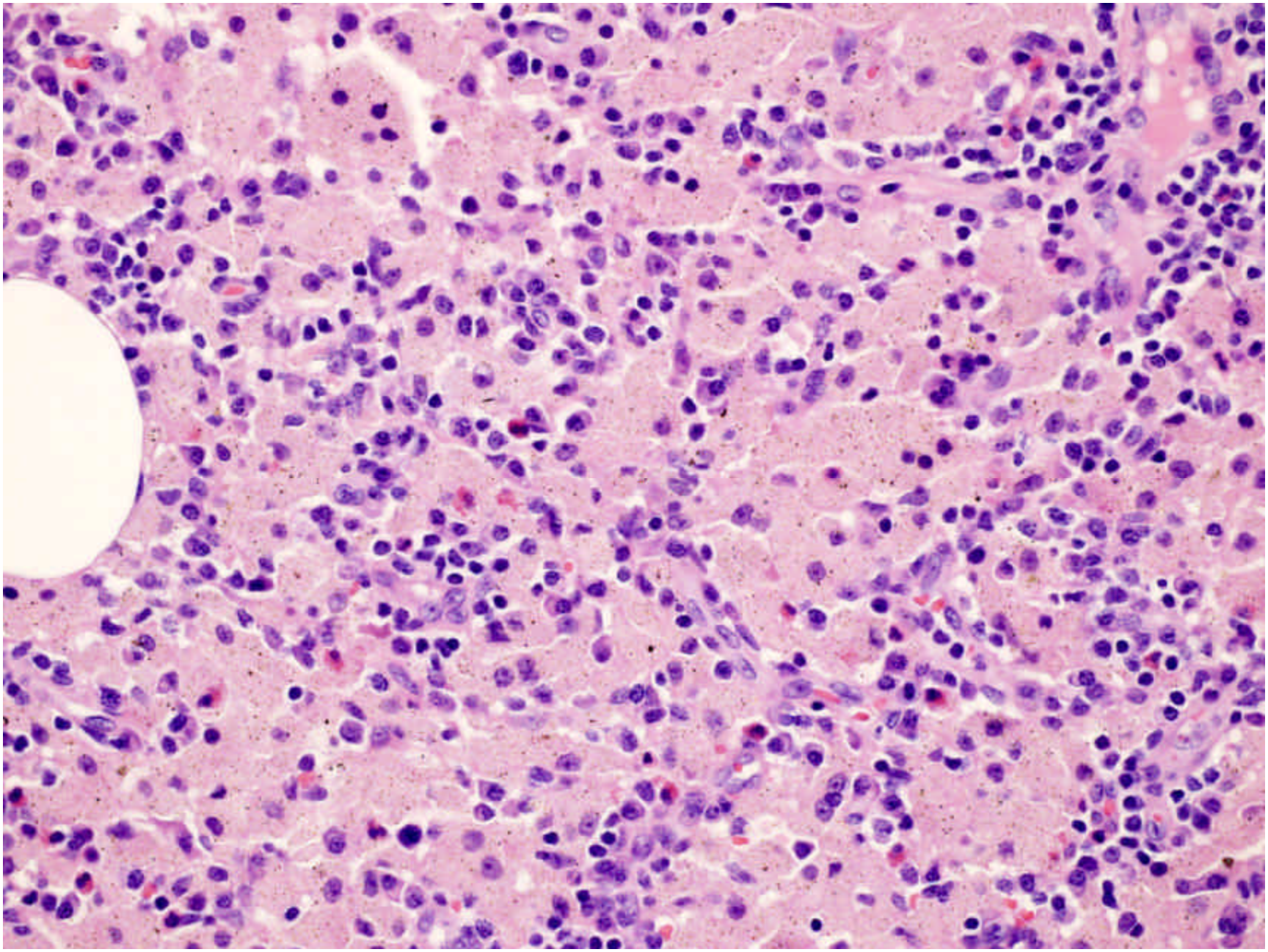
TABLE 2. Clinical Data: Head and Neck Sinus Histiocytosis With Massive Lymphadenopathy

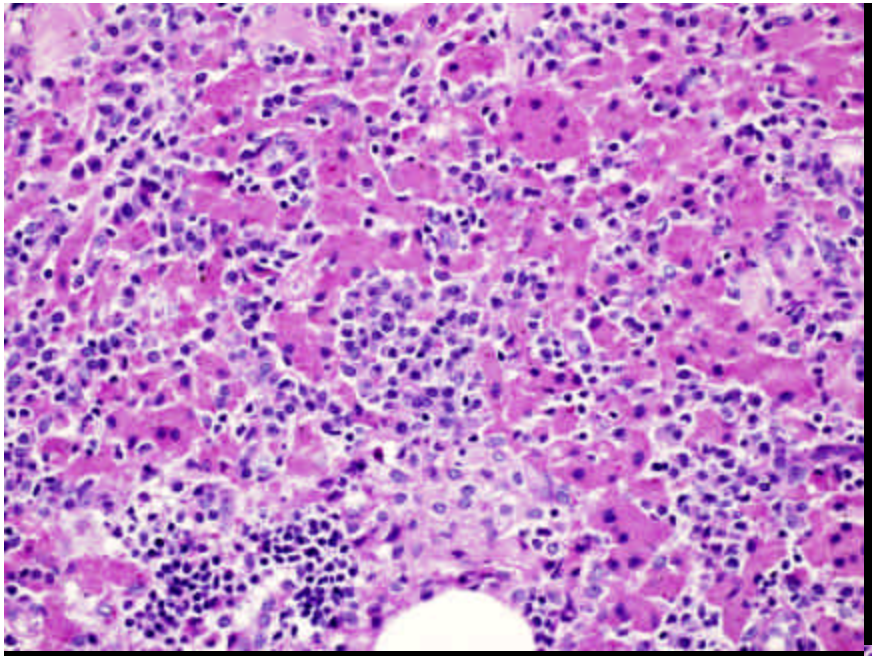
e No./ e (yr)/ Sex	Presentation	Site(s) of Occurrence	Contributor Diagnosis	Recurrences
/50/F	Left ptosis and proptosis with sixth nerve palsy	Left sphenoid bone, floor of temporal fossa, and orbit	Meningioma v eosinophilic granuloma v inflammatory pseudotumor	Four recurrences over a 6-year period predominantly involving the nasal cavity
/40/F	Painless mass in the left parotid gland	Left parotid gland, nasal cavity, left supraglottis, right subglottis, and anterior mediastinum (lymph node)	Granulomatous inflammation of unknown etiology	Progressive enlargement of the anterior mediastinal mass with resulting dyspnea and stridor occurred approximately 1 year following the initial excisions; 16 months following the initial diagnosis a subcutaneous mass on the back was identified
3/64/F	Nasal obstruction	Nasal septum	Granulomatous inflammation of unknown etiology	None
4/70/M	Painless mass in the submandibular gland for 6 months	Submandibular gland	Xanthogranuloma	None
5/16/F	Bilateral proptosis and sinusitis for 3 years with development of a saddle nose deformity	Maxillary and ethmoid sinuses with involvement of the orbit and sphenoid ridge	MMR	Progression of disease with bilateral proptosis, erosion into orbital bones, and destruction of the nasal septum
6/3/M	Painless mass medial to the left eye	Lacrimal gland area	MMR	Recurrence 8 years following initial diagnosis with involvement of the nasal cavities and left maxillary sinus
7/54/F	Decreased vision in right eye and numbness in face for 6 months	Sphenoid bone, temporal bone, orbit, and pterygoid fossa	Inflammatory pseudotumor	—
8/42/F	Nasal obstruction for 2 years; two prior maxillary sinus surgical procedures in Colombia	Ill-defined infiltrates in maxillary sinus	Aggressive fibromatosis	Two recurrences in the cheek within 1 year of initial diagnosis
9/17/F	Left mandibular tenderness	Third molar with extension to buccal and lingual soft tissues and bone	Reparative giant cell tumor	None
10/22/F	Flu-like symptoms for 1 month with development of right-sided facial tenderness and swelling, neck swelling, and progressive stridor	Nasal cavities, nasopharynx, right ethmoid sinus, and subglottis; right cervical adenopathy	Histiocytosis X	Progression of disease over several months following the initial diagnosis with increased facial swelling, cervical adenopathy, and CT scan evidence of progressive sinonasal disease
11/34/M	Epistaxis for 3 years with adenopathy right upper arm region; optic and cochlear nerve deficits preceded the above symptoms by 5 and 4 years, respectively	Nasal cavity (septum); axillary lymph node	Infectious or inflammatory process	Persistent disease in sinonasal region; the cause of the cranial nerve deficits (blindness and deafness) is at present not known
12/39/M	Intermittent nasal obstruction, fever, facial pain, and cervical adenopathy	Nasal septum with bone destruction; cervical lymph nodes	Rhinoscleroma v Gaucher's disease	None
13/09/M	Nasal obstruction of undetermined duration	Nasal cavity	Extramedullary plasmacytoma	One (at the same site as the first lesion) 3 years following the initial mass
14/51/F	Epistaxis for 2 months	Right inferior nasal turbinate with extension into the nasopharynx	Fibrous histiocytoma v infectious disease v malignant lymphoproliferative process	None

Abbreviations: MMR, Malline malignant reticulosis; CT, computed tomography.
* Data from ref 6.









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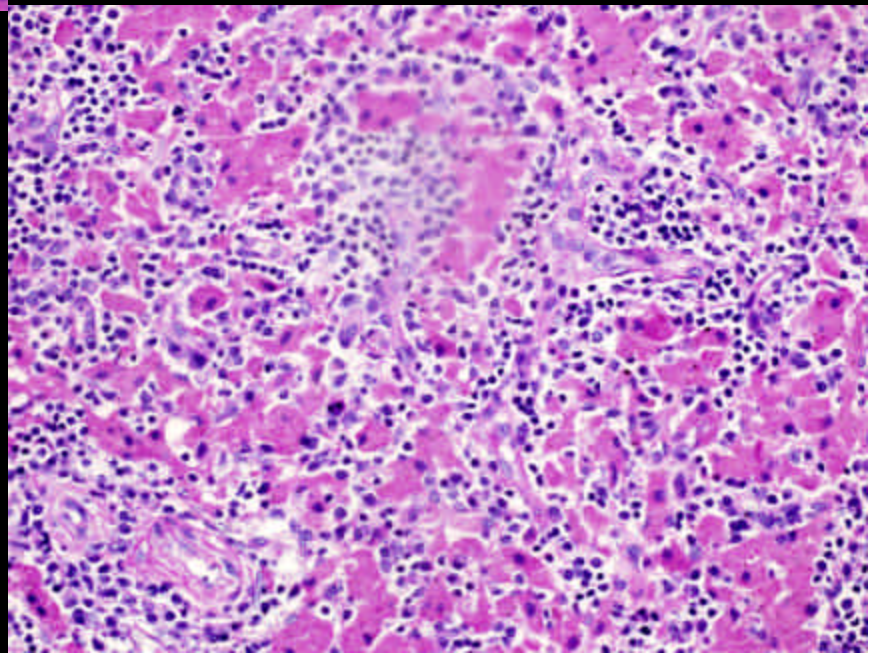

The American Journal of Surgical Pathology 18(1): 51-60, 1994

Sinus Histiocytosis of Pelvic Lymph Nodes after Hip Replacement

A Histiocytic Proliferation Induced by Cobalt–Chromium and Titanium

Jorge Albores-Saavedra, M.D., Frank Vuitch, M.D., Ruby Delgado, M.D., Elizabeth Wiley, M.D., and Herbert Hagler, Ph.D.

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ETIOLOGÍA?

Rosai J. Rosai- Dorfman disease (sinus histiocytosis with massive lymphadenopathy) in Rosai and Ackerman´s Surgical Pathology. Ninth Ed. Mosby 2004, volume 2: 1911.

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Histologic Features of Sinus Histiocytosis With Massive Lymphadenopathy in Patients With Autoimmune Lymphoproliferative Syndrome

Irina Maric, MD,‡ Stefania Pittaluga, MD, PhD,* Janet K. Dale, BA,† Julie E. Niemela, BA,‡ Georges Delsol, MD,§ Judith Diment, MD,‖ Juan Rosai, MD,‖ Mark Raffeld, MD,* Jennifer M. Puck, PhD,¶ Stephen E. Straus, MD,† and Elaine S. Jaffe, MD**

Abstract: Autoimmune lymphoproliferative syndrome (ALPS) is an inherited disorder associated with defects in Fas-mediated apoptosis, characterized most often by childhood onset of lymphadenopathy, splenomegaly, hypergammaglobulinemia, and autoimmune phenomena. Children with sinus histiocytosis with massive lymphadenopathy (SHML) have a somewhat similar clinical phenotype in which prominent adenopathy also is associated with hypergammaglobulinemia, and autoimmune phenomena are reported in 10-15% of cases. We observed histopathological features of SHML in the lymph nodes of some of our ALPS patients, further suggesting an association between these two disorders. We, thus, reviewed the lymph nodes from 44 patients ALPS type Ia, all of whom were confirmed to have germline mutations in the *TNFRSF6* gene encoding Fas (CD95/Apo-1). Eighteen of 44 (41%) patients had a histiocytic proliferation resembling SHML. The affected patients included 15 males and 3 females ranging in age from 11 months to 30 years at the time of the LN biopsy. The lymph nodes contained S-100+ histiocytes with characteristic nuclear features of SHML, and showed evidence of emperipolesis in both hematoxylin and eosin (H and E) and immunostained sections. The extent of the histiocytic proliferation was variable, being confluent in 2 cases, multifocal in 13, and only evident as isolated SHML-type histiocytes in 3. In lymph nodes without confluent SHML changes, increased numbers of $CD3^+CD4^-CD8^-$ (double negative) $\alpha\beta$ T-cells, also negative for CD45RO, a feature of ALPS, could be identified in the paracortex. Furthermore, because SHML shares many clinical features with ALPS, we sought evidence of ALPS in sporadic SHML. We attempted to sequence *TNFRSF6* DNA from archived tissue of 14 cases of Rosai-Dorfman disease. Full sequencing of the gene was successful in 4 of the cases; no mutations were identified. Nevertheless, our observations suggest that histologic features of SHML are part of the pathologic spectrum of ALPS type Ia. It remains to be determined if some cases of apparently sporadic SHML may be associated with heritable defects in Fas-mediated apoptosis.

Key Words: autoimmune lymphoproliferative syndrome, sinus histiocytosis with massive lymphadenopathy, Rosai-Dorfman disease, autoimmune disease, histiocytoses, apoptosis, emperipolesis, Fas gene

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Autoimmune lymphoproliferative syndrome (ALPS) is a recently recognized rare inherited disorder that usually presents in children with generalized, nonmalignant lymphadenopathy, hypergammaglobulinemia, lymphocytosis, splenomegaly, and autoimmune phenomena.[1-4] The syndrome was first reported by Canale and Smith, who identified it as a syndrome of chronic lymphadenopathy simulating lymphoma.[2] More recent work showed that most cases are associated with defects in the Fas-Fas ligand apoptotic pathway.[3,5] Binding of the Fas ligand to Fas initiates B- and T-lymphocyte apoptosis. Fas transduces a death signal through its cytoplasmic "death domain," the binding site for proteins that activate cysteine proteases (caspases) that mediate the apoptosis cascade.[6] Lymphocytes of patients with ALPS fail to undergo apoptosis

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Treatment of Sinus Histiocytosis With Massive Lymphadenopathy (Rosai-Dorfman Disease): Report of a Case and Literature Review

Alessandro Pulsoni,* Gabriel Anghel, Paolo Falcucci, Roberta Matera, Edoardo Pescarmona, Michela Ribersani, Nicoletta Villiva', and Franco Mandelli

Department of Cellular Biotechnology and Hematology, "La Sapienza" University, Rome, Italy

TABLE I. Review of Patients With SHML That Did Not Require Chemotherapy, Radiation, or Surgery

Year	Author	No of patients	Treatment	Response[a]
1972	Rosai [1]	18	Steroids + antibiotics- + tubercolostatics	15 healthy, 3 PD
1976	Lampert [5]	8	No therapy or steroids	6 CR, 1 PD, 1 death
1987	Miettinen [6]	3	2 No therapy 1 steroids	3 CR
1989	Layfield [7]	1	No therapy	1 CR
1989	McAlister [8]	5	Steroids	5 CR
1992	Philipp [9]	1	No therapy	1 CR
1992	Chu [10]	3	Steroids	1 PD, 1PR, 1 CR
1993	Shaver [11]	1	Steroids	CR

[a]CR = complete remission; PD = persisting disease; PR = partial remission.

TABLE II. Review of Patients With SHML That Required Chemotherapy, Radiotherapy, Surgical Debulking, or Interferon

Year	Author	No of patients	Treatment[a]	Response[b]
1972	Rosai [1]	8	4 Chemotherapy, 4 Radiation	3 PD, 1 death, 2 CR, 2 PD
1978	Nawroz [12]	1	Surgery	Healthy
1989	McAlister [8]	2	1 Radiation + steroids, 1 VCR then CHLB then MTX and 6-MP	1 healthy, 1 CR (to MTX and 6-MP)
1992	Baildam [13]	1	Acyclovir	CR
1992	Zagdanska [14]	1	Cyclophosphamide + steroids	PR (subsequent death for infection)
1992	Chu [10]	2	1 Surgery, 1 Chlorambucil	Unknown, PD
1992	Paulli [15]	1	Radiation	PD
1992	Afzal [16]	1	Surgery	Healthy
1993	Wenig [17]	13	5 Surgery, 7 Surgery + steroids + radiation	5 CR, 1 death, 1 CR, 3 PD, 2 unknown
1993	Perrin [18]	1	Cyclophosphamide	PD
1994	Levine [19]	1	Surgery + radiation	Healthy
1994	Foucar [20]	7	3 Radiation, 4 Chemotherapy	3 death, 4 death
1996	Lohr [4]	1	Interferon	CR
1996	Horneff [3]	1	VP-16 then MTX + 6-MP	CR to MTX + 6-MP

[a]VCR = vincristine; CHLB = chlorambucil; MTX = methotrexate; 6-MP = 6-mercaptopurine.
[b]PD = persisting disease; CR = complete remission; PR = partial remission.

TABLE III. Summary of Results of Different Therapeutic Approaches in Patients With SHML That Required a More Intensive Treatment*

	No of patients	CR	PD	PR	Death	Unknown
Chemotherapy (CT)	12	2 (16.6%)	5 (41.7%)	–	5 (41.7%)	–
Surgery	9	8 (88.8%)	–	–	–	1
Radiation (Rx)	9	3 (33.3%)	3 (33.3%)	–	3 (33.3%)	–
Surgery + Rx	1	1	–	–	–	–
Surgery + Rx + CT	7	1 (14%)	3 (43%)	–	1 (14%)	2
Interferon	1	1	–	–	–	–
Acyclovir	1	1	–	–	–	–
Total	40	17 (42.5%)	11 (27.5%)	–	9 (22.5%)	3

*CR = complete response; PD = persisting disease; PR = partial remission.

Sinus histiocytosis with massive lymphadenopathy (SHML) is a rare disorder of unknown etiology, usually associated with lymph node enlargement in various superficial or deep sites. It usually shows a prolonged clinical course with occasional exacerbation and remission phases. We describe the long-term follow-up of a case of SHML that showed typical clinical features and in which various therapeutic strategies were attempted. Chemotherapy and α-interferon (IFN) were ineffective; surgery was ultimately required with satisfactory results. From an extensive literature review we found different treatment strategies in SHML in the 80 cases published between 1969 and 2000. Spontaneous resolution of adenopathies is frequently observed: 32 out of 40 cases which did not receive chemotherapy, radiotherapy, or surgery were healthy at the time of publication. Radiotherapy alone showed conflicting results: 3 complete remissions (CR) were obtained in the 9 patients treated. Surgical debulking when required was effective—8/9 CR—while chemotherapy showed generally negative results. IFN has been previously employed in only one case. In conclusion, clinical observation without treatment is advisable when possible. In the presence of vital organ compression and/or extranodal localization with important clinical signs, surgical debulking may be necessary. Radiotherapy has shown limited efficacy, while chemotherapy is in general ineffective. More experience is needed to evaluate the role of IFN. Am. J. Hematol. 69:67–71, 2002.

Key words: Rosai-Dorfman disease; sinus histiocytosis; lymphadenopathy; chemotherapy; surgery

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