Overview of some lymphoma mimics

淋巴瘤近亲概况

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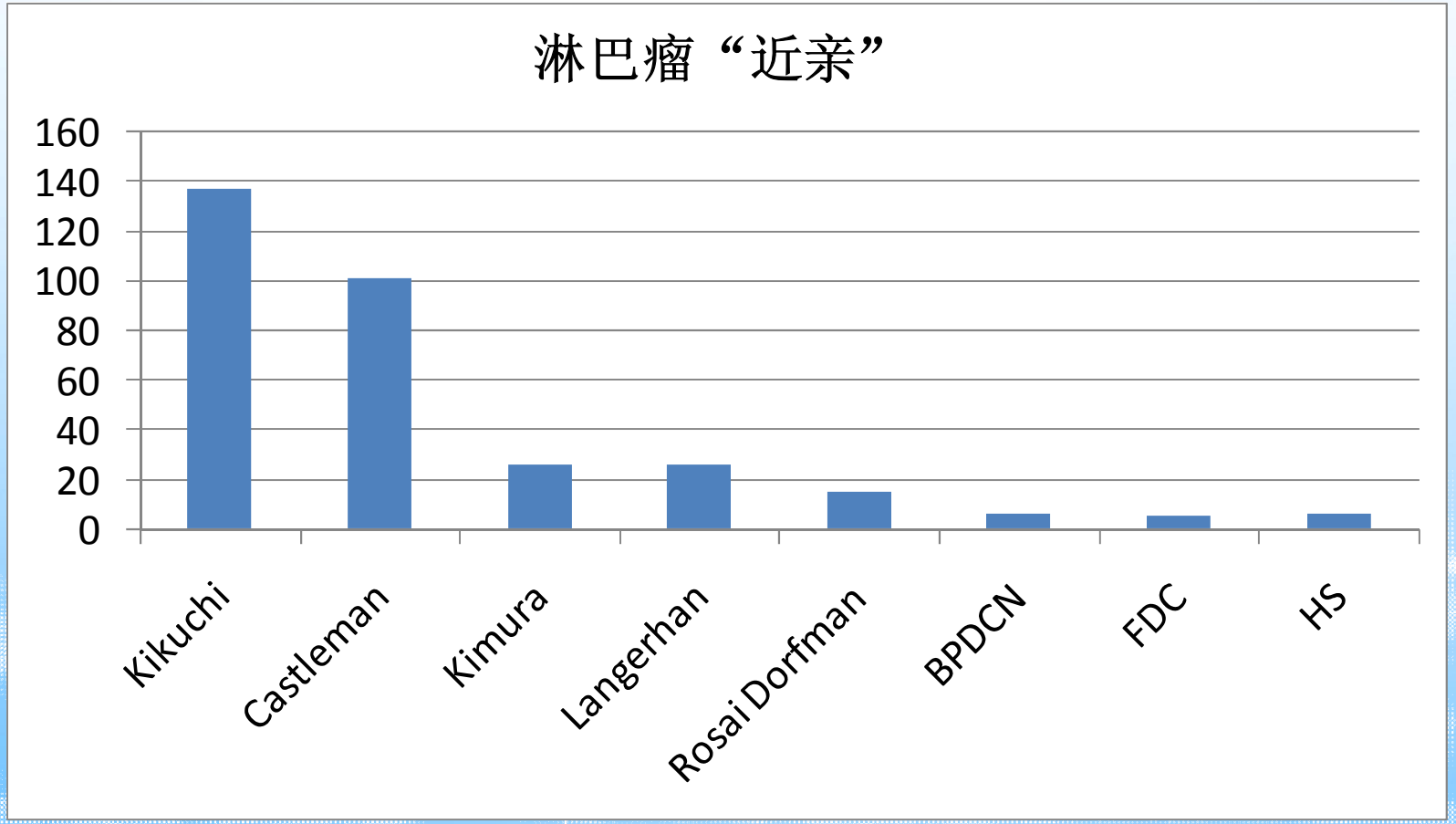
BCH “淋巴瘤近亲”近五年发病情况统计（2008-11~至今）

疾病类型	例数	男/女	年龄范围	平均年龄	中位年龄	部位（结内/外）	组织类型	系统性病变
Kikuchi 淋巴结炎	137	44/93	5-77	32	29	淋巴结		
Castleman 病*	101	58/43	10-72	42	43	91/10	HV(59), PC (11), 混合型（26）	10 例 1 例淋巴结发生者合并 MALT
Kimura 病	26	25/1	12-77	39	40	淋巴结或软组织		
Langerhans 组织细胞增生症	26	17/9	1-77	26.7	26	14 例发生在骨，		1 例淋巴结发生者合并 ALCL
Rosai Dorfman 病*	15	9/6	1-64	36	35	淋巴结、脾结外		
BPDCN*	6	2/4	20-78	51.8	62	淋巴结（1）/皮肤（4）		
FDC 肿瘤*	5	1/4	29-69	50	48	脾（2）、肠，颈部，腹膜后		
组织细胞肉瘤	6	4/2	15-67	38	37	淋巴结（4），软组织（1），硬膜外（1）		


淋巴瘤“近亲”
160
140
120
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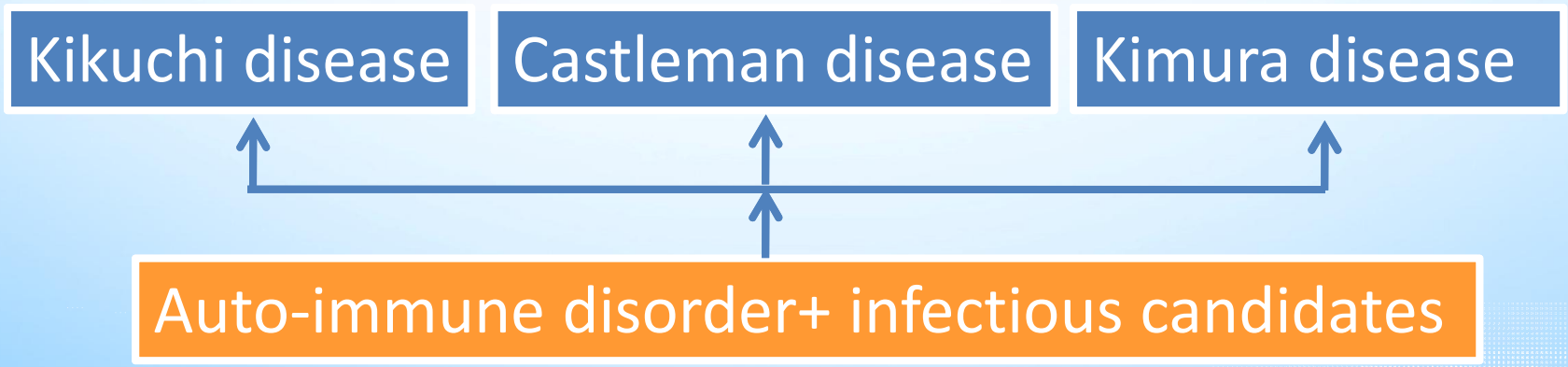
Kikuchi
Castleman
Kimura
Langerhan
Rosai Dorfman
BPDCN
FDC
HS

Lymphoma mimics



Kikuchi lymphadenitis

One of reactive lesions often misdiagnosed as lymphoma

Kikuchi lymphadenitis

- Kikuchi-Fujimoto disease (KFD) was first described in Japan by Dr Masahiro Kikuchi in 1972 and independently by Y. Fujimoto.
- It is also known as **Kikuchi disease**, histiocytic necrotizing lymphadenitis, Kikuchi necrotizing lymphadenitis, phagocytic necrotizing lymphadenitis, subacute necrotizing lymphadenitis, and necrotizing lymphadenitis .

Kikuchi lymphadenitis

Epidemiology

- Kikuchi-Fujimoto disease (KFD) is a rare disorder that typically affects the cervical lymph nodes. It is mainly a disease of young adults (mean age, 20–30 years), with a slight bias towards females.
- Course of the disease is generally benign and self-limiting. Lymphadenopathy most often resolves over several weeks to six months. Recurrence rate is about 3%. Mortality is extremely rare and usually due to hepatic, respiratory, or cardiac failure.

Kikuchi lymphadenitis

Pathogenesis

- Some studies have suggested a genetic predisposition to the proposed autoimmune response.
- Several infectious candidates have been associated with Kikuchi's disease.
- Mycobacterium szulgai, Yersinia and Toxoplasma
- Epstein-Barr virus, HHV6, HHV8, Parvovirus B19, HIV- and HTLV-1

Kikuchi lymphadenitis

- It is possible that KFD may represent an exuberant T-cell mediated immune response in a genetically susceptible individual to a variety of non-specific stimuli.

Kikuchi lymphadenitis

Clinical Features

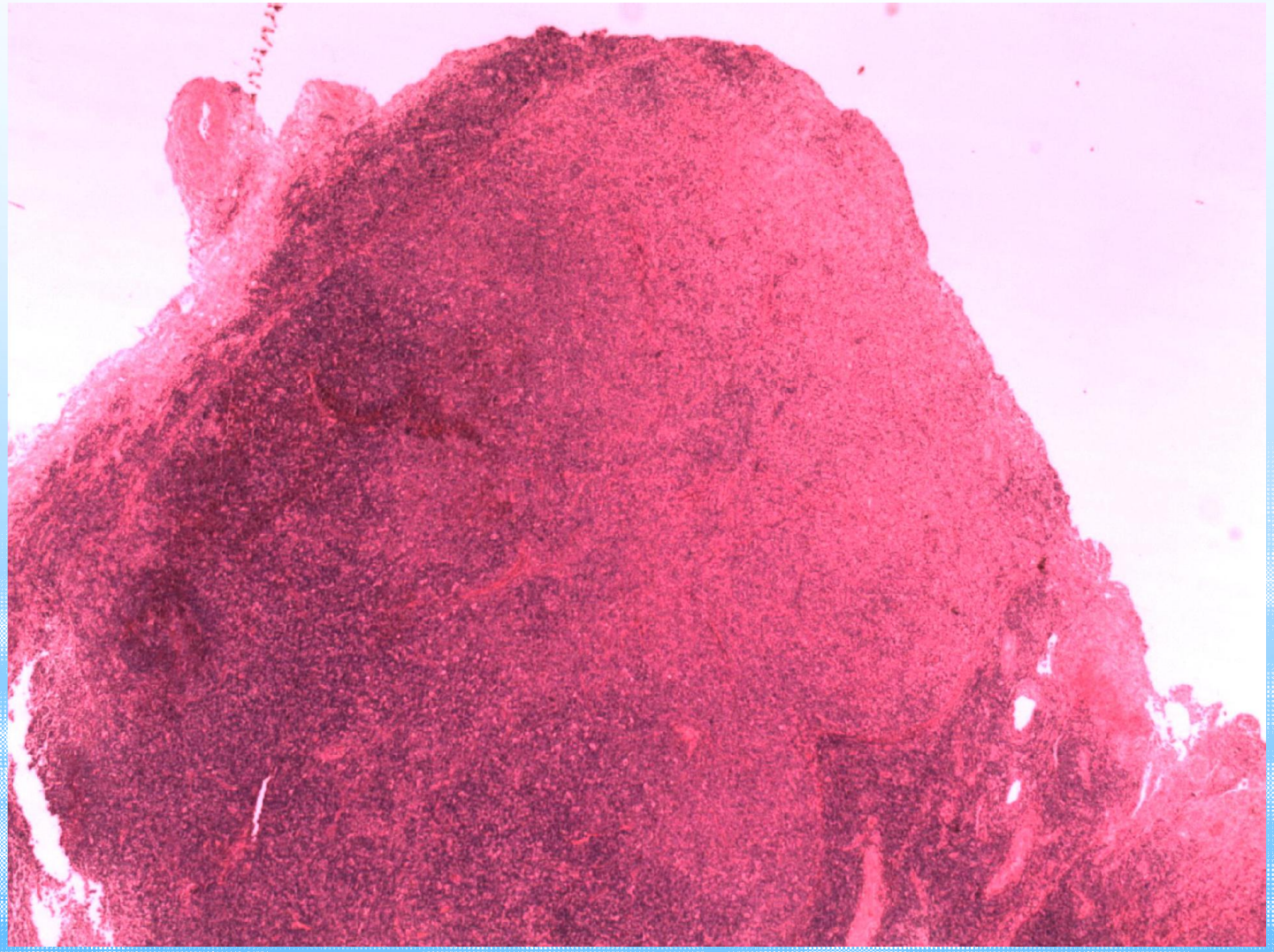
- The signs and symptoms of Kikuchi's disease are fever, lymphodenopathy, skin rashes and head-ache. Rarely hepatosplenomegaly and nervous system involvement resembling menigitis is seen.
- Typical laboratory findings are an increased ESR, lymphocytosis, and neutropenia.
- Differential diagnosis includes SLE, disseminated tuberculosis , lymphoma, sarcoidosis, and viral lymphodenopathy.

Kikuchi lymphadenitis

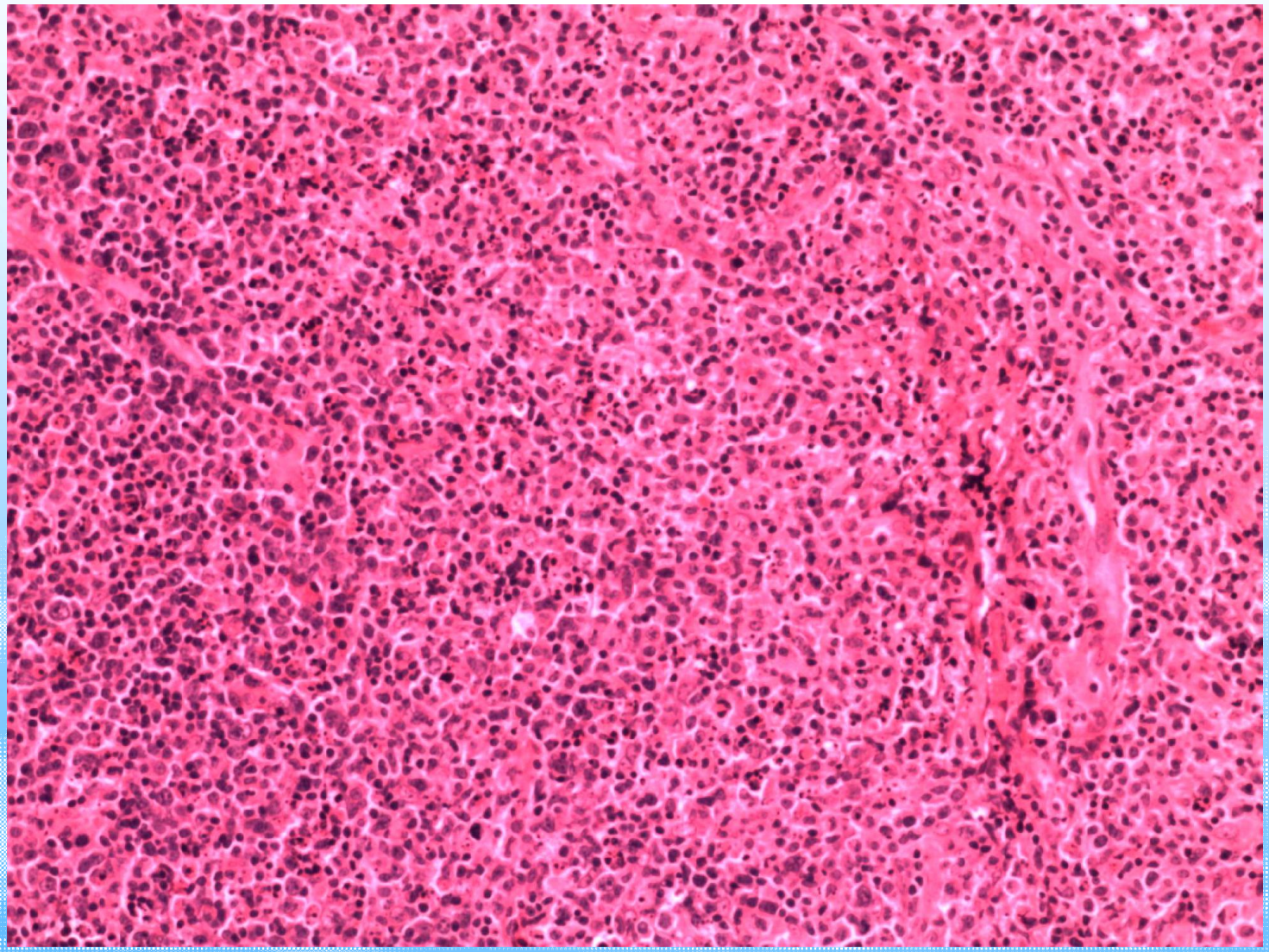
Morphological features

- Patchy distribution and non-expansile quality of the lesional areas
- Abundance of karyorrhectic debris, and presence of admixed medium-sized cells with round nuclei (plasmac ytoid dendritic cells).
- In addition to the presence of large T cells (CD3-positive) in the lesion, there are many CD68-positive histiocytes coexpressing myeloperoxidase, and also many CD68-positive CD123-positive plasmacytoid den-d ritic cells.

Kikuchi lymphadenitis



Kikuchi lymphadenitis



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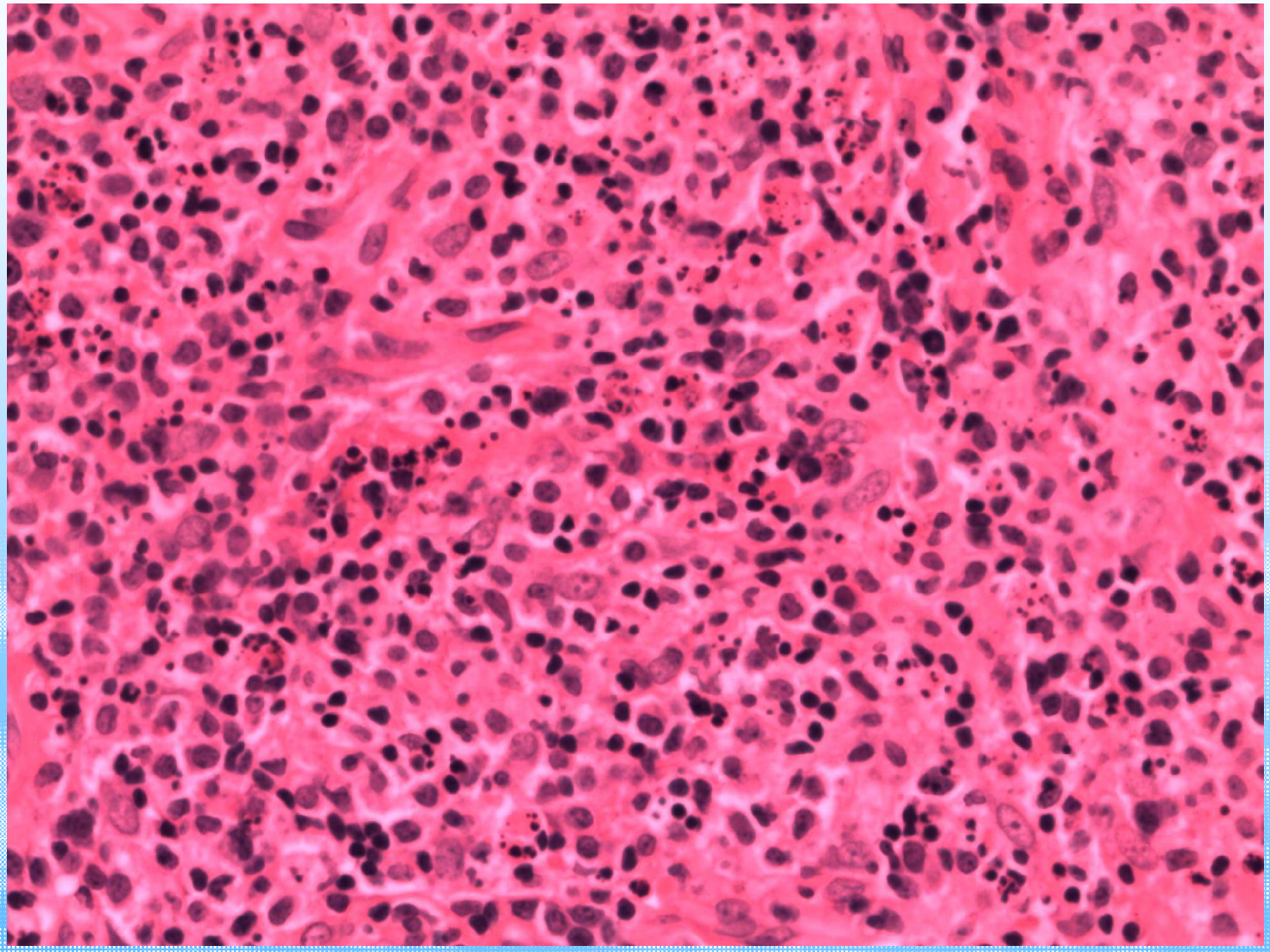

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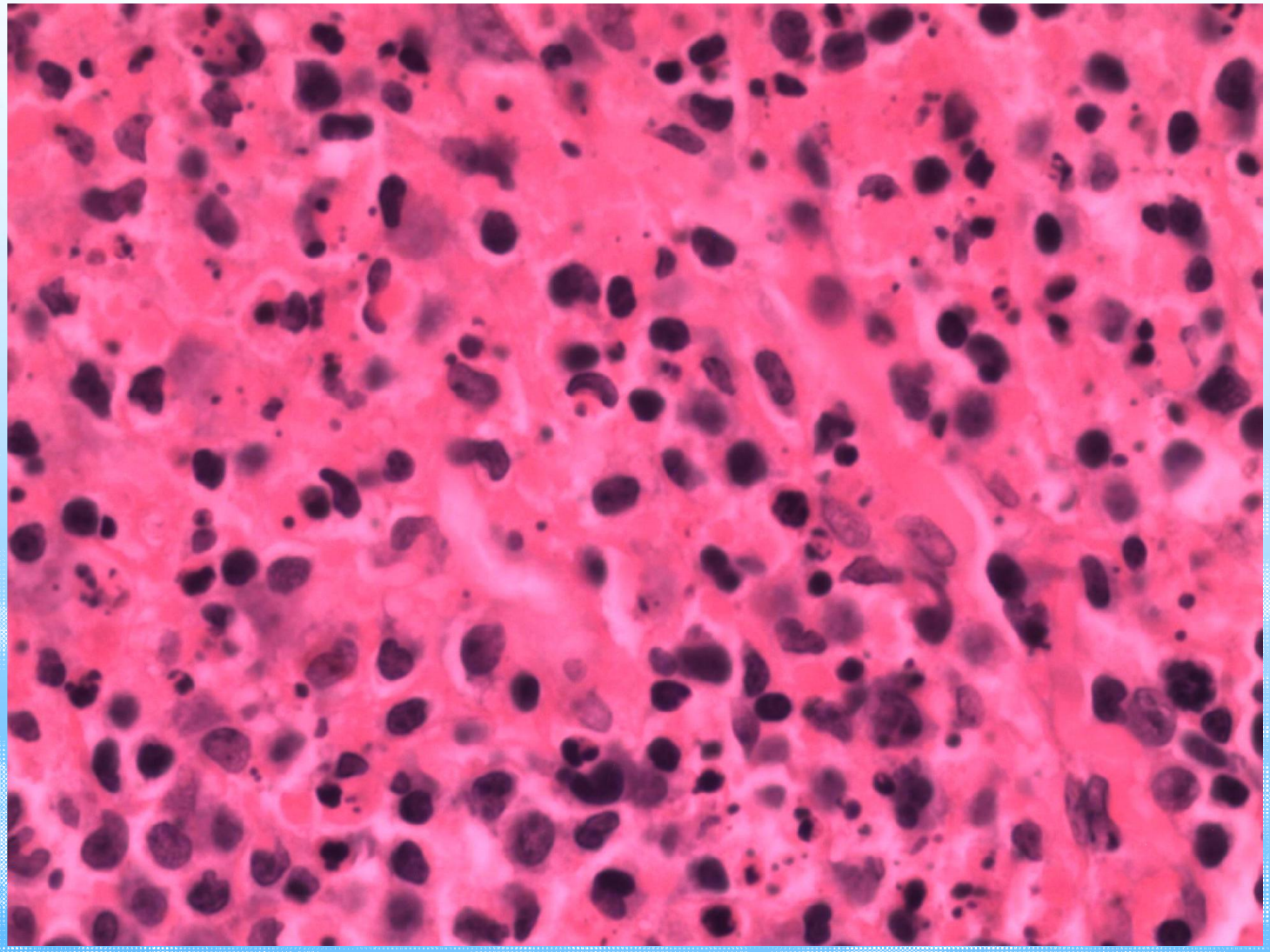
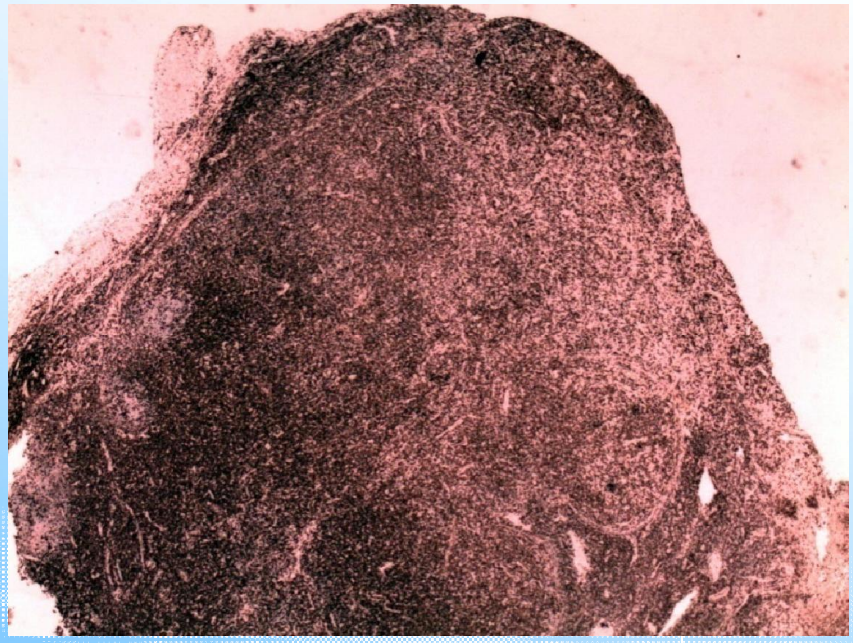
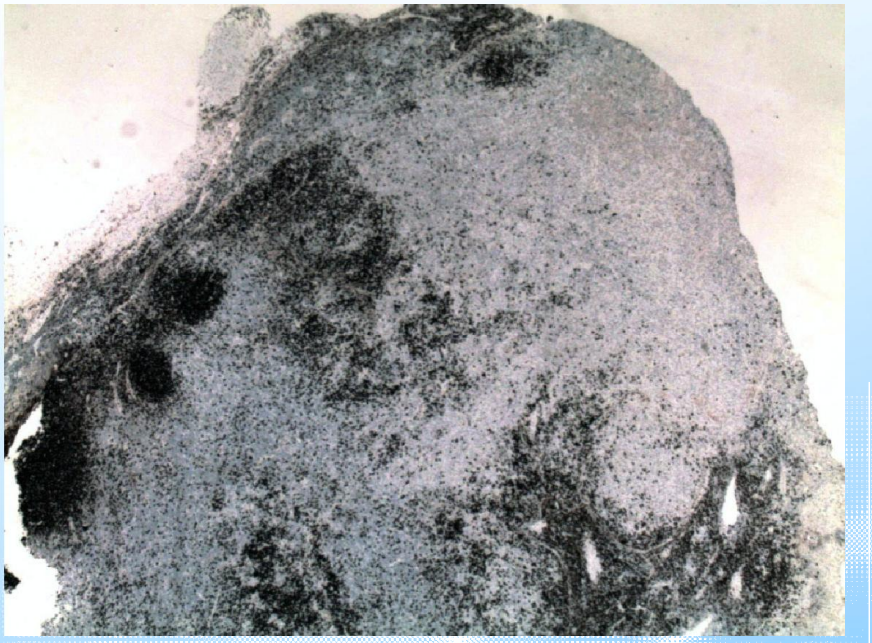


Kikuchi lymphadenitis

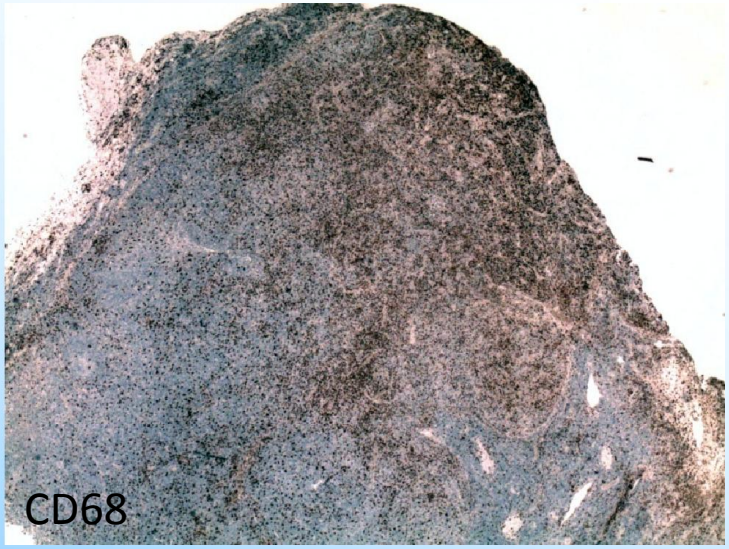


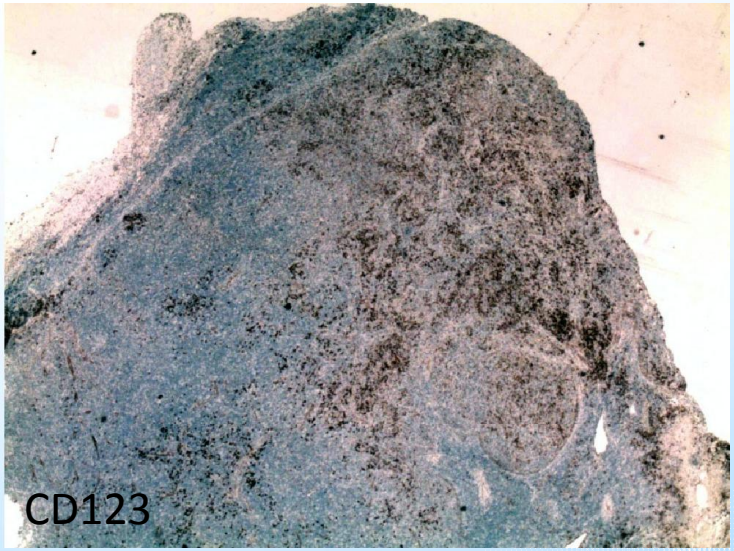
CD3

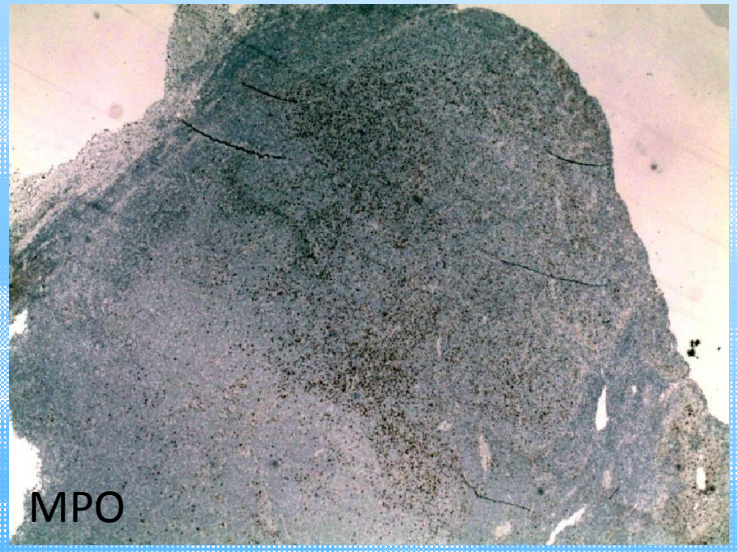


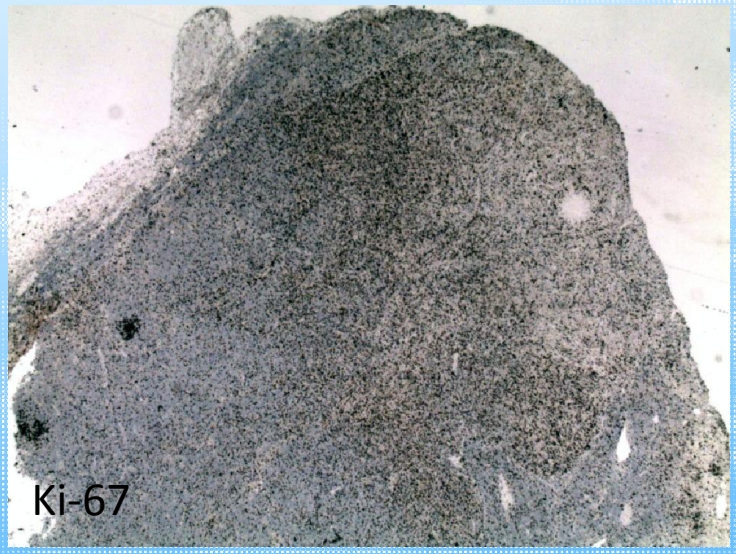
CD20

Kikuchi lymphadenitis









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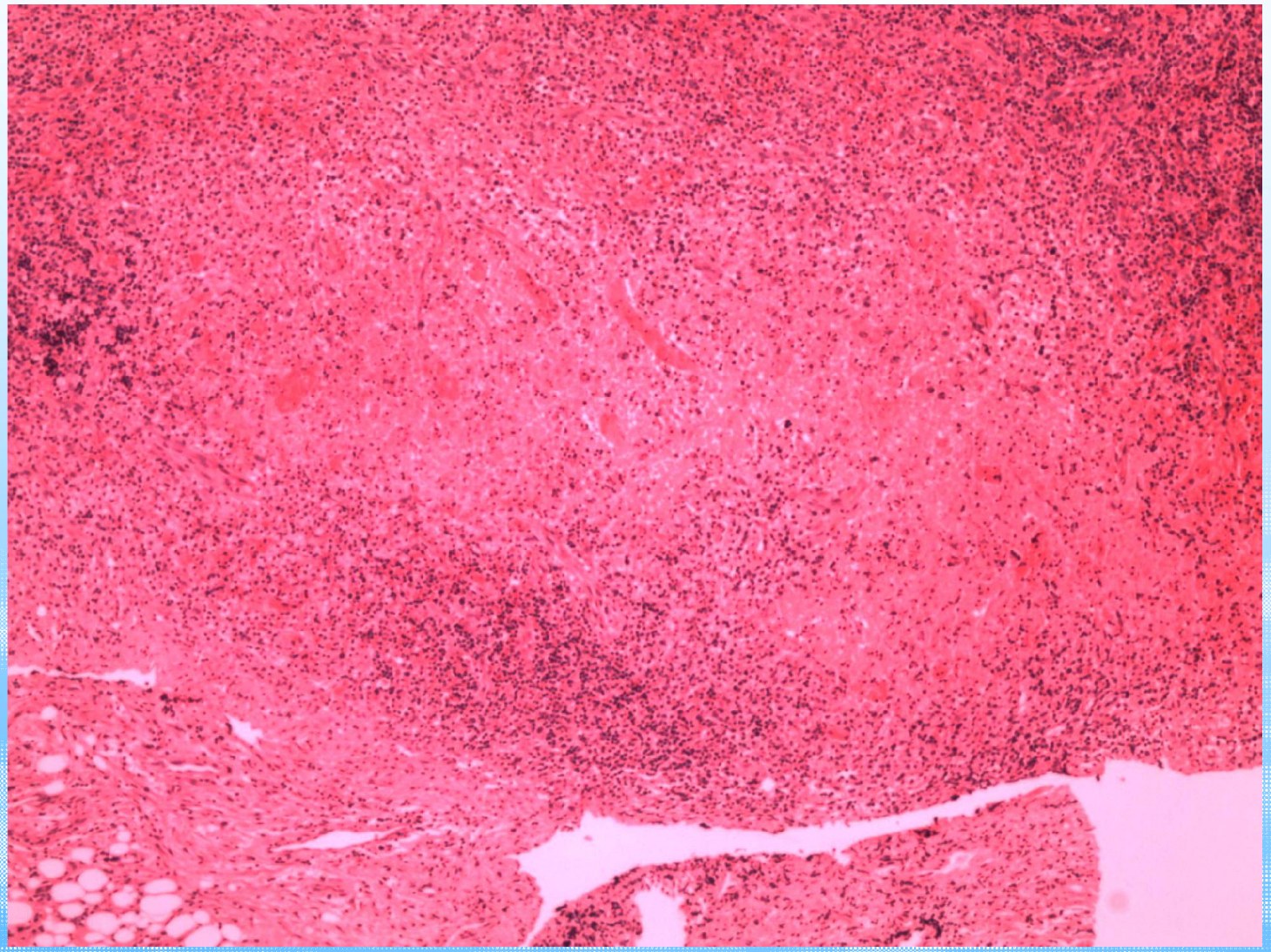

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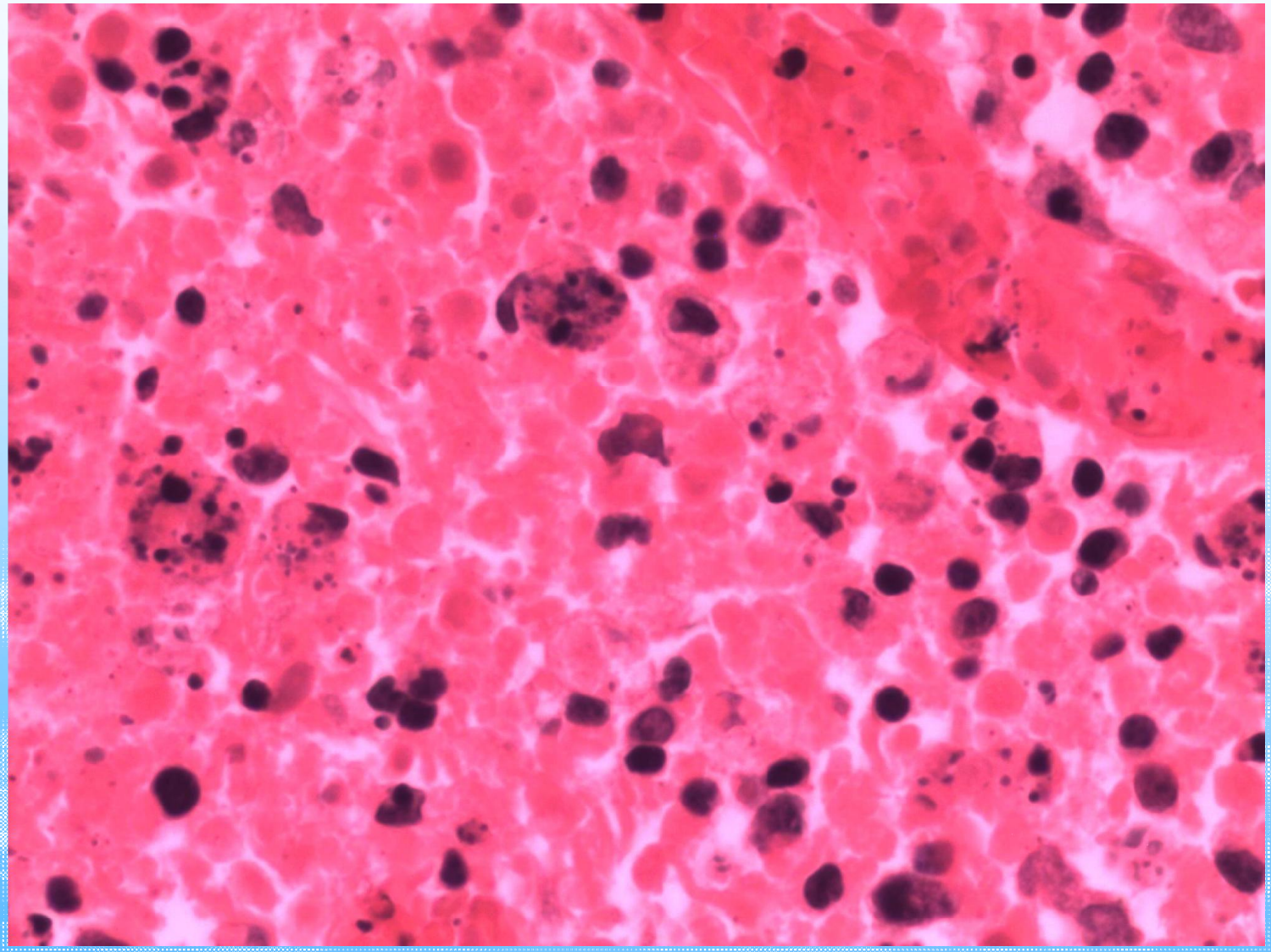
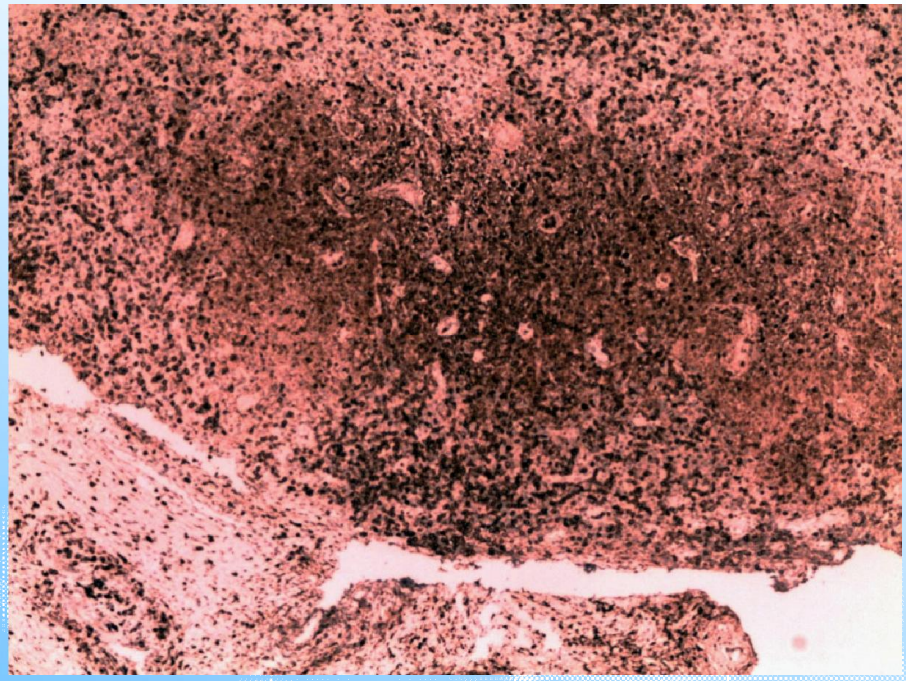
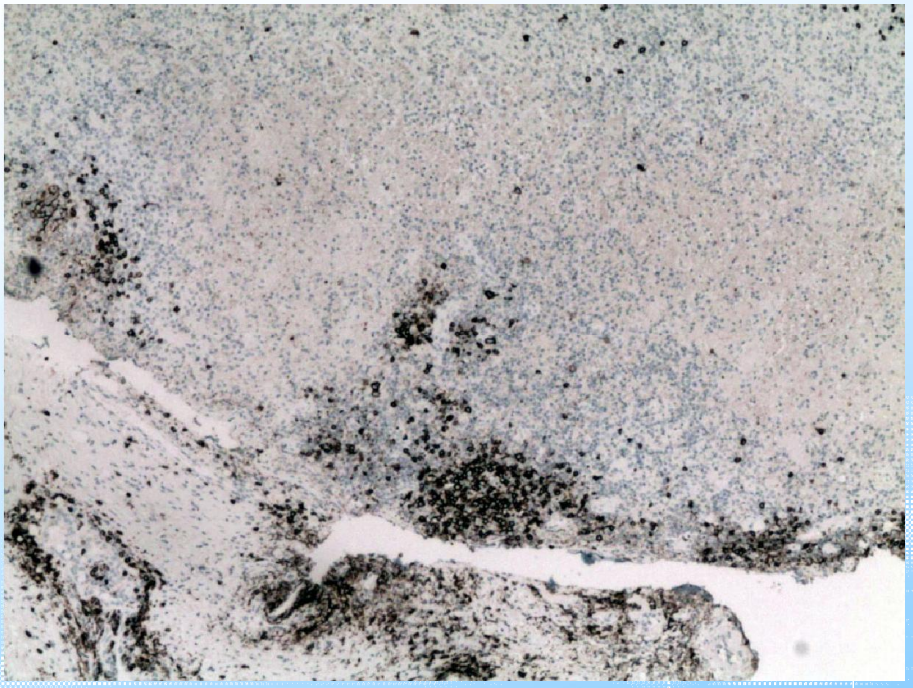


Kikuchi lymphadenitis

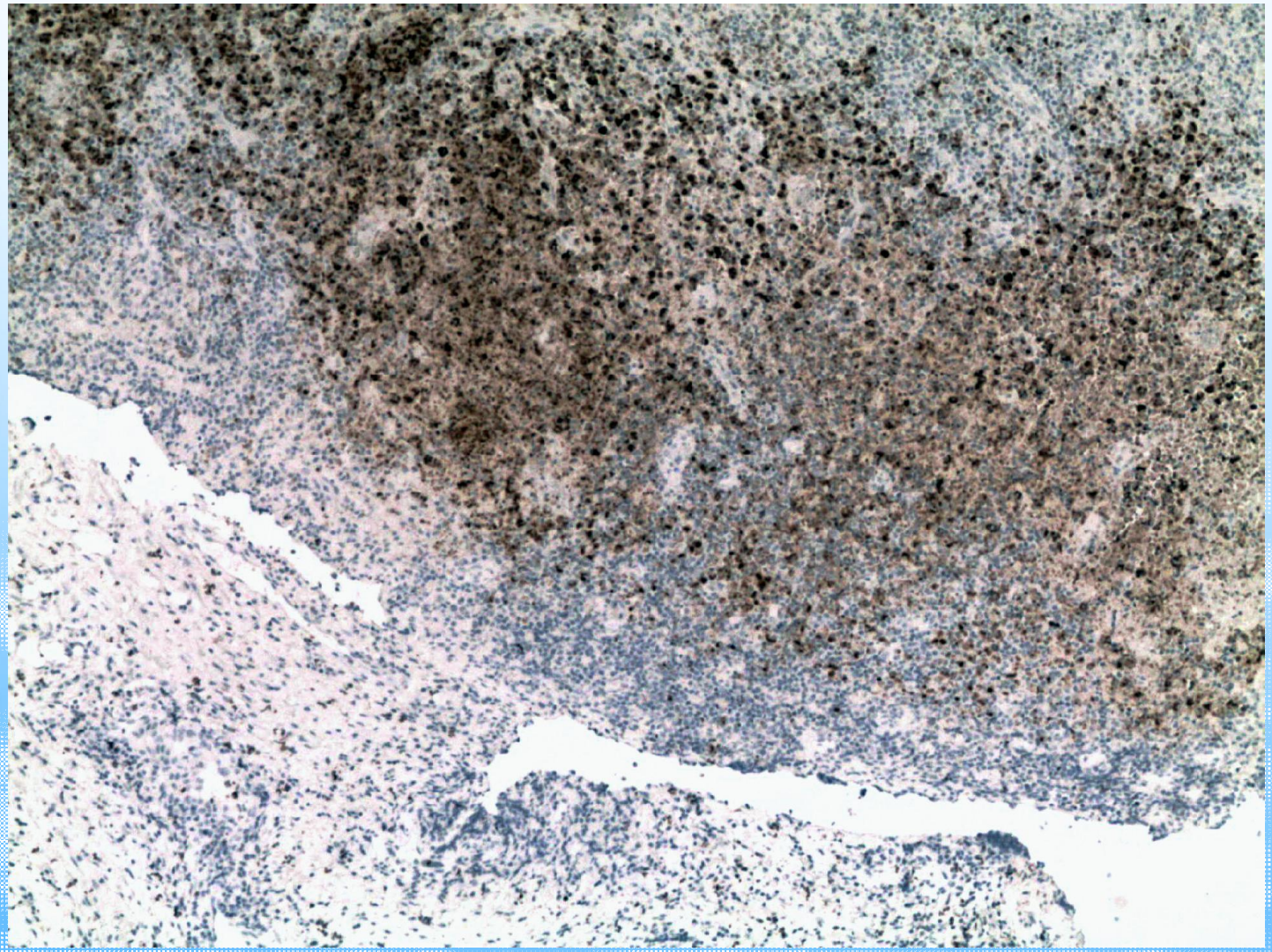


CD3

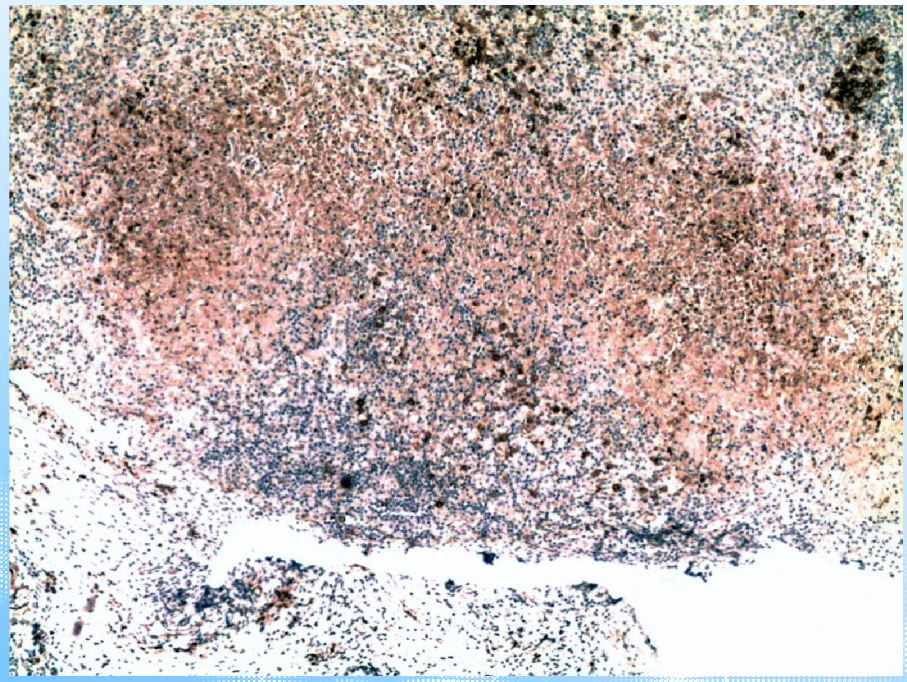


CD20

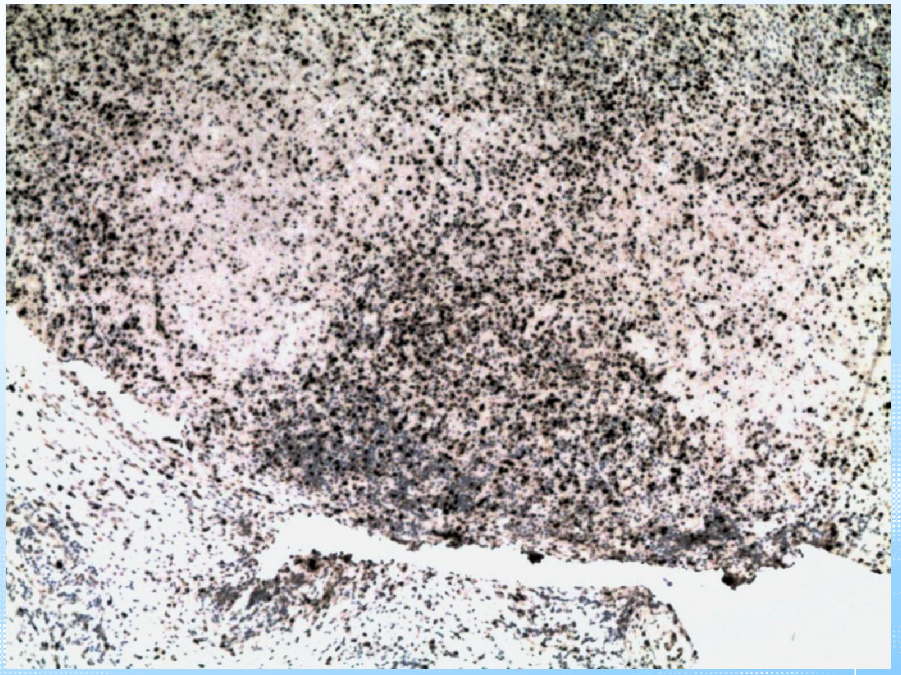
Kikuchi lymphadenitis



Kikuchi lymphadenitis

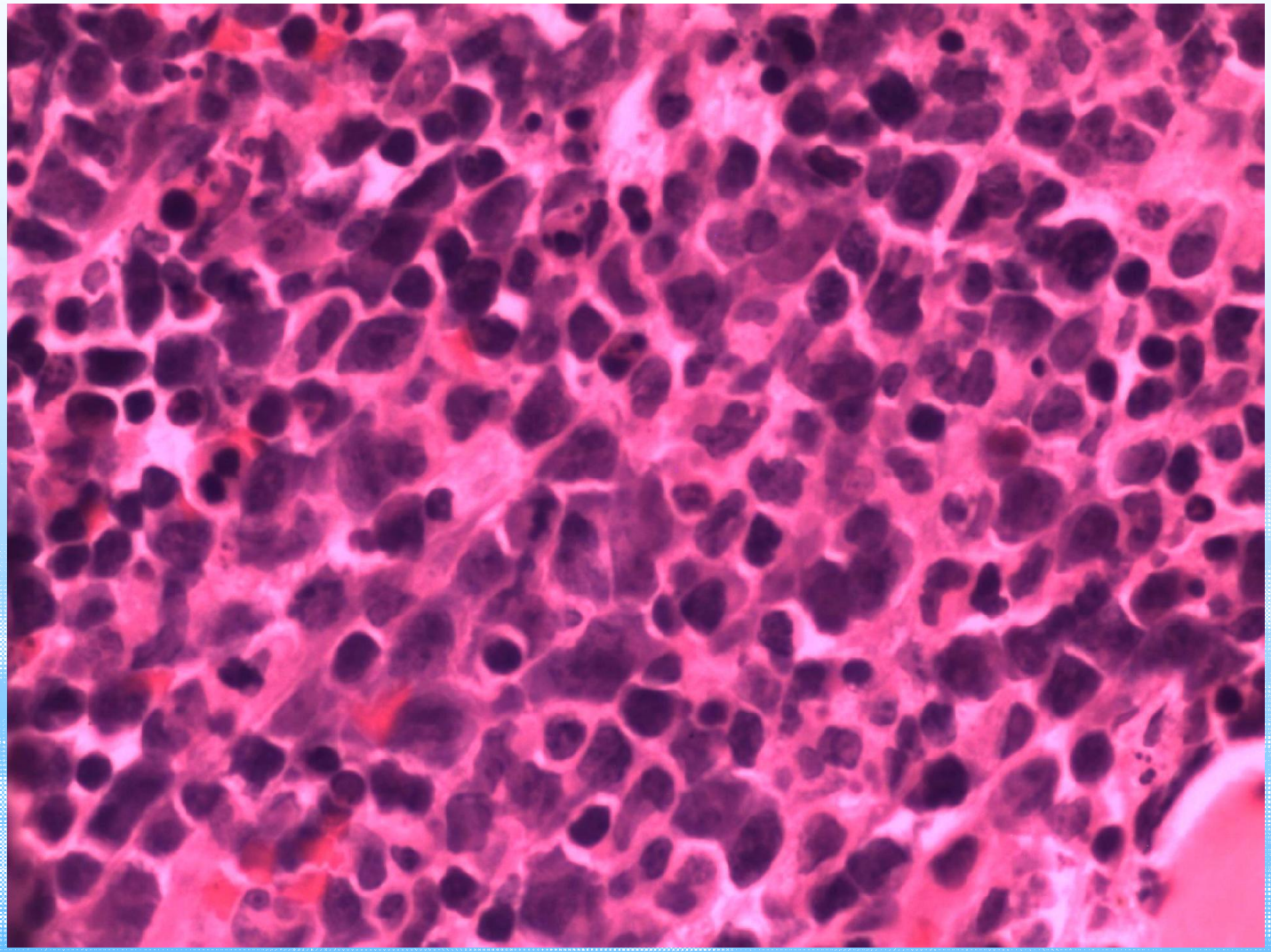


CD123



Ki-67

Kikuchi lymphadenitis



Kikuchi lymphadenitis

Management

- No specific cure. Treatment largely supportive. NSAIDs for tender lymphnodes and fever, corti costeroids are useful in severe extranodal or g eneralized disease.

Kimura disease

- The first report of Kimura disease was from China in 1937, in which Kimm and Szeto descri bed seven cases of a condition they termed "eosinophilic hyperplastic lymphogranuloma."
- The disorder received its current name in 1948, w hen Kimura et al noted the vascular compo- nent and referred to it as an "unusual granulation combined with hyperplastic changes in lymphoid tissue."

Kimura disease

- Whether Kimura disease and angiolymphoid hyperplasia with eosinophophilia (ALHE) are the same entity?
- Some authors believe that Kimura disease represents a chronic, deeper form of ALHE
- Recent papers distinguish the two on the basis of clinical and histopathologic characteristics.
  - ALHE appears to represent an arteriovenous malformation with secondary inflammation.
  - Kimura disease may represent a primary inflammatory process with secondary vascular proliferation.

Kimura disease

Epidemiology

- The exact prevalence of Kimura disease is not known.
- Most cases of this rare disease are reported in East and Southeast Asia, with a small number of cases reported in Europe and US.
- Males are affected by Kimura disease more commonly than females, with a 3.5:1 to 9:1 male-to-female ratio in most series reported, with the exception of one series in which the male-to-female ratio was 19:1.

Kimura disease

Pathogenesis

- The pathophysiology of Kimura disease remains unknown.
- It has been hypothesized that an infection or toxin may trigger an autoimmune phenomenon or lead to a type I (immunoglobulin E [IgE]–mediated) hypersensitivity reaction.

Kimura disease

Clinical Features

- Kimura disease is usually seen in young adults during the third decade of life, with the median age being 28-32 years
- Presents as a painless mass or masses in the head and neck region, especially in the parotid and submandibu lar regions, often associated with lymphadenopathy.
- Less frequently, the orbit (including the eyelids, conju nctiva, and lacrimal glands), paranasal sinuses, epiglot tis, tympanic membrane, parotid gland, and paraphar yngeal space may be involved.

Kimura disease

Clinical Features

- Renal disease, nephrotic syndrome in particular, is pr e-sent in up to 20% of patients
- Involvement of the extremities and inguinal lymph nodes has been reported
- A presentation of Kimura disease as a pulmonary hila r mass has recently been described
- Hypercoagulable state in patients without associated nephrotic syndrome
- Nearly all patients with Kimura disease demonstrate peripheral eosinophilia and elevated levels of serum IgE.

Kimura disease

Morphological features

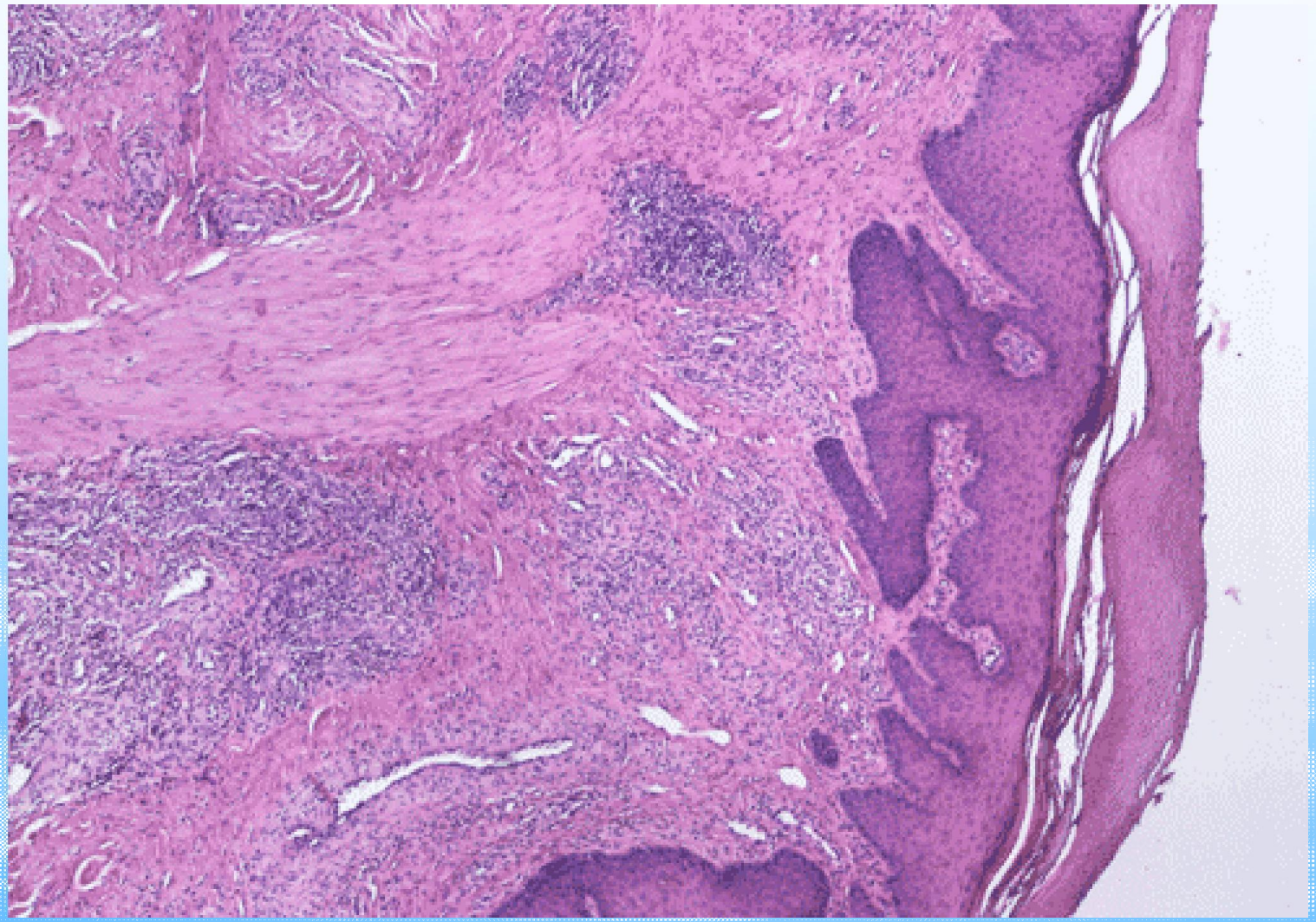
- Lymphoid nodules with discrete germinal centers can occupy an area extending from the reticular dermis to the fascia and muscle.
- A marked eosinophilic infiltrate and eosinophilic abscesses are present.
- Centrally, thick-walled vessels are present with hobnail endothelial cells.

Kimura disease

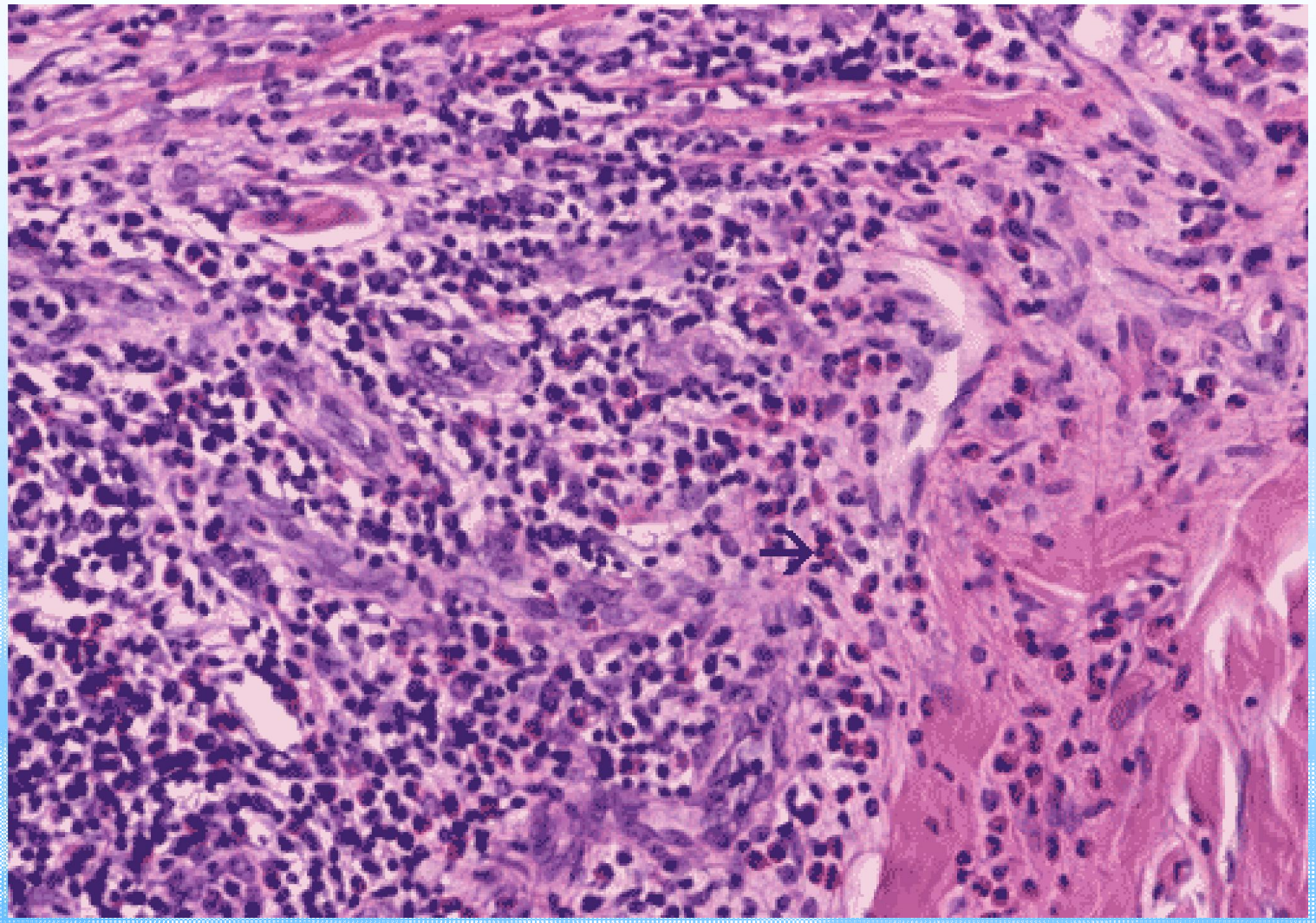
Morphological features

- Immunohistochemical evaluation of the lymphoid nodules demonstrates a polymorphous infiltrate without clonality.
- Reports have also demonstrated the presence of plasmacytoid dendritic cells in a lesion of Kimura disease.

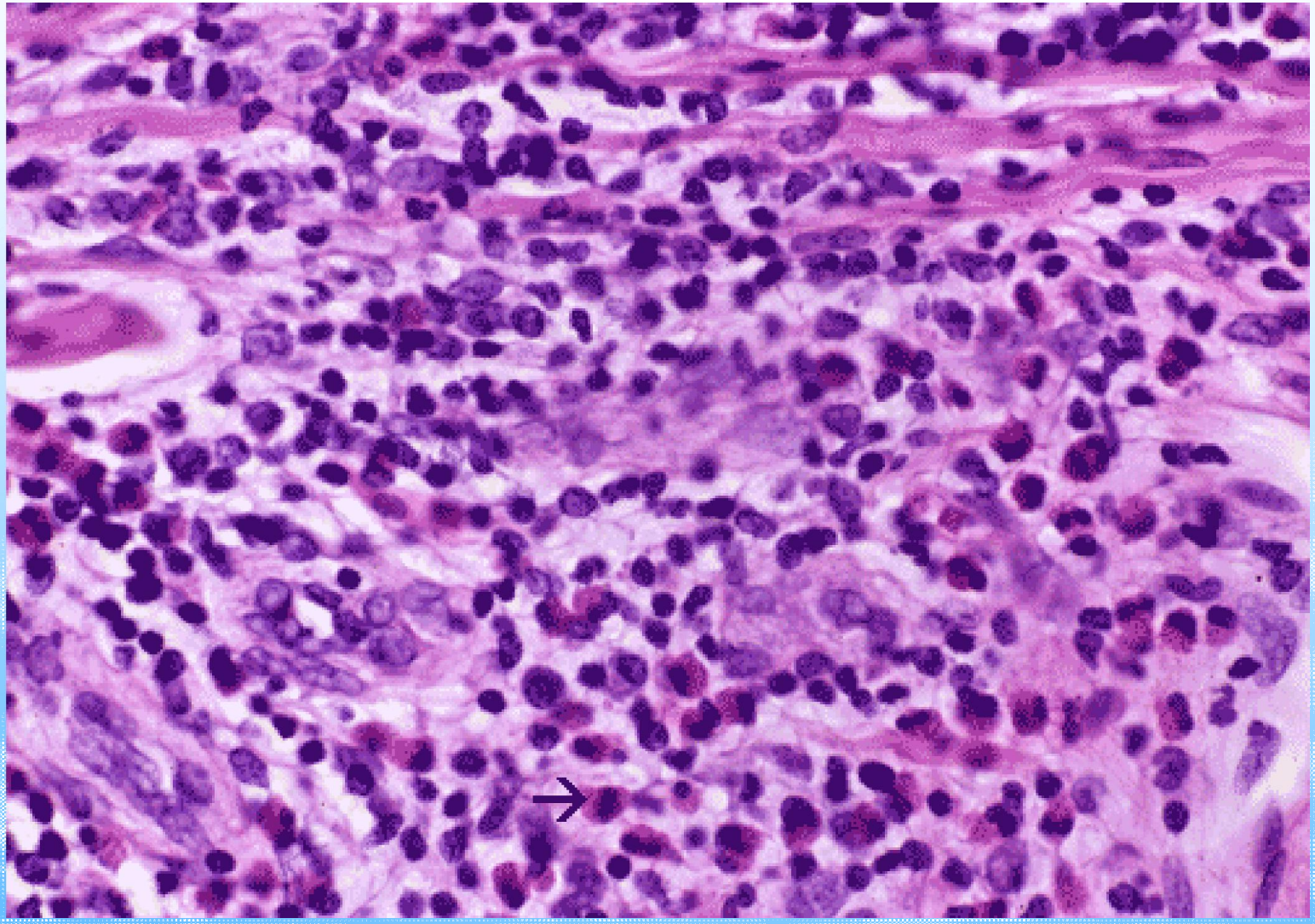
Kimura disease



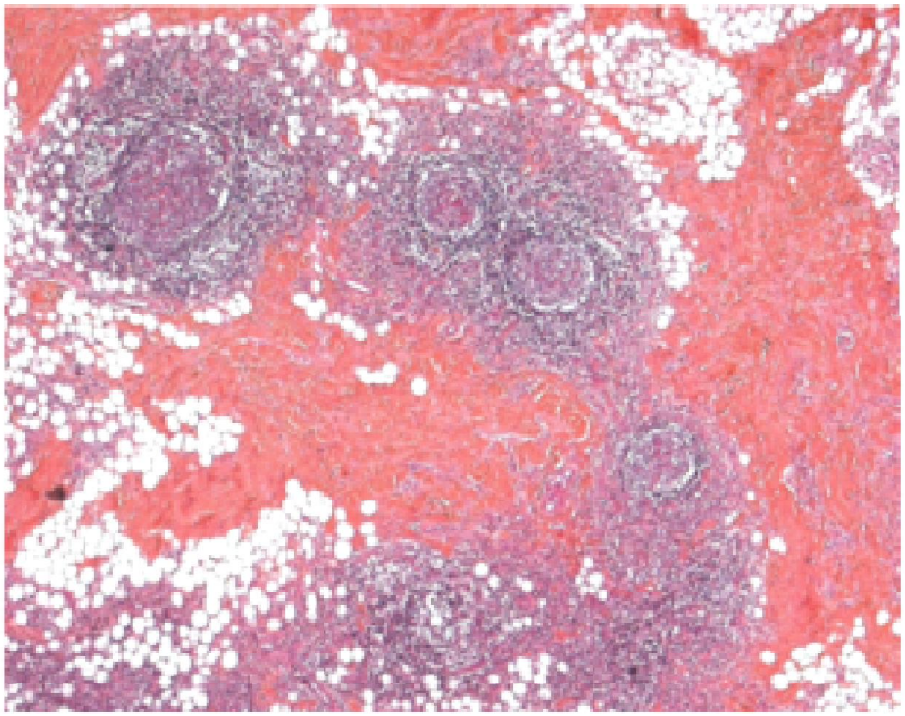
Kimura disease

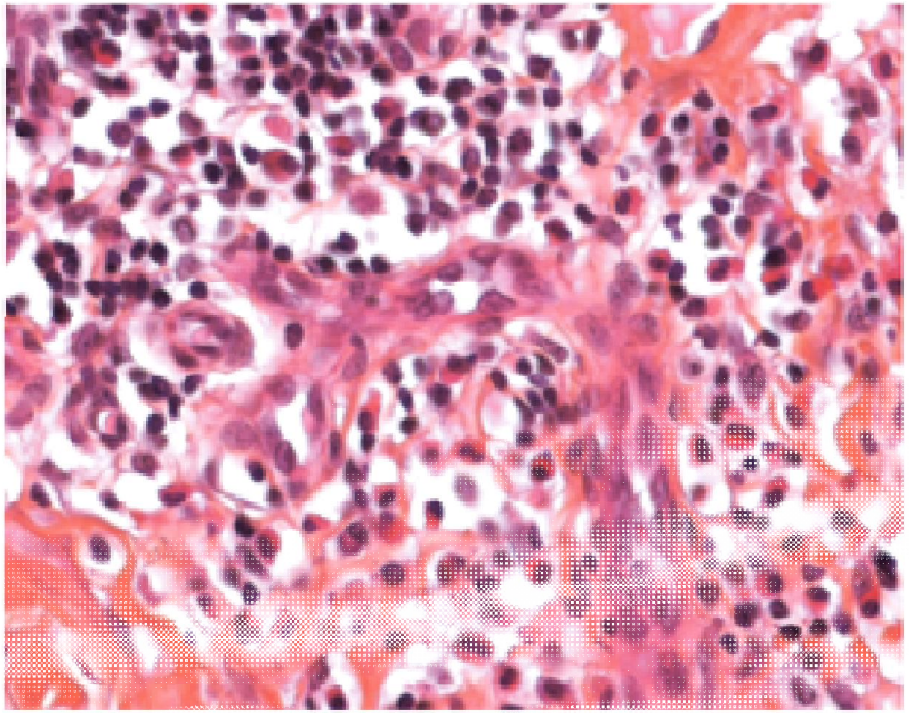


Kimura disease



Kimura disease



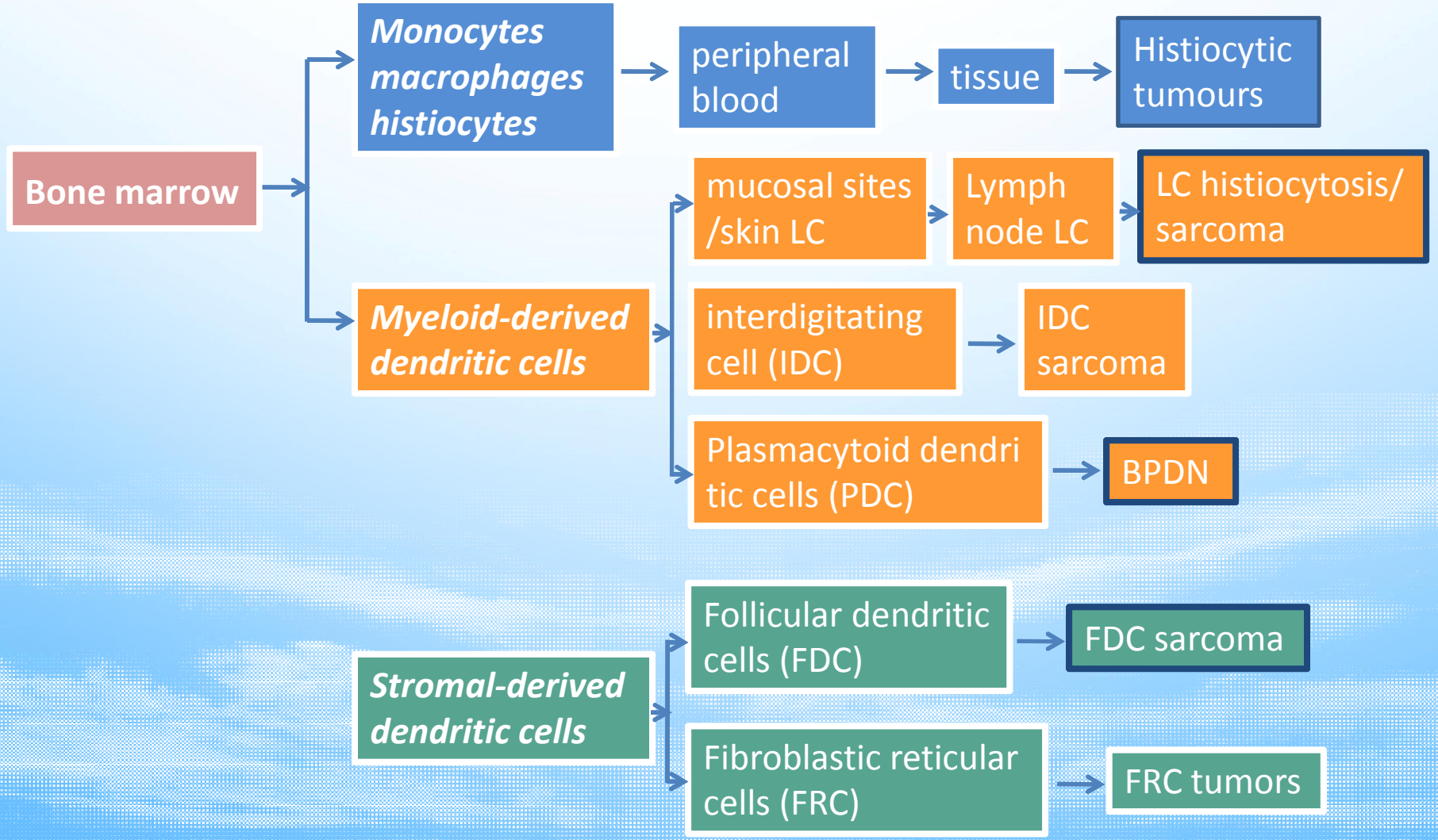


Kimura disease

Management

- Observation, Oral corticosteroids, Cyclosporine Intravenous immunoglobulin (IVIG), Oral pentoxifylline, All *trans*-retinoic acid in combination with prednisone, Imatinib may be an effective treatment
- Conservative surgical excision has been considered the treatment of choice for Kimura disease. Recurrence after surgery is frequently observed.

Histiocytes and Dendritic cells



Langerhans cell histiocytosis

- **Langerhans cell histiocytosis** (**LCH**) is a rare disease involving clonal accumulation and pro liferation of dendritic cells deriving from bone marrow and capable of migrating from skin to lympho nodes, hence sometimes called Dendr itic Cell Histiocytosis.

Langerhans cell histiocytosis

Eidemiology

- LCH usually affects children between 1 and 15 years old, with a peak incidence between 5 and 10 years of age. Yearly incidence is thought to be 1 in 200,000 (<10 y)
- 1 in 560,000 in, vanishingly rare in elderly
- It is most prevalent in Caucasians, males:females 2:1

Langerhans cell histiocytosis

Pathoenesis

- Whether LCH is a reactive or neoplastic process is a matter of debate.
- Reactive: spontaneous remissions, the extensive secr etion of multiple cytokines,favorable prognosis and r elatively good survival rate
- Neoplastic: the infiltration of organs by monoclonal population of pathologic cells, the successful treatm ent of subset of disseminated disease using chemoth erapeutic regimens, the BRAF gene was detected in 35 of 61 (57%) with mutations being more common in patients younger than 10 years (76%) than in patie nts aged 10 years and older (44%).

Langerhans cell histiocytosis

Clinical Features

- LCH is clinically divided into three groups:

  unifocal, multifocal unisystem, and multifocal multisystem

- **Unifocal LCH** is a slowly progressing disease

  characterized by an expanding proliferation of Langerhans Cells in various bones. It is a mono stotic or polystotic disease with no extraskelet al involvement.

Langerhans cell histiocytosis

- **Multifocal unisystem LCH**
  Characterized by fever, bone lesions and diffu-se eruptions, usually on the scalp and in the ear canals.
  50% of cases involve the pituitary stalk leading to diabetes insipidus. The triad of diabetes insip idus, exopthalmos, and lytic bone lesions is known as the *Hand-Schüller Christian* triad

Langerhans cell histiocytosis

- **Multifocal multisystem LCH**
  also called *Letterer-Siwe disease*, is a rapidly progressing disease in which Langerhans cells proliferate in many tissues. It is mostly seen in children under age 2, and the prognosis is poor : even with aggressive chemotherapy, the 5-year survival is only 50%.

Langerhans cell histiocytosis

- **Pulmonary LCH**
  Occurs almost exclusively in cigarette smokers. It is now considered a form of smoking-related interstitial lung disease. Some patients recover completely after stopping smoking, but others develop long-term complications such as pulmonary fibrosis and pulmonary hypertention

Langerhans cell histiocytosis

Morphological features

- Langerhans cells in combination with lymphoc ytes, eosinophils, , and normal histiocytes form typical LCH lesions that can be found in almost any organ

Langerhans cell histiocytosis

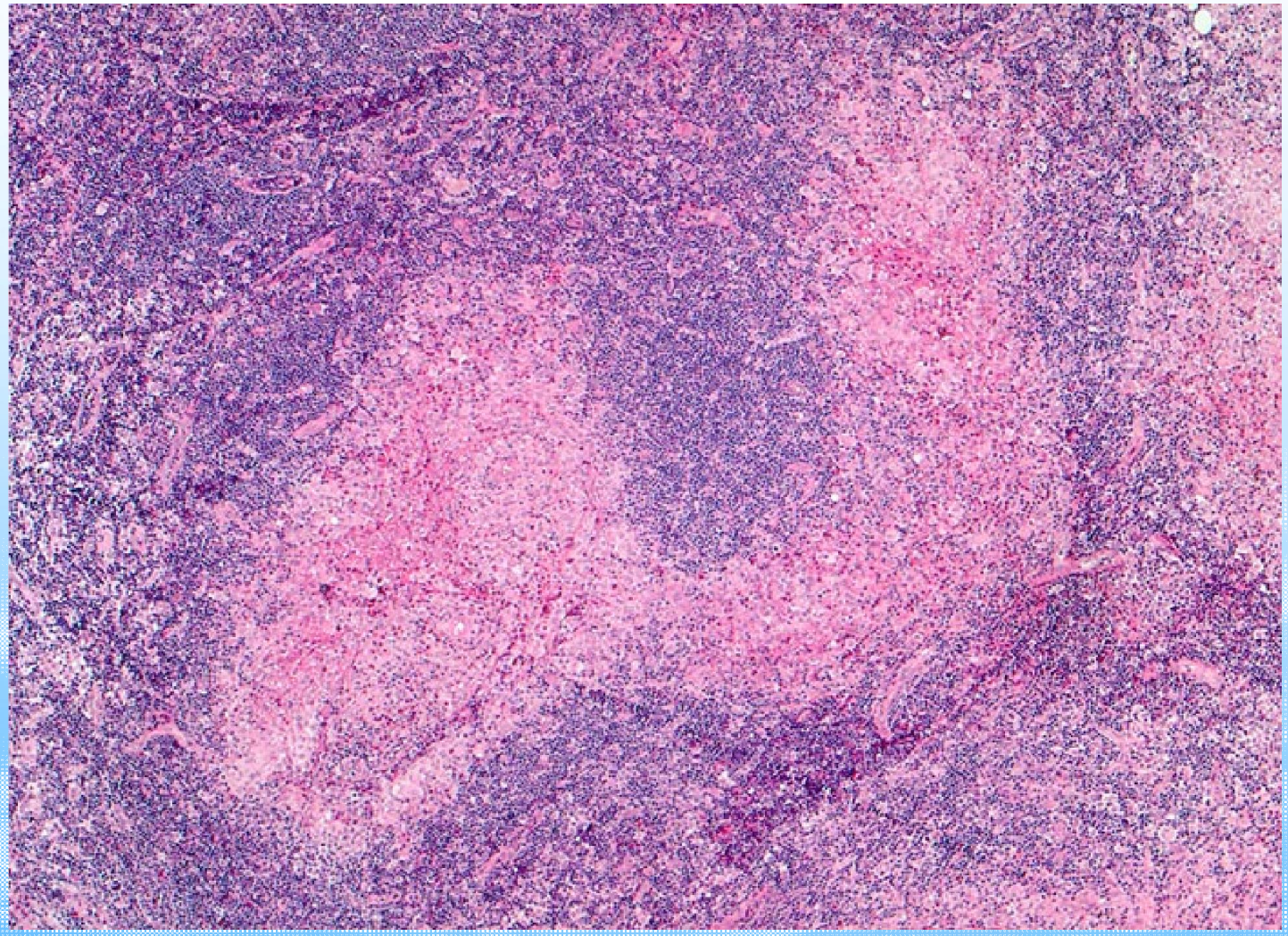
- Features of Langerhans Cell
  - distinct cell margin, pink granular cytoplasm,
  - presence of Birbeck granules on EM
  - immunohistochemistry S-100 protein, peanut agglutinin(PNA), MHC class II, CD1a, Langerin(CD207) positivity

Langerhans cell histiocytosis

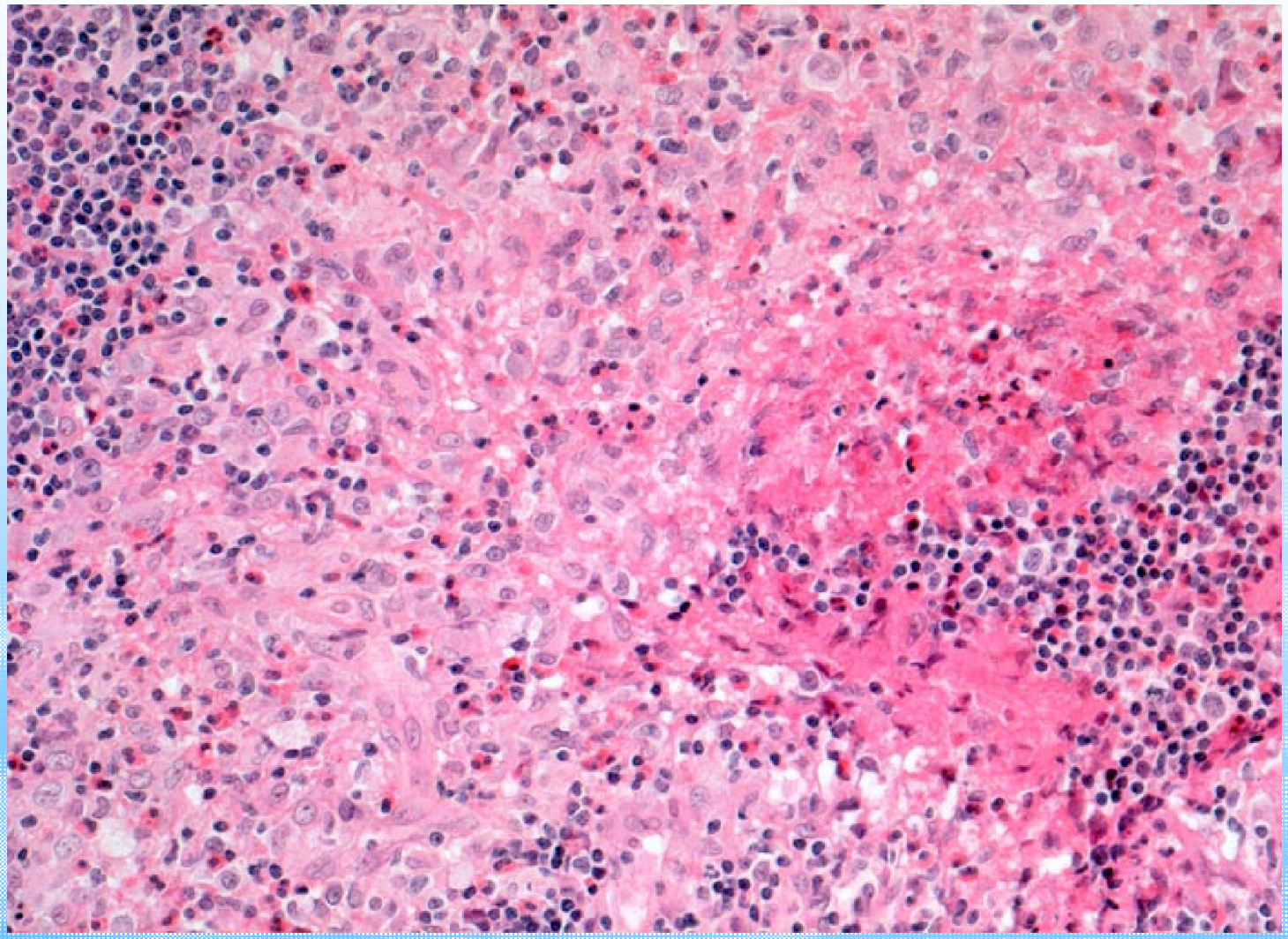
Treatment

- Treatment is guided by extent of disease.
  - Solitary bone lesion may be amenable through excision or limited radiation,
  - Systemic diseases often require chemotherapy.

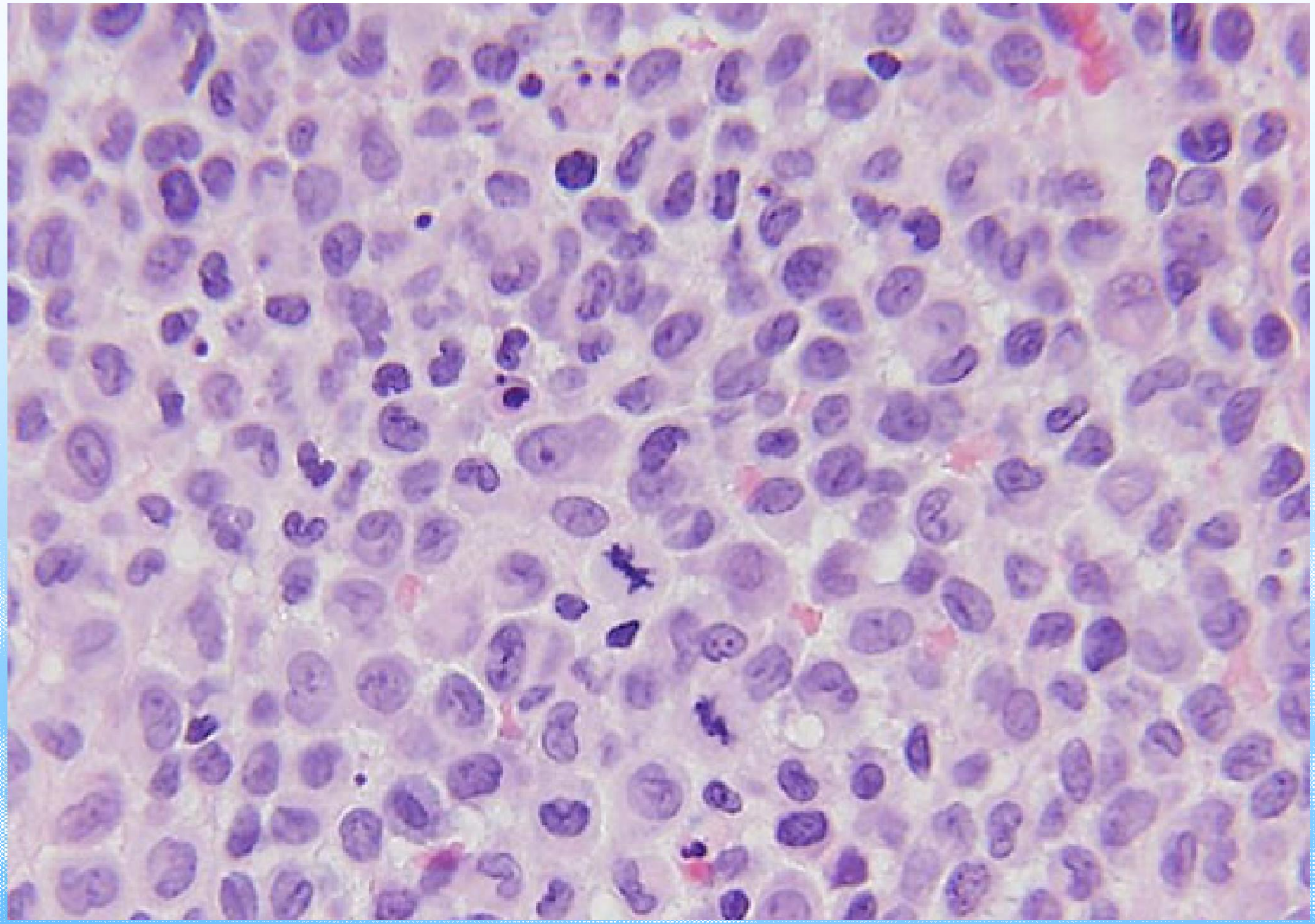
Langerhans cell histiocytosis



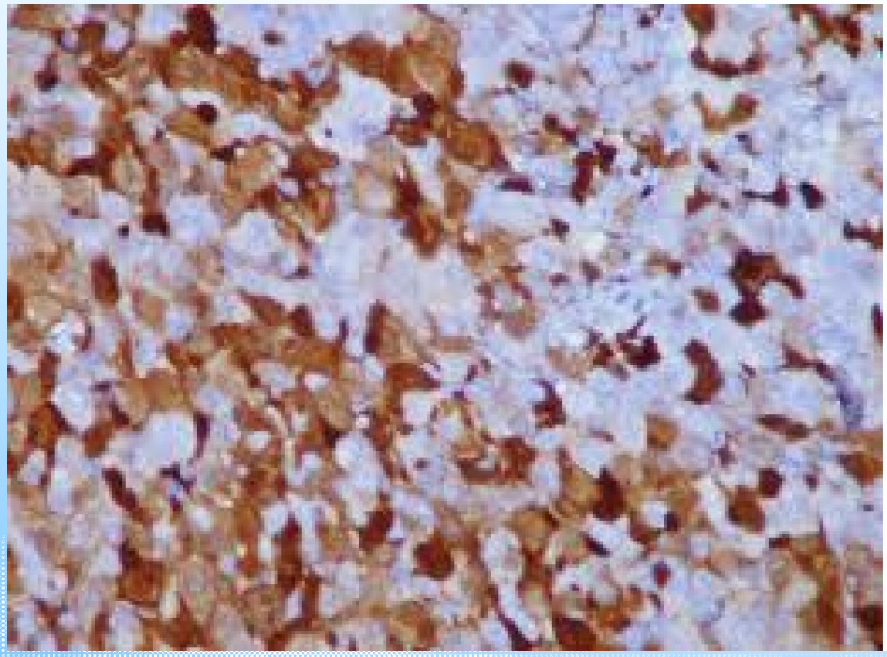
Langerhans cell histiocytosis



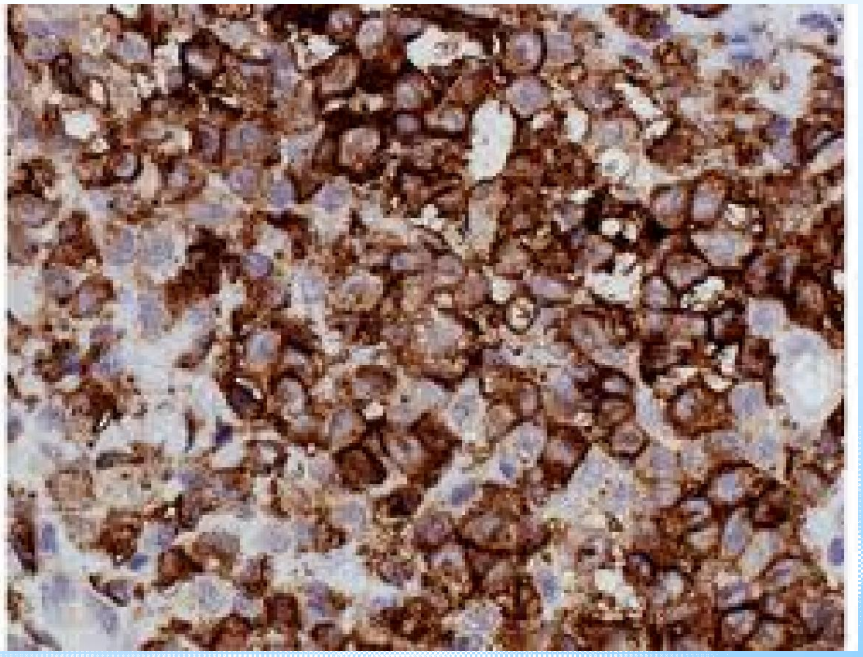
Langerhans cell histiocytosis



Langerhans cell histiocy

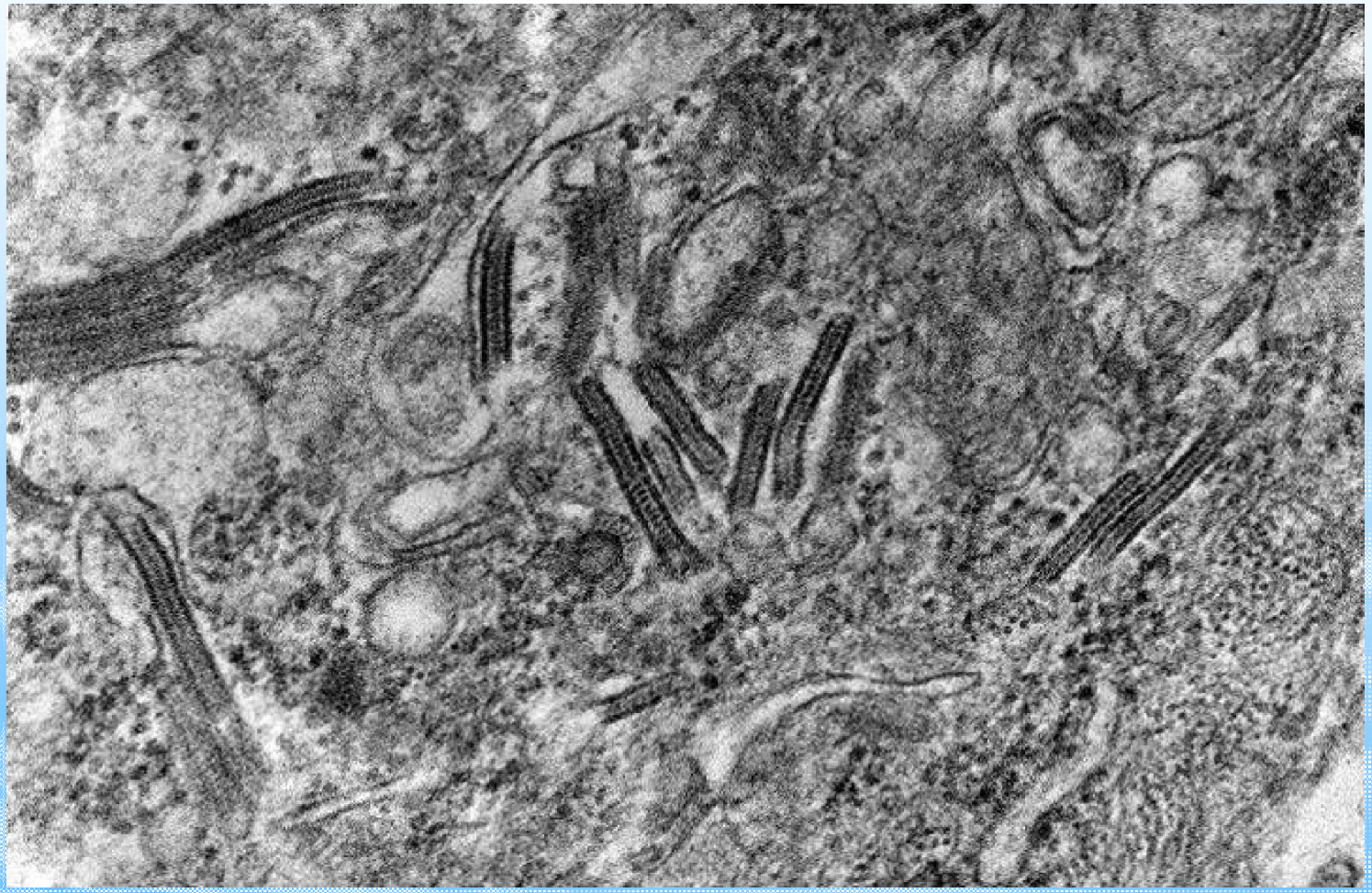


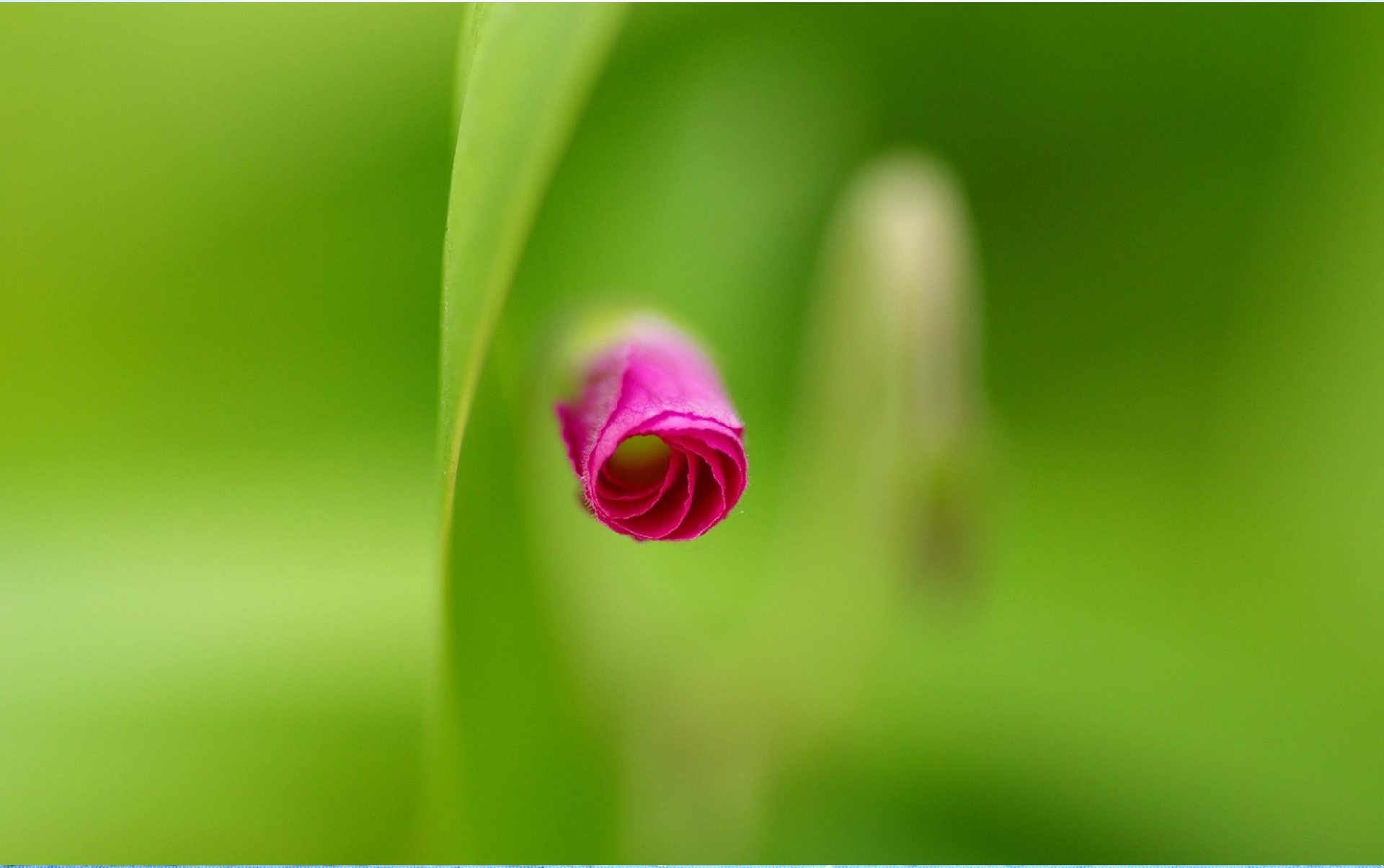
S-100



CD1a

Langerhans cell histiocytosis





Histiocytic Sarcoma
Malignant Histiocytosis

- **Histiocytic sarcoma (HS)**, formerly designated as true histiocytic lymphoma, consists of exce edingly rare hematopoietic neoplasms, repre-senting <1% of all non-Hodgkin's lymphomas.
- The term 'histiocytic sarcoma' was introduced in 1970 by Mathé *et al*

Histiocytic Sarcoma
Malignant Histiocytosis

- **Histiocytic sarcoma** Histiocytic neoplasia which originates at a single site**.**
- **Disseminated histiocytic sarcoma** When spread to distant sites
- **Malignant histiocytosis (MH)** is an aggressive histiocytic neoplasm which arises in multiple sites simultaneously

Histiocytic Sarcoma
Malignant Histiocytosis

- **Epidemiology**
  Tumours of histiocytes are among the rarest of tumours affecting lymphoid tissues, probably representing less than 1% of tumours presenting in lymph nodes or soft tissues

Histiocytic Sarcoma
Malignant Histiocytosis

Clinical features

- 20-73 years (mean, 57.8 years)
- Lymph node, extranodal site
- Late stage
- No leukemic component

Jeffrey A Vos et al
Histiocytic sarcoma: a study of five cases including the histiocyte marker CD163
Modern Pathology (2005) 18, 693–704

Histiocytic Sarcoma
Malignant Histiocytosis

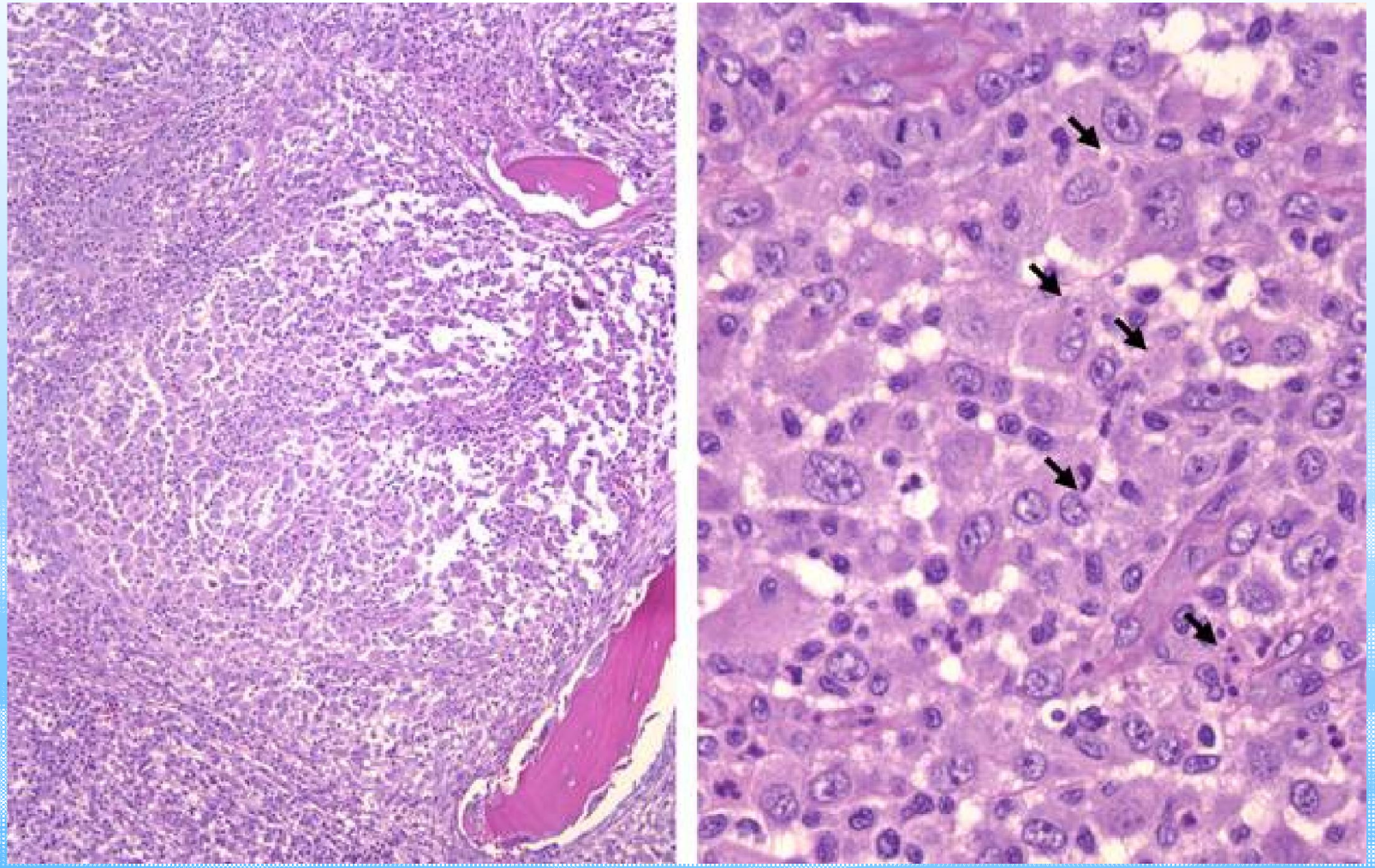
Mophological features

- Diffuse architecture with large, discohesive polygonal cells.
- Spindling of cells focally present
- Hemophagocytosis identified in some
- A prominent inflammatory background

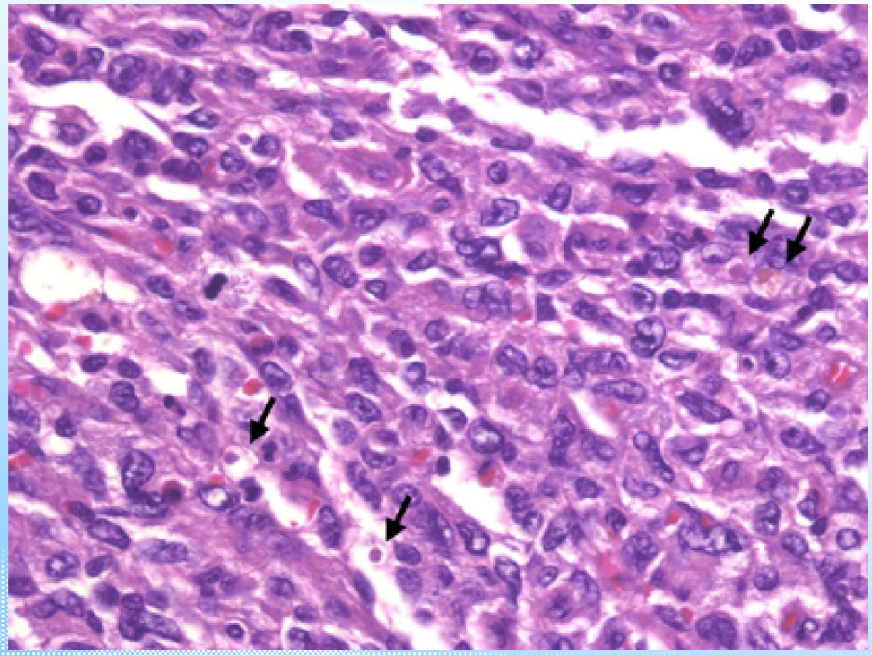
Histiocytic Sarcoma
Malignant Histiocytosis

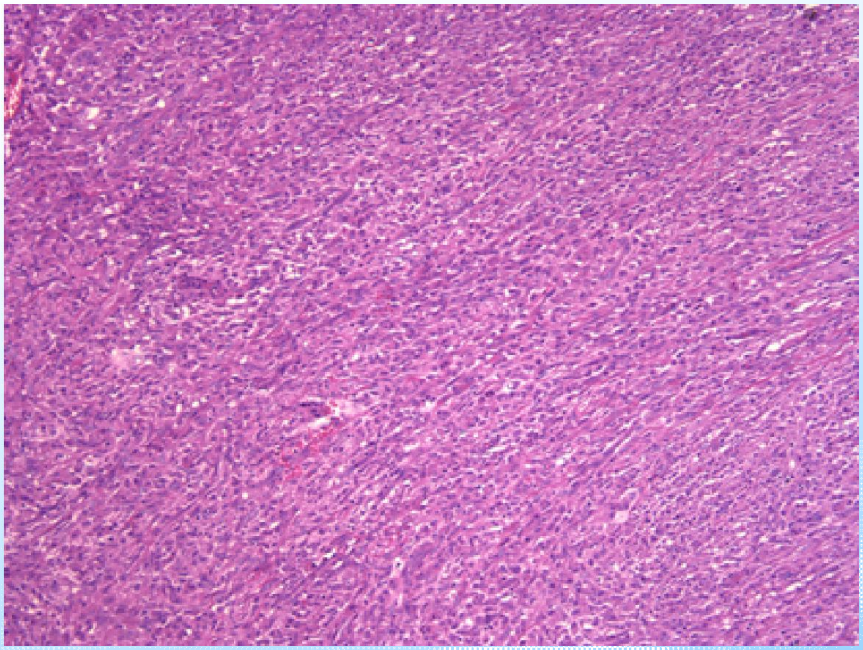
- **Immunohistochemistry**
  - CD45, CD163, CD68 positive
  - lysozyme, S-100 was focally
  - Antibodies for melanocytic, epithelial, lymphoid, and dendritic cell markers were negative.
- **Molecular studies** showed monoclonal IgH gene rearrangements in some

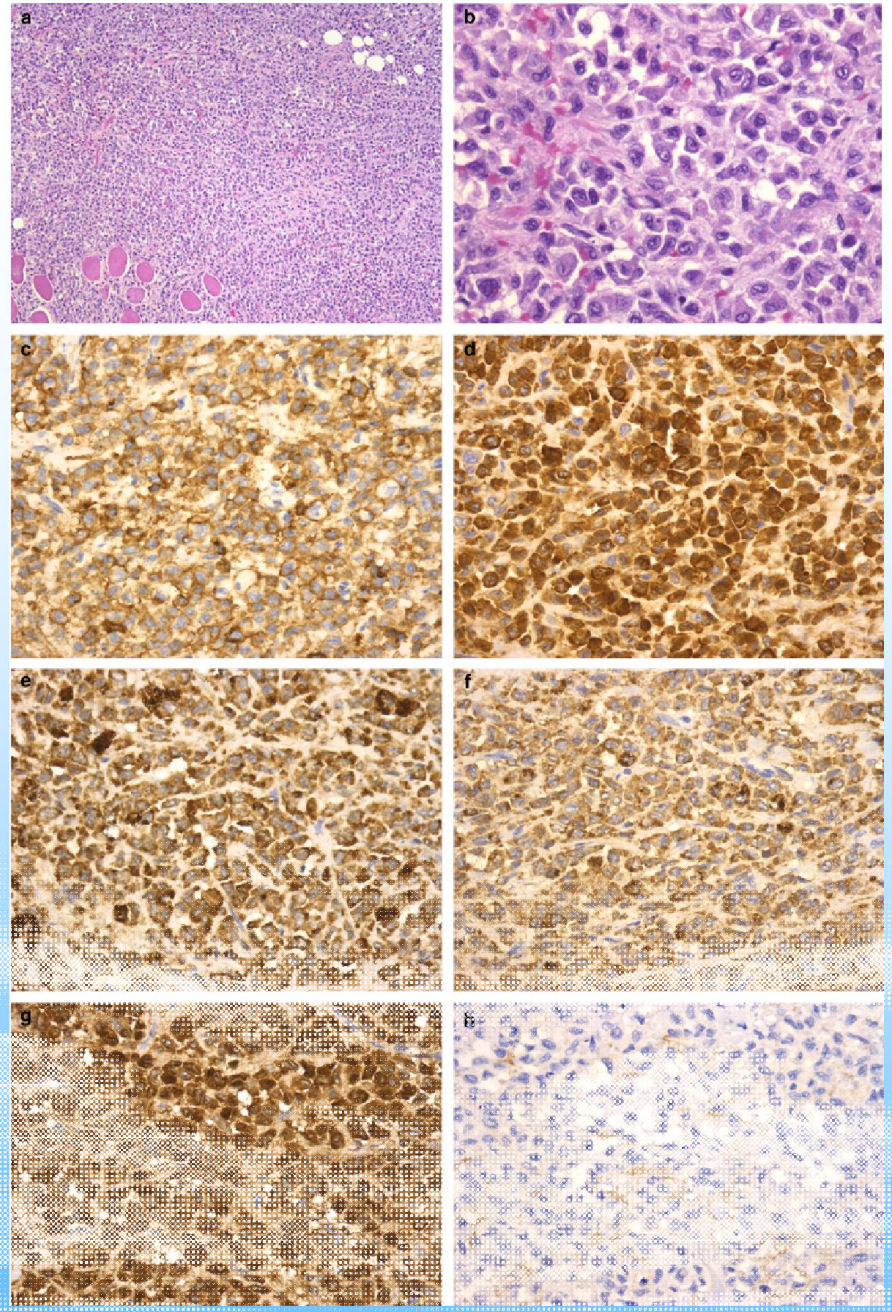
Histiocytic Sarcoma
Malignant Histiocytosis



Histiocytic Sarcoma
Malignant Histiocytosis







CD45

CD163

CD68

lysozyme

MAC387

S-100

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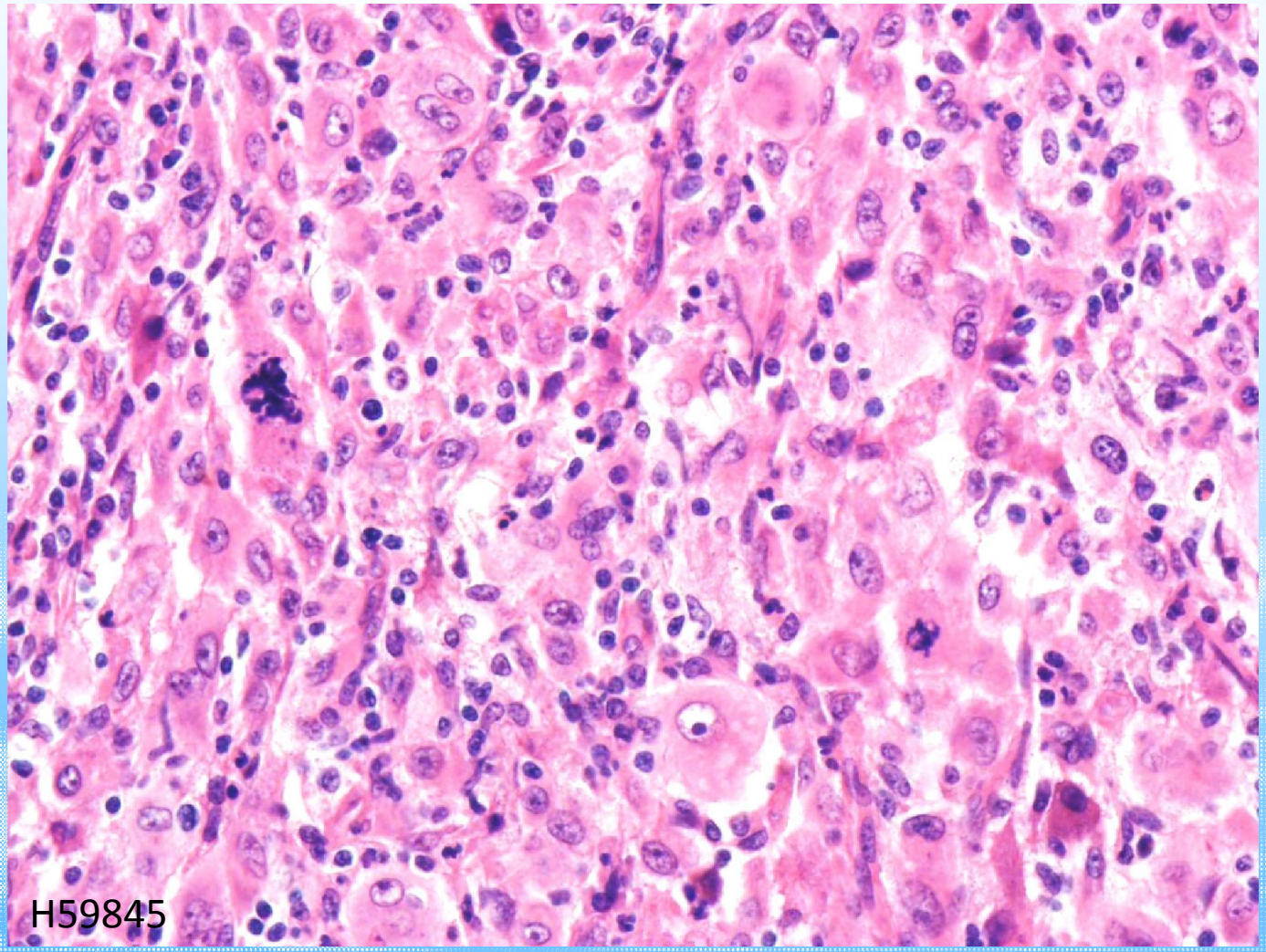

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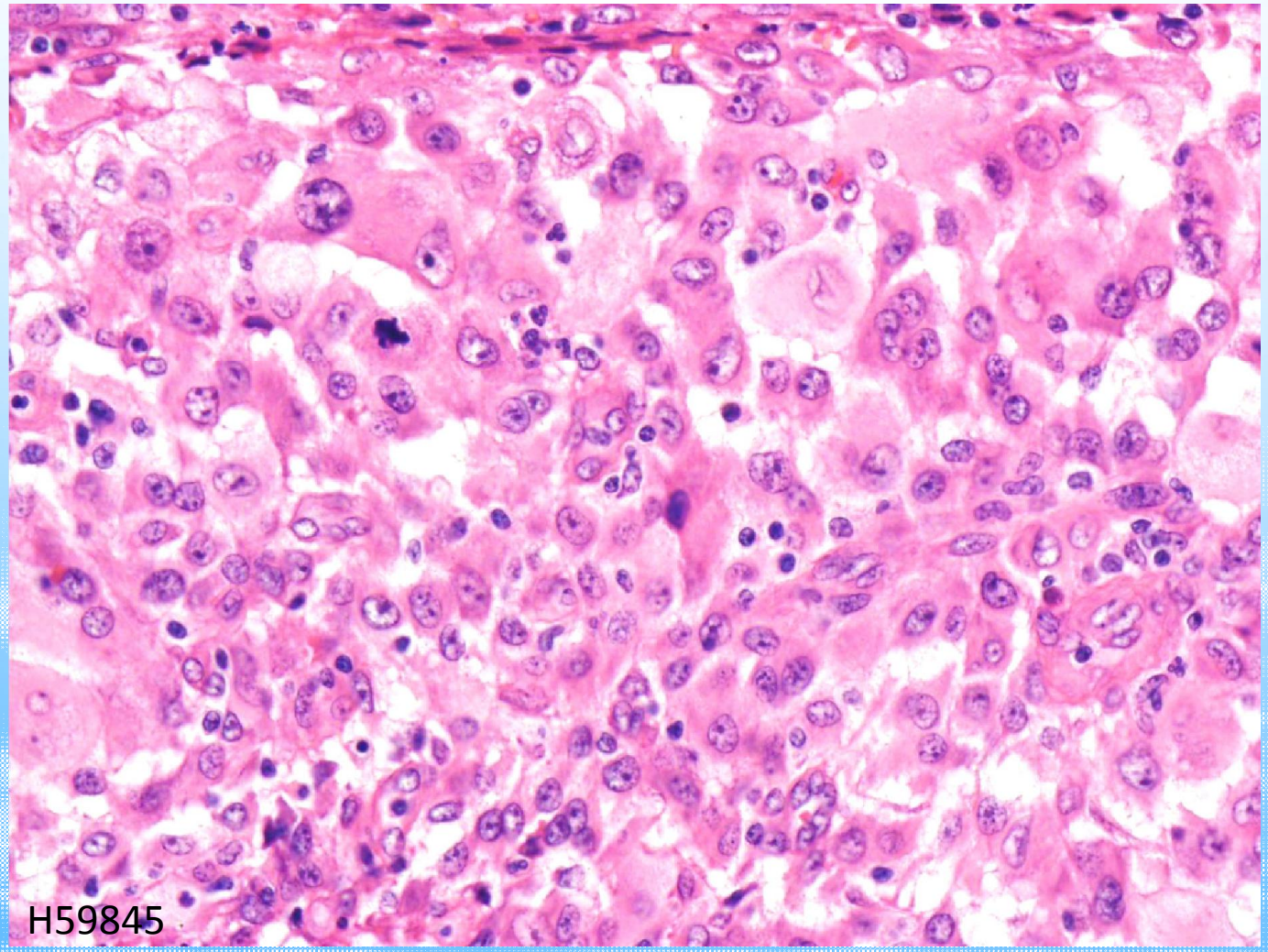

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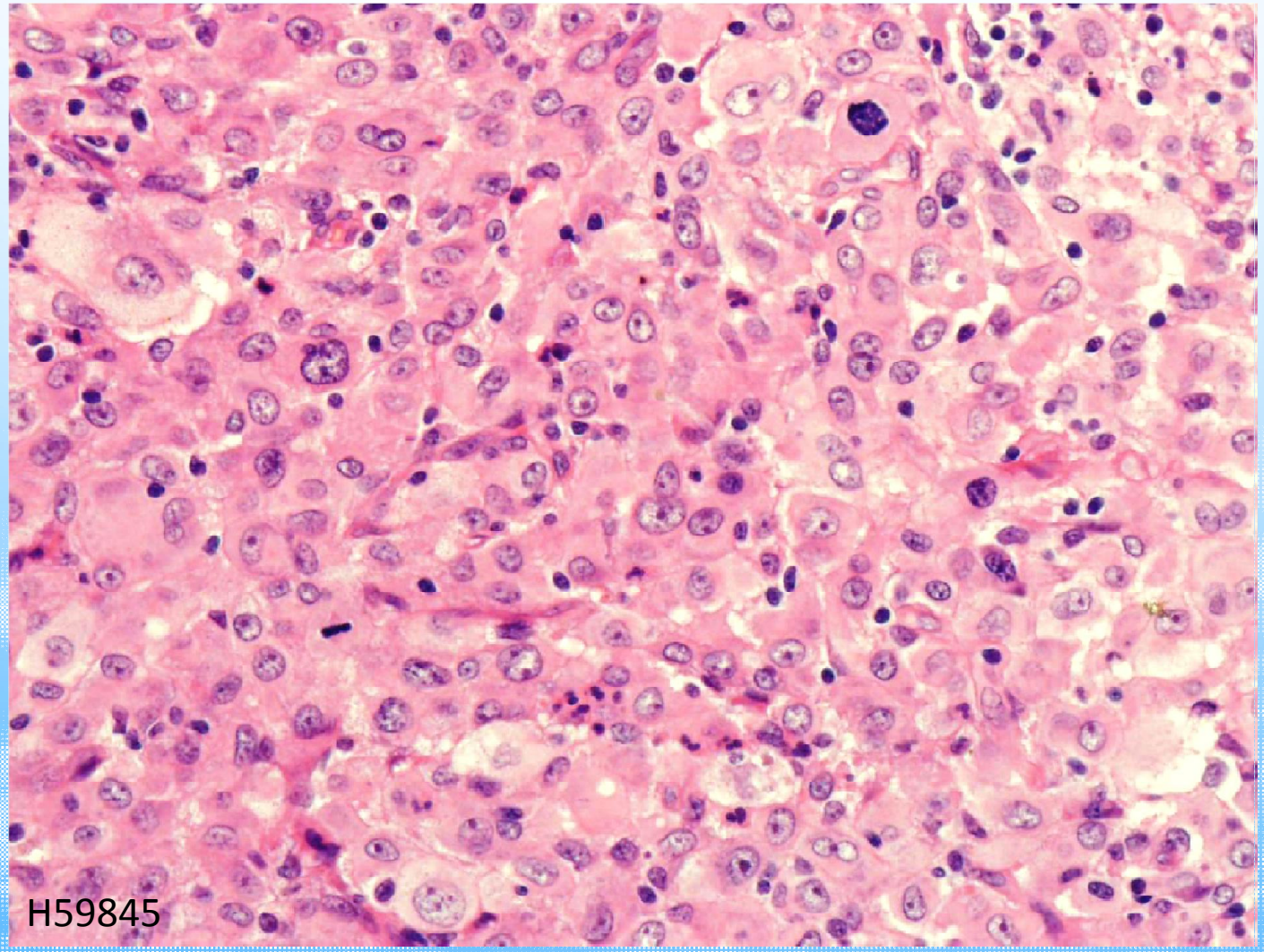

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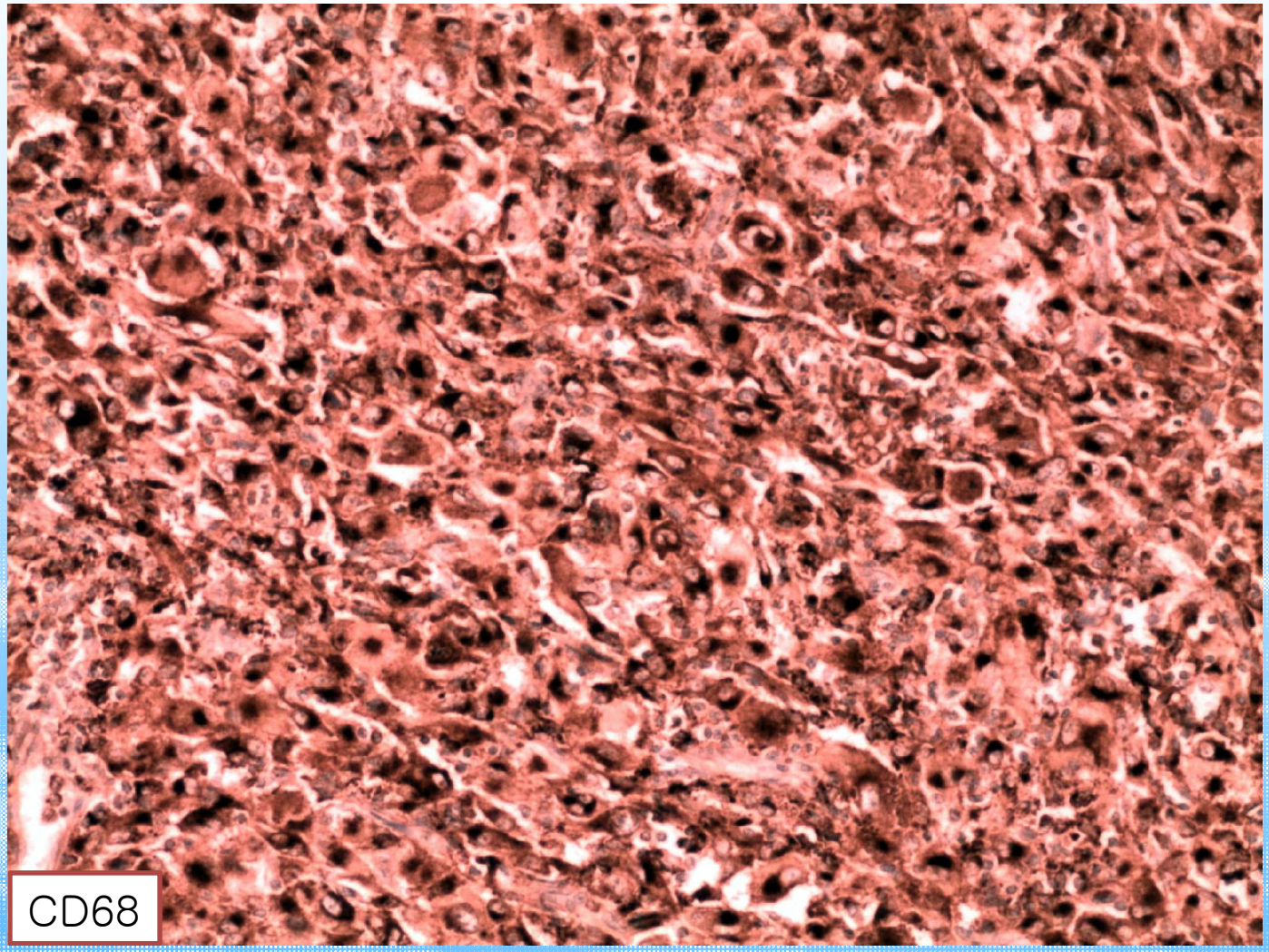

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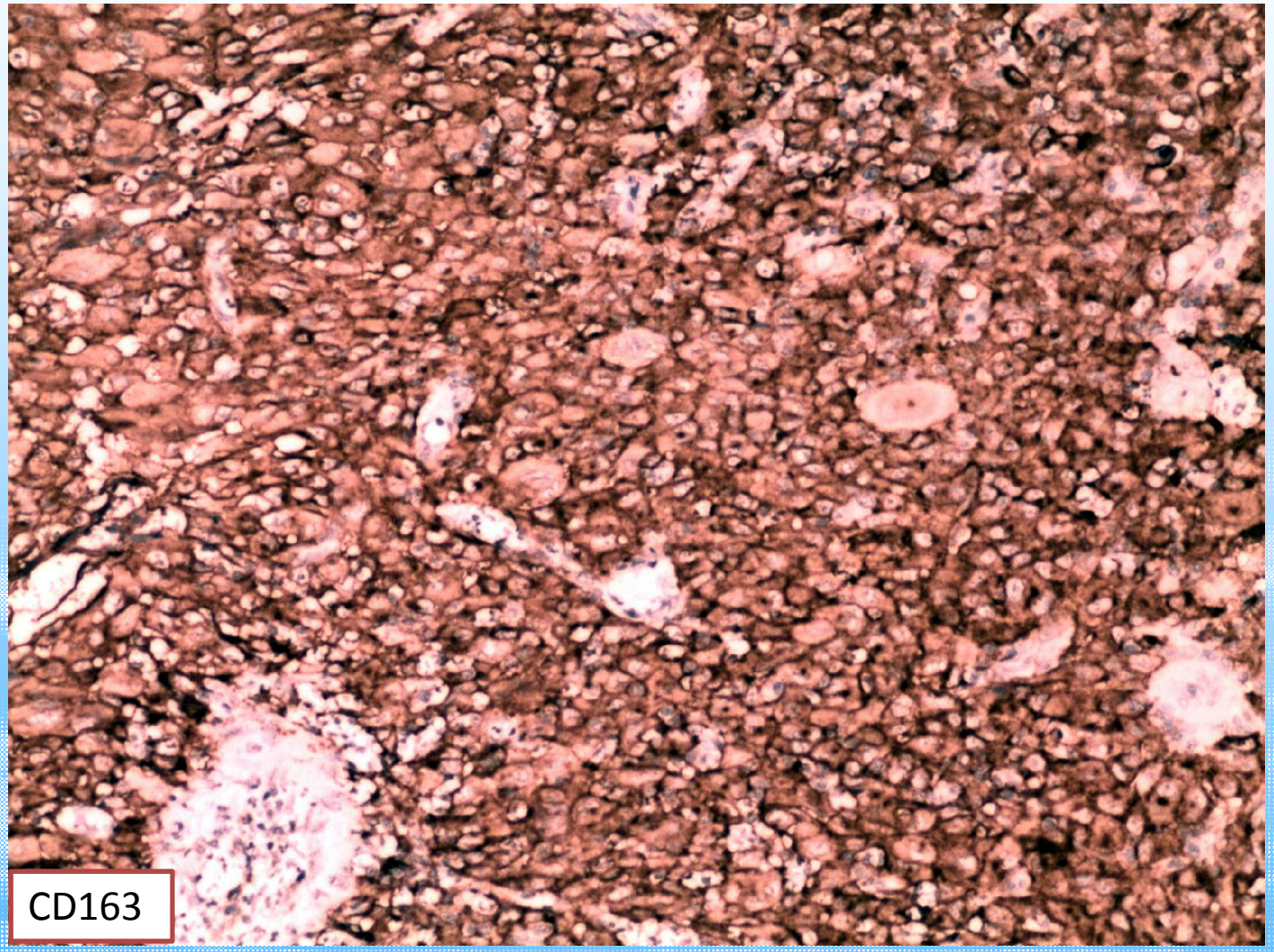

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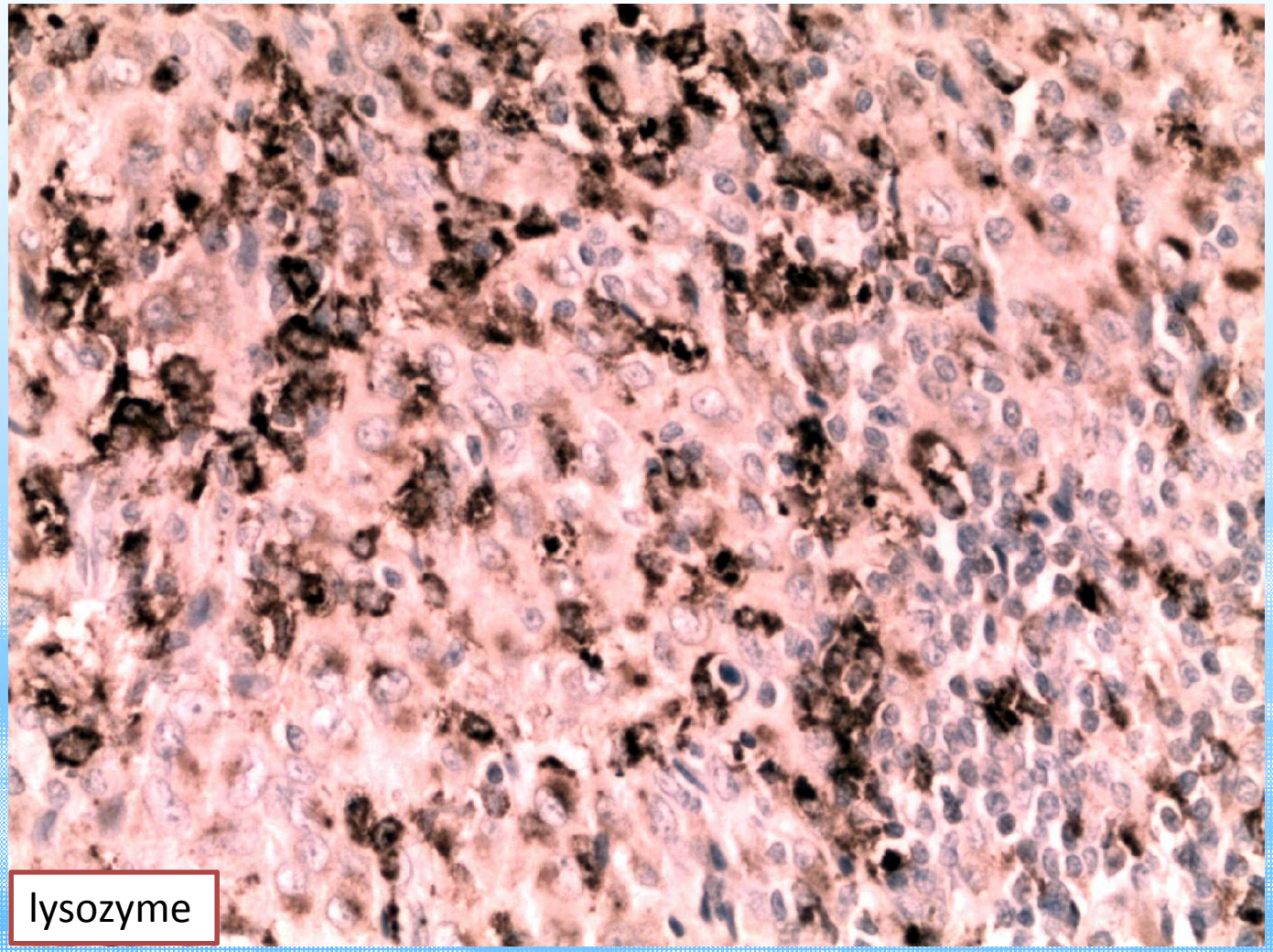

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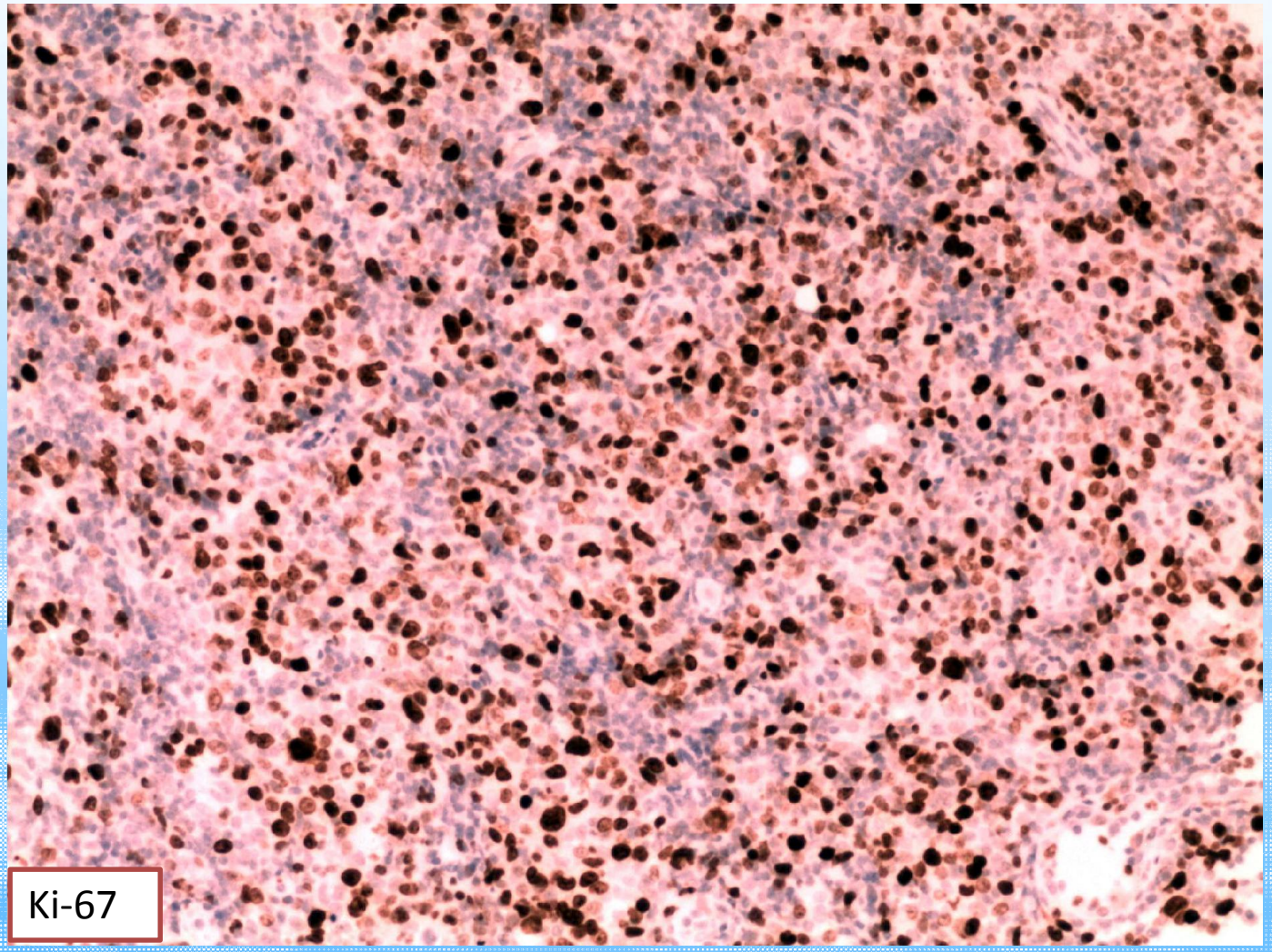

Histiocytic Sarcoma
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Management.

- Localized HS affecting skin and subcutis have been cured by early surgical excision.
- In the case of periarticular HS which occurs in the sub-synovial tissues of the extremities, amputation of the a ffected limb is enforced
- Disseminated HS (including MH) is not readily treated surgically, since even in the splenic form, early metasta sis to the liver has often occurred. Response to chemo-therapy has been at best brief, and the disease progres ses rapidly (weeks to months) to death or euthanasia.


Thank you!