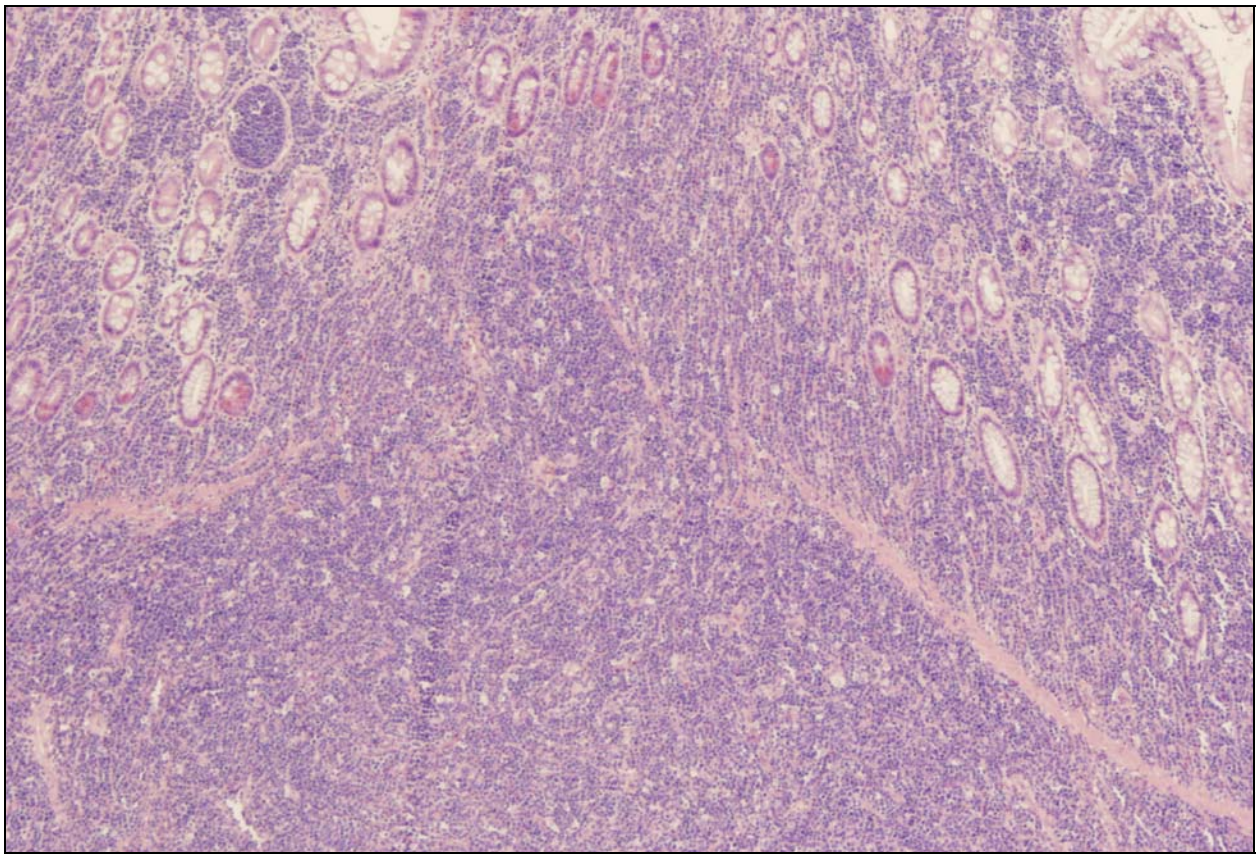
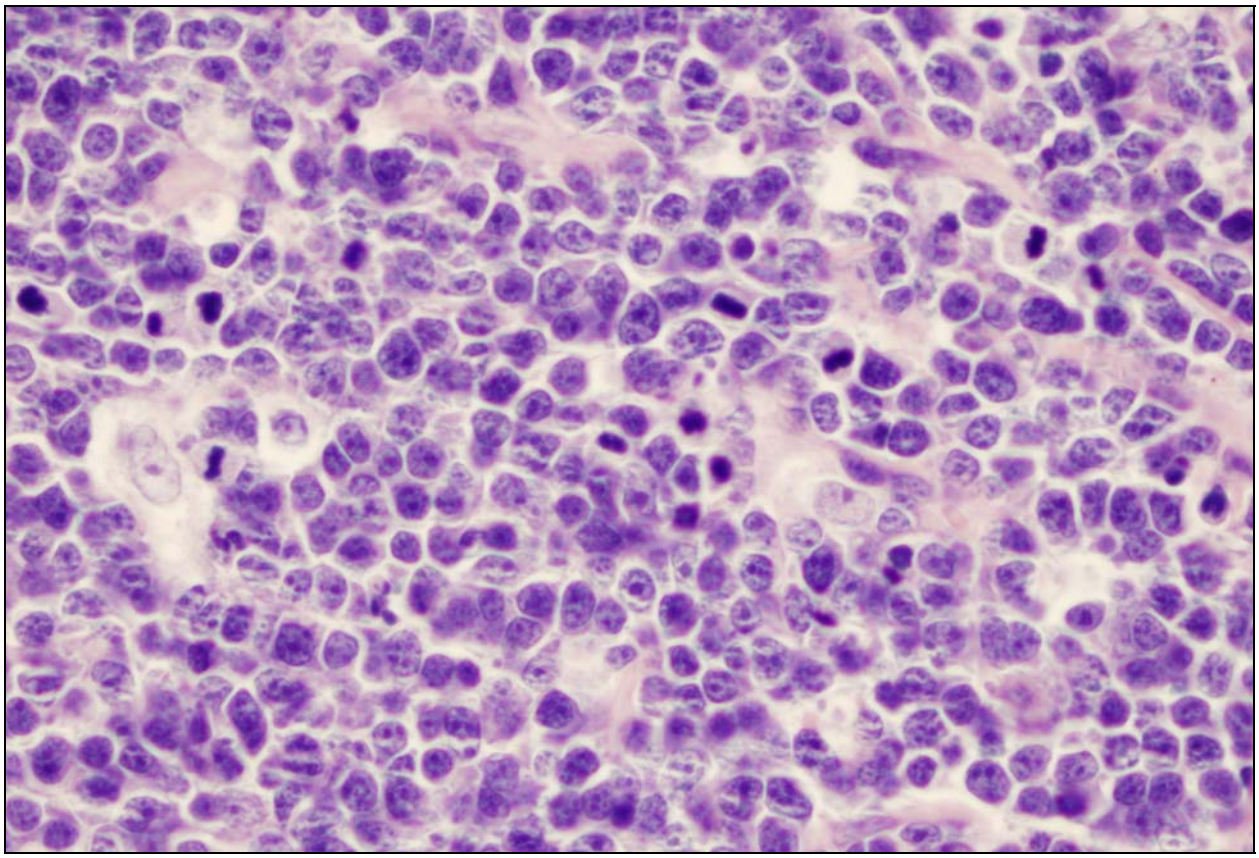
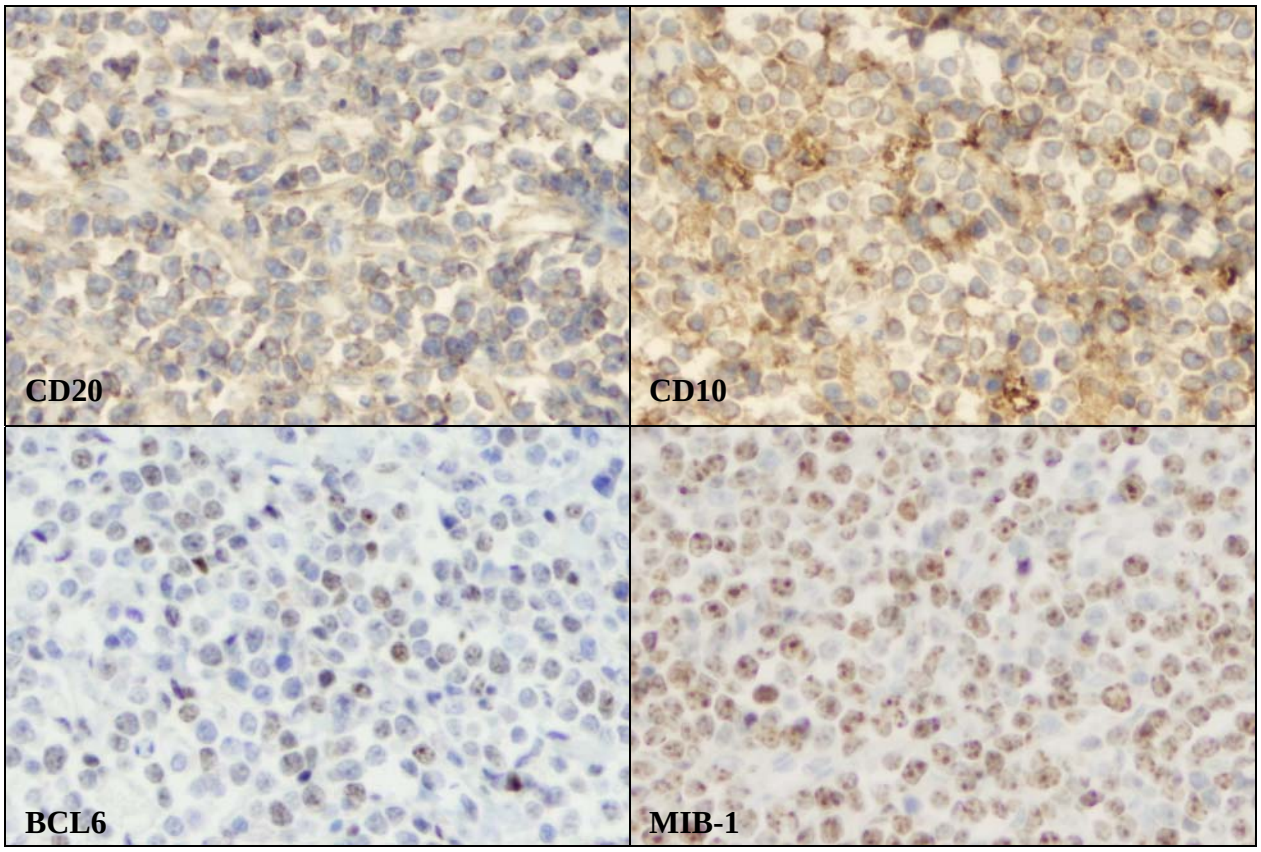
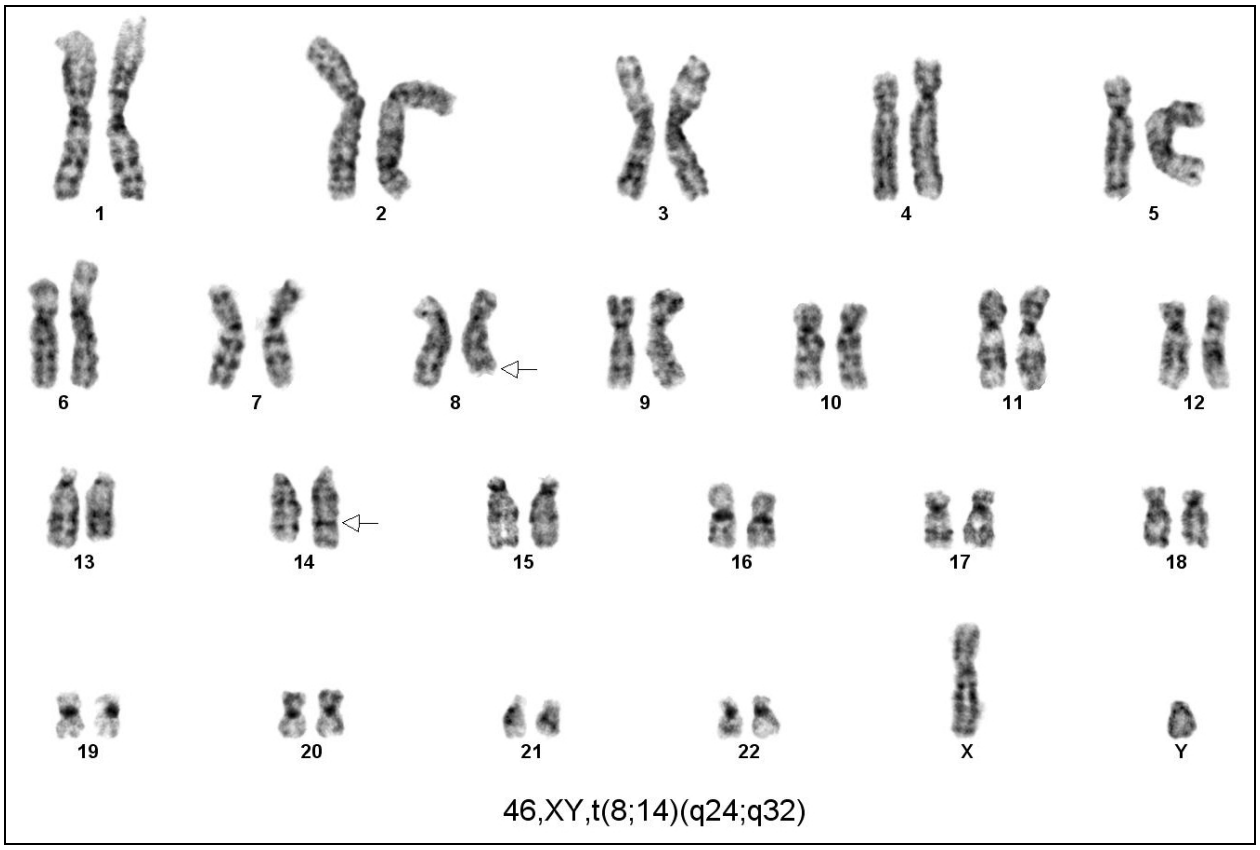
Case

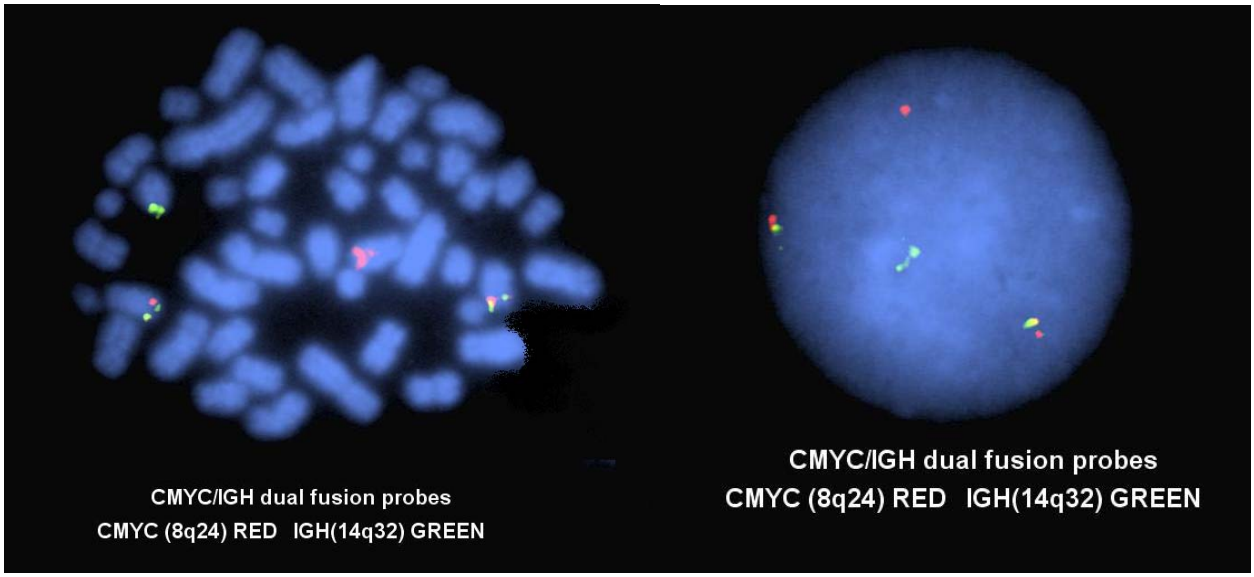
The patient is a 55 year old male with a history of epithelioid hemangioendothelioma that metastasized to his lung, status post resection and chemotherapy 3 years before. He now presents with an 8-week history of severe paroxysms of crampy epigastric pain with abdominal distension, nausea, and bilious vomiting. A CT scan revealed a small bowel intussusception and retroperitoneal lymphadenopathy. An ileocolic resection was performed. Representative images from the patient's resection specimen and cytogenetics are shown below.






CD20
CD10
BCL6
MIB-1





What is your diagnosis?

A) Metastatic hemangioendothelioma
B) Undifferentiated sarcoma
C) B-cell lymphoma, unclassifiable
D) Poorly differentiated adenocarcinoma with neuroendocrine features

Answer and discussion

C) B-cell lymphoma, unclassifiable. More specifically, B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL).

Permeating diffusely throughout the mucosa and muscle wall are heteromorphic malignant lymphocytes, both intermediate and large in size. Some areas have a "starry sky" pattern, characterized by macrophages ingesting apoptotic debris, which is typical of BL. However, the cytology is not as uniform as typically seen in BL. The malignant cells are larger and more pleomorphic, which are features more consistent with DLBCL.

Immunohistochemistry was performed, confirming a B-cell origin for the lymphoproliferative neoplasm: CD20+ and CD3– (not shown). Further stains were used to characterize the lymphoma and the staining profile was suggestive of BL: CD20+, CD10+, BCL6+, BCL2 – (not shown). The proliferation rate (MIB-1) was ~ 90%, which is typical in BL and higher than what is often seen in DLBCL.

Cytogenetics, which can also aid in the diagnosis of high-grade B-cell lymphomas, was performed. Most cases of BL have a MYC translocation. Common cytogenetic abnormalities in DLBCL include translocations involving BCL6 and BCL2. In the current case, the cytogenetic results revealed a translocation between chromosomes 8 and 14 (MYC/IGH translocation). This translocation was confirmed by FISH.

The immunohistochemical and cytogenetic profile of this tumor fits with a diagnosis of BL. However, the histologic morphology does not support this diagnosis. Therefore, it is best designated as a B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and BL (intermediate DLBCL/BL; 2008 WHO criteria). As the name implies, this lymphoma lies somewhere in the biological continuum between DLBCL and BL. These cases classically have morphologic and genetic features of both entities. They were previously called Burkitt-like lymphomas or erroneously misdiagnosed as simply DLBC or BL. They express pan B-cell markers (CD19, CD20, CD22, and/or CD79a) and, as in this case, often are immunophenotypically similar to BL (positive for CD10 and BCL6, and high MIB-1 rate). They can occasionally be BCL-2 positive. Nearly half of intermediate DLBC/BL cases have a MYC rearrangement and 15% have a BCL2 translocation, with or without a MYC translocation.

Intermediate DLBCL/BL lymphomas are aggressive and are frequently diagnosed at advanced stages with extranodal involvement. Our patient had a subsequent bone marrow biopsy positive for intermediate DLBC/BL lymphoma and clinical suspicion for liver involvement by imaging. Prognosis is poor particularly for those that have both the MYC and BCL2 translocations (so called "double hit" lymphomas), as they are generally refractory to standard chemotherapy regimens.

References

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