Case -4
Bone Lesion in an Adolescent Patient

14-18 OCT 2018

Amman, Jordan

XXXII International Academy of Pathology Congress

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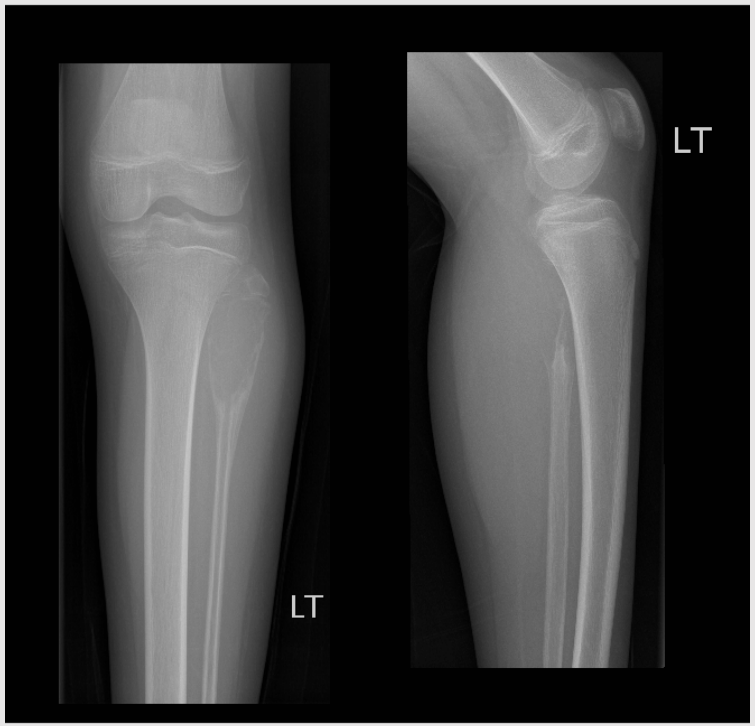
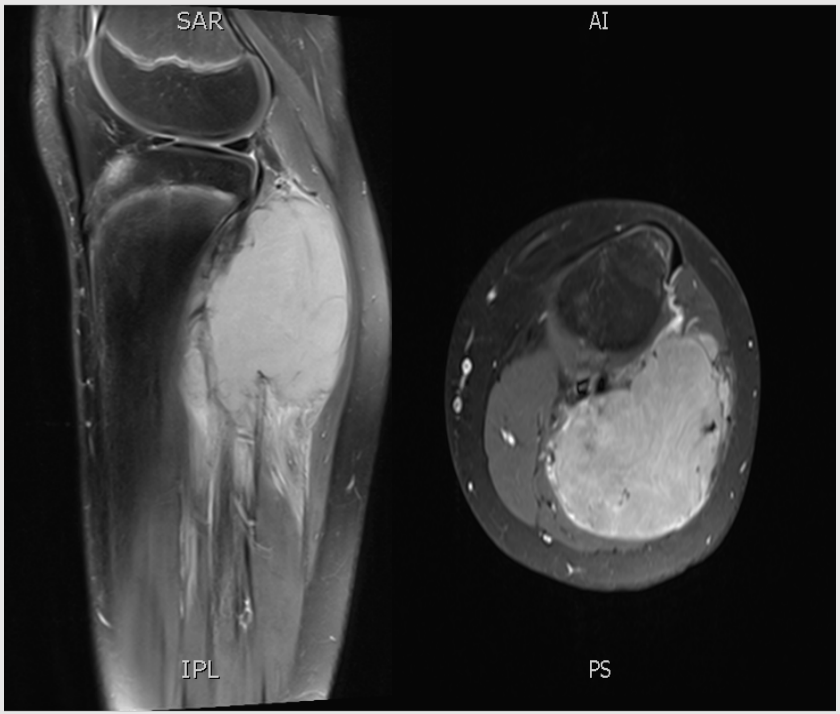
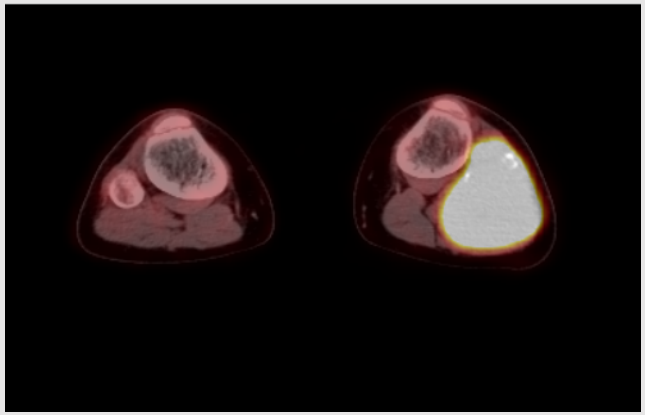
Case history

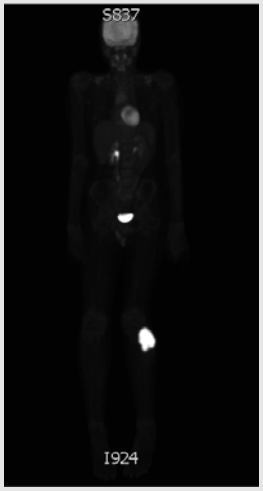
- 14 years old male patient presented with Proximal leg pain and swelling for four months duration
- Clinical examination: firm and tender left leg posterolateral swelling , No palpable regional or distant lymph nodes, No organomegaly

Radiological investigations





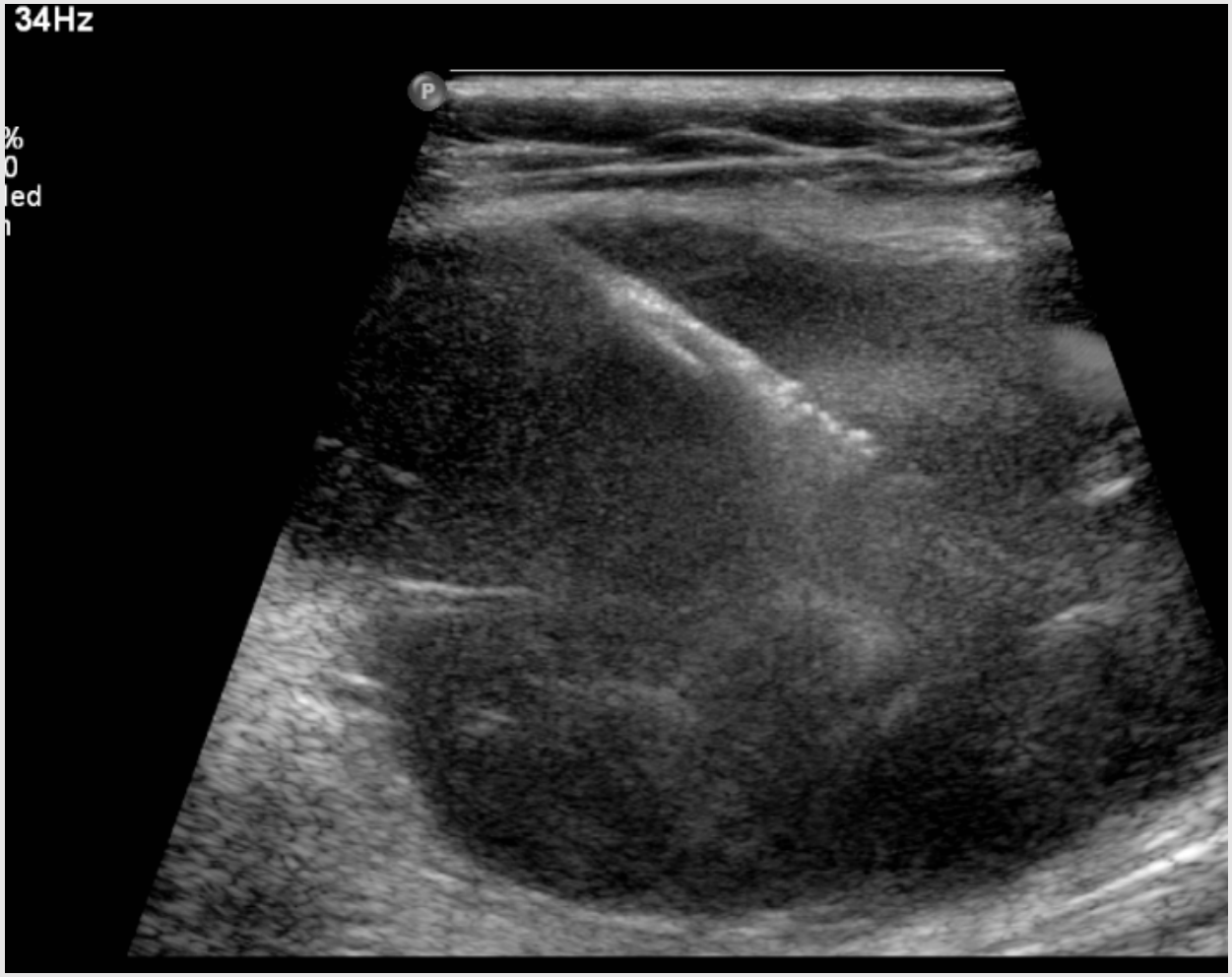


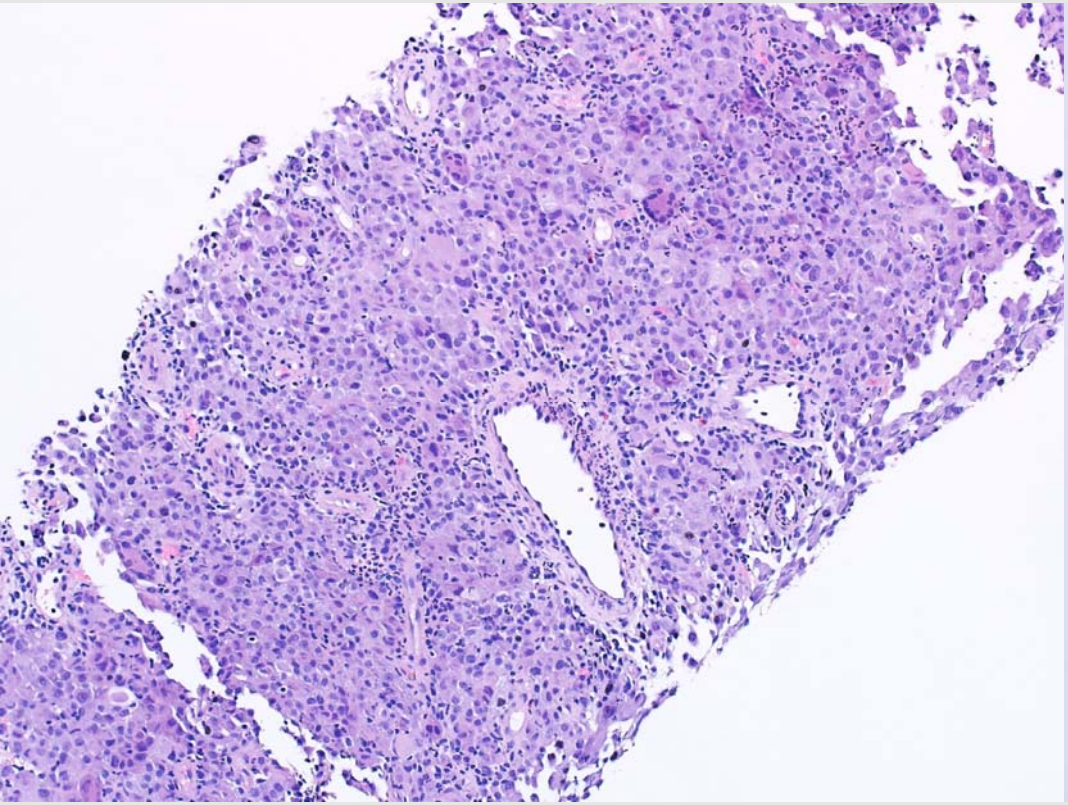


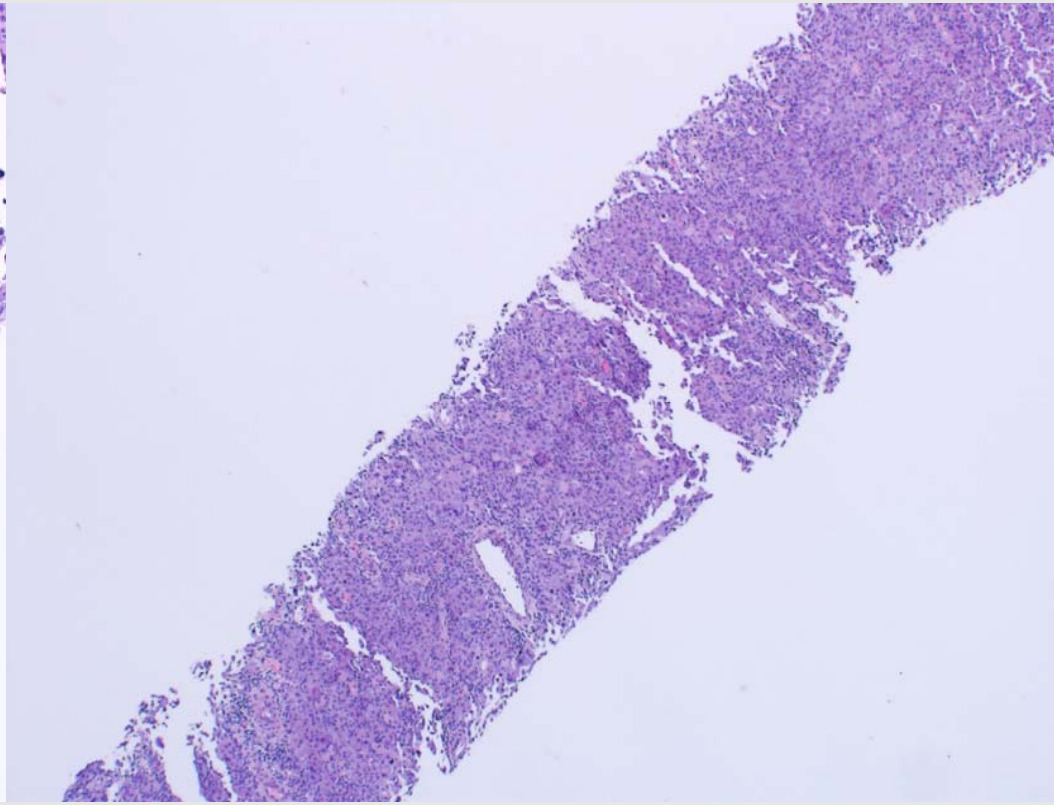
PET Scan

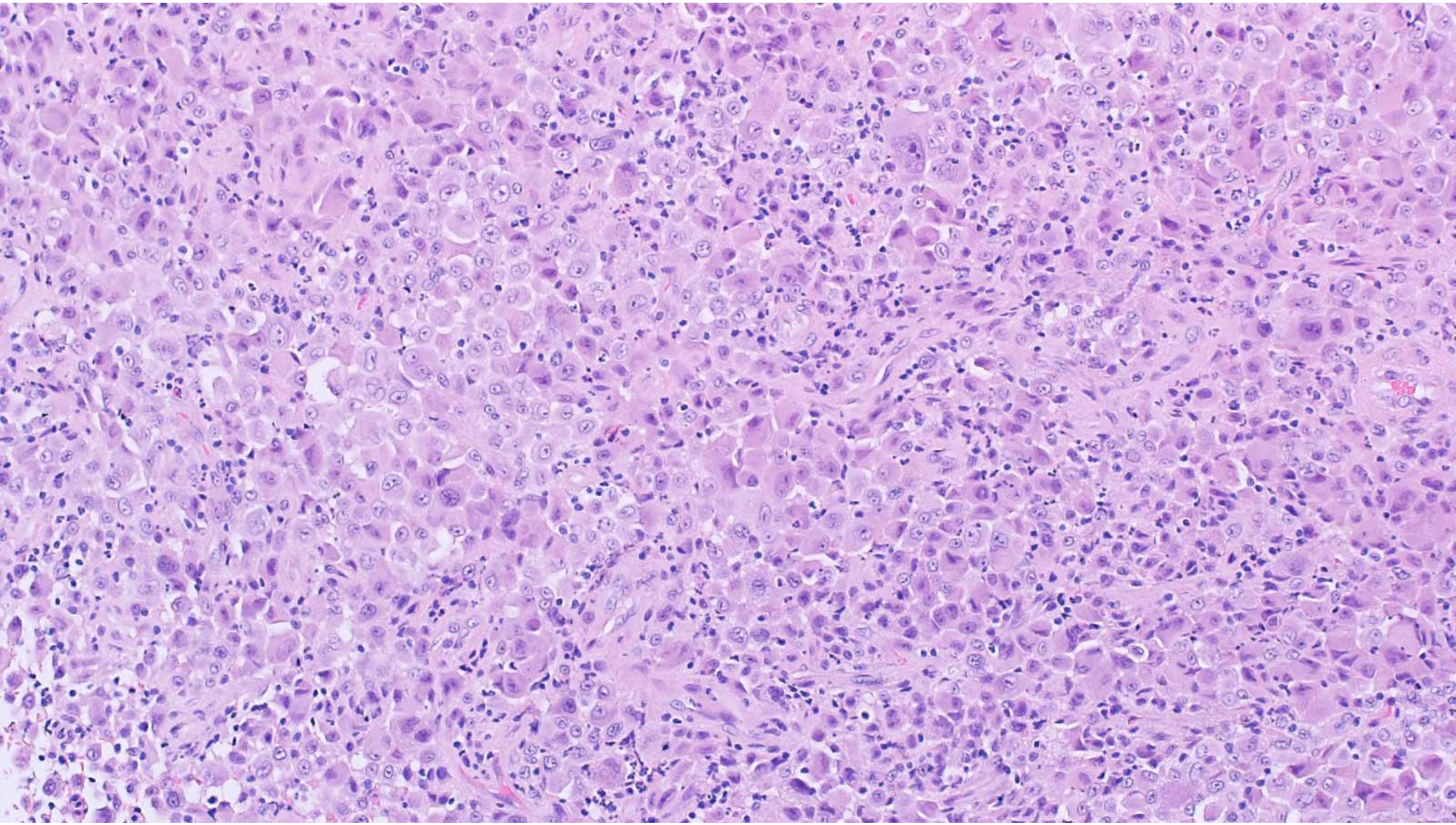
- There is markedly FDG avid large mass lesion seen at the proximal left fibula involving the head measuring 6 x 8 x 6.5 cm (SUVmax 23.7).
- There is no evidence of skip lesion.
- There is no FDG avid or enlarged loco-regional lymph nodes.
- The rest of FDG distribution is within physiological limits with no focal FDG avid cerebral, cerebellar, pulmonary, hepatic, pancreatic, adrenal, splenic or bone lesion.

Ultrasound guided biopsy



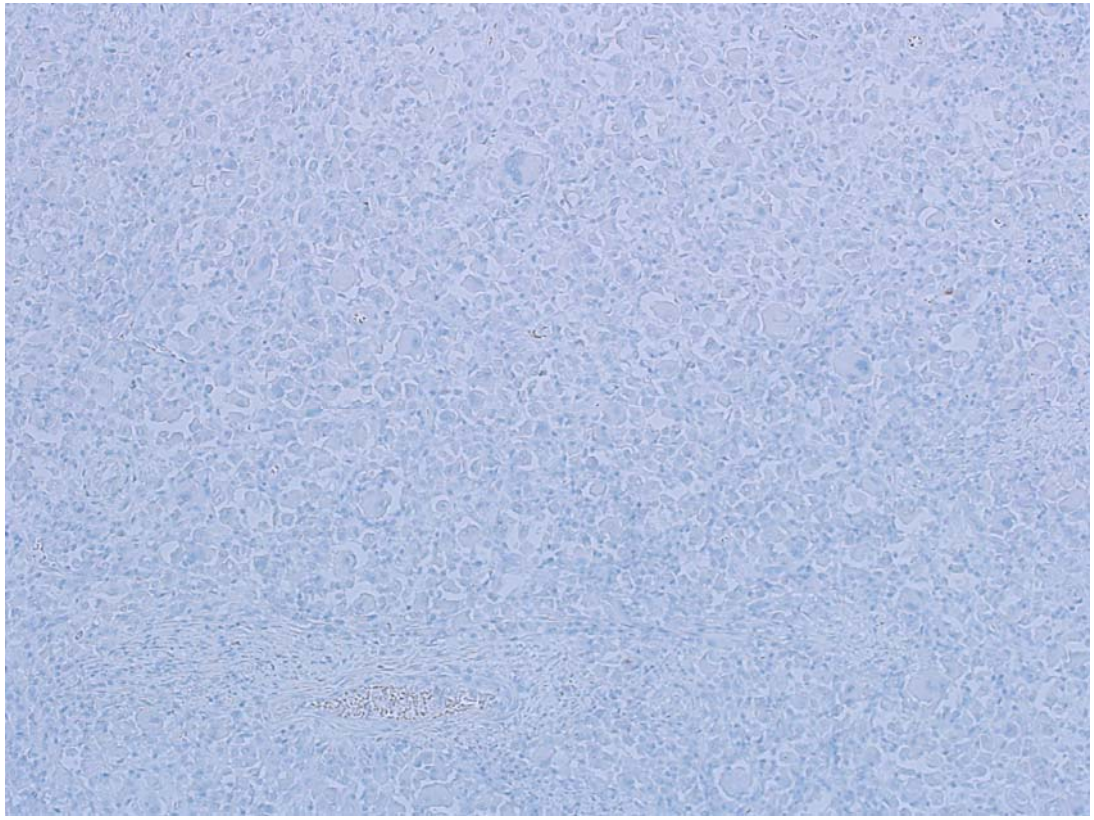


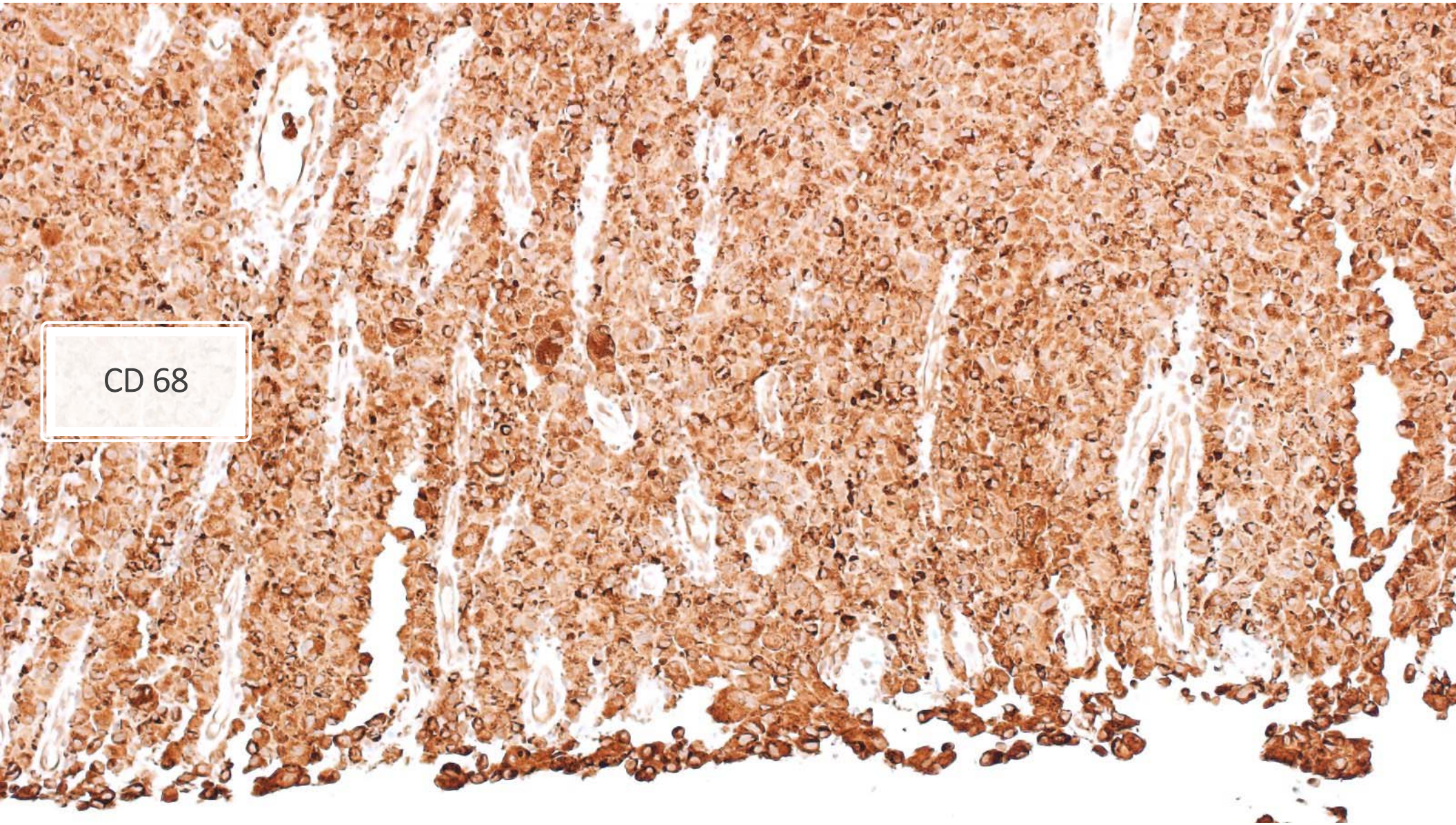




Negative Stains

- PAN CK, CAM 5.2 , EMA
- CD 20 , CD3 , CD 30 , ALK-1
- HMB45
- CD 1a
- CD 117
- CD 21, CD23
- Desmin , SMA




CD 68

Histological Diagnosis

Non-Langerhans Cell Histiocytic Proliferation

That is

Radiologically and Clinically Locally Aggressive and Destructive

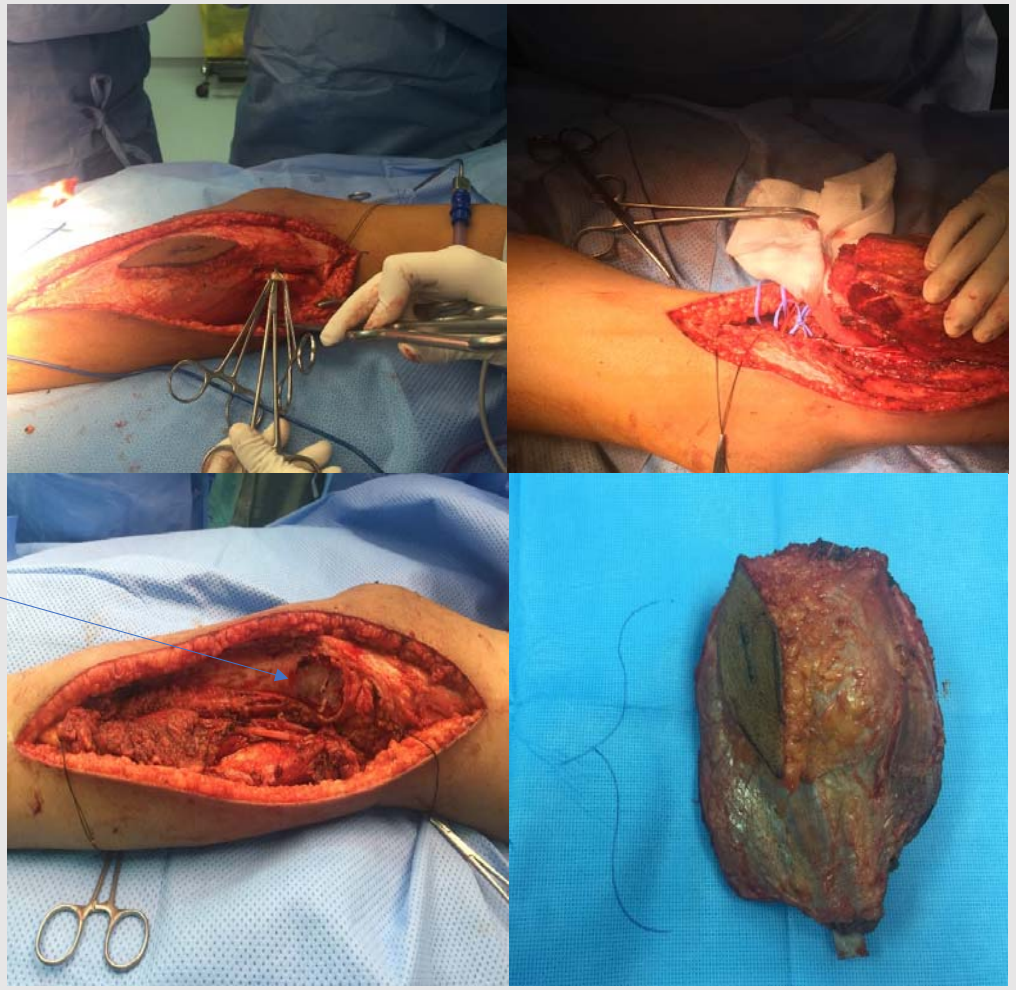
“Likely Malignant”

Pediatric Tumor Board Decision

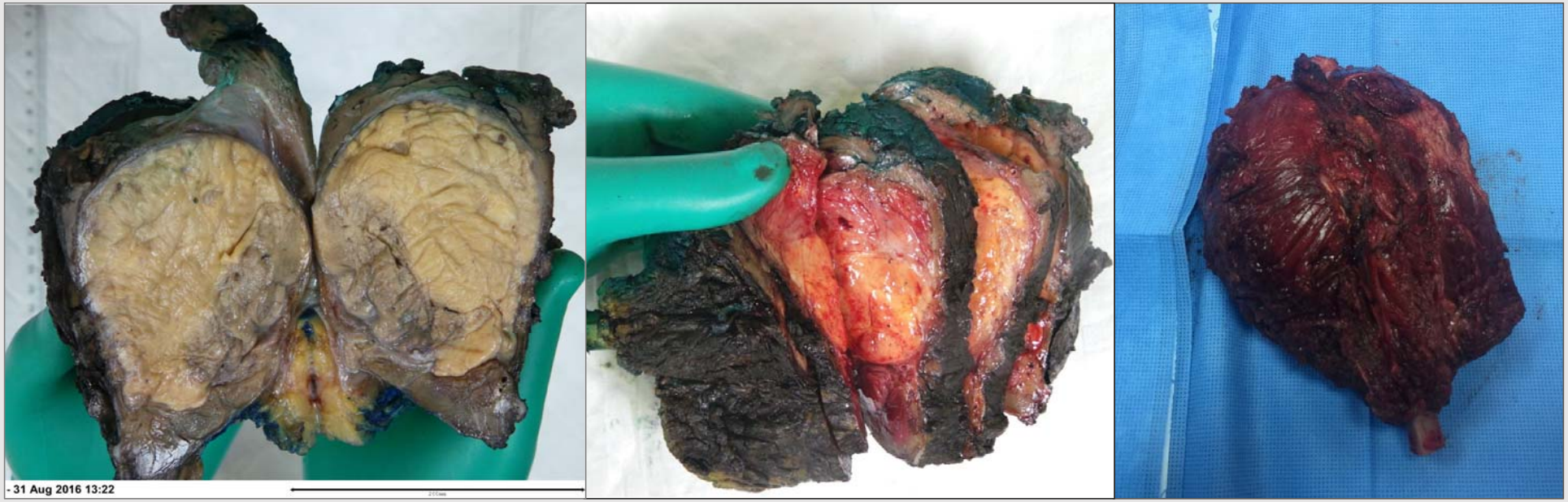
- Extremely rare disease in bones
- Wide local resection
- Post operative local and systemic surveillance

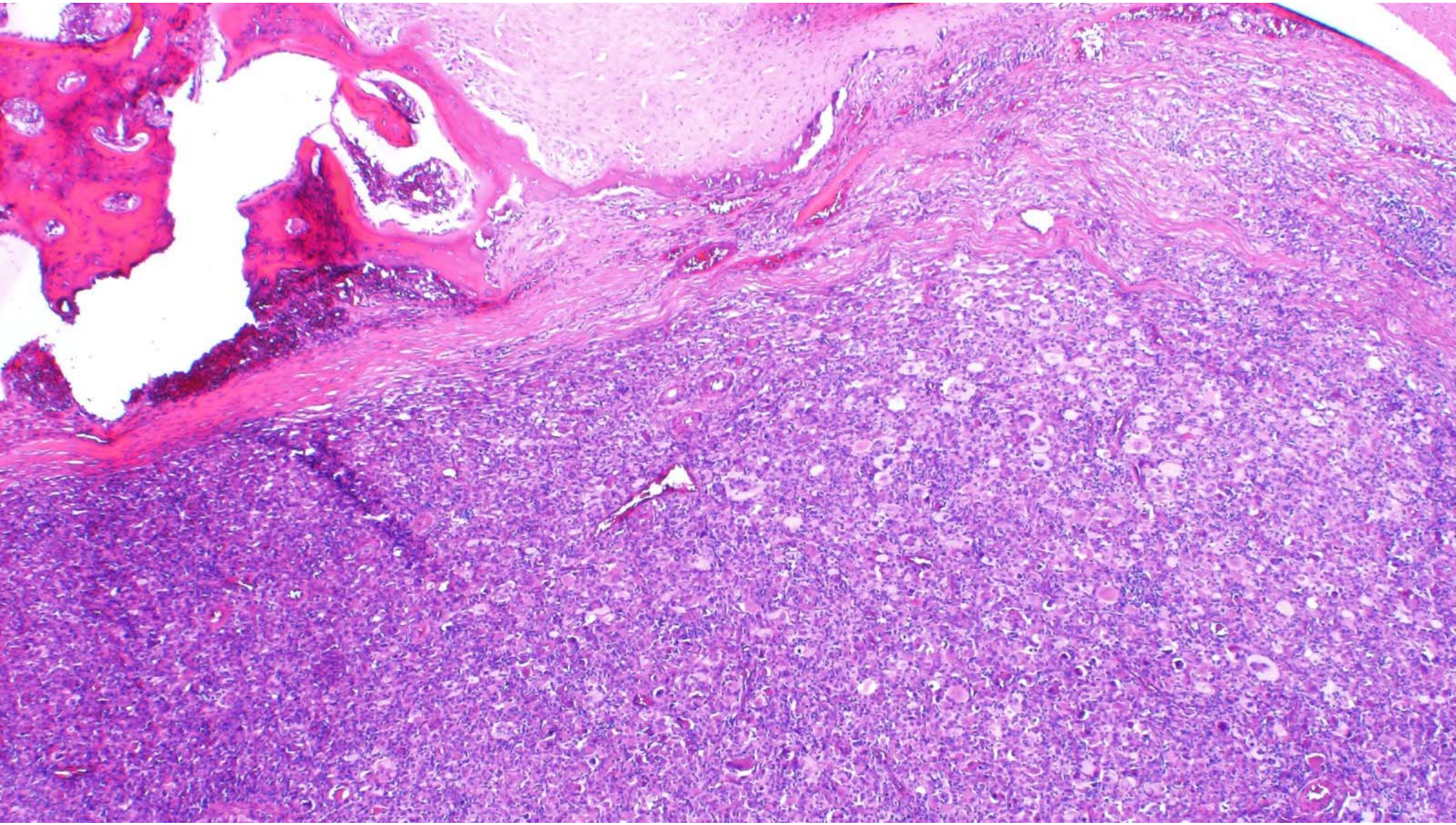
Surgical Management

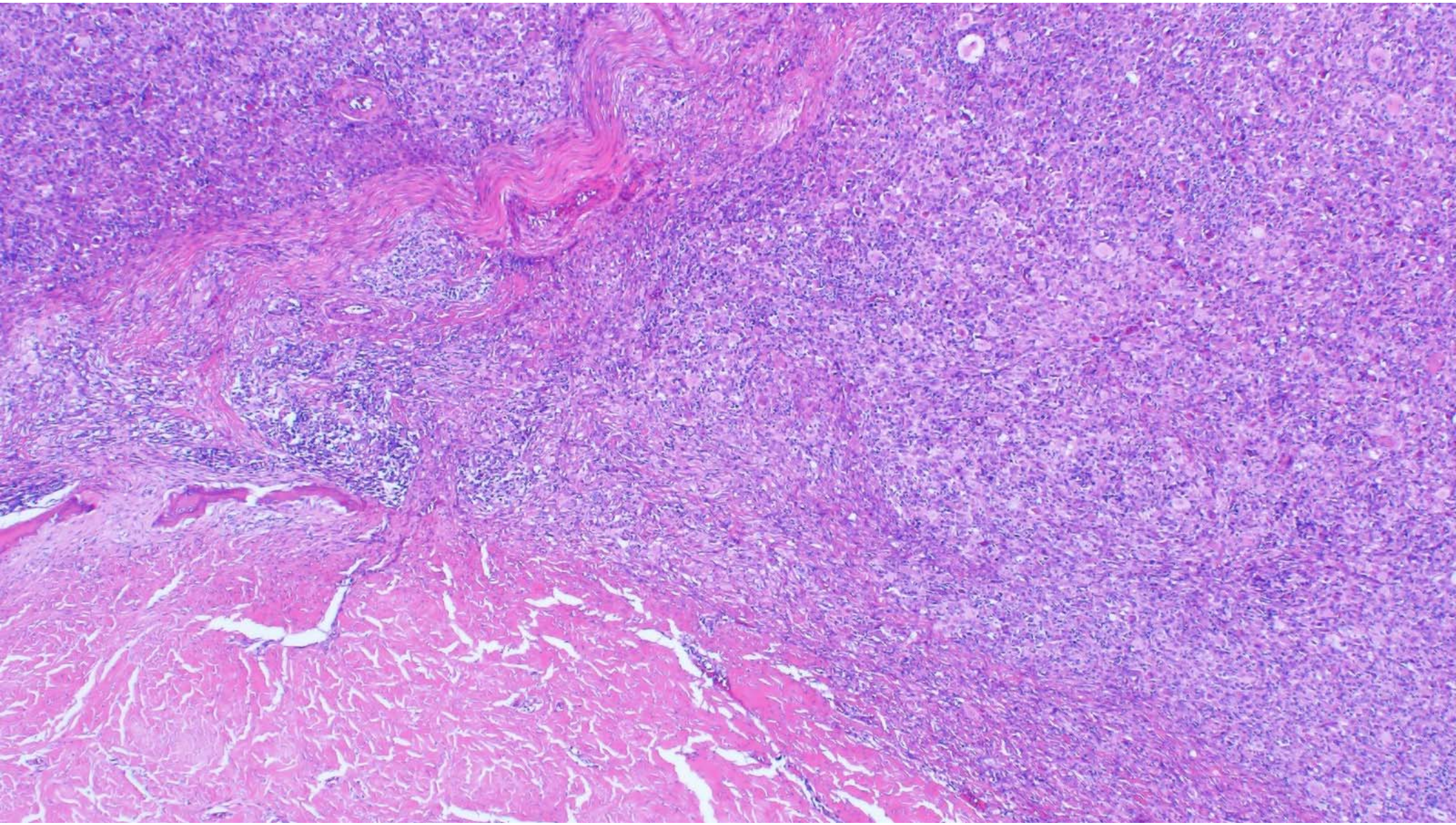
- Wide local resection
- Bone soft tissue component
- Tibio Fibular Joint resection
- Intraoperative frozen section

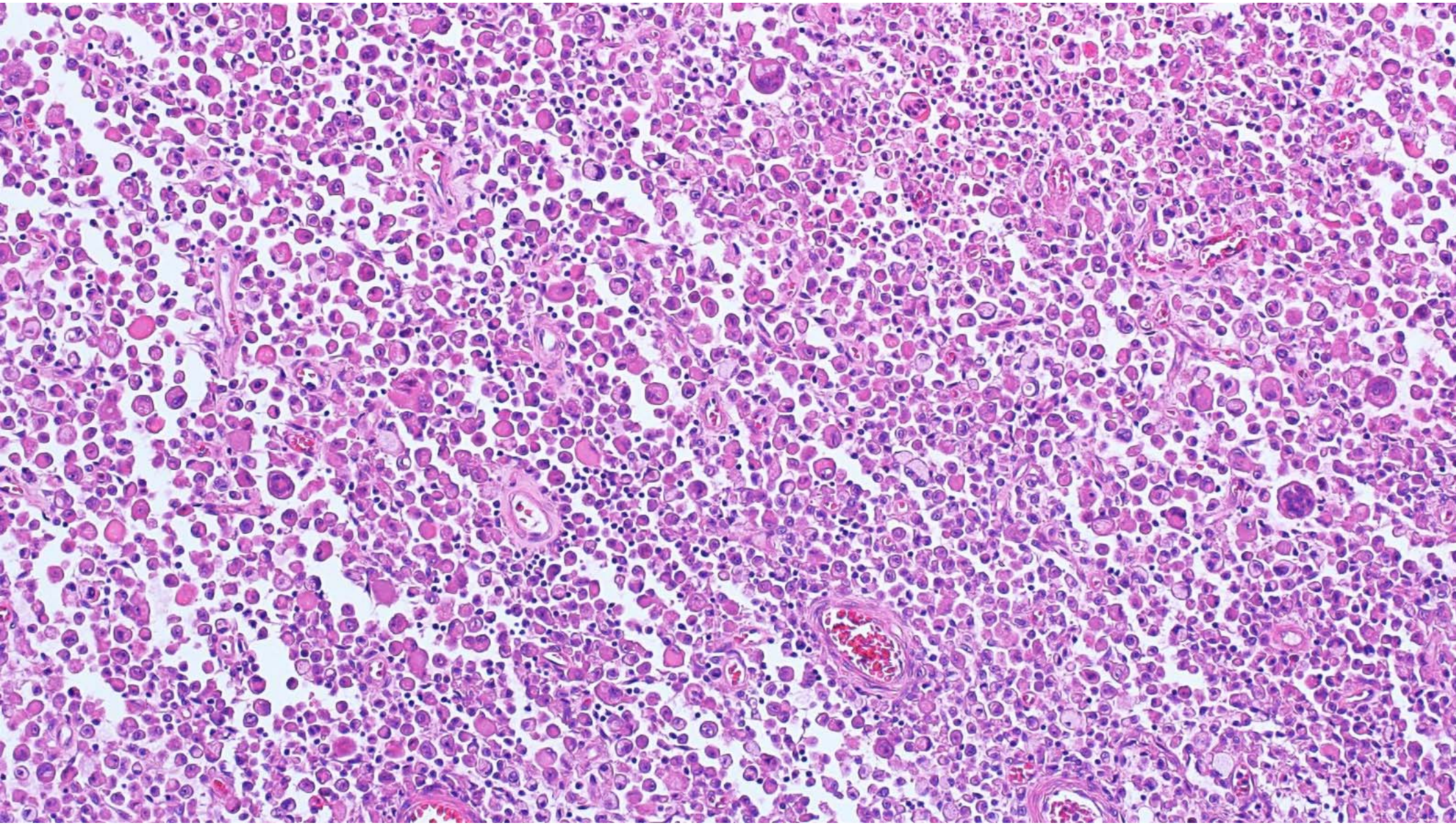


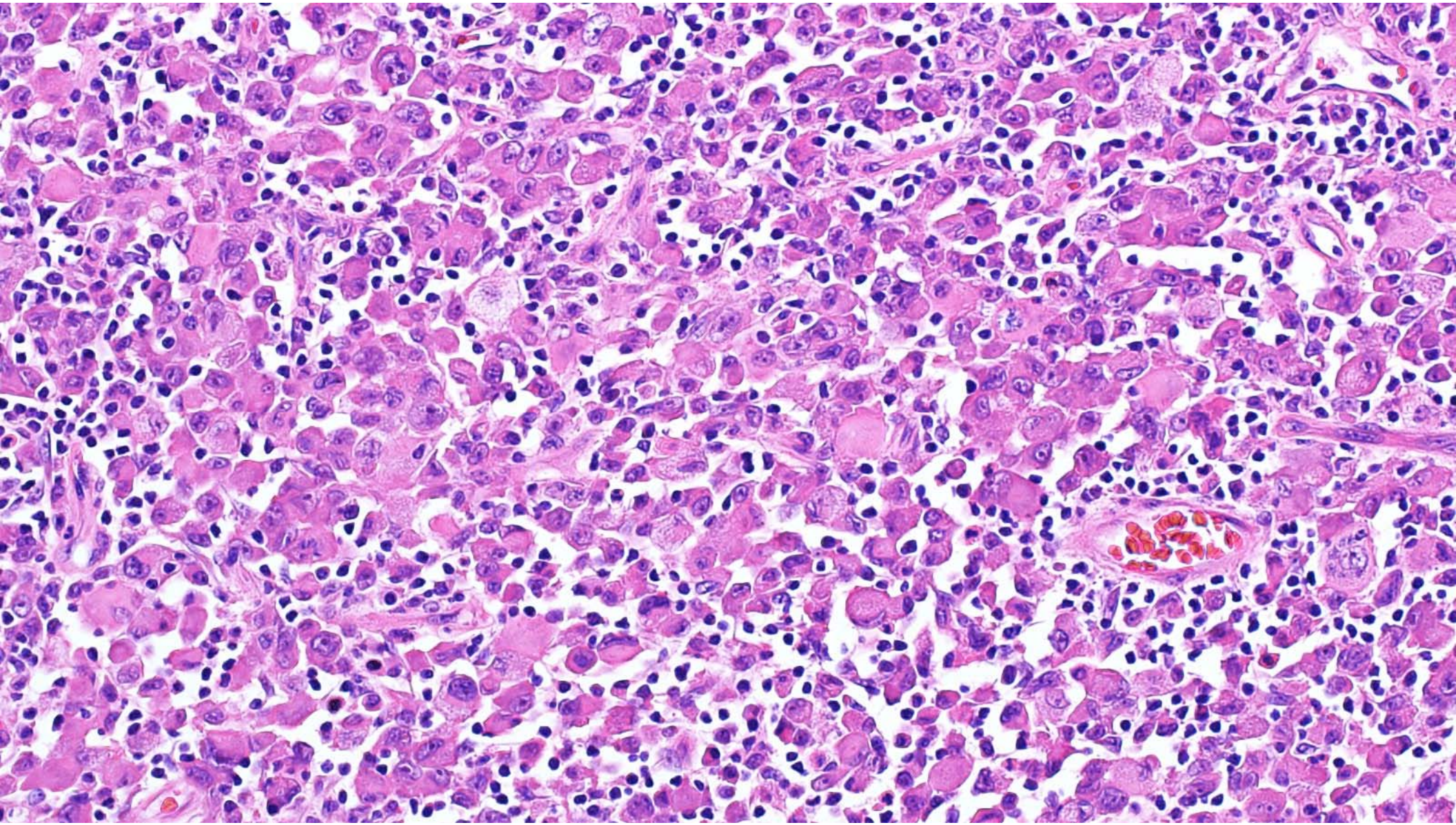
Gross Pathology

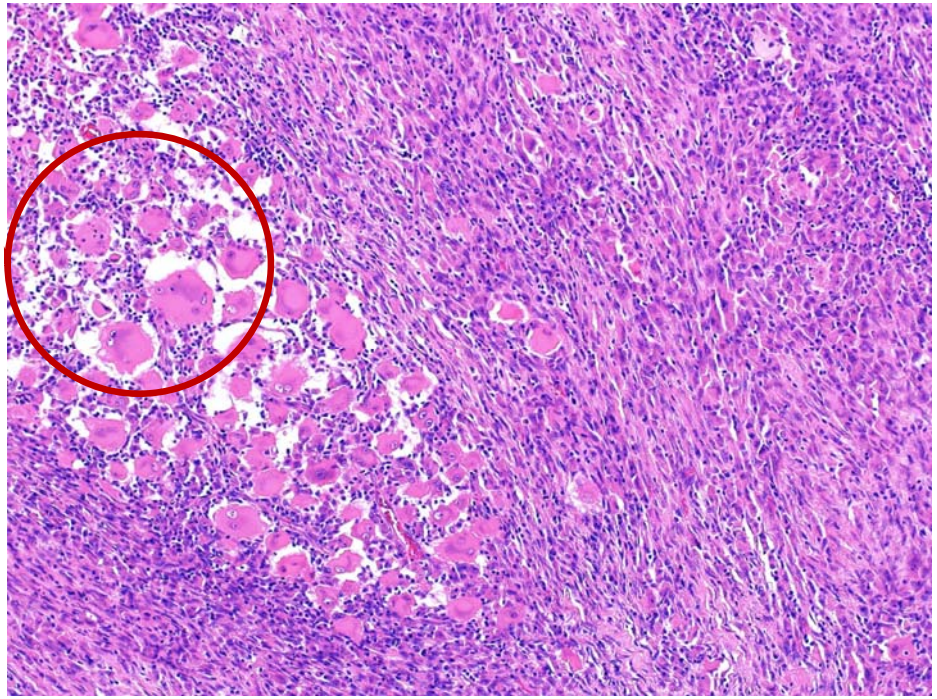


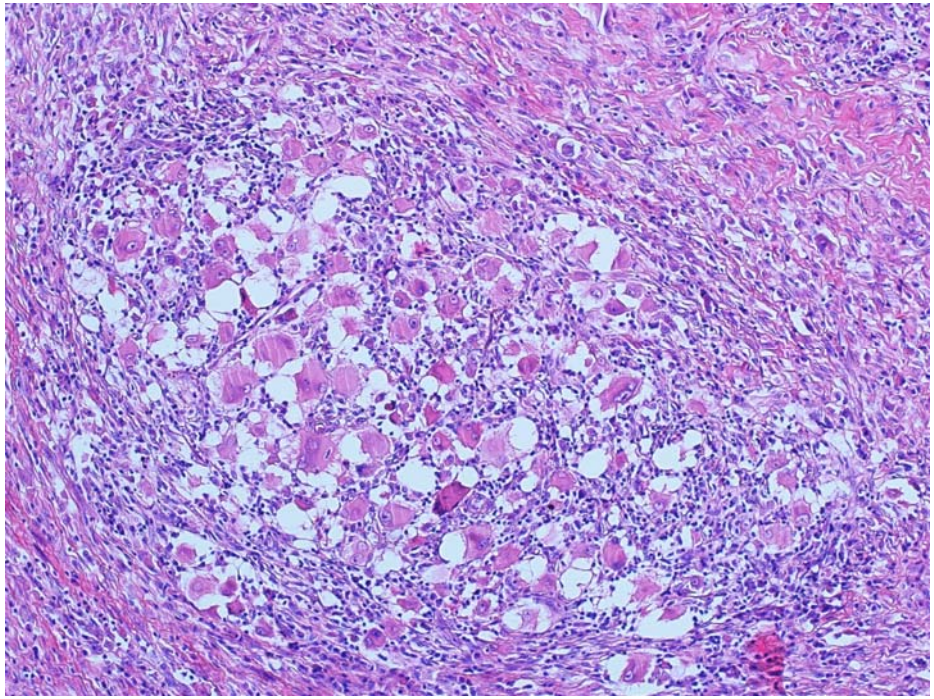




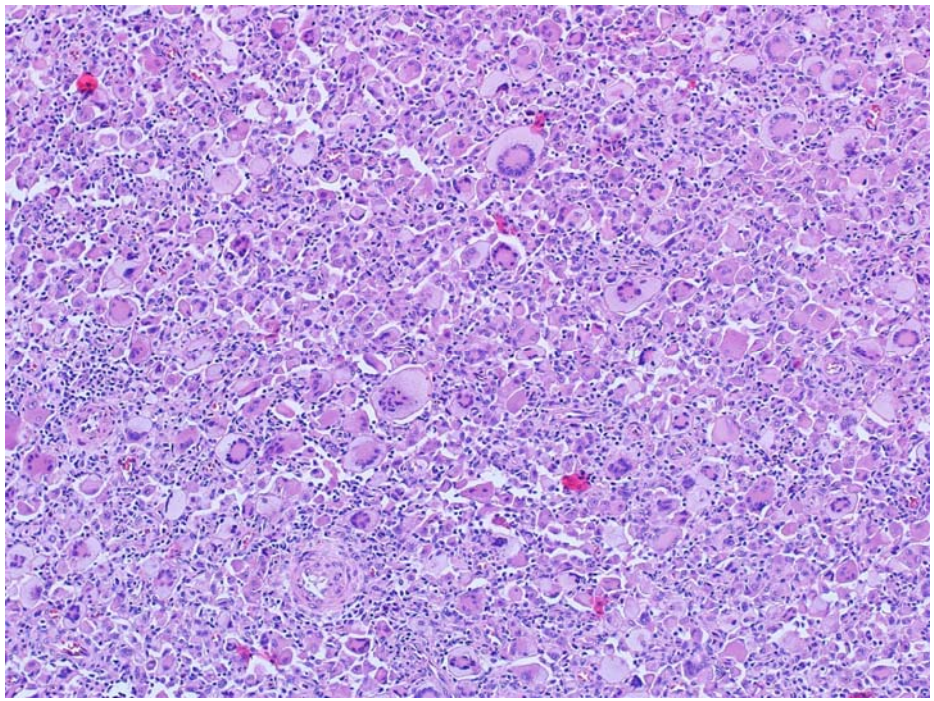


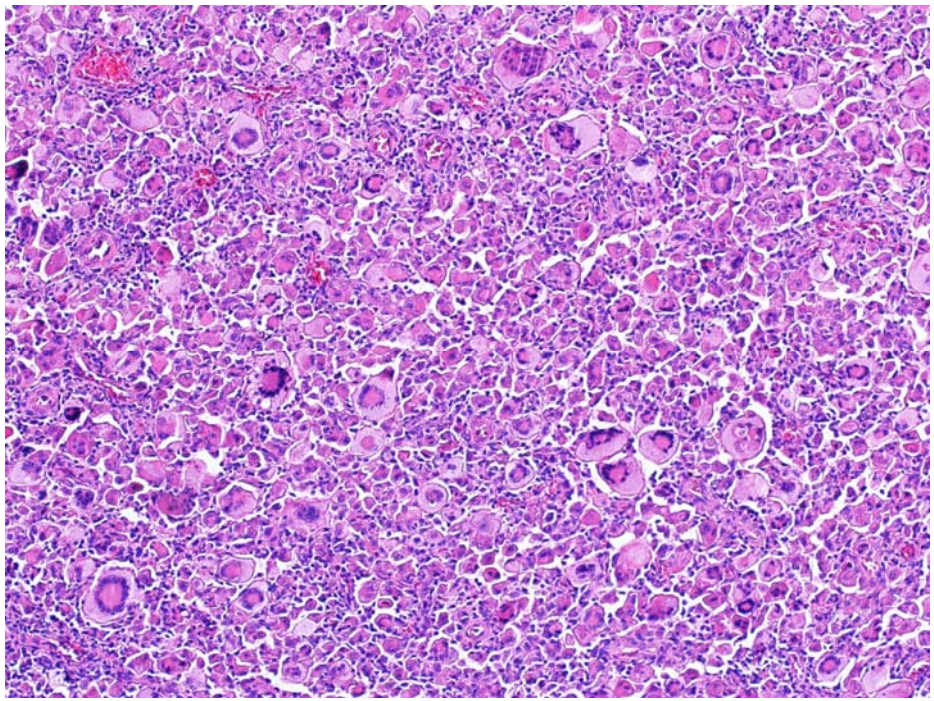




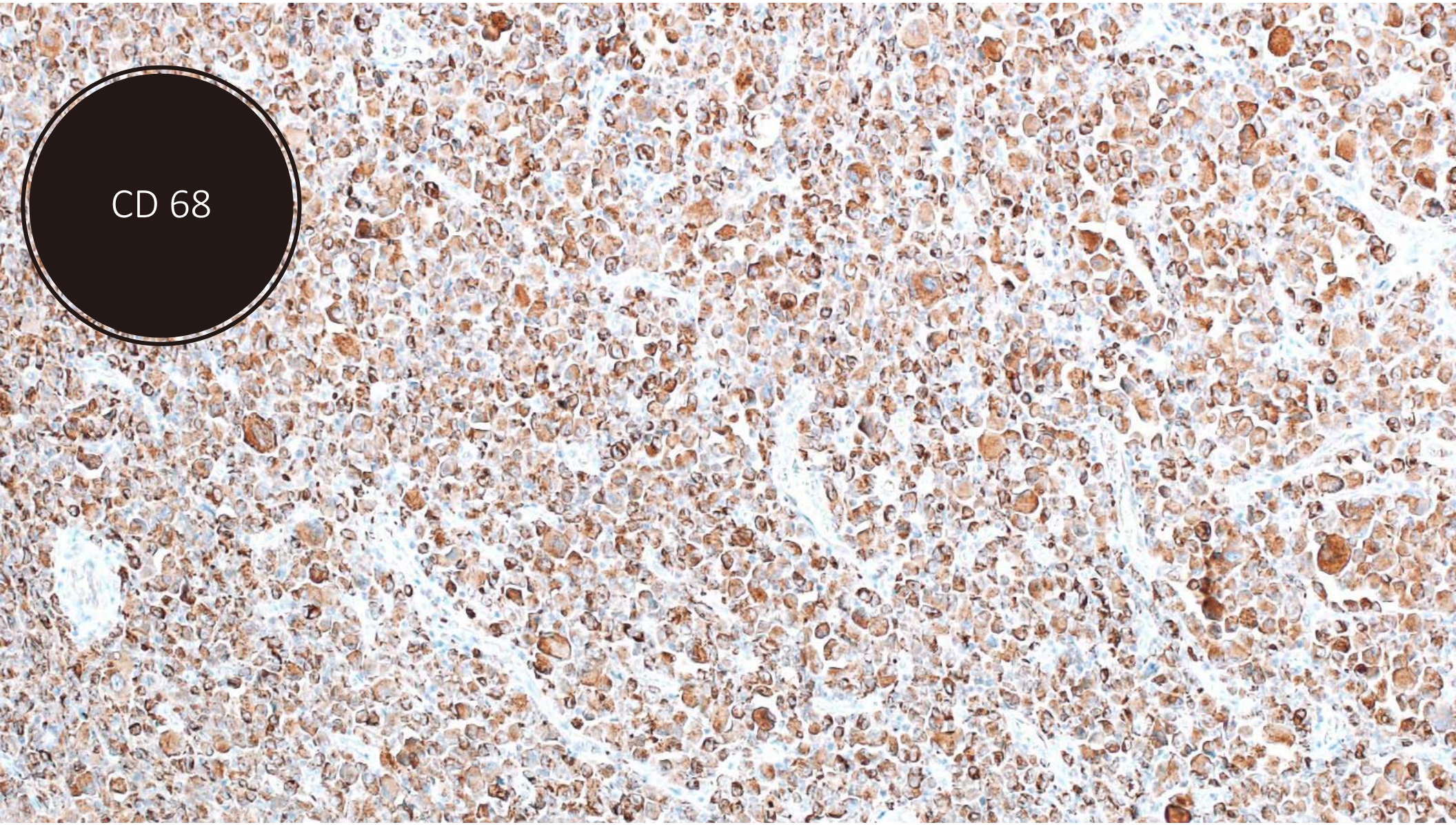


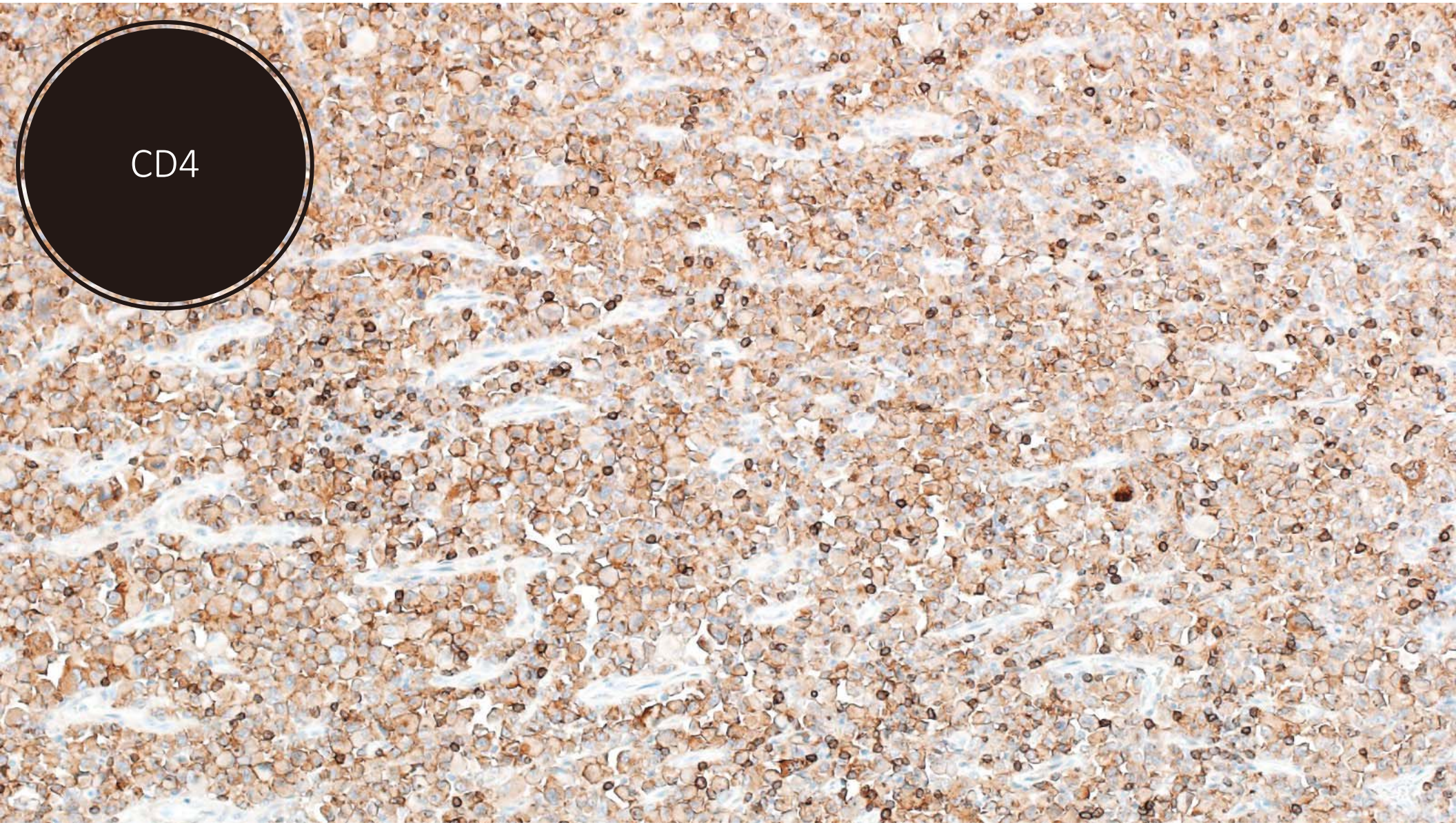
Spindle Cell Morphology and Emperipolesis

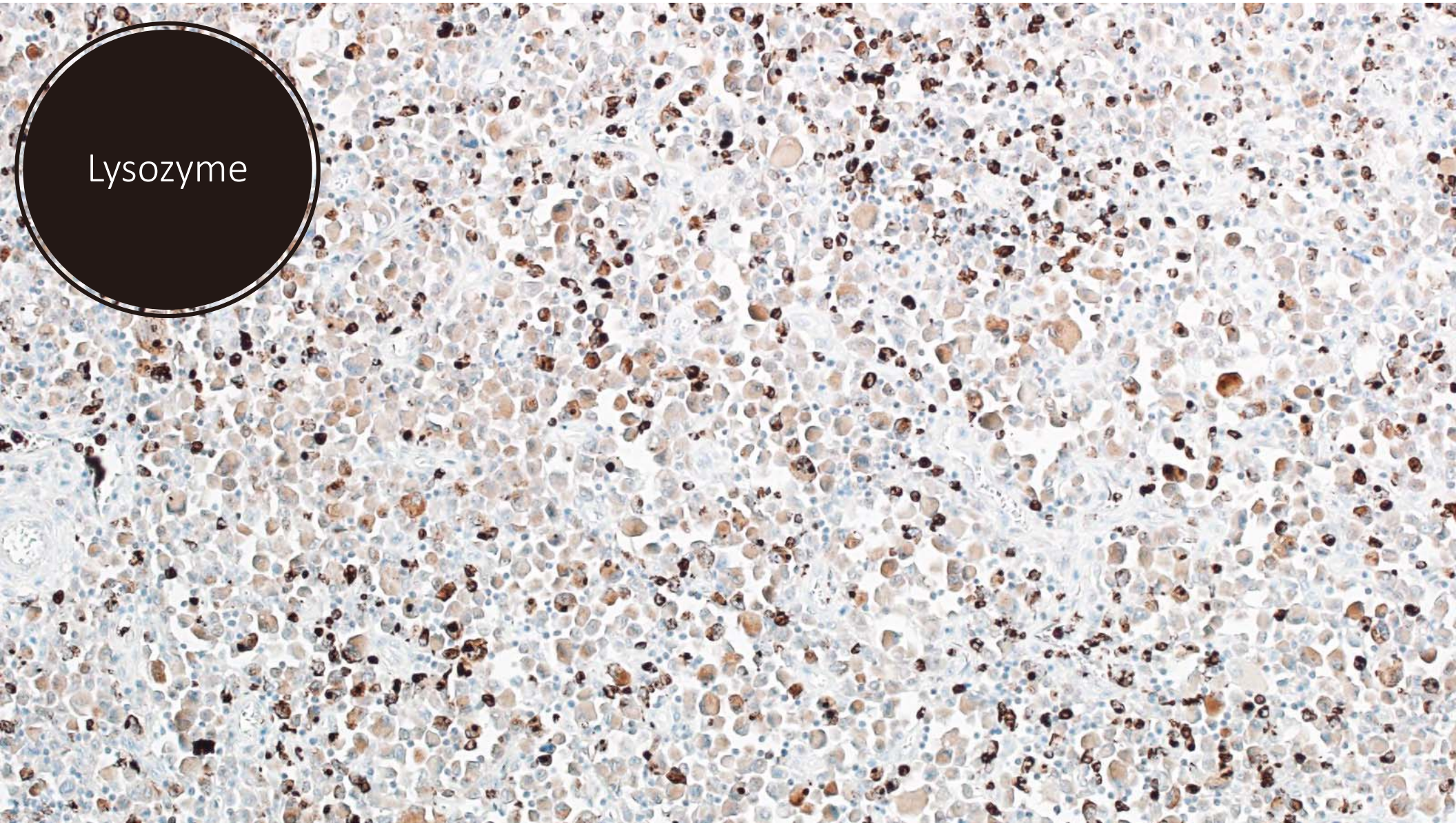


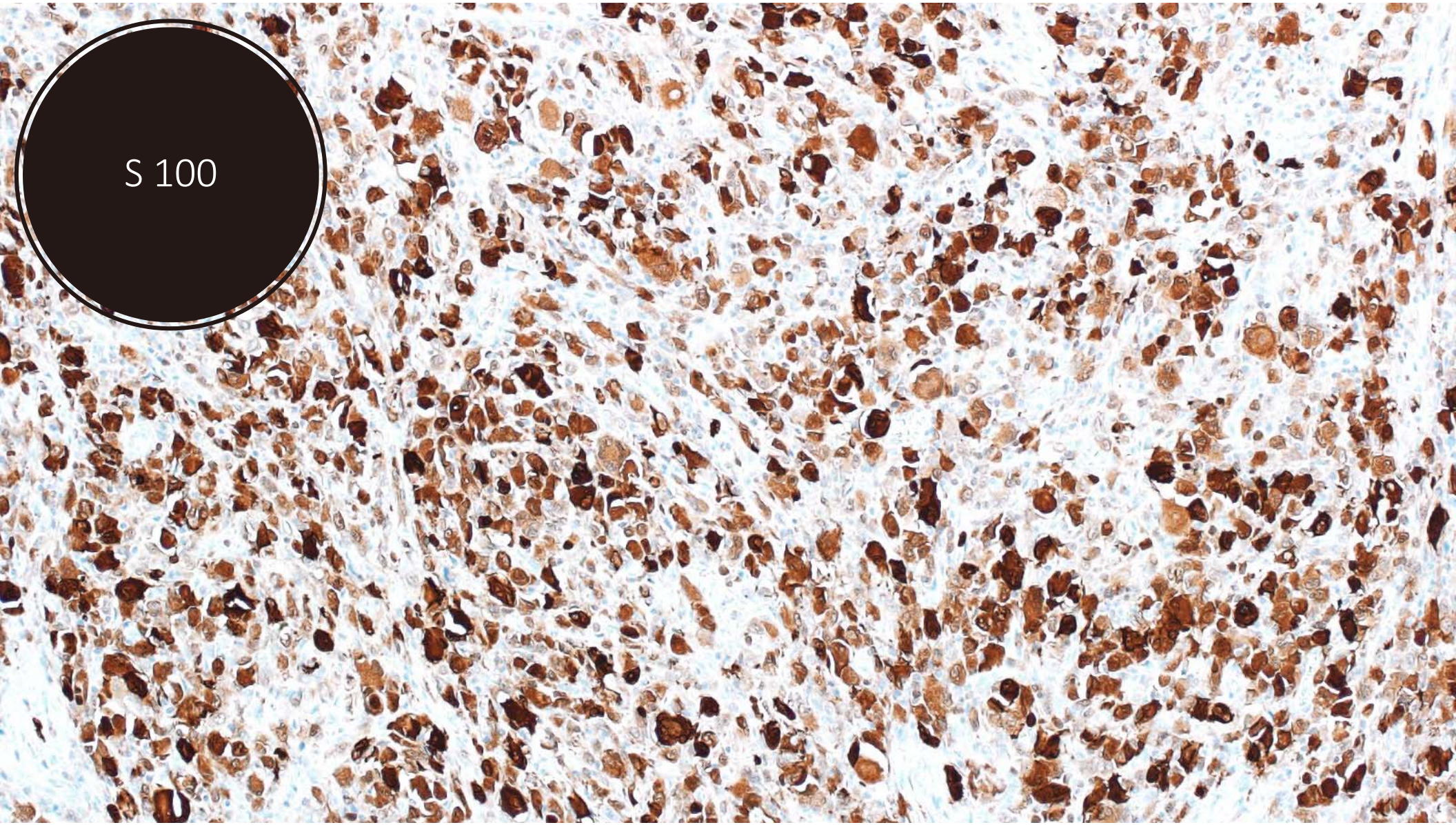


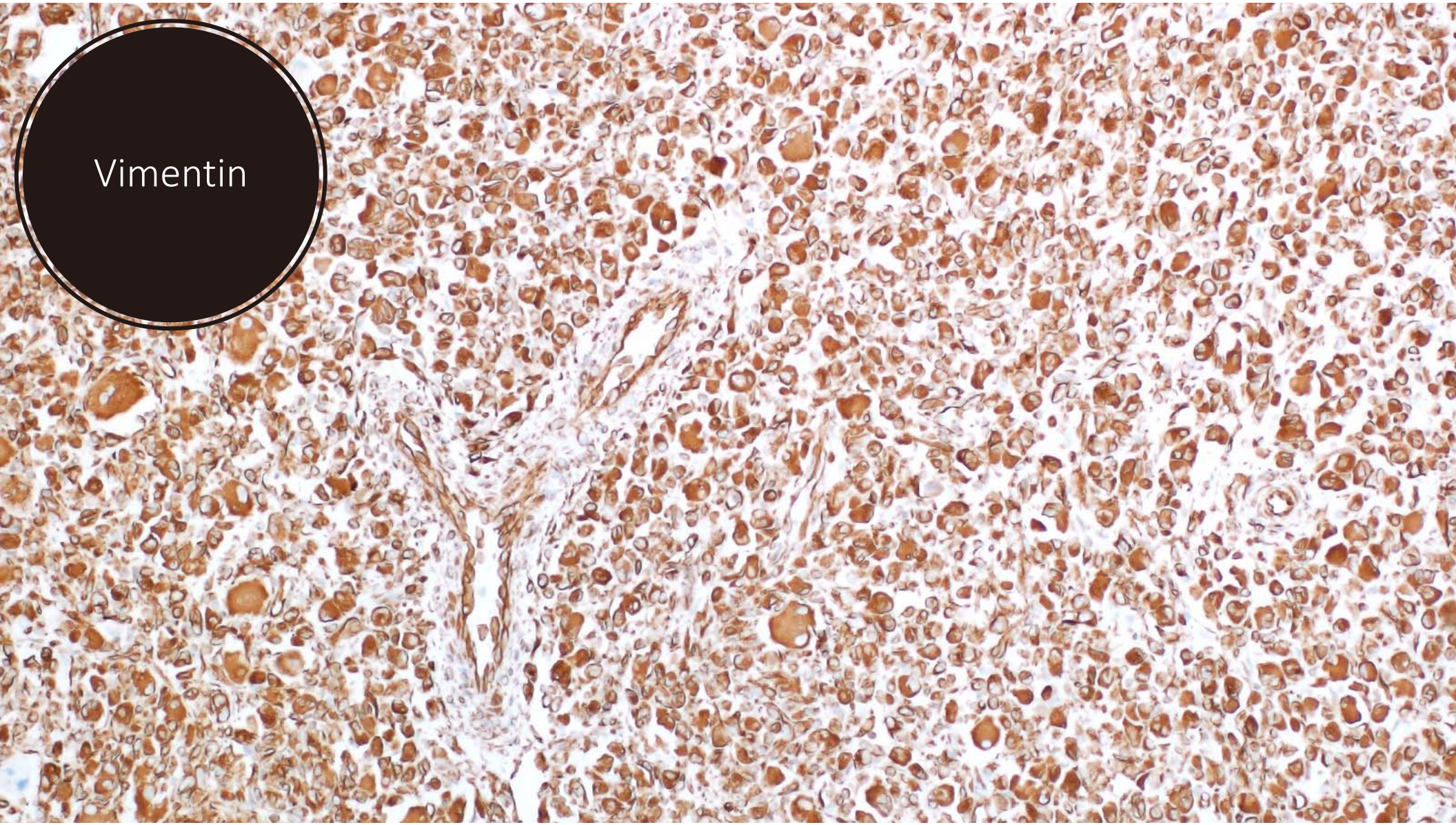
Touton Cells


CD 68


CD4


Lysozyme


S 100


Vimentin

Negative Stains

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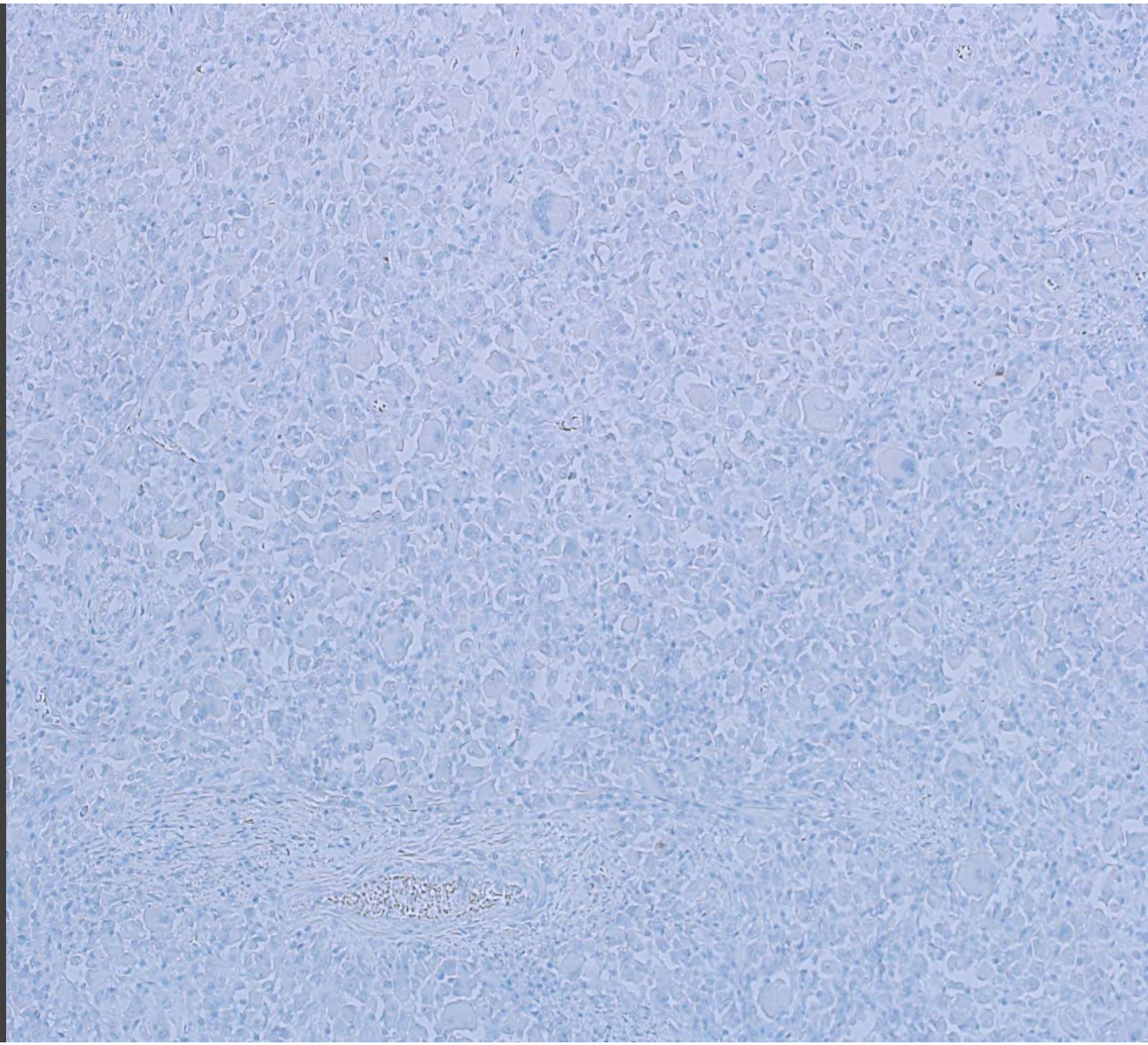

Review Article

Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages

Jean-François Emile,[1,2] Oussama Abla,[3] Sylvie Fraitag,[4] Annacarin Horne,[5] Julien Haroche,[6,7] Jean Donadieu,[1,8] Luis Requena-Caballero,[9] Michael B. Jordan,[10] Omar Abdel-Wahab,[11] Carl E. Allen,[12] Frédéric Charlotte,[7,13] Eli L. Diamond,[14] R. Maarten Egeler,[3] Alain Fischer,[15,16] Juana Gil Herrera,[17] Jan-Inge Henter,[18] Filip Janku,[19] Miriam Merad,[20] Jennifer Picarsic,[21] Carlos Rodriguez-Galindo,[22] Barret J. Rollins,[23,24] Abdellatif Tazi,[25] Robert Vassallo,[26] and Lawrence M. Weiss,[27] for the Histiocyte Society

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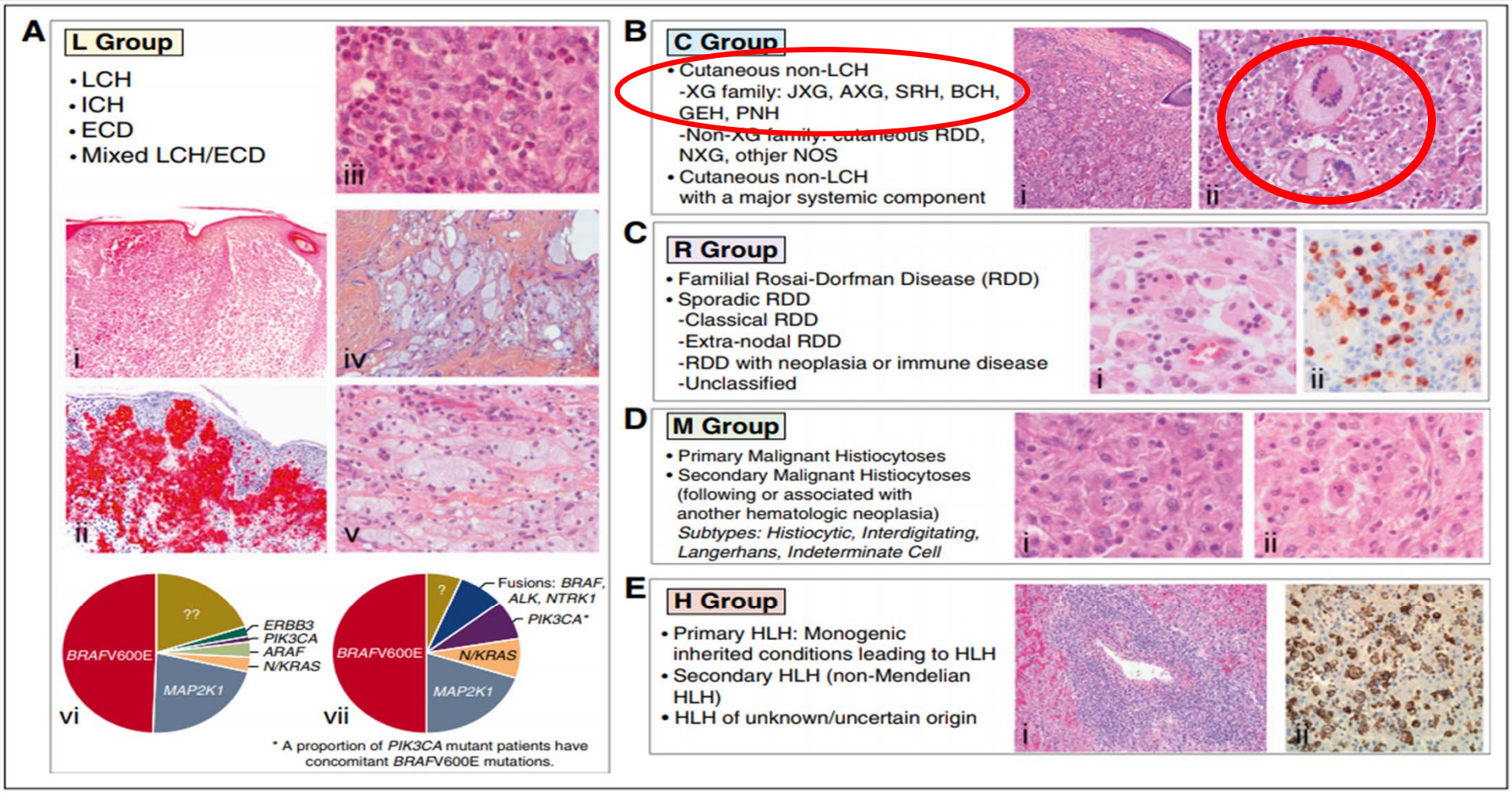
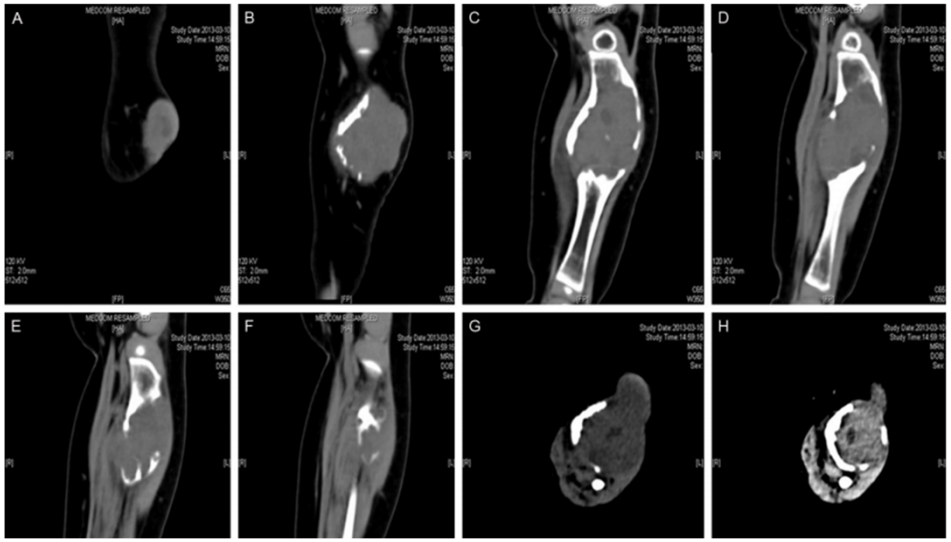


Figure 1. Histology and somatic mutations of histiocytoses of group L, C, R, M, and H. (A) L group: Histology of LCH (skin [i-ii] and bone [iii]) and of ECD (perirenal [iv-v]). Pie chart of relative frequencies of activating kinase mutations in LCH (vi) and ECD (vii). (B) C group: Histology of JXG (i-ii). (C) R group: Histology of RDD (meningeal with high IgG4$^+$ plasma cell infiltration [i-ii]). (D) M group: Histology of MH (i-ii). (E) H group: Histology of inherited HLH (liver [i-ii]). Staining with CD1a (Lii in red), IgG4 (Rii in brown), CD163 (Hii in brown), or hematoxylin and eosin (all others). NOS, not otherwise specified.

Juvenile Xanthogranuloma

- Typical presentation as solitary cutaneous lesion in young children
- Benign and self-limiting
- Infiltration by bland-looking histiocytes (non-lipidized and foamy), touton giant cells, often admixed with inflammatory cells
- Show overlapping histological features of Rosai-Dorfman Disease (S100 +, Emberiopolesis)
- Histiocytic differentiation by IHC (CD68 +, CD4, Lysozyme+)
- Few reported cases of solitary extracutaneous JXG (CNS and Bone)



Original Article

Solitary juvenile xanthogranuloma with tibial involvement: a case report

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Departments of [1]Pediatric Surgery, [2]Neurosurgery, [3]Pathology, [4]Organ Transplantation Center, [5]Digital Computer-aided Medicine and Surgery Key Laboratory, The Affiliated Hospital of Qingdao University, Qingdao, Shandong, China

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Abstract: Juvenile xanthogranuloma (JXG) is a rare disease that is part of a spectrum of histiocytic dendritic cell disorders. Most patients present with a solitary cutaneous lesion; however, others present with extracutaneous manifestations or even with systemic involvement. We present the first report of an 11-month-old girl in whom was diagnosed a unifocal extracutaneous JXG involving the tibia. Histological and immunohistochemical staining results are presented. A review of the literature on these unusual lesions is conducted, along with discussion of their differential diagnosis and key aspects of the patient's evaluation, management, and pathological diagnosis.

Keywords: Juvenile xanthogranuloma, Langerhans cell histiocytosis, tibia

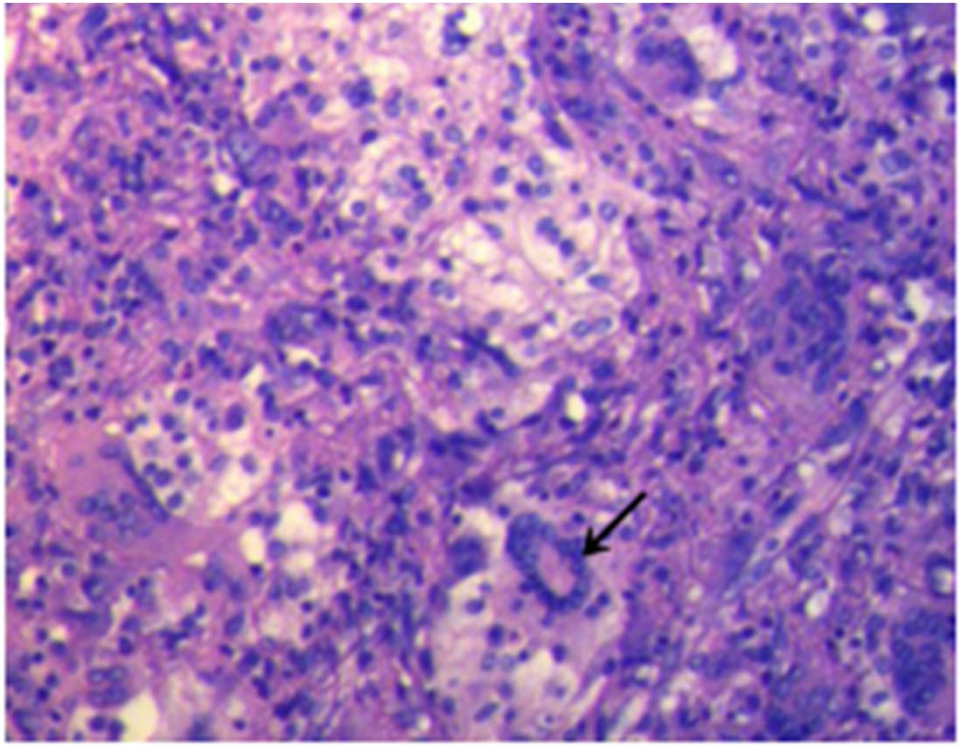
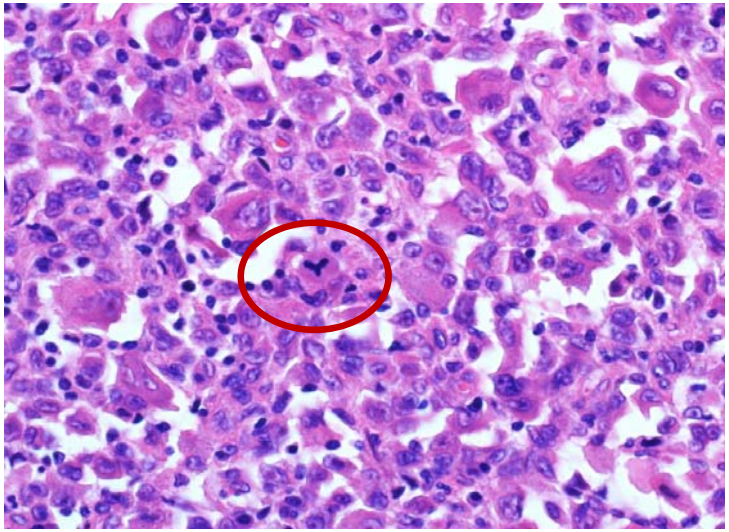
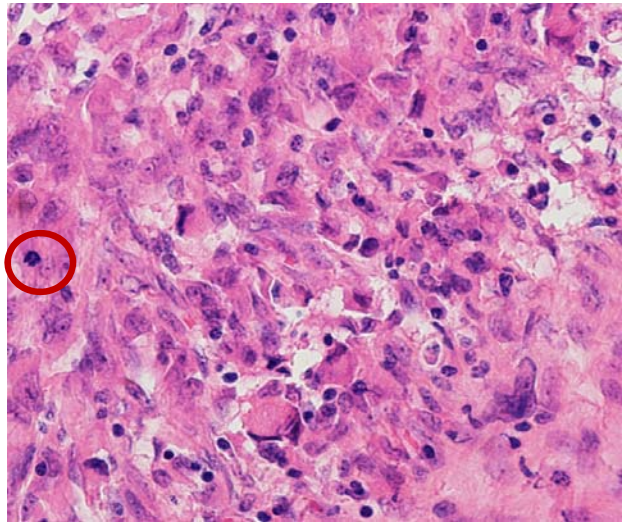
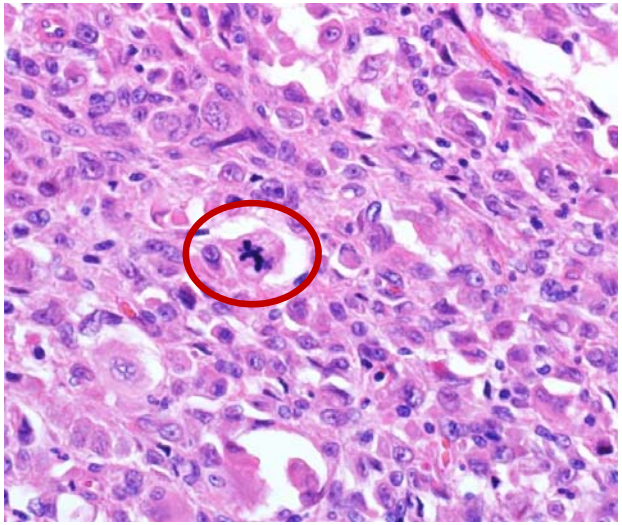
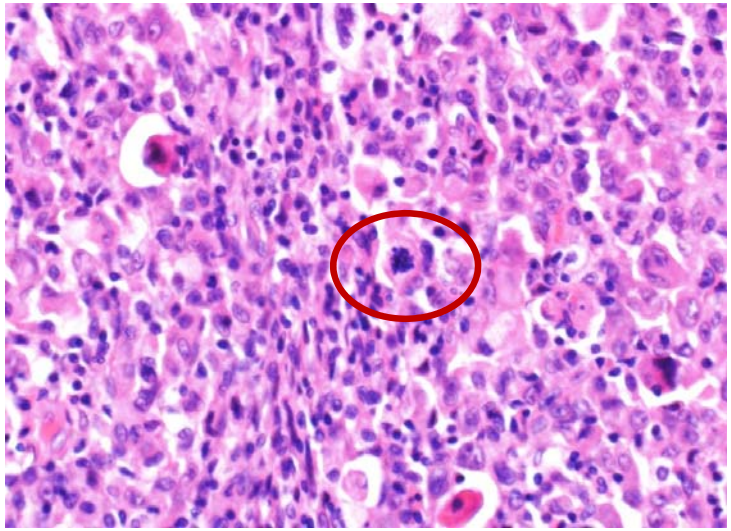
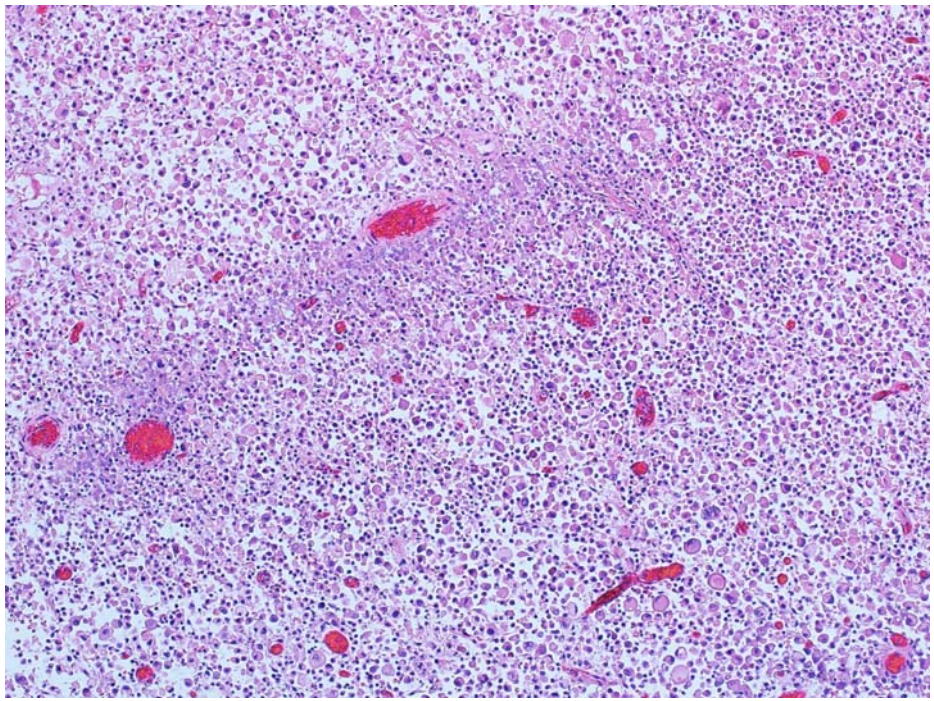
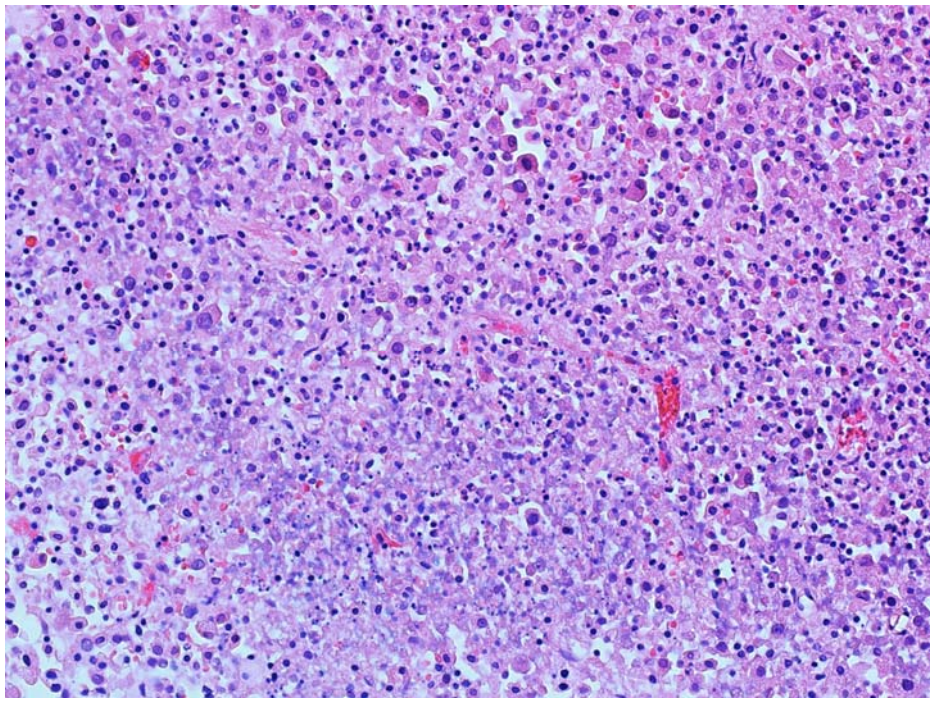


Figure 7. Monomorphic histiocytic cells with characteristic admixed eosinophils, Touton giant cells (arrows), and cells with intracytoplasmic microvesicular lipid, no prominent cytological atypia or mitotic figures were identified (H&E, original magnification ×200).

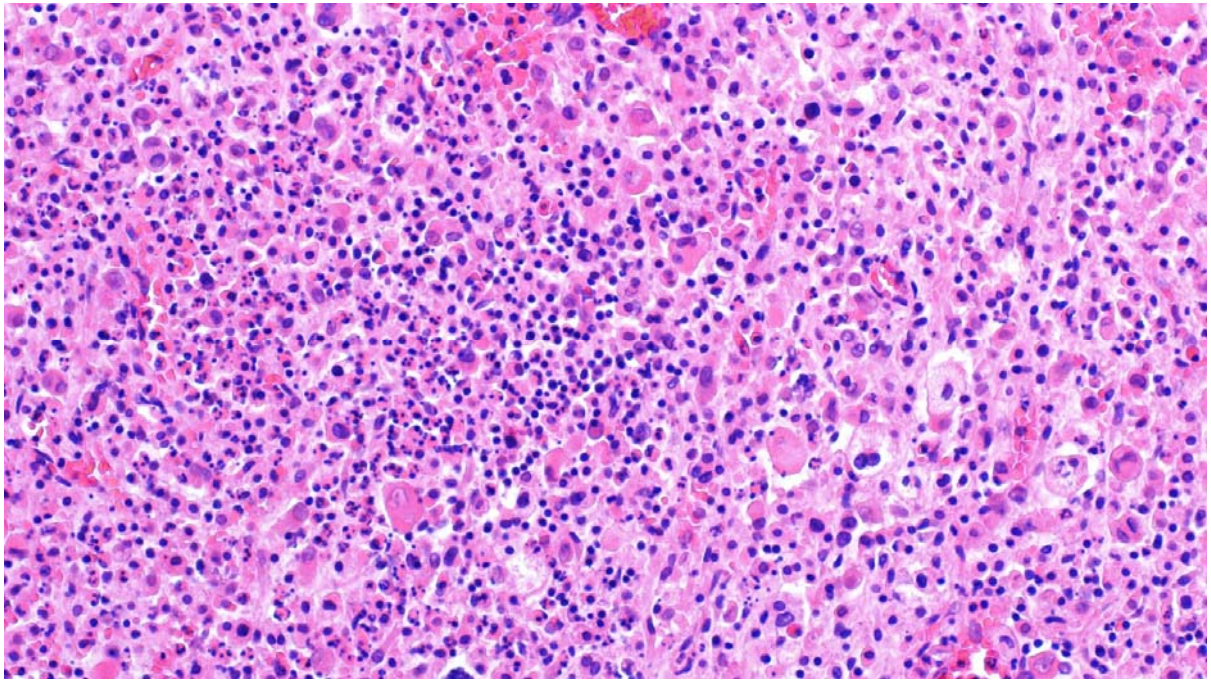
Atypical Mitotic figures

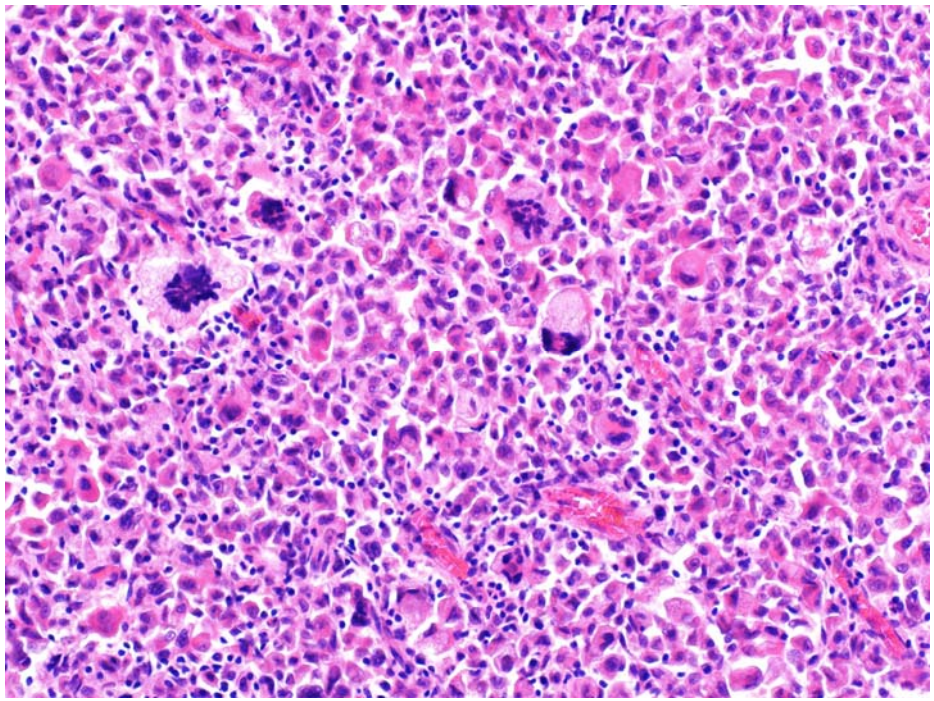


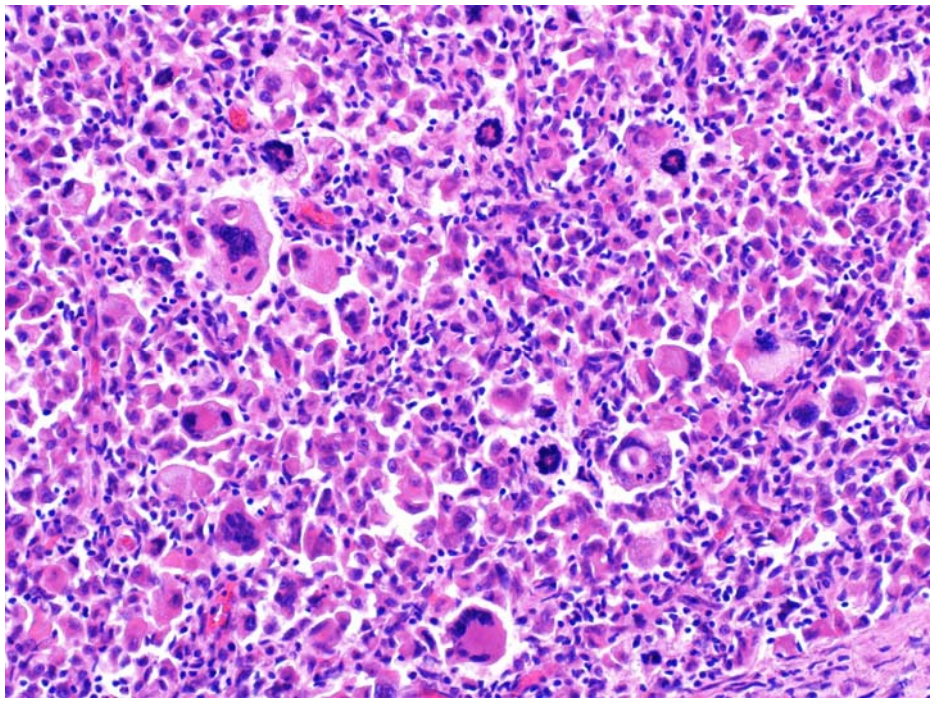


Necrosis

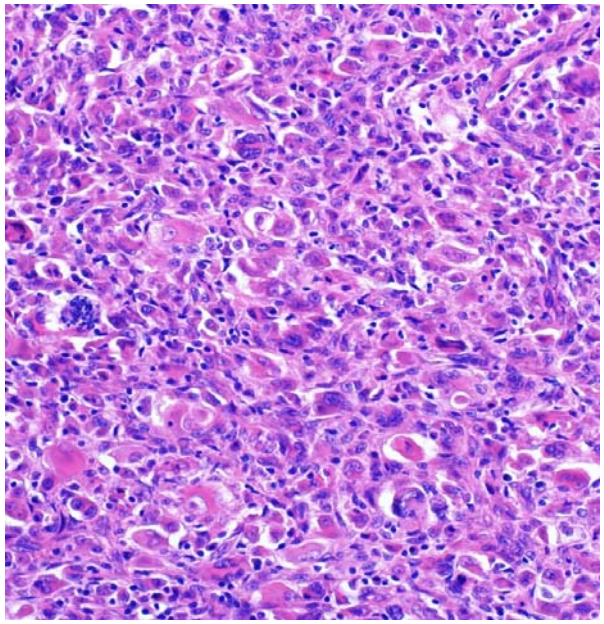
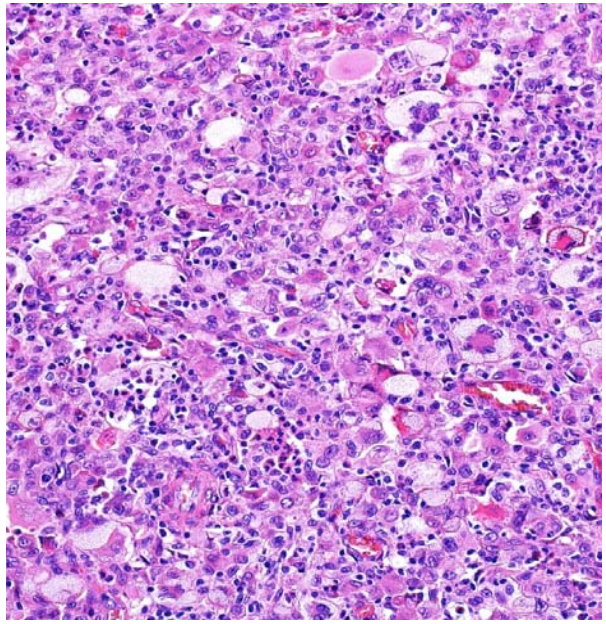
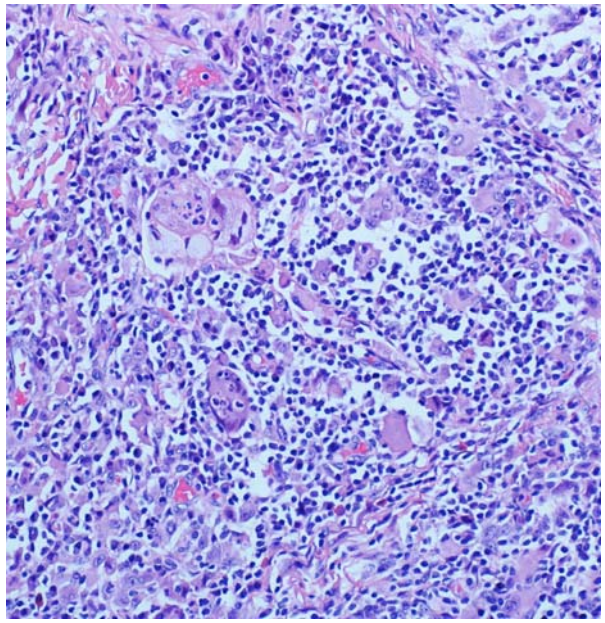
Apoptosis



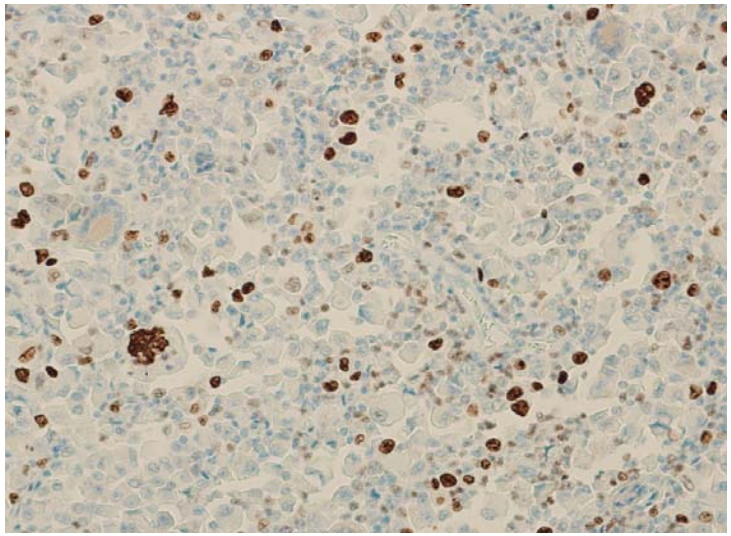


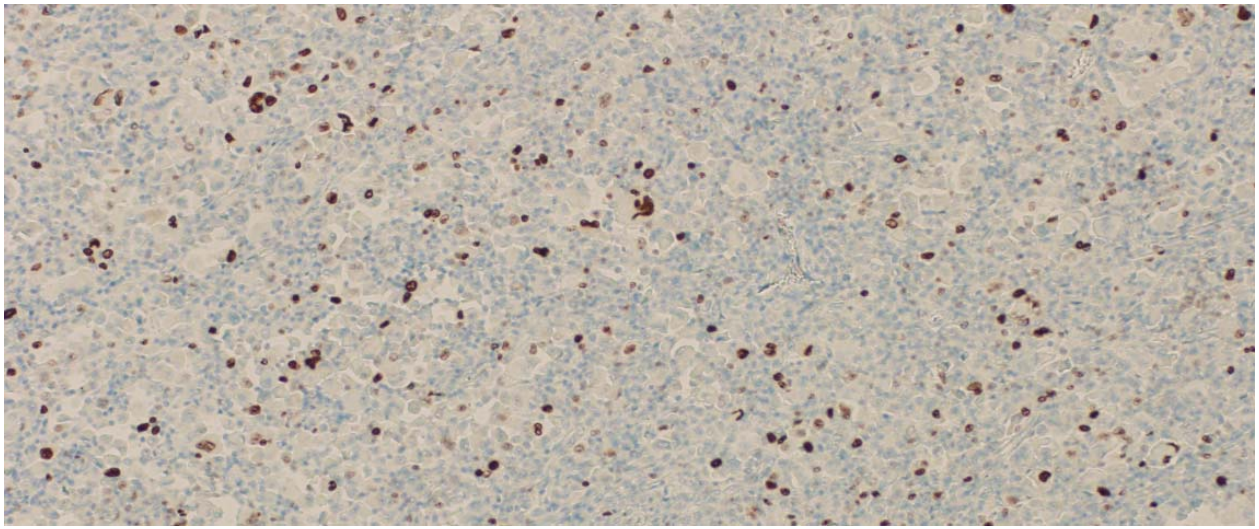


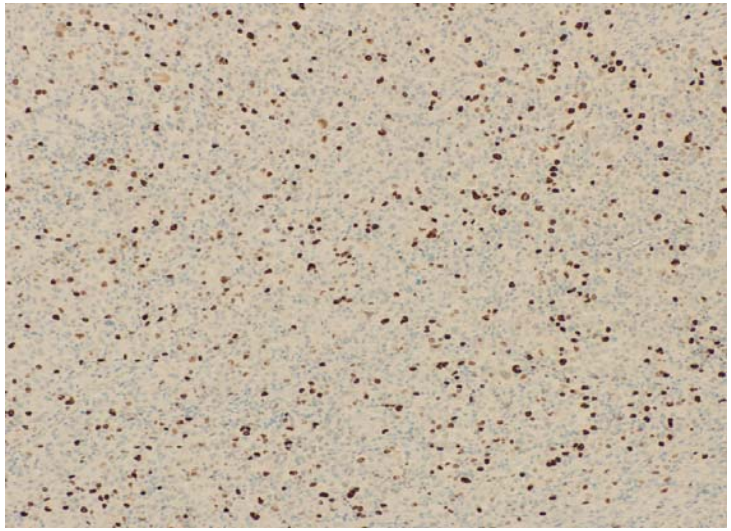
Severe cytological Atypia

Severe Emperipolesis (Phagocytosis)







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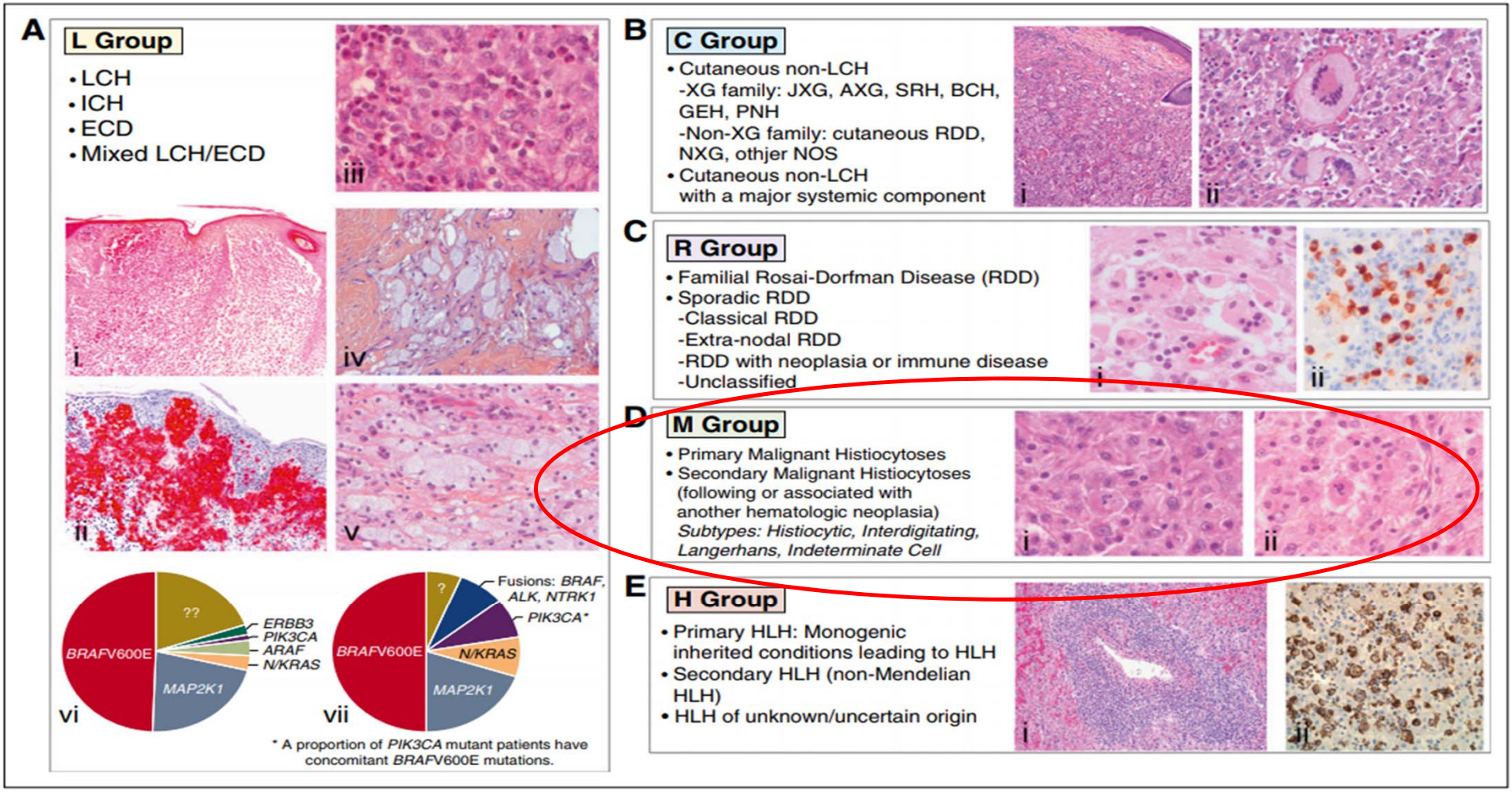

Figure 1. Histology and somatic mutations of histiocytoses of group L, C, R, M, and H. (A) L group: Histology of LCH (skin [i-ii] and bone [iii]) and of ECD (perirenal [iv-v]). Pie chart of relative frequencies of activating kinase mutations in LCH (vi) and ECD (vii). (B) C group: Histology of JXG (i-ii). (C) R group: Histology of RDD (meningeal with high IgG4^{+} plasma cell infiltration [i-ii]). (D) M group: Histology of MH (i-ii). (E) H group: Histology of inherited HLH (liver [i-ii]). Staining with CD1a (Lii in red), IgG4 (Rii in brown), CD163 (Hii in brown), or hematoxylin and eosin (all others). NOS, not otherwise specified.

Malignant Histiocytic Neoplasms
Histiocytic Sarcoma

Molecular Studies

No genetic mutations in BRAF V 600 E and NRAS genes

Post-Operative

- Radiotherapy 3 weeks post surgery
- Back to walking in three months
- Back to full functional activities
- Surveillance: **No any local or systemic recurrence of the disease for 3 years post diagnosis**

Histiocytic Sarcoma

- Rare hematopoietic neoplasm (non-Langerhans histiocytic cells of the monocyte/macrophage system)
- Less than1% of all malignancies of the hematopoietic system.
- Sporadic illness (Primary HS)
- A separate synchronous or metachronous hematologic malignancy (Secondary HS) (18%)
- Mean age of 46 years(6months-75 years) with slight male predilection (2.6/1).
- Secondary HS share the same clonal IGH / light chain rearrangements and chromosomal translocations of the primary tumor
- Some cases are associated with BRAF V600E mutations.

- HS occurs in lymph nodes (27%) , or more commonly extranodal (55%)
- Unifocal or systemic (18%) (Malignant histiocytosis) .
- Metastatic at presentation (60%) (stage III-IV)
- Aggressive (50%progressive disease and die, 30% relapse after CR, 20% alive in CR)
- HS is managed using different types of treatment including surgery, radiotherapy, chemotherapy and combinations depending on the stage of the disease.

Pathological Findings

- Malignant proliferation of cells showing morphological and immunophenotypic features of mature tissue histiocytes.
- **Diagnosis can be challenging owing to unclear distinction between neoplastic and non-neoplastic proliferation of histiocytes (atypia, necrosis, atypical mitoses)**
- Expression of at least two histiocytic markers (CD163, CD68 , S-100 protein (patchy), CD4 and lysozyme)
- Negativity for Keratins, EMA, Melan-A, HMB-45, B and T lymphocyte markers, and follicular DC markers

Histiocytic Sarcoma of Appendicular Bones

- Extremely rare

- Most reported cases are secondary following other hematological malignancies (secondary HS)

To the best of our knowledge, this case is:

- First case of primary appendicular bone histiocytic sarcoma (fibula) in humans
- Presented in a child who was only treated by surgical excision and radiotherapy
- Excellent disease-free follow-up for three years

Dilemma of the case

Does this lesion represent a primary bone Juvenile Xanthogranuloma with malignant transformation ?

OR

Primary Histiocytic Sarcoma with Juvenile Xanthogranuloma like-changes ?

Thank You