Adventist HealthCare

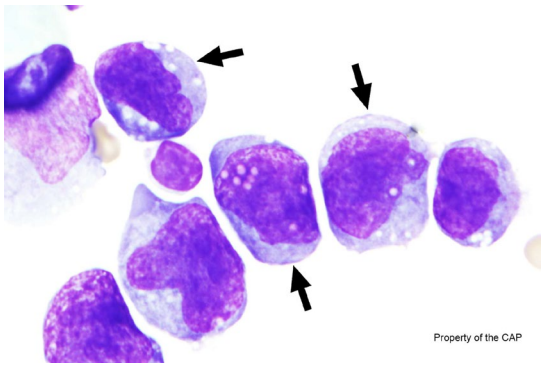
TRAINING UPDATE

Lab Location:	All sites	**Date Distributed:**	4/1/25
Department:	Hematology	**Due Date:**	6/30/25

Reason for MTS:

The arrowed cells were missed at all four sites. They were incorrectly identified by 77.4% of CAP participants as Macrophage/Monocyte, including us. Therefore, the slide was determined a non-consensus and does not count against us. It is however an educational opportunity.

Description:



The arrowed cells are lymphoma cells.

Lymphoma cells can exhibit a variety of appearances depending on the lymphoma subtype, and definitive diagnosis can be difficult. These cells can exhibit a variety of sizes, shapes, and nuclear and cytoplasmic characteristics. Cell size ranges from 8 to 30 µm and the N:C ratio varies from 7:1 to 3:1. Supplemental studies, such as immunophenotyping, are often necessary to arrive at a diagnosis. The most important distinction between these cells is the difference in their N:C ratios. The N:C ratio tends to be low in reactive lymphocytes, while it is high in lymphoma cells. In addition, reactive lymphocytes are characterized by their wide range of morphologic appearances within the same blood smear. While lymphoma cells can exhibit a wide range of morphologic appearances, any individual case tends to show a more monotonous population of the abnormal cells. In this case, the lymphoma cells are much larger than normal lymphocytes (also present in the image and CMP-08 for comparison), with irregular nuclear contours, somewhat condensed chromatin, and a moderate amount of cytoplasm. These cells are also singly dispersed while non-hematopoietic malignant cells are often in clusters.

While both monocyte/macrophages and the arrowed lymphoma cells are larger than a normal lymphocyte, the abnormal features of the cells are not consistent with monocytes/macrophages. **The arrowed lymphoma cells have a higher nuclear-to-cytoplasmic ratio and much more irregular nuclear contours than a typical monocyte/macrophage which has round to ovoid to kidney bean shaped nuclei with abundant cytoplasm.**

Document your compliance with this training update by taking the quiz in the MTS system.

Clinical Presentation:
This patient is a 61-year-old woman with rapidly progressive shortness of breath and decreasing oxygen saturations. Pleural fluid sample laboratory findings include: WBC = 7842/µL (7.842× 10E3/µL); RBC = 3365/µL (3.365 × 10E3/µL).

(PLEURAL FLUID, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 100X)

CASE DISCUSSION: Large B-cell lymphoma in pleural fluid

The abnormal cells in this case are very large (much larger than the normal lymphocyte shown for comparison) with high nuclear-to-cytoplasmic ratios, irregular nuclear contours, condensed chromatin, and a minimal to moderate amount of cytoplasm, with cytoplasmic vacuoles. These are large atypical lymphoid cells, morphologically compatible with a large cell lymphoma.

Lymphomas are often clinically divided into two types: Hodgkin and non-Hodgkin lymphoma. Non-Hodgkin lymphoma encompasses a wide variety of disorders, the most common of which is diffuse large B-cell lymphoma (DLBCL). Only rarely do certain subtypes of large cell lymphomas manifest solely as effusion-based lymphoma, such as primary effusion lymphoma, which is mostly seen in immunocompromised patients. More commonly, patients with DLBCL involving lymph nodes can develop pleural effusions with lymphomatous involvement, which has been reported in up to 20% of cases. The presence of a malignant effusion in DLBCL is associated with a worse prognosis.

While the cells in this case are morphologically suggestive of a large cell lymphoma, additional studies such as flow cytometry would be needed to further classify them. Alternatively, immunostains can be performed on cytopathology specimens for further evaluation. These studies will identify the cells as abnormal B cells and aid in definitive diagnosis and classification. They are also important in preventing misclassification of these cells as non-hematopoietic tumor cells.

Involvement of pleural fluid by small B-cell lymphomas can be more challenging to morphologically distinguish from reactive lymphocytoses as the cells tend to be more similar to normal lymphocytes. In such cases, flow cytometry and/or immunocytochemical stains, as well as molecular testing, are essential in confirming that the cells are malignant.

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References:

1. Chen YP, Huang HY, Lin KP, Medeiros LJ, Chen TY, Chang KC. Malignant effusions correlate with poorer prognosis in patients with diffuse large B-cell lymphoma. *Am J Clin Pathol*. 2015;143(5):707-715.
2. Das DK. Serous effusions in malignant lymphomas: a review. *Diagn Cytopathol*. 2006;34(5):335-347.
3. WHO Classification of Tumours Editorial Board. *Haematolymphoid tumours.* International Agency for Research on Cancer. 2024. (WHO classification of tumours series, 5th ed.; vol. 11).