

Primary Non-Hodgkin's Lymphoma of the Cervix: A Case Report

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Conflict of Interest Statement:

We certify that there is no conflict of interest with any commercial entities or other associations regarding the material discussed in this case report.

Abstract

Primary non-Hodgkin's lymphoma is extremely rare in the uterine cervix with approximately 150 cases reported to date. We report a case of primary non-Hodgkin's lymphoma of the cervix. A 48-year-old woman presented with vaginal bleeding and rapid weight loss along with a cervical mass upon pelvic examination. A Pap test and cervical biopsy was performed. The Pap test showed malignant cells morphologically consisted with lymphoma. Cervical biopsy and immunohistochemical studies confirmed the diagnosis of diffuse large B cell lymphoma (DLBCL), germinal center type. The similarities of this disease to common cancers of the uterine cervix can pose a diagnostic challenge both clinically and cytologically. Histologic and immunohistochemical studies are necessary to confirm a diagnosis of primary non-Hodgkin's lymphoma of the cervix.

Key Words: primary non-Hodgkin's lymphoma; diffuse large B cell lymphoma; DBCL

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Introduction

Primary non-Hodgkin's lymphoma is a rare disease that accounts for less than 1% of extranodal lymphomas arising from the uterine cervix.¹ As of 2006 approximately 150 cases of the disease have been reported.² Clinical symptoms include abnormal bleeding and enlarged cervix upon pelvic examination.^{3,4,5} Primary non-Hodgkin's lymphoma of the female genital tract can clinically mimic primary carcinoma of the cervix. We report a case of primary non-Hodgkin's lymphoma located in the uterine cervix and describe the Pap test and cervical biopsy findings.

Case Report

A 48-year-old woman presented with vaginal bleeding every day for a period of several weeks along with a 25 lb weight loss over a two month period. Upon pelvic examination a 14 cm cervical mass was noted. A ThinPrep Pap test along with a cervical biopsy was performed by the gynecologist. The cervical biopsy sample consisted of a 1.5x0.8x0.1 cm aggregate of irregular, hemorrhagic soft tissue fragments and mucus. The patient did not have a history of lymphoma. After the diagnosis of lymphoma the patient was sent to a different physician for treatment.

Findings

The Pap test revealed a background of blood and tumor diathesis. Numerous single-lying abnormal cells were present that were large and monotonous in size with scant cytoplasm. Most nuclei were lobulated with irregular granular chromatin. Many nuclei possessed multiple prominent nucleoli. The cytologic diagnosis was malignant tumor cells consistent with lymphoma. The cervical biopsy revealed a cell pattern identical to that observed on cytology. A diffuse pattern of malignant lymphocytes with a mixture of large cleaved and noncleaved cells was present with lobulated and irregular nuclear

membranes and occasional nucleoli. Initial immunohistochemical analysis showed diffusely positive staining for CD20, while staining for cytokeratin was negative. Additional immunohistochemical stains were performed to further classify the lymphoma. The large neoplastic B cells were positive for CD10 and BCL6. They were negative for MUM1, cyclin D1, CD3 and CD5. CD3 and CD5 highlighted small background T cells. The final pathologic diagnosis was diffuse large B cell lymphoma (DLBCL), germinal center type.

Discussion

Primary non-Hodgkin's lymphoma of the uterine cervix is extremely rare. There is a wide age range of this disease, from 20-80 years with a median age in the early 40's.⁶ The rare occurrence of this disease presents a diagnostic challenge for the clinician and pathologist. Most patients present with abnormal uterine bleeding and a cervical mass or lesion.^{3,4,5} Because abnormal uterine bleeding is a common symptom of cancer in the uterine cervix, many cases have been reported as a primary tumor of endometrial or cervical origin. Durson et al.⁶ reported other symptoms include pelvic pain, post coital bleeding, and postmenopausal bleeding. Typical symptoms of lymphomas such as night sweats, fever, and weight loss have been rare occurrences in primary cervical lymphomas.^{4,5,7} Harris and Scully⁸ reported that 67% of tumors reveal a subepithelial mass without a visible ulcerated lesion or abnormal epithelium. Because the disease typically does not arise in cervical mucosa, cytology is not a reliable screening tool. In most cases patients present with negative Pap cytology, and malignant lymphocytes are not exfoliated unless a lesion is present.⁹ Differential cytologic diagnoses of primary non-Hodgkin's lymphoma include chronic inflammation, poorly

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differentiated cervical carcinoma, and sarcoma.^{3,10}

Histologic and immunohistochemical or molecular analyses must be performed to confirm a diagnosis of lymphoma. In order to be considered a primary lymphoma of the cervix, the tumor must meet three criteria: 1) be confined to the cervix, 2) no evidence of lymphoma elsewhere for at least several months, and no evidence of leukemia.¹¹ The most common histologic type of primary cervical lymphoma is diffuse large B cell lymphoma.¹⁰ This case showed the patient had a diffuse large B cell lymphoma, germinal center type. Large neoplastic B cell lymphomas show a positive staining reaction to CD10 and BCL6, and a negative staining reaction for MUM1, CD3, and CD5. Germinal center subtype (CD10+, BCL6+, MUM1-) lymphomas have superior treatment outcomes compared to non-germinal center subtype (CD10-, BCL6-, MUM1+) lymphomas.¹²

It is important that a correct diagnosis of this rare disease is made due to the differences in treating primary cervical lymphoma and common cancers of the cervix.

The most common first treatment for large diffuse B-cell lymphoma is combined rituximab and CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy^{13,14}.

Several studies have reported localized treatment with radio therapy and surgery along with rituximab and CHOP improve the overall outcome of patients and is considered to be the favored course of treatment among many clinicians^{14,15,16}. When compared to nodal lymphomas, extranodal lymphomas typically have a poorer prognosis due to challenges in diagnostic accuracy of the disease.

However, Pham et al⁷ reported that patients who are diagnosed in the early stage of the disease have a better prognosis that is comparable to other cancers of the uterine cervix.

In summary, primary non-Hodgkin's lymphoma of the uterine cervix is extremely rare. Cytology alone is not a reliable method for an accurate diagnosis of the disease. Histopathologic analysis along with immunohistochemical stains are needed to confirm a diagnosis of primary cervical lymphoma. Combination chemotherapy with either surgery or radiation therapy is the most frequent published recommendation of treatment for the disease.

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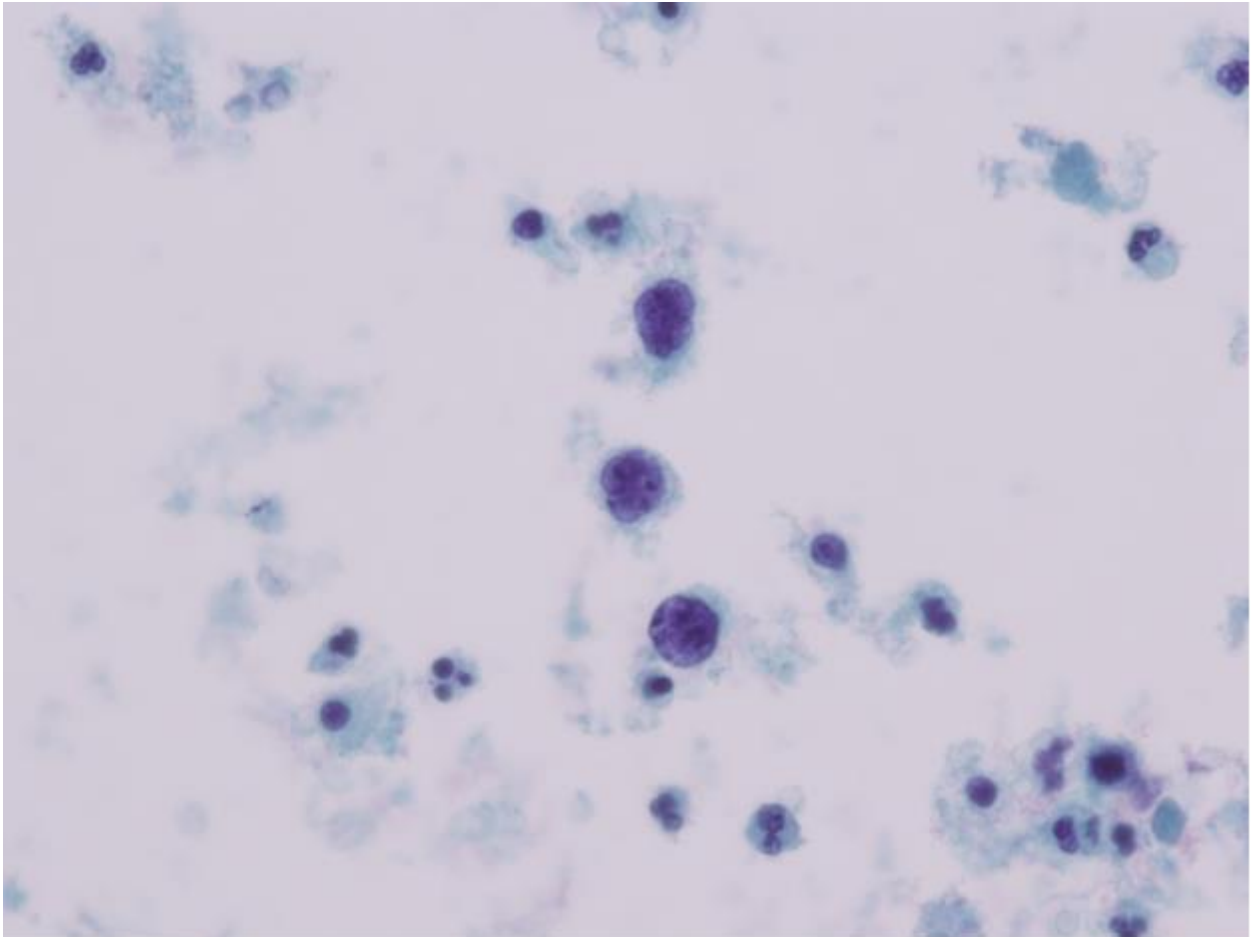


Figure 1: ThinPrep Pap Test

Single-lying malignant lymphocytes with irregular, lobulated nuclear membranes are present. The nuclei possess multiple nucleoli. Diathesis can be seen in the background. (Papanicolaou stain, X400)

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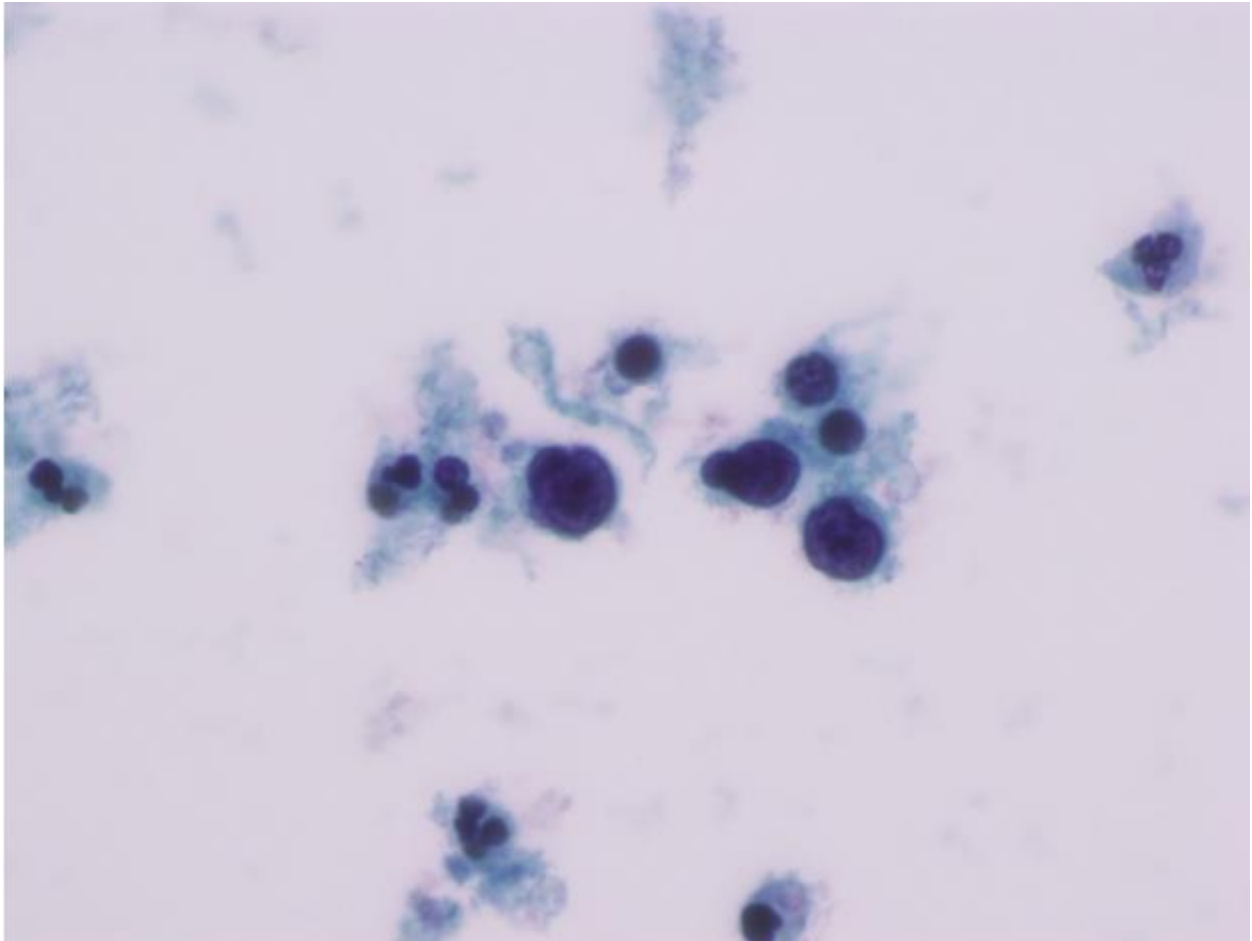


Figure 2: ThinPrep Pap Test

Single-lying malignant lymphocytes are 2-3X the size of normal lymphocytes and possess irregular nuclear membranes as opposed to the smooth nuclear membranes of normal lymphocytes. (Papanicolaou stain, X600)

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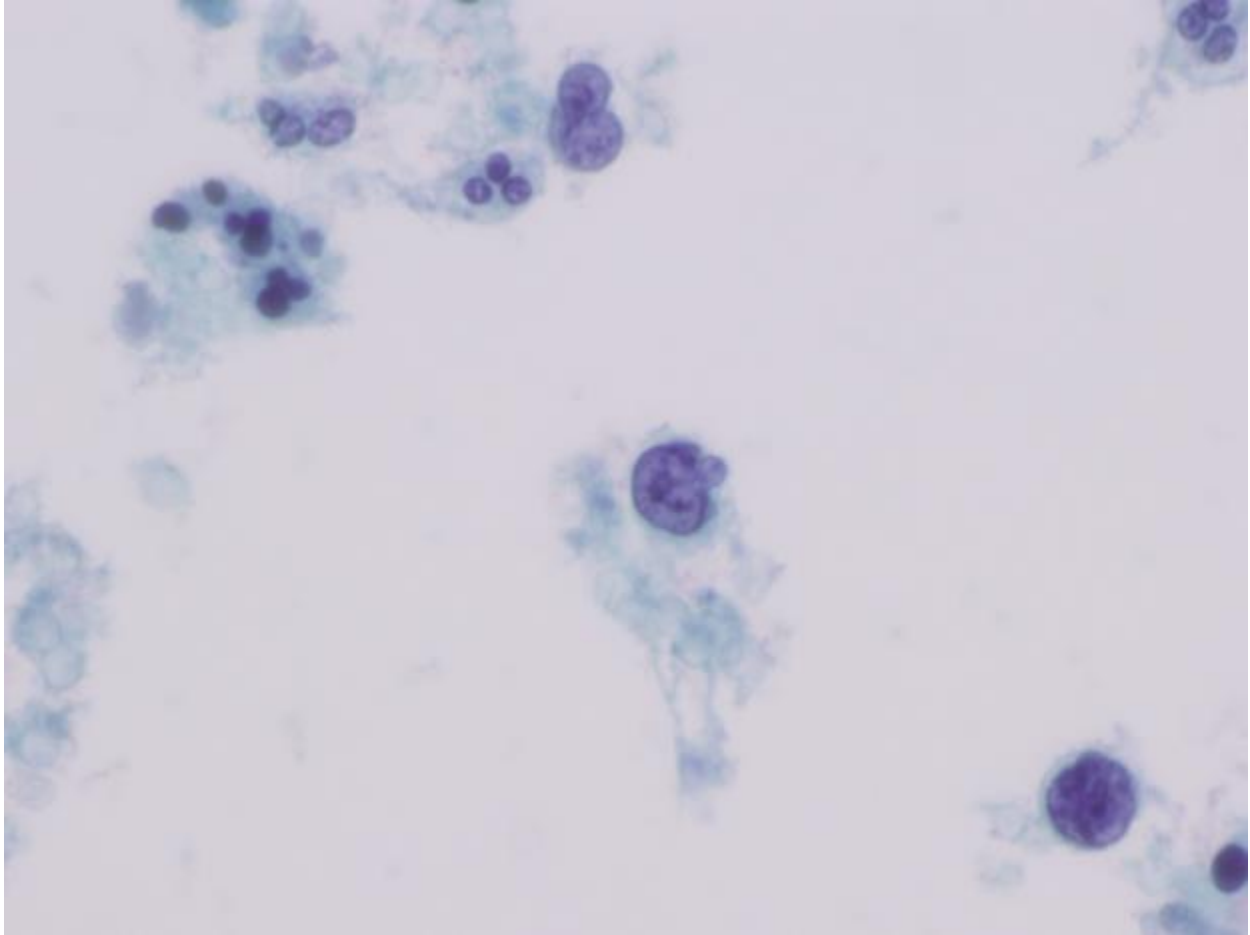


Figure 3: ThinPrep Pap Test

Several single-lying malignant lymphocytes, one with a prominent Koss's nose (center).
(Papanicolaou stain, X600)

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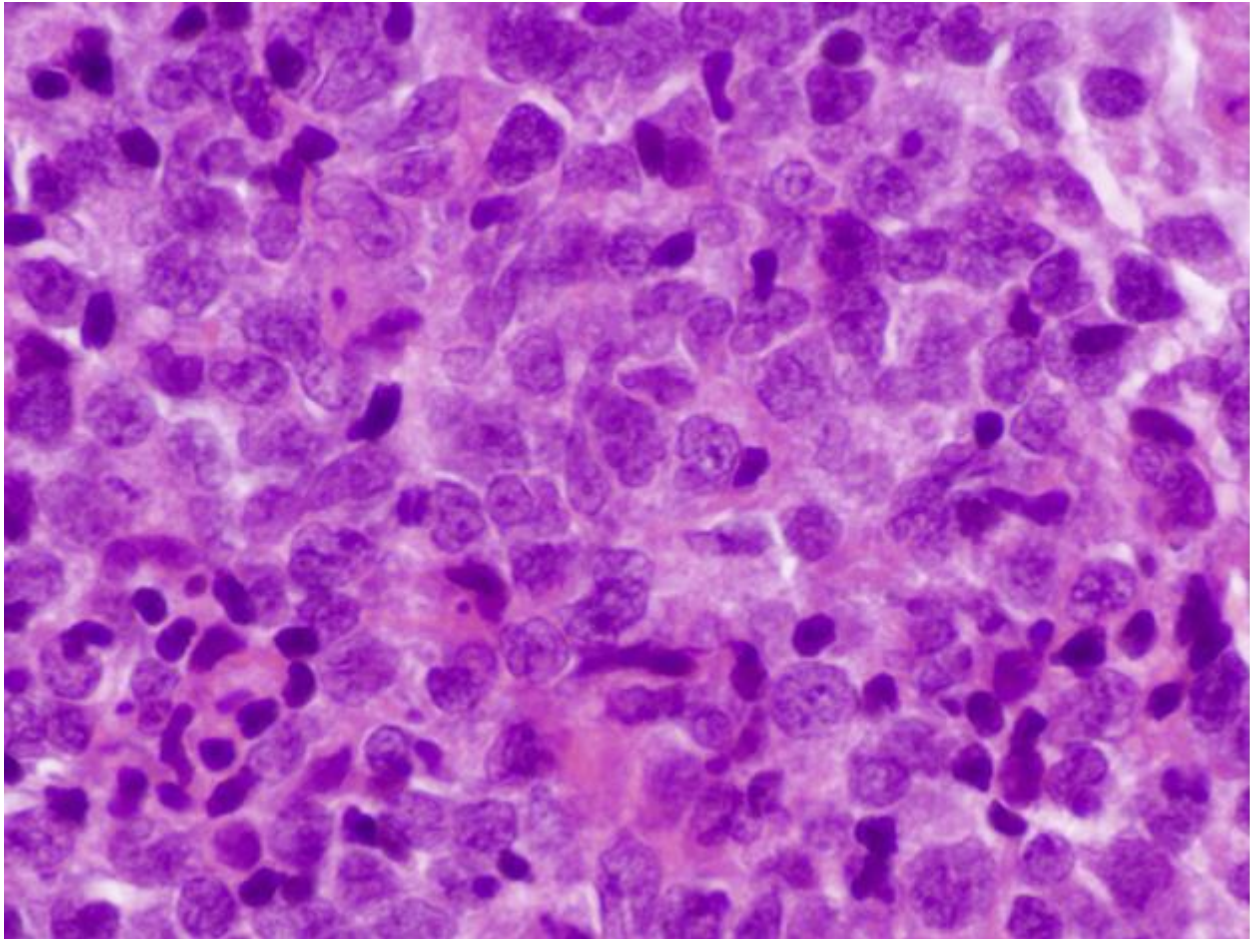


Figure 4: Histological Section Cervix

Sheets of large neoplastic lymphoid cells many with irregular, lobulated nuclear membranes. (H & E, X600)

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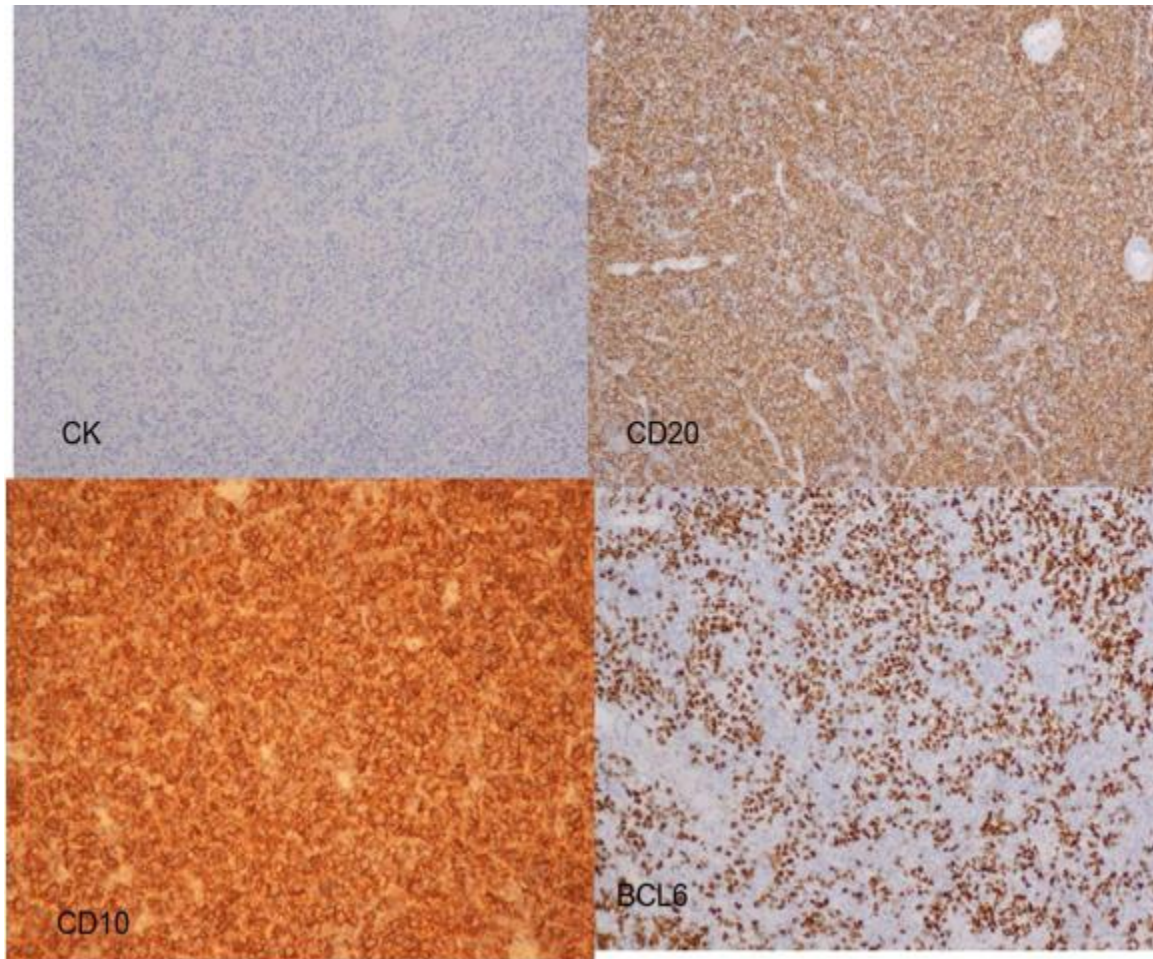


Figure 5:
CK Stain: Negative (rules out an epithelial cancer)
CD20 Stain: Positive
CD10 Stain: Positive
BCL 6 Stain: Positive