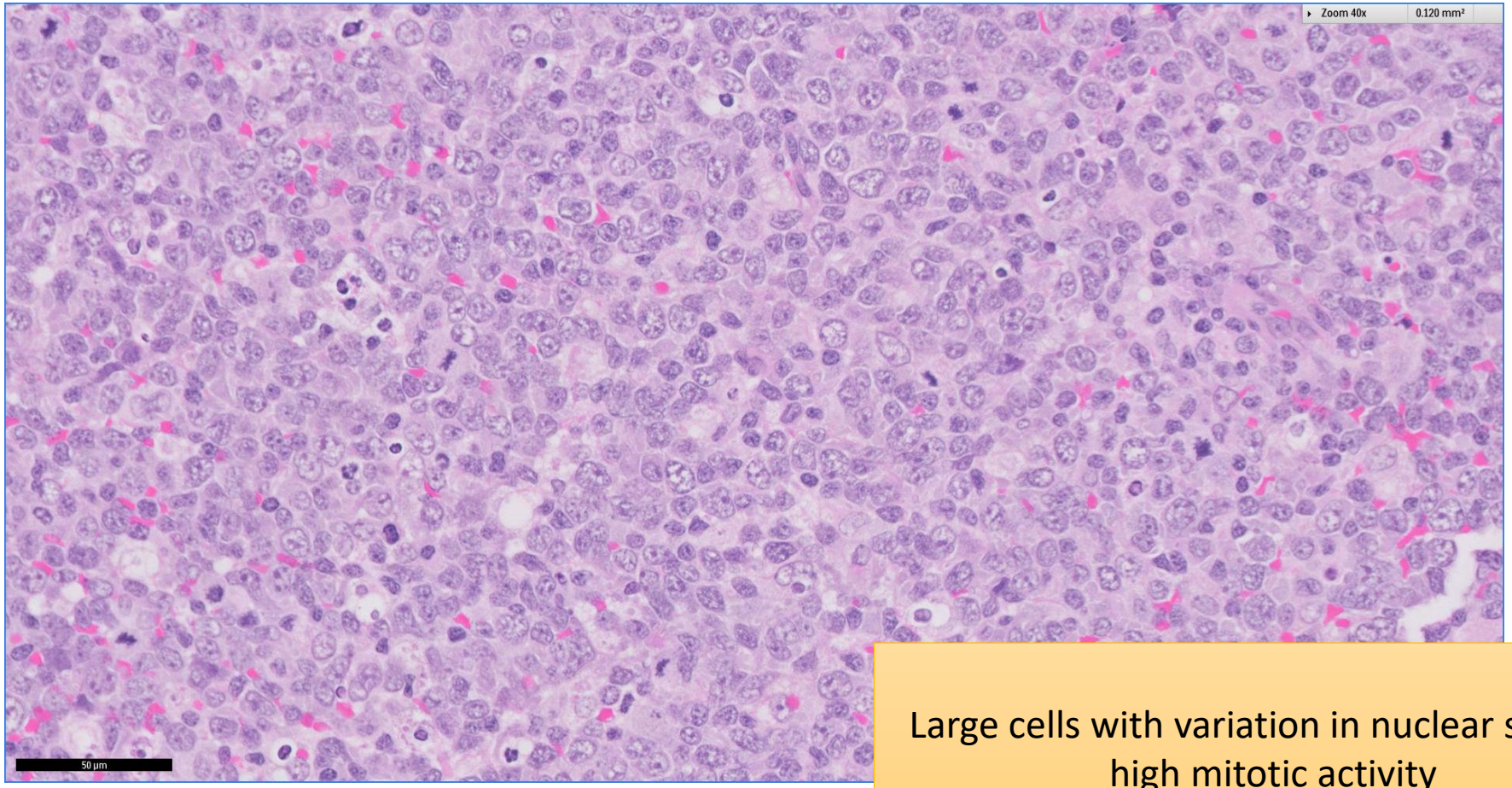
SGH CASE 19: 17RE125

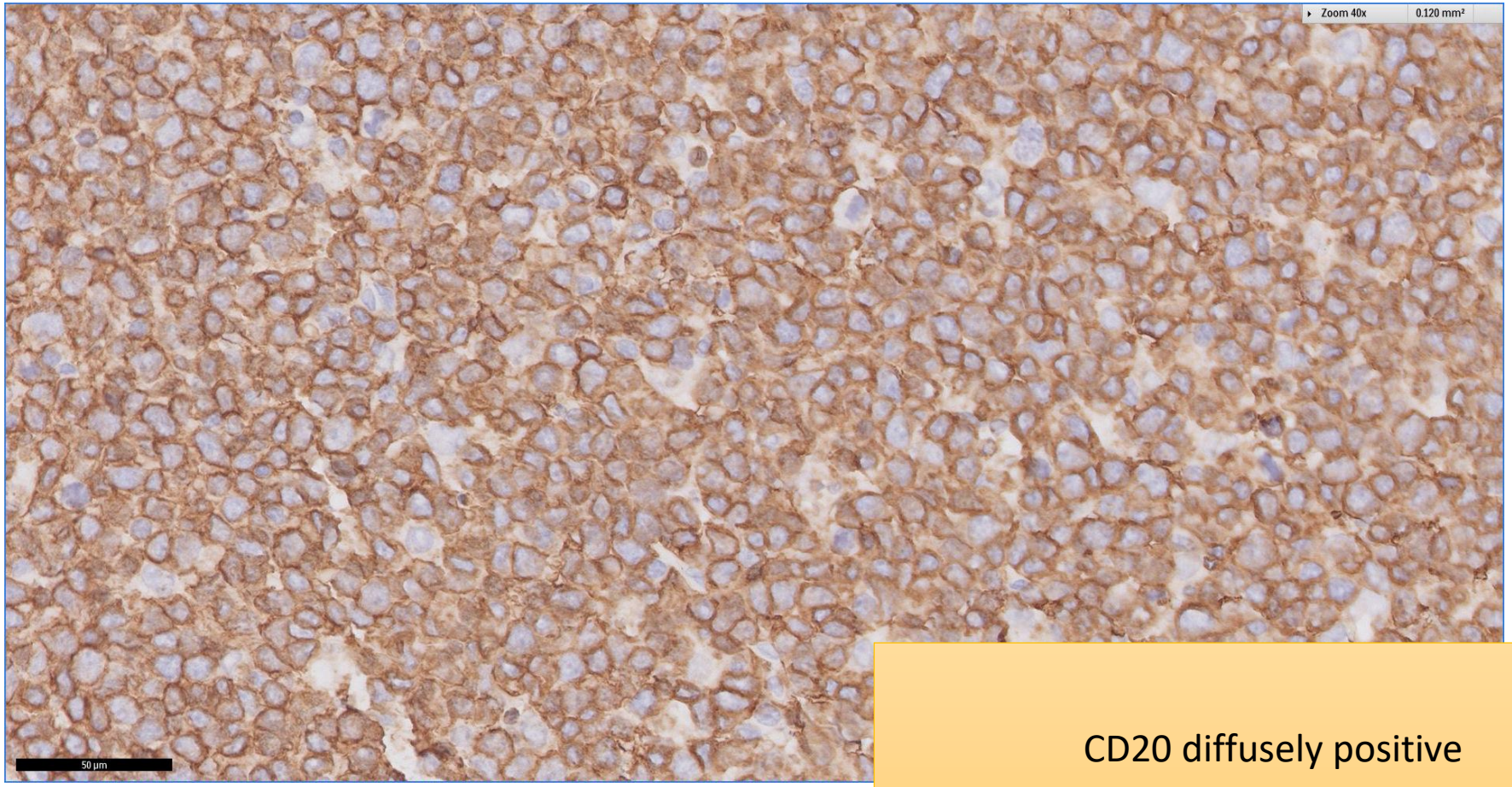
- Clinical History:
  - 40+ years old (late 40s). Female. Presented with cough, night sweats, loss of appetite and loss of weight. CT scan showed large right perirenal soft tissue mass, splenomegaly with multiple splenic infarcts, destructive lesions in right iliac bone and left hemisacrum. Atypical lymphocytes in blood and bone marrow aspirate (both about 20%).
- Specimen:
  - Right cervical lymph node excision biopsy.

SGH CASE 19: 17RE125 H&E



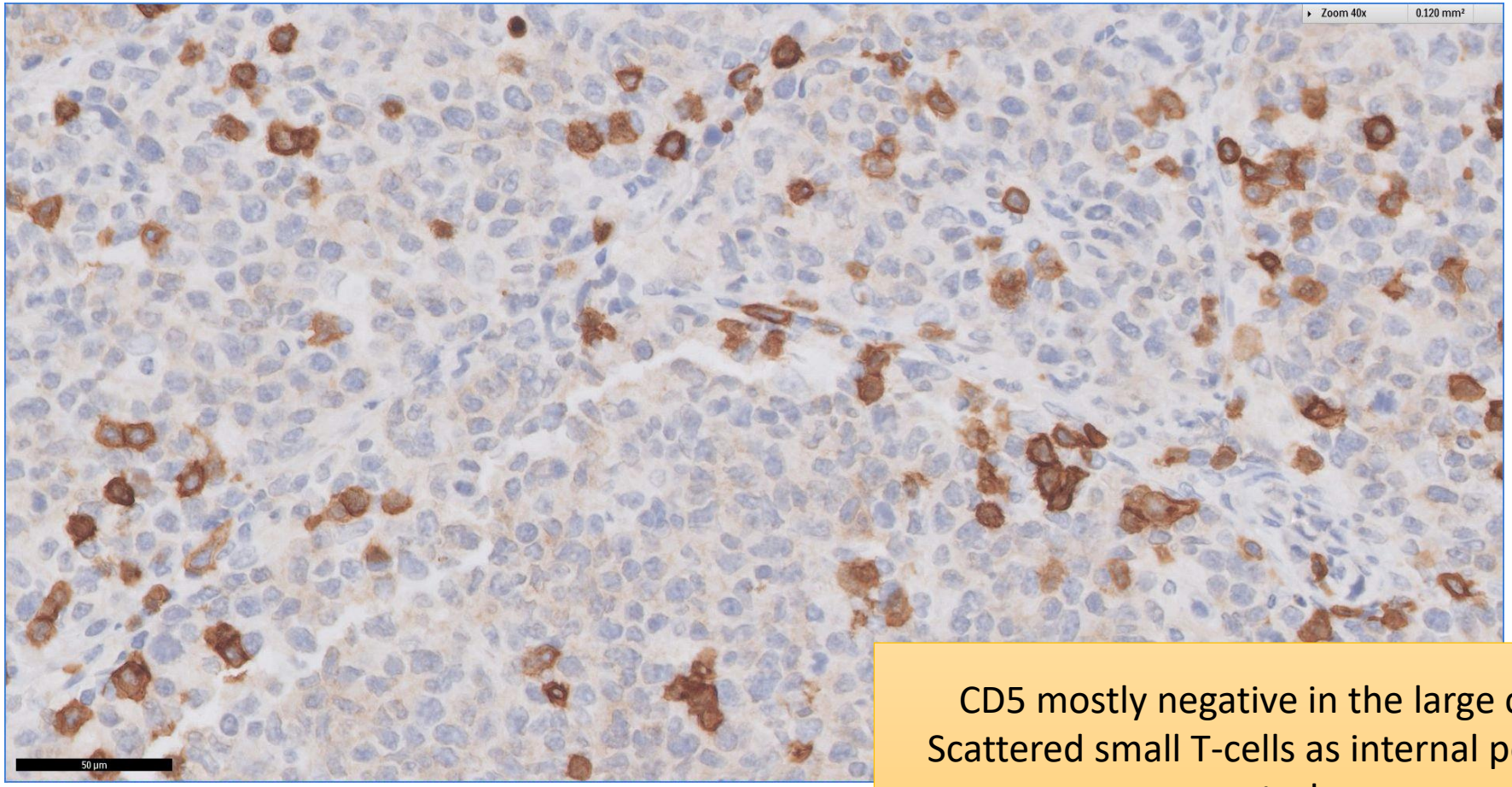
Large cells with variation in nuclear size and high mitotic activity

SGH CASE 19: 17RE125 CD20



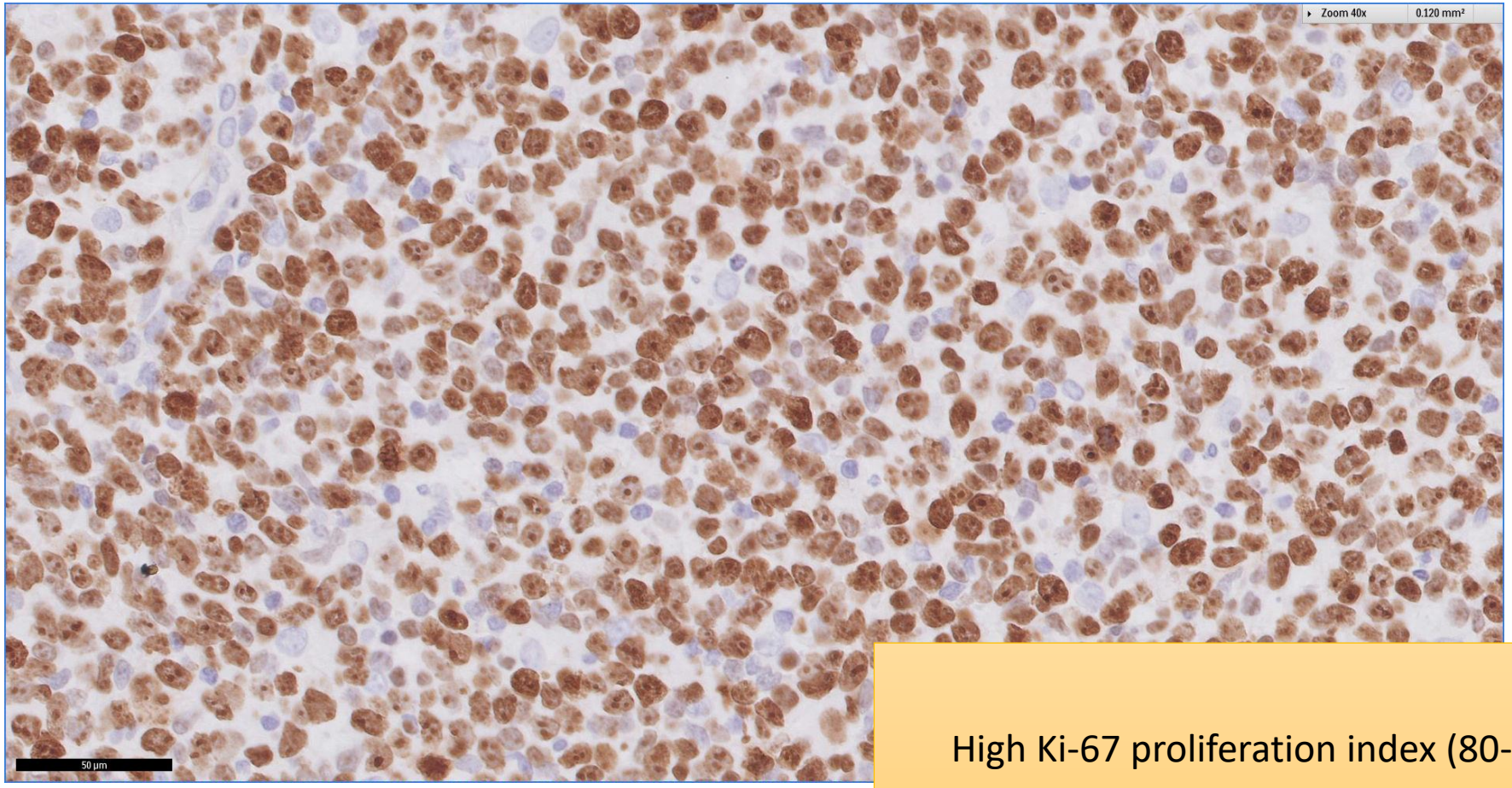
CD20 diffusely positive

SGH CASE 19: 17RE125 CD5



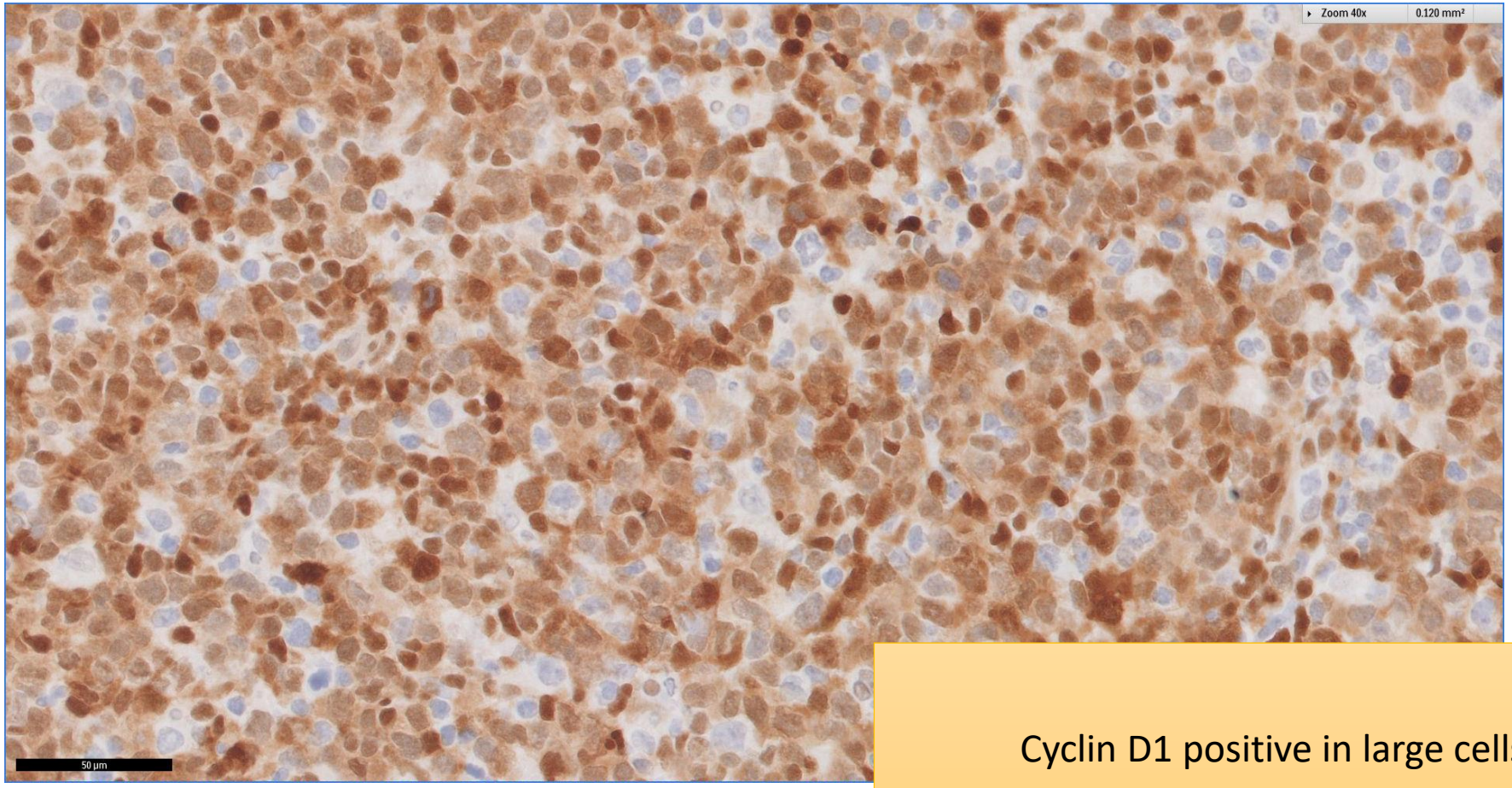
CD5 mostly negative in the large cells.
Scattered small T-cells as internal positive controls.

SGH CASE 19: 17RE125 KI67



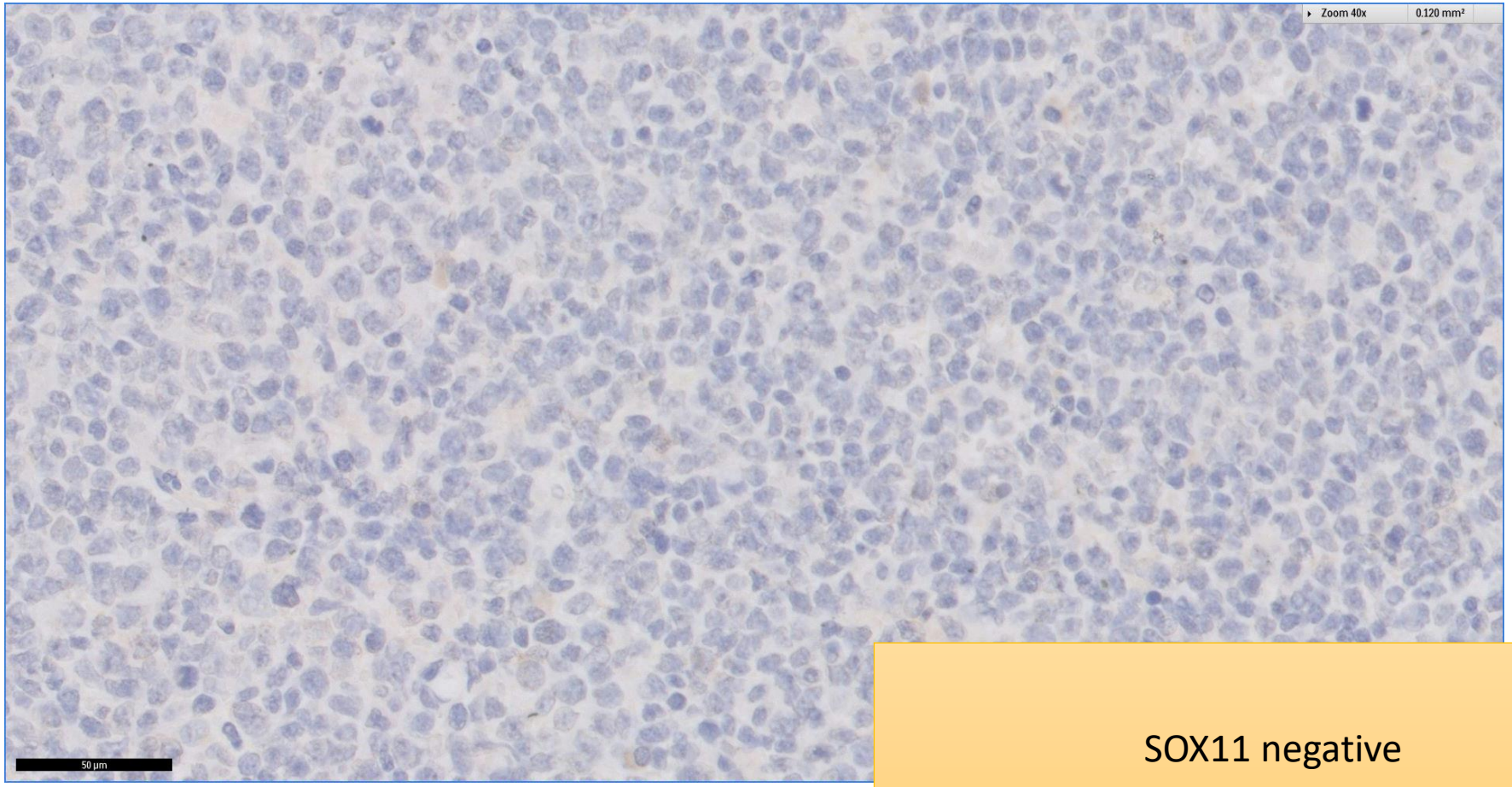
High Ki-67 proliferation index (80-90%)

SGH CASE 19: 17RE125 CYCLIN D1



Cyclin D1 positive in large cells

SGH CASE 19: 17RE125 SOX11



SOX11 negative

SGH CASE 19: 17RE125 Discussion (1)

- Apart from perirenal soft tissue mass, lymphadenopathy is not a significant feature; lymph node biopsied is palpable but small (slightly less than 1cm)
- Immunophenotype of lymphomatous large cells
  - CD20 and Cyclin D1 positive
  - SOX11 and CD5 negative
  - Ki-67 80-90%; c-myc 20-30%
  - Bcl-6 and MUM-1 variably positive; CD10 negative
- CCND1(11q13)/IGH(14q23) fusion probes is positive for CCND1/IGH fusion
- Blood and bone marrow involved by lymphomatous cells
  - Flow cytometry in both blood and bone marrow show medium to large atypical lymphoid cells which are CD20+, CD10-, CD5-, TdT-.

SGH CASE 19: 17RE125 Discussion (2)

- Morphological variants of mantle cell lymphoma (MCL)
  - Blastoid: Cells resemble lymphoblasts with high mitotic rate
  - Pleomorphic: Cells are pleomorphic, with large oval to irregular nuclear contours enclosed by pale cytoplasm. Some prominent nucleoli.
  - Small cell: small round lymphocytes with clumped chromatin, resemble CLL/SLL.
  - Marginal zone-like: Foci of cells with abundant pale cytoplasm resembling marginal zone or monocytoid B-cells.
- Key differential for pleomorphic variant MCL is cyclin D1-positive diffuse large B-cell lymphoma (DLBCL).
  - DLBCL: Usually no cyclin D1 rearrangements and cyclin D1 immunohistochemistry is more heterogeneous than MCL; SOX11 usually negative.
  - Rare cases of cyclin D1-positive DLBCL has been described in literature to have cyclin D1 rearrangements (including *IGH–CCND1* translocation). Genetic copy number analysis showed that some of these cases may be a 'grey-zone' lymphoma with features intermediate between DLBCL and MCL. (not a formal WHO entity)

SGH CASE 19: 17RE125 Discussion (3)

- WHO 2017 described a sub-entity of MCL called “Leukaemic non-nodal mantle cell lymphoma”.
  - Usually indolent with peripheral blood, bone marrow and sometimes splenic involvement without significant lymphadenopathy
  - Usually “small cell” morphologically resembling CLL/SLL.
  - Usually SOX11 negative and less CD5 expression; somatic hypermutation present.
  - More genetically stable than conventional MCL.
  - Some cases of this subtype may progress to blastoid or pleomorphic variant.
- Our case do not have a detectable “low grade” component or prior history, so unable to determine if this may represent progression from leukaemic non-nodal subtype of MCL.

SGH CASE 19: 17RE125 Discussion (4)

- For our case:
  - Is this cyclin D1+ DLBCL with cyclin D1 rearrangement or pleomorphic MCL (possible progression or relation to leukaemic non-nodal MCL)?
  - In view of the clinical and haematological picture, as well as strong cyclin D1 expression with classic cyclin D1 gene rearrangement, best classified as “pleomorphic MCL” but acknowledge the unusual SOX11 and CD5 negativity as well as limited experience with such findings.

SGH CASE 19: 17RE125 Discussion (5)

- Final diagnosis:
  - Mantle Cell Lymphoma, Pleomorphic Variant

Reference

- Swerdlow et al. WHO classification of Tumours of Haematopoietic and Lymphoid Tissue. Revised 4th Edition. IARC, Lyon, 2017.
- Chuang WY, Chang H, Chang GJ, Wang TH, Chang YS, Wang TH, Yeh CJ, Ueng SH, Chien HP, Chang CY, Wan YL, Hsueh C. Pleomorphic mantle cell lymphoma morphologically mimicking diffuse large B cell lymphoma: common cyclin D1 negativity and a simple immunohistochemical algorithm to avoid the diagnostic pitfall. Histopathology. 2017 May;70(6):986-999.
- Sander B, Quintanilla-Martinez L, Ott G, Xerri L, Kuzu I, Chan JK, Swerdlow SH, Campo E. Mantle cell lymphoma--a spectrum from indolent to aggressive disease. Virchows Arch. 2016 Mar;468(3):245-57.