A Rare Case of EBV-Positive Nodal T- and NK-cell Lymphoma; A Distinct Clinicopathological WHO-5 Entity

Conor Browne, Haematology Registrar, St Vincent's University Hospital.

Michael Craughwell, Histopathology Senior House Officer, St Vincent's University Hospital.

December 2021

- 40 year old male presented with a 6 week history of:
  - Fevers
  - weight loss
  - cervical with axillary lymphadenopathy
- PMHx:
  - prior spontaneous pneumothorax
  - non-smoker

- Bloods:
  - Hb 11.8, WCC 4.7, lymph 1.3, Plt 283
  - Transaminitis
  - LDH >1,000
  - EBV IgG (VCA + EBNA) positive, EBV VCA IgM negative
  - EBV-DNA titre >54,000 copies/ml

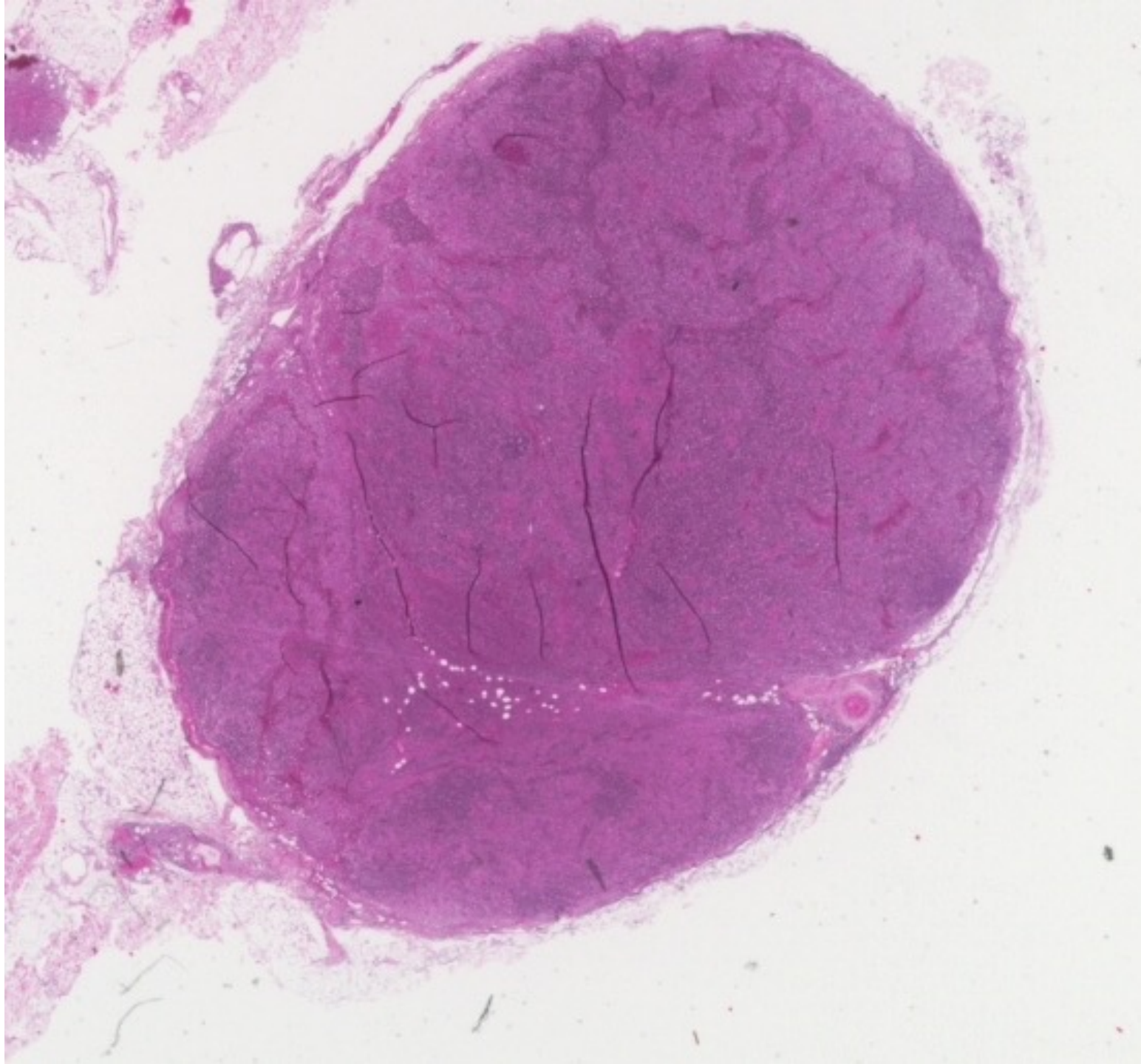
December 2021

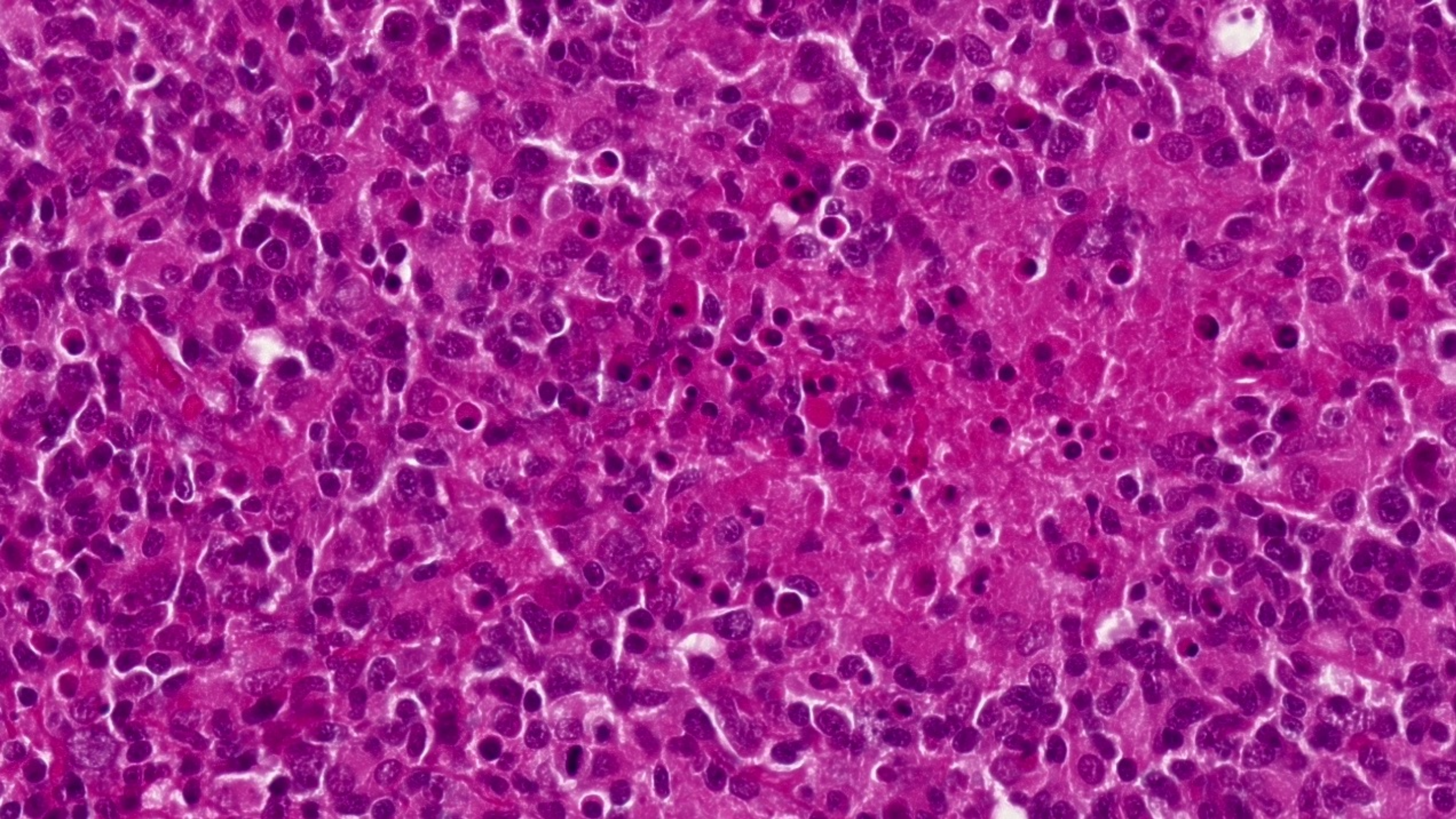
- 40 year old male presented with a 6 week history of:
  - Fevers
  - weight loss
  - cervical with axillary lymphadenopathy
- PMHx:
  - prior spontaneous pneumothorax
  - non-smoker

- Bloods:
  - Hb 11.8, WCC 4.7, lymph 1.3, Plt 283
  - Transaminitis
  - LDH >1,000
  - EBV IgG (VCA + EBNA) positive, EBV VCA IgM negative
  - EBV-DNA titre >54,000 copies/ml

- CT: lymphadenopathy involving the cervical, axillary, mediastinal, abdominal and retroperitoneal regions.

Cervical Excisional Nodal Biopsy





Cervical nodal excisional biopsy

- Paracortical expansion: CD45, CD3, CD8, CD4 positive (CD8 > CD4)
- High Ki-67
- Strongly EBV-ISH positive
- Residual background lymphoid follicles CD20, PAX5 positive
- AFB and PAS negative for organisms

Cervical nodal excisional biopsy

Paracortical expansion: CD45, CD3, CD8, CD4 positive (CD8 > CD4)

High Ki-67

Strongly EBV-ISH positive

Residual background lymphoid follicles CD20, PAX5 positive

AFB and PAS negative for organisms

Conclusion

- Acute lymphadenitis with features suggestive of EBV infection
- No evidence of lymphoma.

January 2022

EBV-DNA titre >4,000,000 copies/ml

HLH:

Persistent fevers

Ferritin >1,000

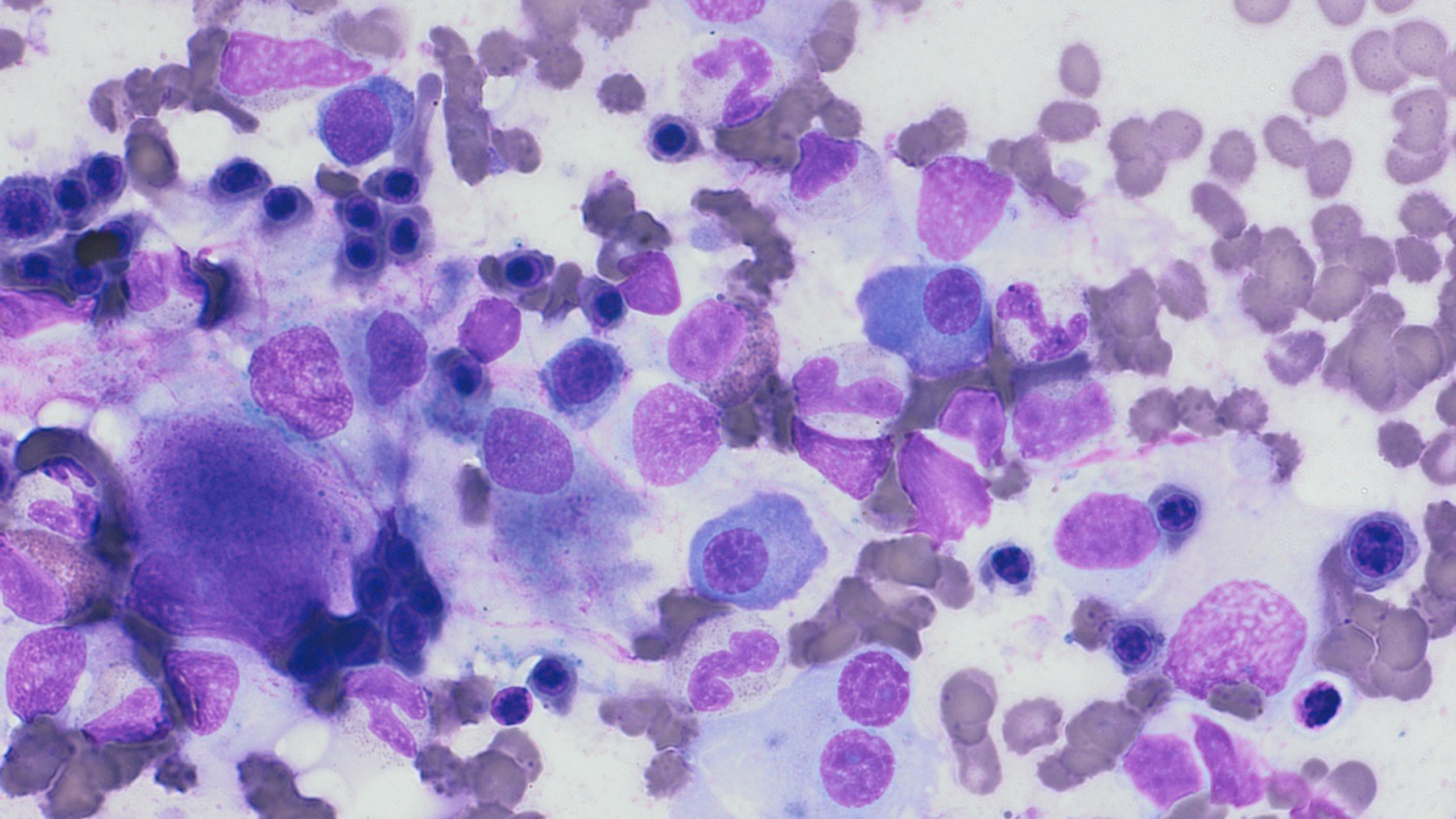
Reduced NK cell subsets

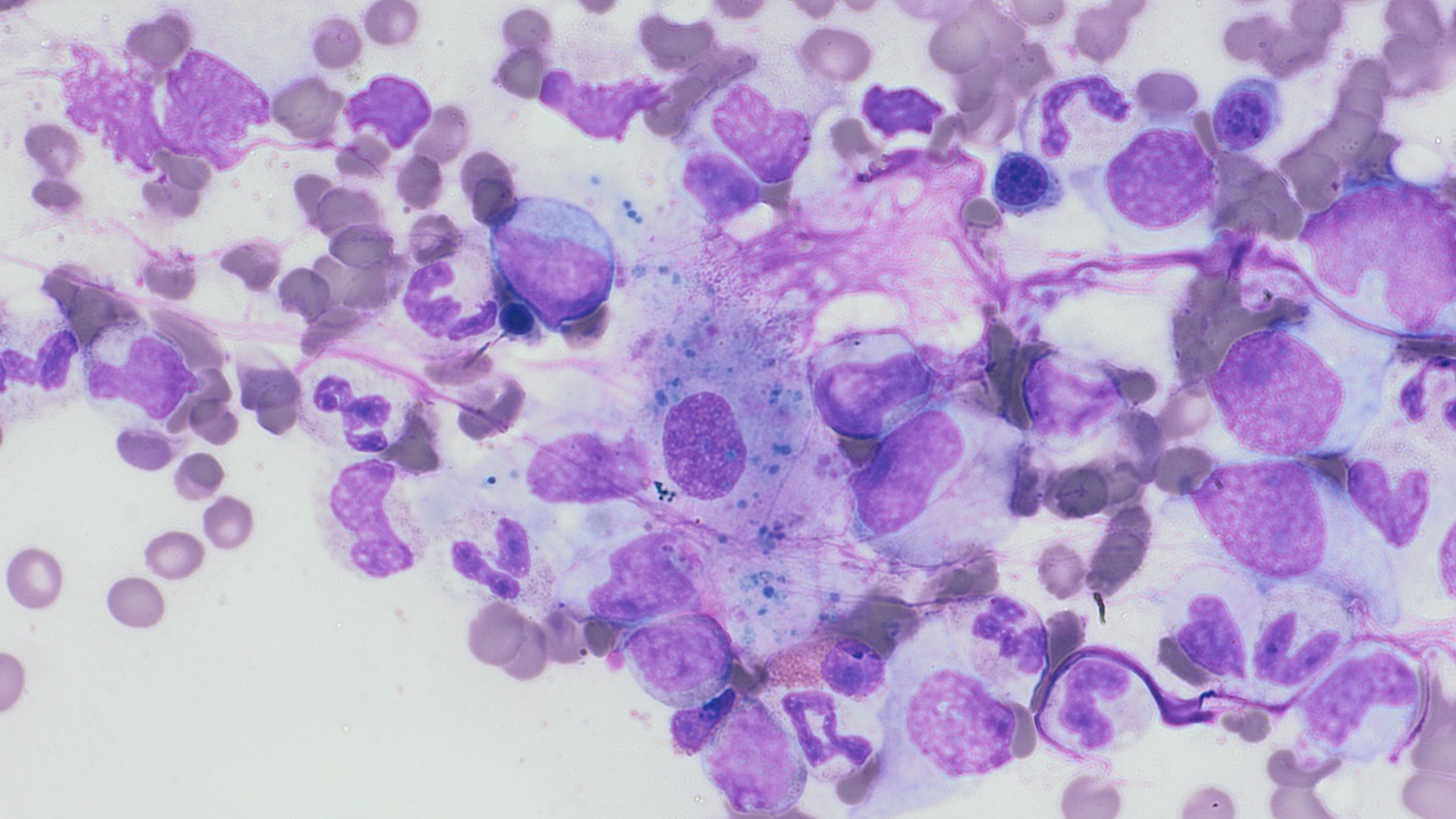
Transaminitis (ALT 377, AST 307)

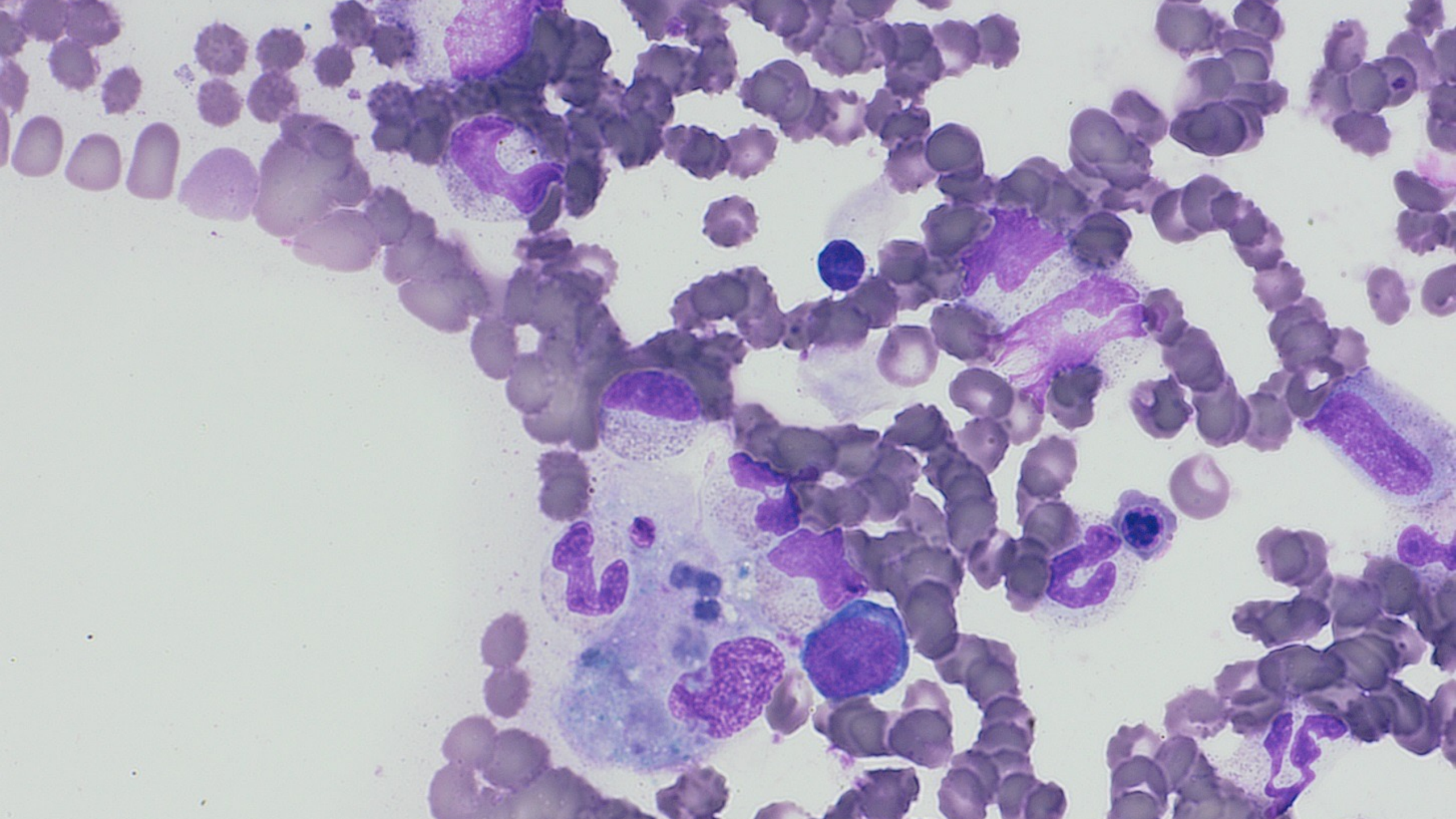
Splenomegaly

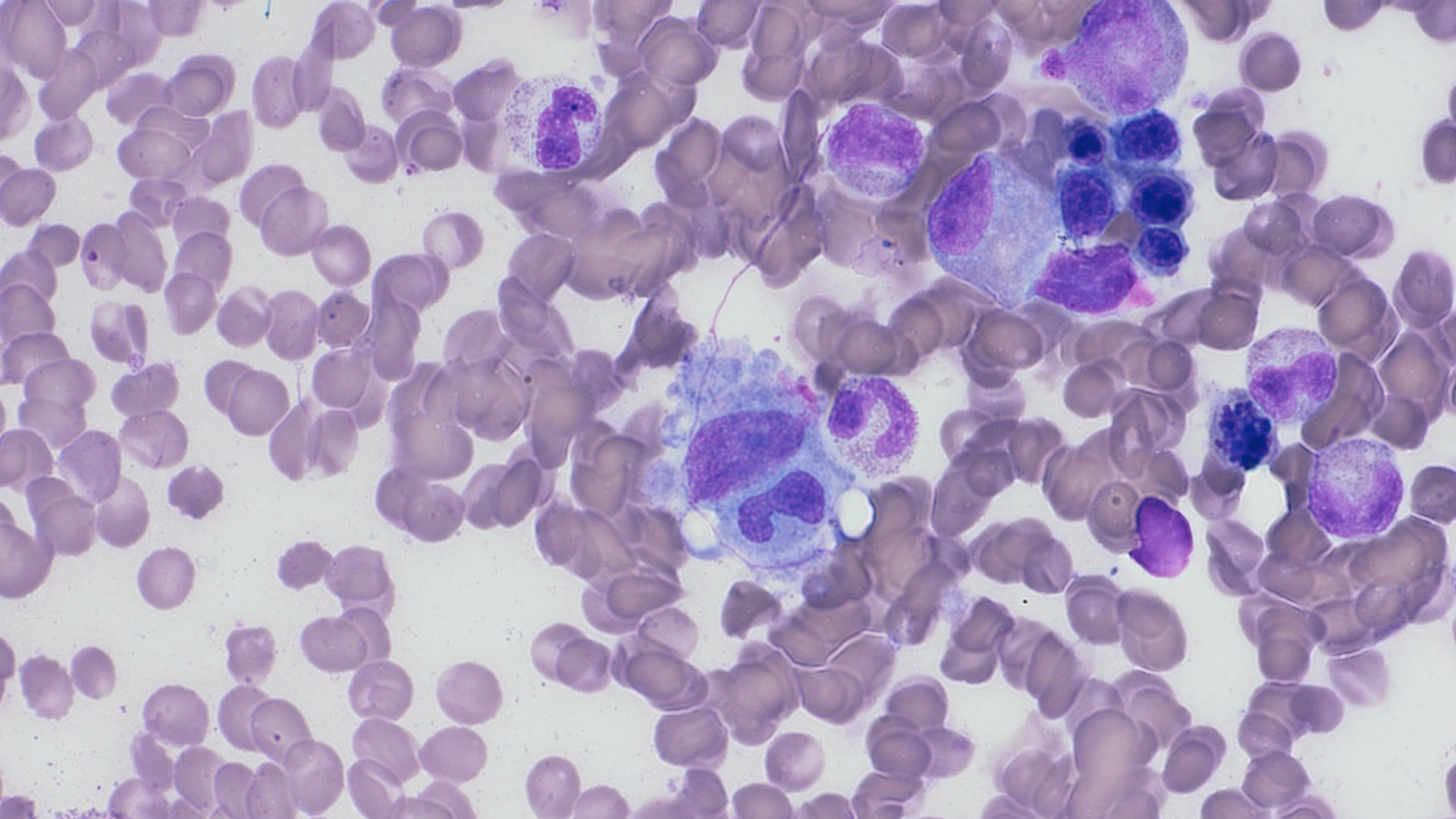
CT: progressive lymphadenopathy and widespread pulmonary nodules.

Worsening respiratory failure requiring intubation.

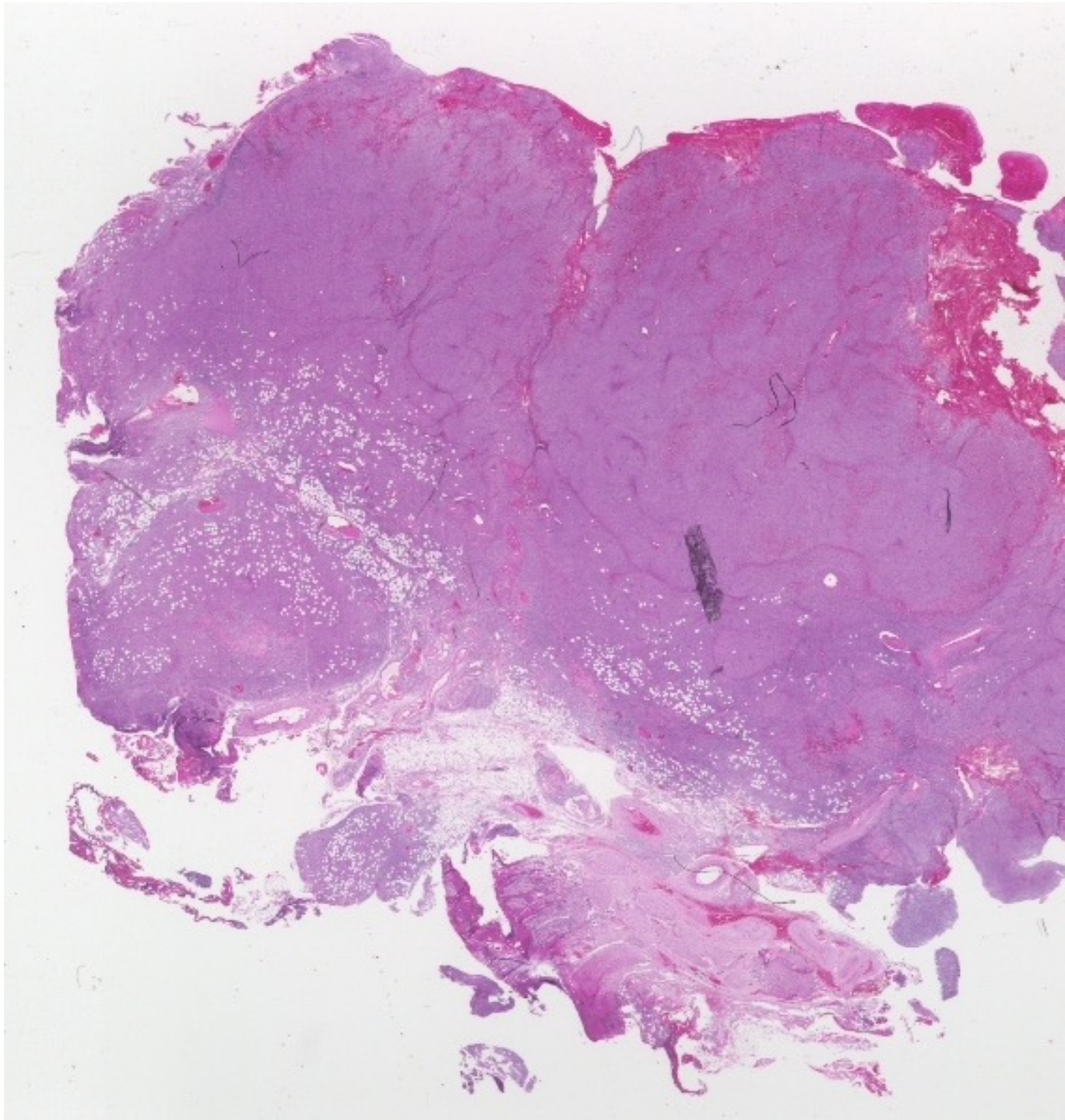


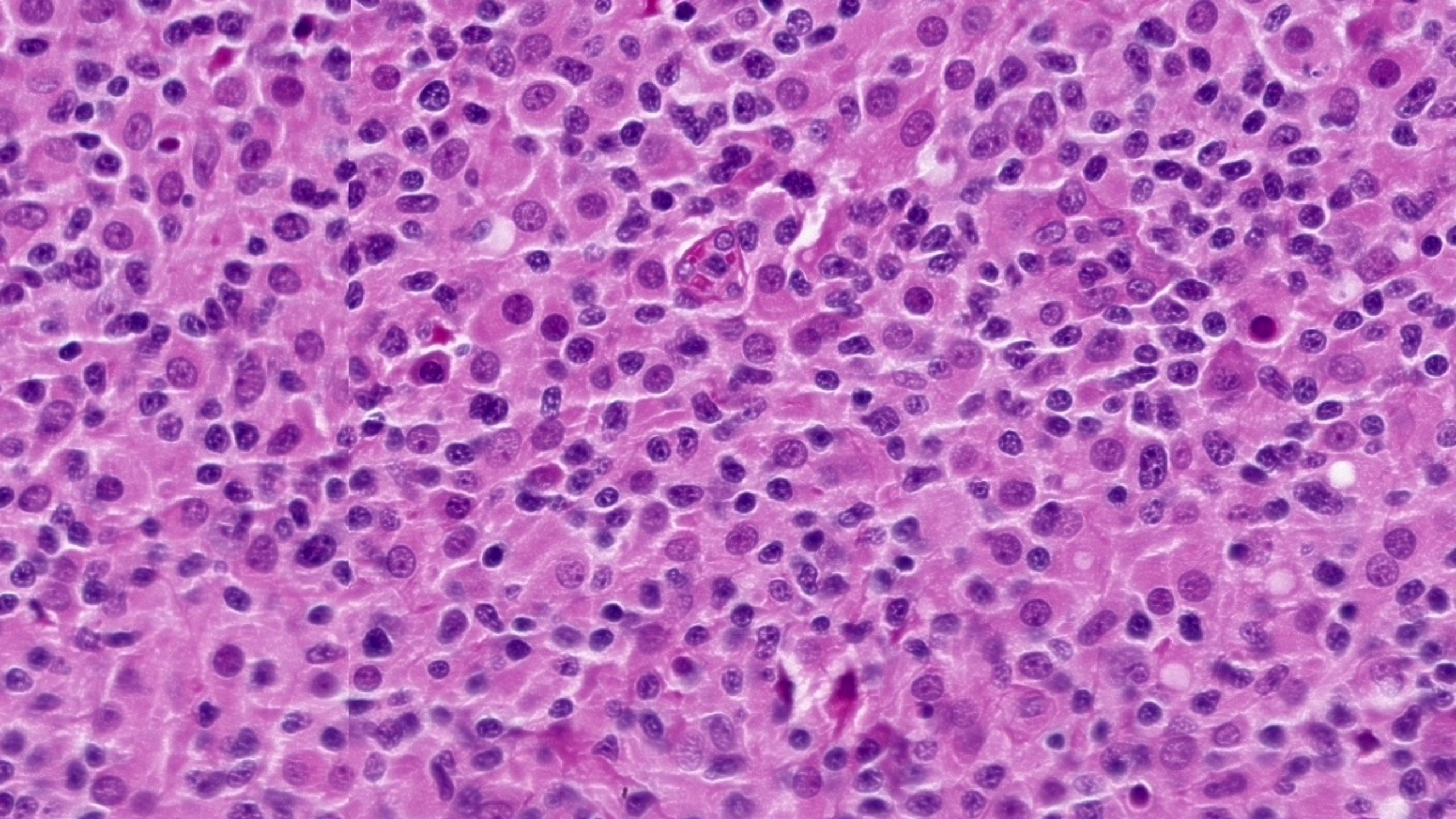


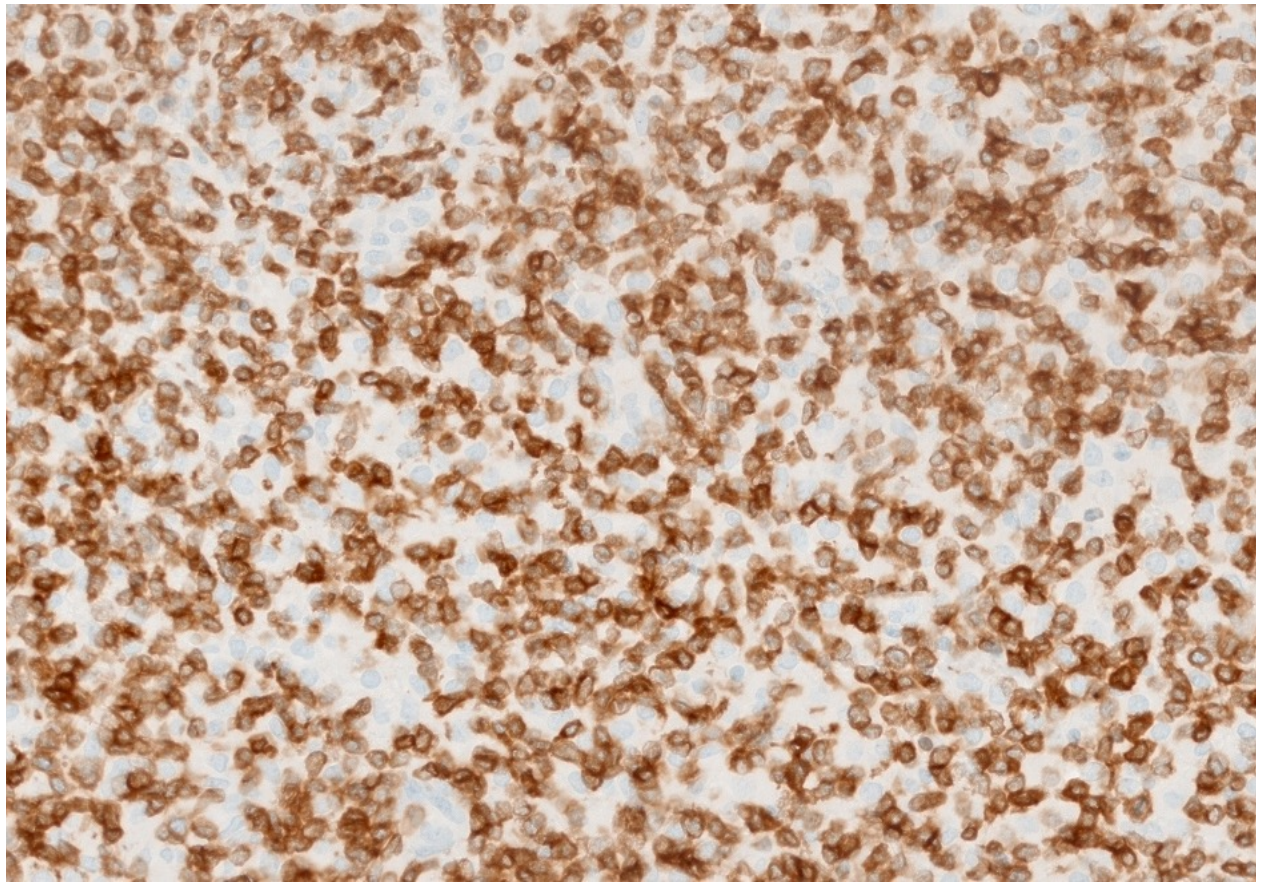




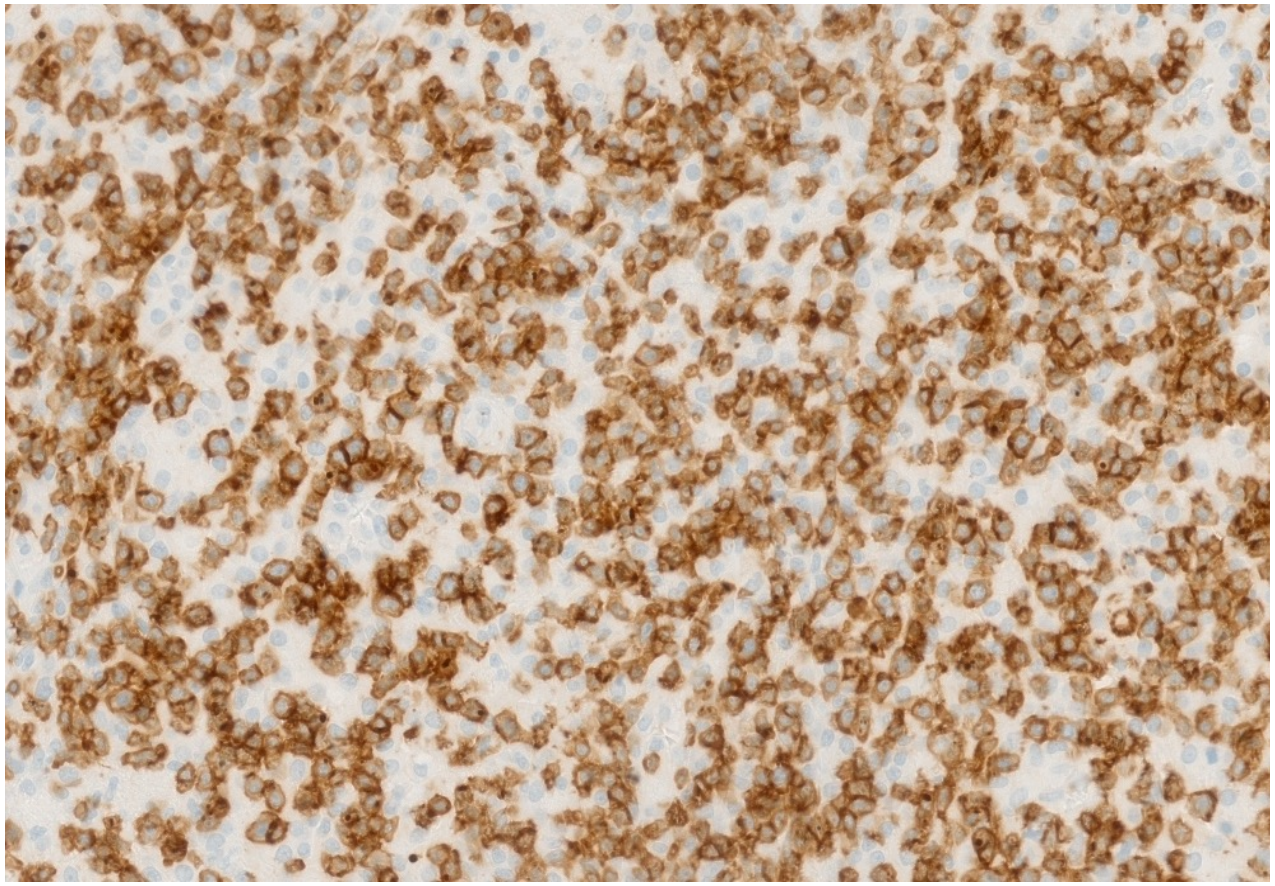
Axillary Excisional Nodal Biopsy





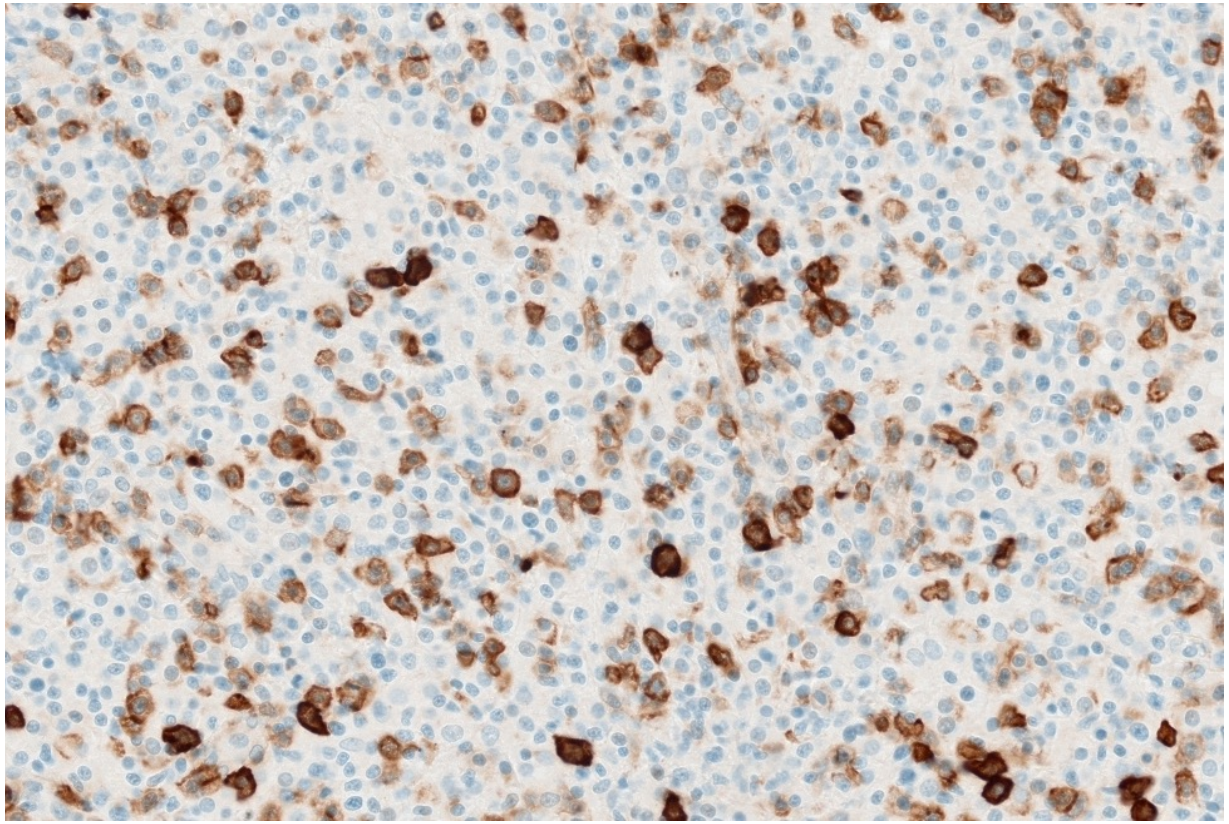


CD3

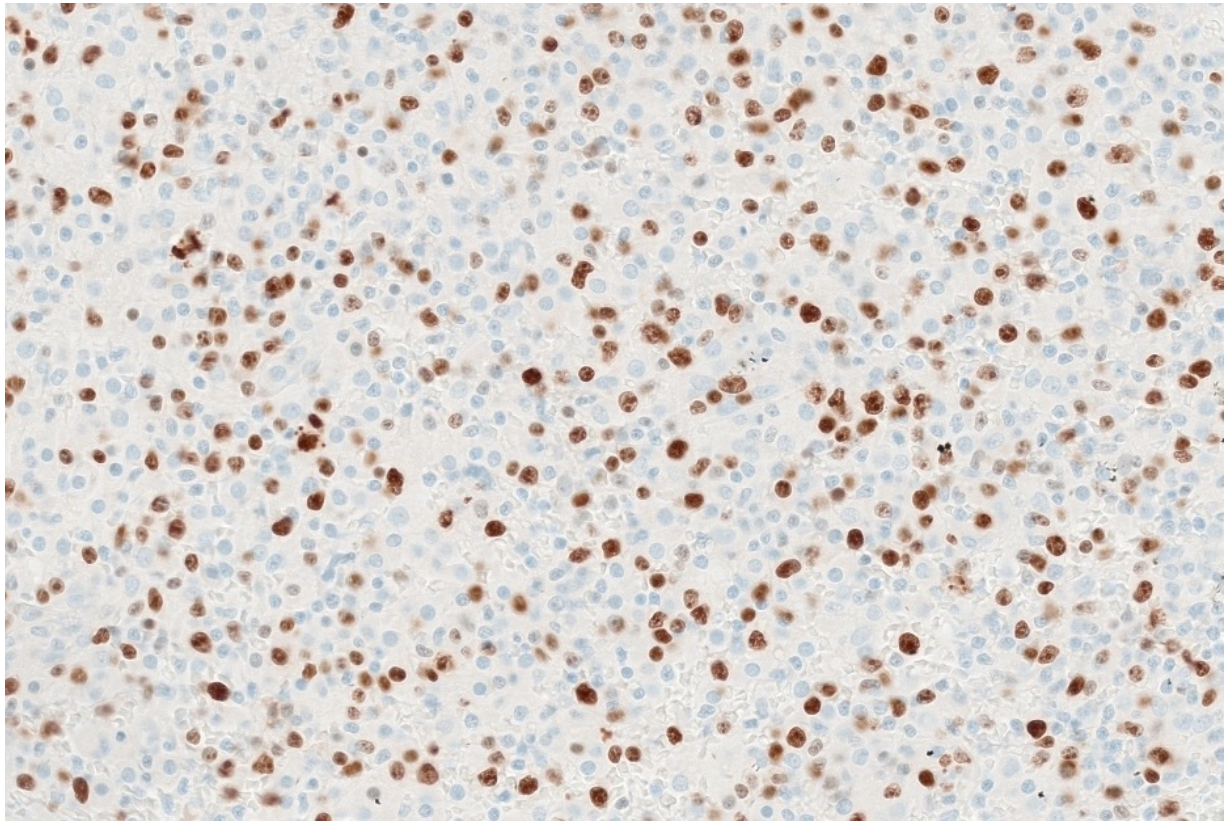


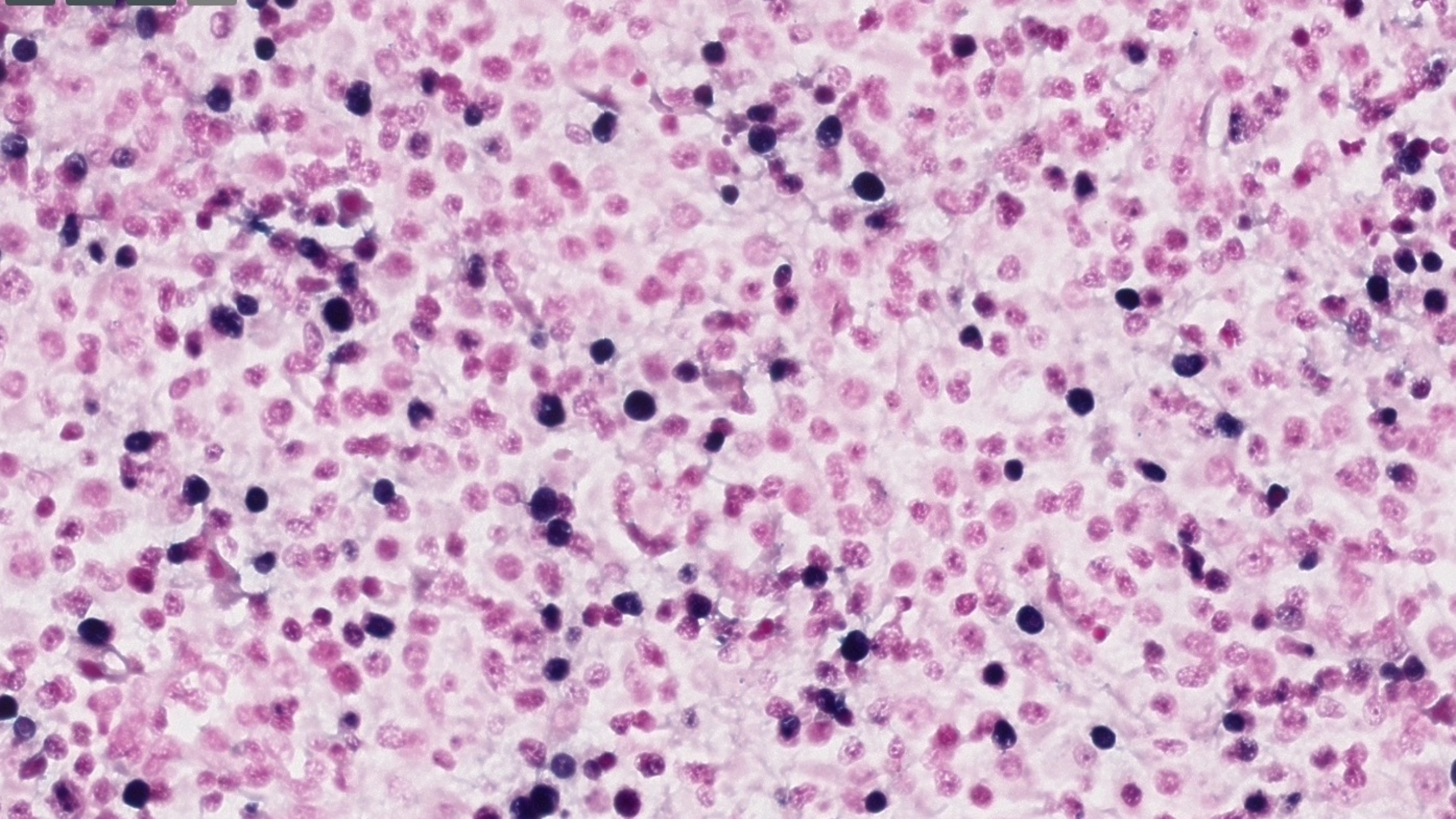
CD8

CD56



Ki-67: 70%





Histopathology

BMAT: no evidence of lymphoma morphologically or via flow cytometry.

Peripheral T-Cell Lymphoma NOS, Stage IV, diagnosed as per WHO-4 criteria.

Re-evaluation of the prior biopsy confirmed EBV lymphadenitis without evidence of lymphoma.

Management

CHOEP x6

PET-CT: CMR (Deauville 2)

Management

CHOEP x6

PET-CT: CMR (Deauville 2)

BEAM autologous SCT June 2022

Day 100 PET-CT CMR.

July 2023

Fevers, night sweats, weight loss

abdominal discomfort

EBV-DNA titre >4,000,000 copies/ml.

H-Score 243 (>99% probability HLH)

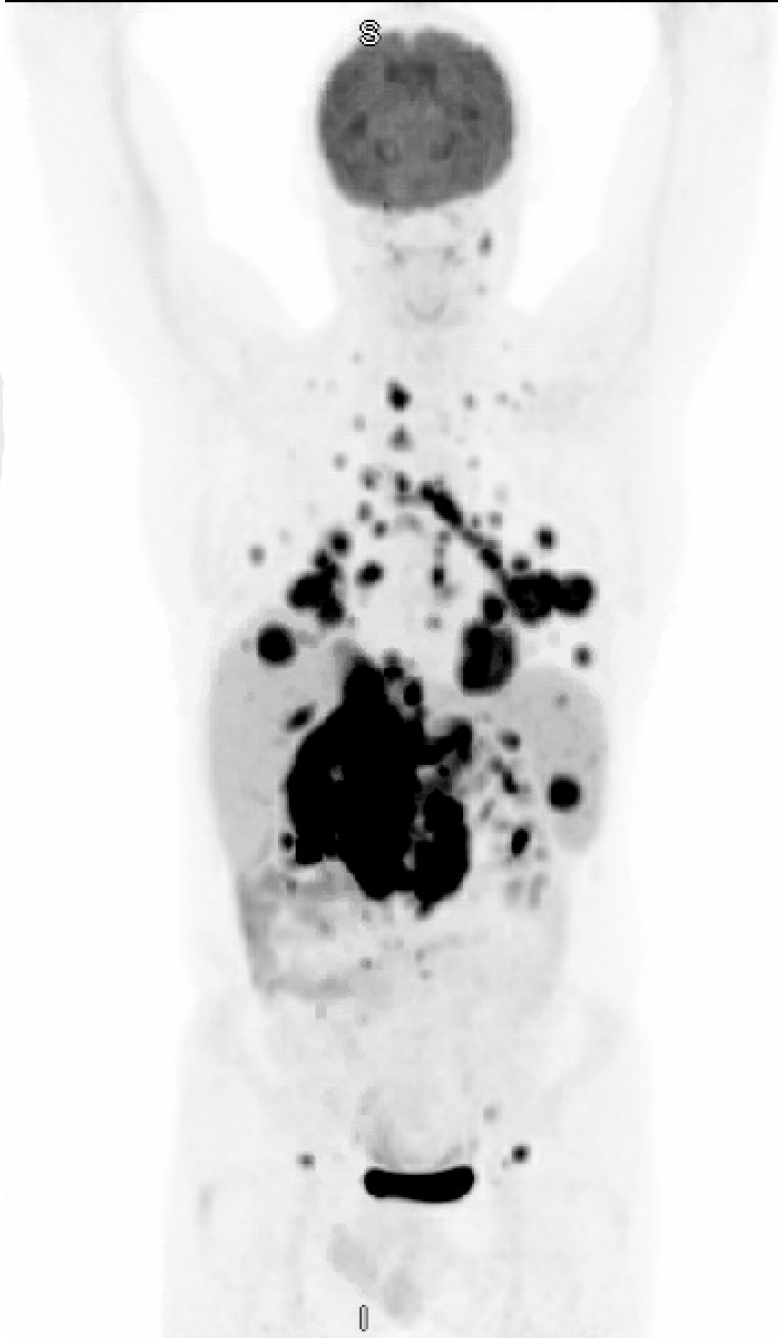
July 2023

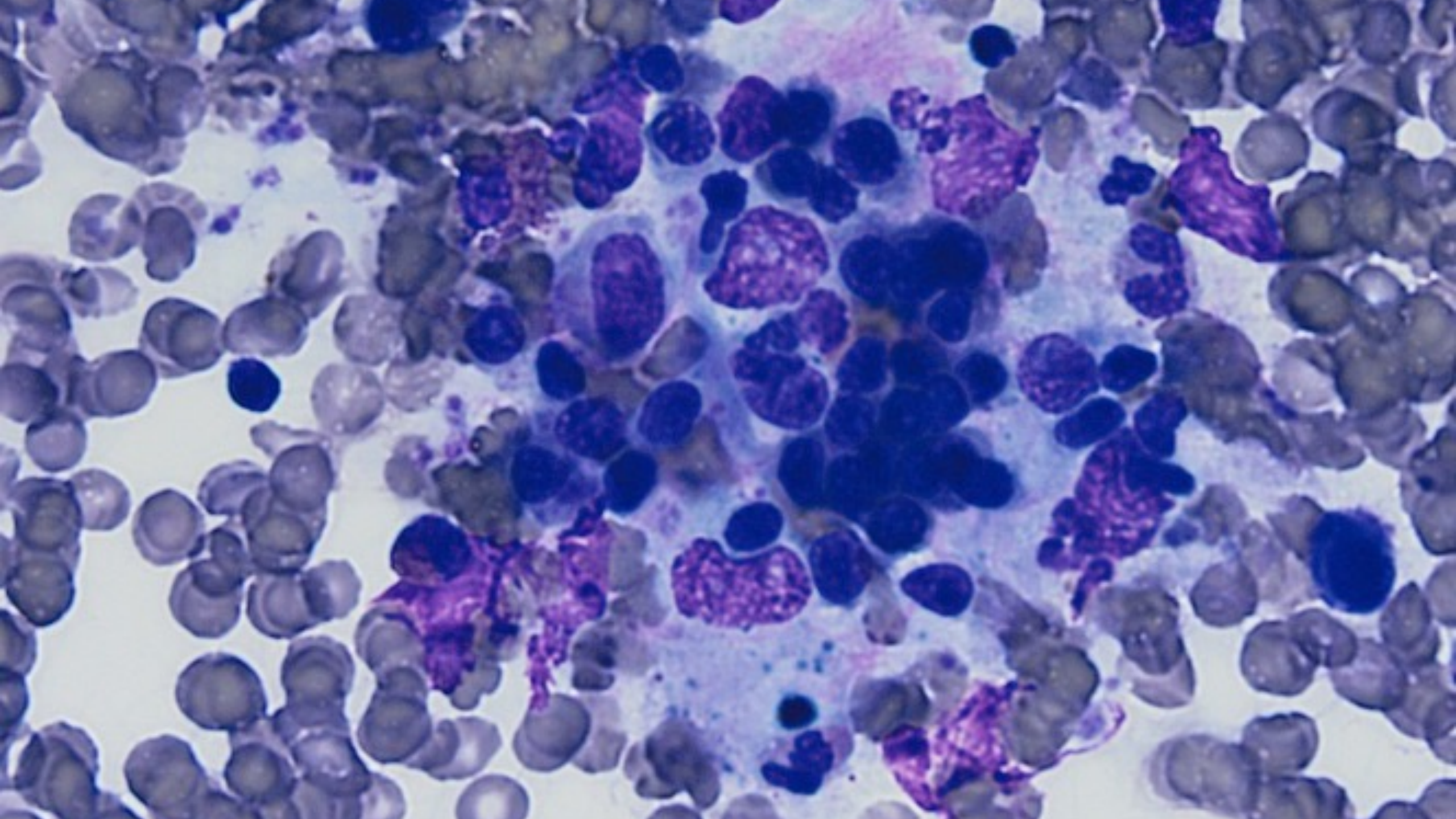
Fevers, night sweats, weight loss

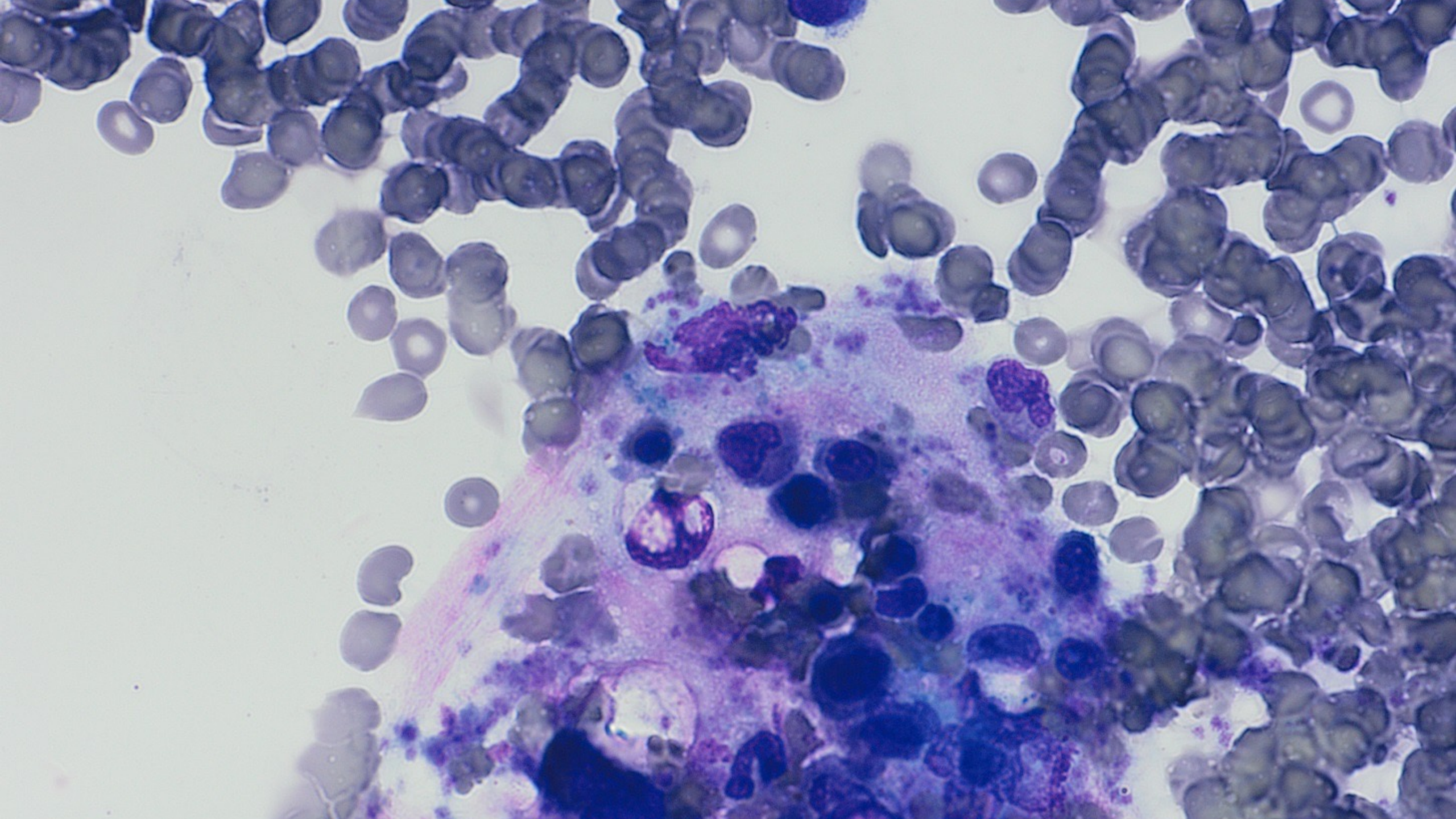
abdominal discomfort

EBV-DNA titre >4,000,000 copies/ml.

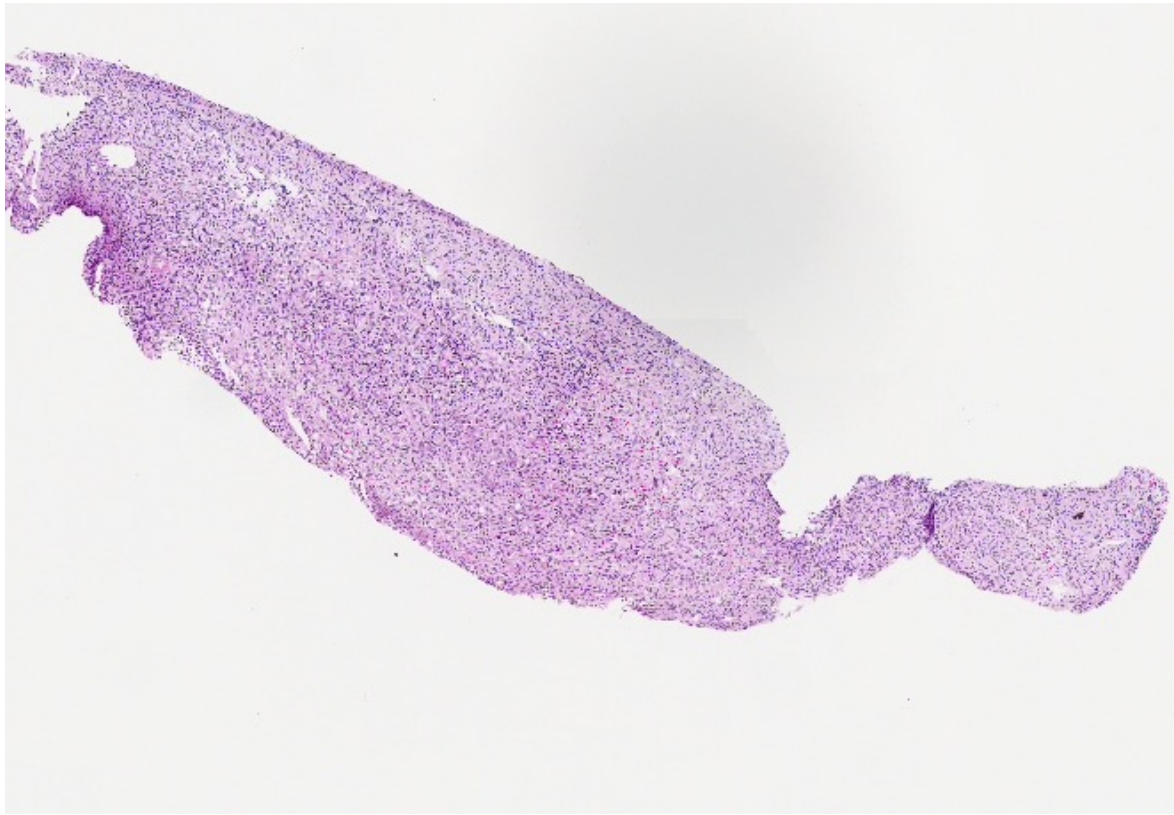
H-Score 243 (>99% probability HLH)

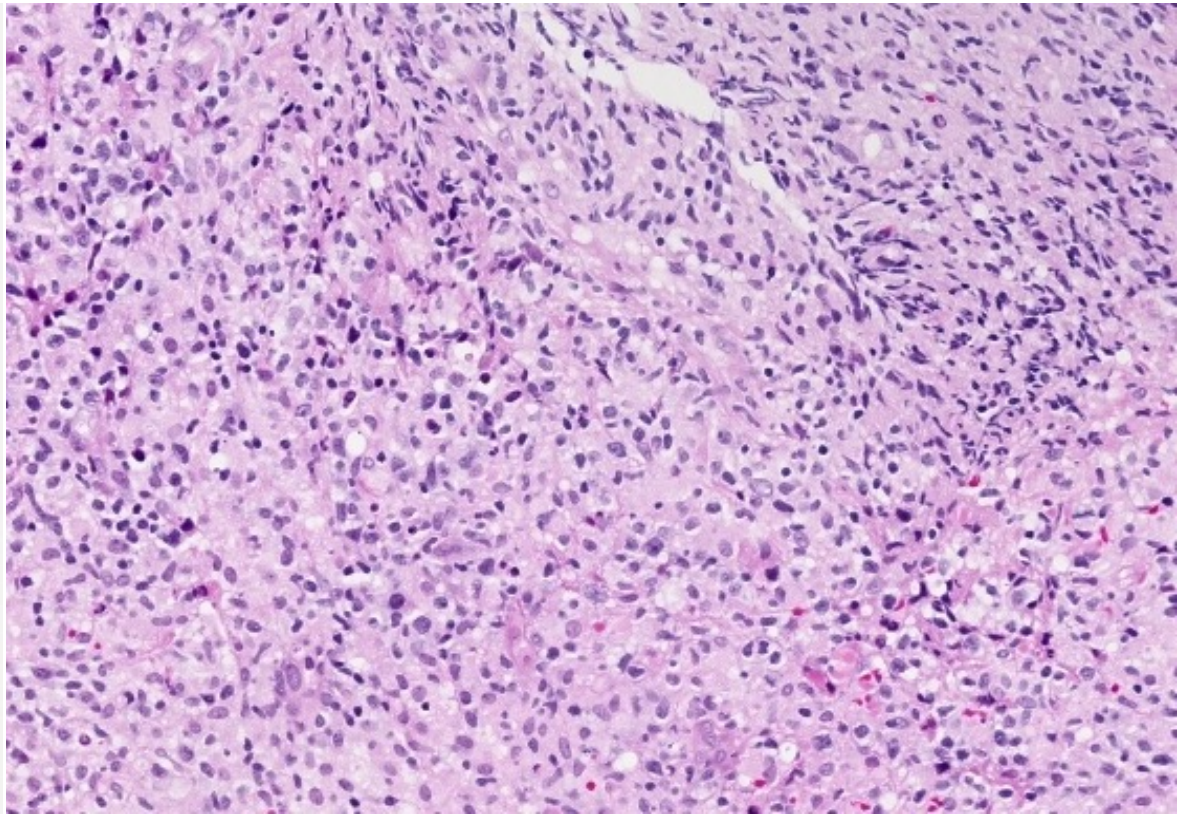






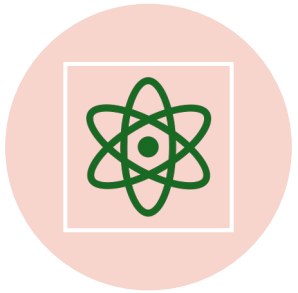
Left Inguinal Core Nodal Biopsy





A WHO-5 Entity

Diagnostic material from both presentations externally reviewed.

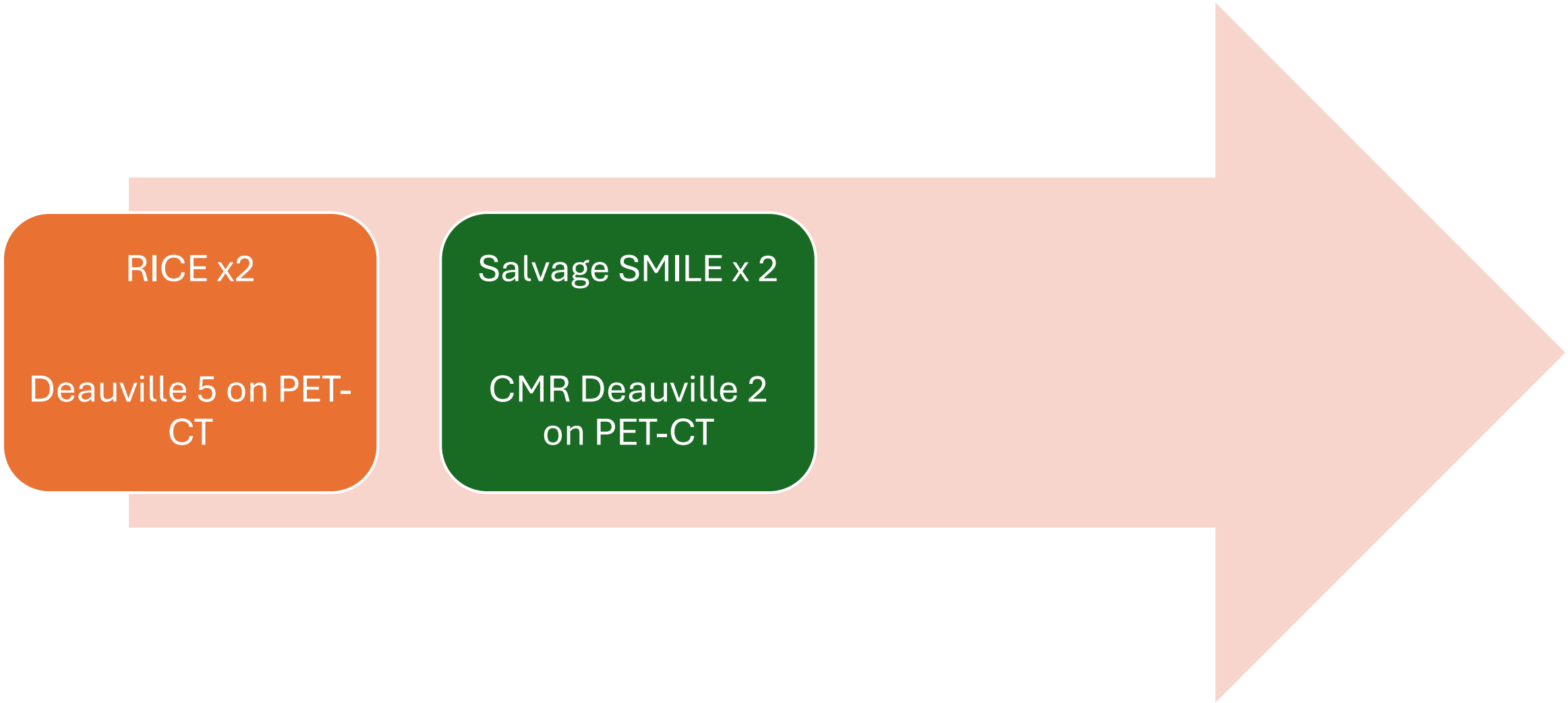


PCR confirmed clonal TCR gamma-chain rearrangements.

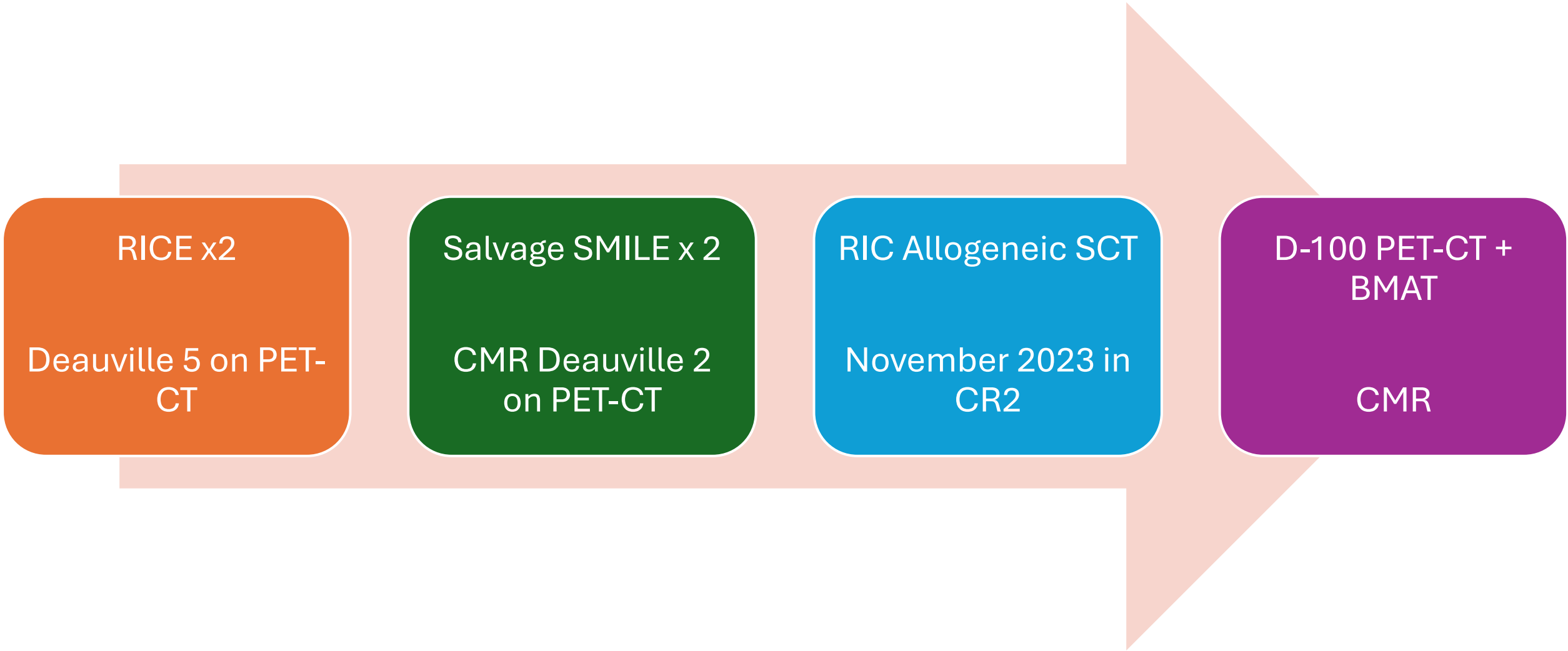
NGS panels showed no pathogenic variants.

Overall features were consistent with a diagnosis of EBV-positive nodal T- and NK-cell lymphoma.

Management


RICE x2
Deauville 5 on PET-CT
Salvage SMILE x 2
CMR Deauville 2 on PET-CT

Management


RICE x2
Deauville 5 on PET-CT
Salvage SMILE x 2
CMR Deauville 2 on PET-CT
RIC Allogeneic SCT
November 2023 in CR2
D-100 PET-CT + BMAT
CMR

April 2024

- Rising EBV titre to 7300 copies/ml

April 2024

- Rising EBV titre to 7300 copies/ml

April 2024

- Rising EBV titre to 7300 copies/ml
- Rituximab x4 weekly

April 2024

- Rising EBV titre to 7300 copies/ml
- Rituximab x4 weekly
- BMAT:
  - Minor clonal TCR gene rearrangement detected.
  - Flow revealed very low-level aberrant T/NK CD8, 56+ve.

EBV-Positive Nodal T- and NK-cell Lymphoma

New entity in the WHO-5

Rare with poor prognosis

Distinct clinicopathological features

Role for L-asparaginase based regimens

Acknowledgements

- **Dr Liam Smyth**
- **Dr Lindsey Clarke**

- Prof Niall Swan, Prof David Gibbons
- Dr Maryse Power

- Dr Richard Flavin, Dr Robert Henderson.

- Dr Elaine Jaffe M.D.

- Any Questions?

ST. VINCENT'S UNIVERSITY HOSPITAL
Elm Park

OSPIDÉAL SAN SÉAMAS
ST JAMES'S HOSPITAL

References

1. Alaggio, R., Amador, C., Anagnostopoulos, I., Attygalle, A. D., Araujo, I. B. de O., Berti, E., Bhagat, G., Borges, A. M., Boyer, D., Calaminici, M., Chadburn, A., Chan, J. K. C., Cheuk, W., Chng, W. J., Choi, J. K., Chuang, S. S., Coupland, S. E., Czader, M., Dave, S. S., … Xiao, W. (2022). The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. In *Leukemia* (Vol. 36, Issue 7, pp. 1720–1748). Springer Nature. https://doi.org/10.1038/s41375-022-01620-2

2. Kato, S., Hamada, M., Okamoto, A., Yamashita, D., Miyoshi, H., Arai, H., Satou, A., Gion, Y., Sato, Y., Tsuyuki, Y., Miyata-Takata, T., Takata, K., Asano, N., Takahashi, E., Ohshima, K., Tomita, A., Hosoda, W., Nakamura, S., & Okuno, Y. (2024). EBV+ nodal T/NK-cell lymphoma associated with clonal hematopoiesis and structural variations of the viral genome. *Blood Advances*, *8*(9), 2138–2147. https://doi.org/10.1182/bloodadvances.2023012019

3. Wai, C. M. M., Chen, S., Phyu, T., Fan, S., Leong, S. M., Zheng, W., Low, L. C. Y., Choo, S. N., Lee, C. K., Chung, T. H., Ban, K. H. K., Ghosh, S., Lie, S., Kato, S., Nakamura, S., Takahashi, E., Ko, Y. H., Khoury, J. D., Chuang, S. S., … Ng, S. B. (2022). Immune pathway upregulation and lower genomic instability distinguish EBV-positive nodal T/NK-cell lymphoma from ENKTL and PTCL-NOS. *Haematologica*, *107*(8), 1864–1879. https://doi.org/10.3324/haematol.2021.280003

Post Transplant Course