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CD20-Negative Diffuse Large B-Cell Lymphoma of the Colon: Exposing the Great Mimicker with IHC

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Introduction

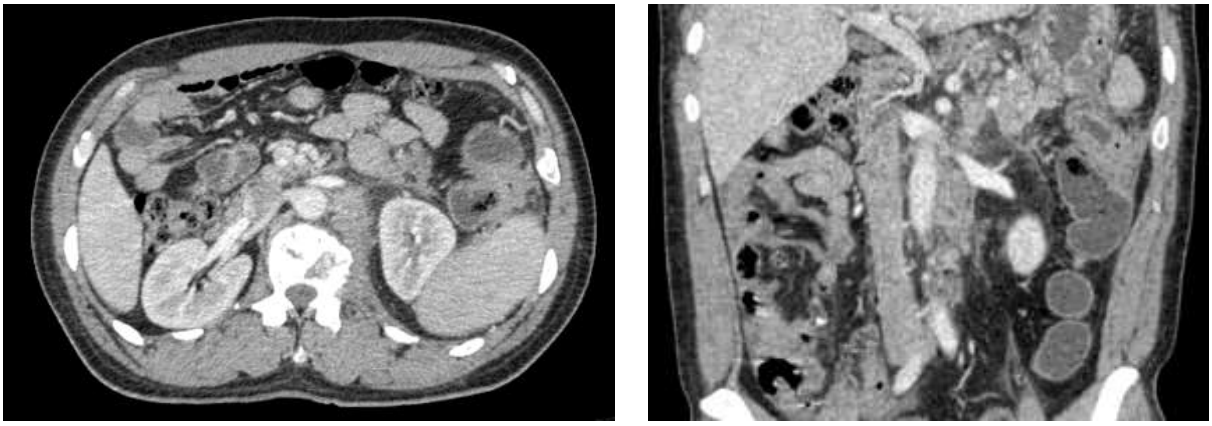
Diffuse Large B-Cell Lymphoma (DLBCL) is the most common subtype of non-Hodgkin's lymphoma (NHL) and it accounts for 30-40% of cases. (1) CD20-negative diffuse large B-cell lymphoma (DLBCL) are NHL subtypes that confer a poorer prognosis due to its atypical morphology, predilection for extranodal involvement, aggressive clinical course and resistance to chemotherapy. (2-3) In addition, it poses a diagnostic challenge due to its rarity and highly variable clinical presentation. We report a case of primary CD20-negative DLBCL of the colon which responded to the standard CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) based chemotherapy.

Case Report

Our patient is a 45-year-old gentleman with underlying Chronic Hepatitis B who presented with history of left hypochondrium pain for the past 1 year. There was associated weight loss of 10kg during that period with intermittent fever. On clinical assessment blood pressure was 106/68 mmhg and a pulse of 70 /minute. The temperature was 38oC. The clinical examination was unremarkable. Blood parameters were notable for deranged Full blood count with white cell count of 24 x 103 u/L.; hemoglobin 11 g/dl, platelet 175 x10/uL and an elevated C reactive protein of 214 mg/L . Apart for hypoalbuminemia, his renal profile and liver function tests were unremarkable. Other work-up which included autoimmune profile, tumor markers, viral screening and tuberculosis workup were negative.

An ultrasound imaging of the abdomen revealed an ill-defined splenic collection. He was commenced on a course of antibiotics for a total of 2 weeks in view of a presumptive diagnosis of splenic abscess. However a reassessment ultrasound abdomen did not reveal radiological improvement. Additional evaluation with CT imaging demonstrated intra-abdominal lymphadenopathy with focal circumferential thickening of the descending colon resulting in luminal narrowing (Figure 1a and Figure 1b). There was a heterogenous hyperdensity at the splenic hilum measuring 4 x 8 x 5 cm in keeping with a necrotic node.

We proceeded with a colonoscopy that revealed circumferential segmental colitis at the descending colon in keeping with TB colitis. (Figure 2a). Narrow-band Imaging (NBI) assisted characterization of the lesion (Figure 2b) did not demonstrate malignant features.



A **B**

Figure 1a &1b: Circumferential thickening of the descending colon resulting in luminal narrowing

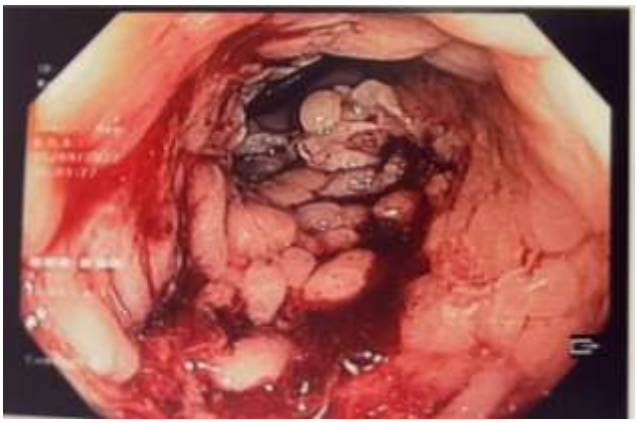


Figure 2a. Circumferential, continuous, friable and nodular appearance with a narrowed lumen at the descending colon

Figure 2b. Characterization with NBI did not demonstrate malignant features

The histopathological examination **(**HPE**)** of the descending colon which displayed atypical lymphoid cells was non-diagnostic. In view of a high index of suspicion of TB, a repeat colonoscopy and biopsy of the lesion was performed which revealed malignant lymphoid cells with immunoblastic appearance. An initial negative result for CD20 and CD3 markers as well as CD30 positivity had resulted in a preliminary misdiagnosis of ALK negative Anaplastic Large Cell Lymphoma. Further immunohistochemistry evaluation which revealed reactivity to primitive B-cell line markers ; CD79a and PAX5 with high ki67 proliferative index **(**>90%**) (** Figure 3a and Figure 3b **)** resulted in a revision of the diagnosis to CD20-negative Diffuse Large B-Cell Lymphoma of the colon.

He was subsequently referred to the hematology unit and was commenced on 1 cycle of Bendamustine due to its better tolerability profile followed by 5 cycles of CHOP chemotherapy **(** cyclophosphamide ,doxorubicin, vincristine and prednisolone **)**. During clinic follow up patient had notable clinical improvement. Repeat CT imaging after completion of chemotherapy showed good treatment response evidenced by marked reduction of proximal descending colon thickening and regression in the size of the splenic node. **(**Figure 4a and Figure 4b**)** Reassessment colonoscopy showed endoscopic resolution of the previously seen area of segmental colitis with the presence of pseudopolyps.

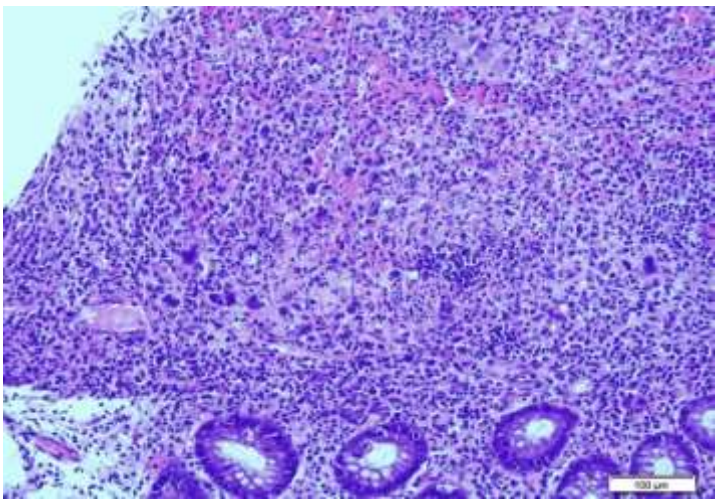


Figure 3a Individually dispersed malignant lymphoid cells with immunoblastic appearance within the lamina propria.

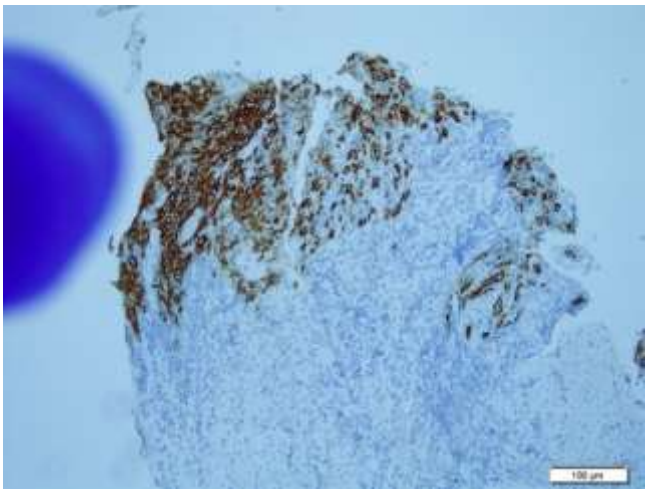


Figure 3b

- Malignant lymphoid cells exhibit the following immunoprofile: positive for leucocyte common antigen **(**LCA**)**, CD79a, CD30 and paired box containing **(**PAX5 **)(**strong nuclear expression**)** with high ki67 proliferative index **(**>90%**)**.
- Consistent with CD20-negative DIFFUSE LARGE B-CELL LYMPHOMA.

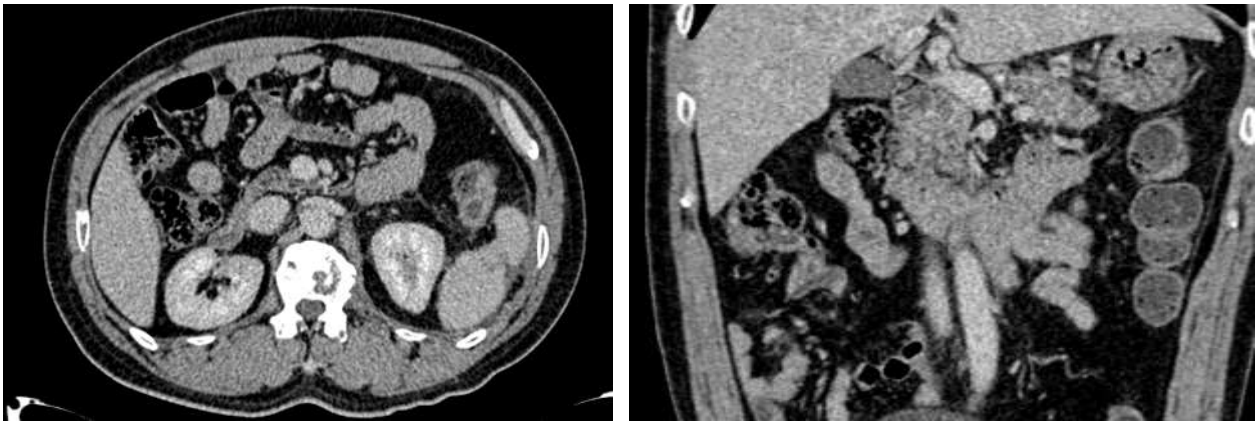


Figure 4a) and 4b) Near complete resolution of the proximal descending colon thickening

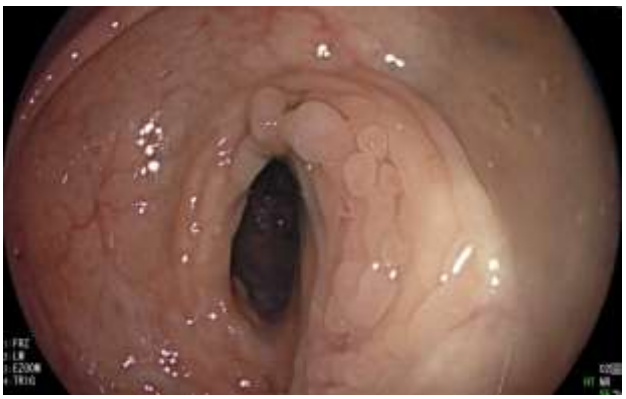
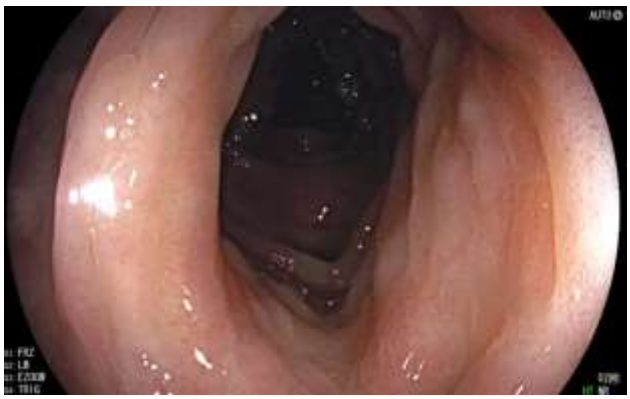



Figure 5a) and 5b) : Post chemotherapy reassessment colonoscopy revealed resolution of colitis and presence of pseudopolyps.

Discussion

CD20-negative diffuse large B-cell lymphoma **(**DLBCL**)** are a rare group of lymphoproliferative disorders with a pronounced proclivity for extranodal involvement. **(**2**)**

The lack of an overarching histological classification, for DLBCL variants that do not express CD20, as illustrated in our case render these entities unclassifiable. Current recognised variants of CD20-negative DLBCL are plasmablastic lymphoma, primary effusion lymphomas, Anaplastic lymphoma kinase positive large B-cell lymphoma, and human immunodeficiency-virus associated plasmablastic lymphoma. **(**4**)**

In East Malaysia, a legitimate concern, owing to a disproportionately high prevalence is the diagnosis of intra-abdominal tuberculosis. **(**5**)** The absence of malignant features on NBI **(**Narrow-band Imaging**)** during the index colonoscopy and the features on CT imaging had raised suspicion of TB. Nevertheless, the immunostaining which was positive for LCA markers confirmed that the cells were of lymphoid lineage. A preliminary misdiagnosis of ALK negative Anaplastic Large Cell Lymphoma did occur in our case owing to the initial negative result for CD20 and CD3 markers as well as CD30 positivity. However, immunoreactivity to CD79a and PAX5 had assisted in elucidating the diagnosis. This highlights the importance of having an extensive repertoire of antibody panel in diagnostic immunohistochemistry.

In our patient the chemotherapy regime was initiated with Bendamustine followed by 5 cycles of CHOP. The patient's initial clinical presentation warranted the use of Bendamustine due to its better

safety profile. He responded radiologically and endoscopically following treatment with the conventional CHOP based chemotherapy.

It is worth noting that in the event of a relapse in our patient, a targeted agent towards CD30, such as Brentuximab would be a prudent choice given the immunohistochemical expression of the aforementioned antibody.

Conclusion

To the best of our knowledge, this is the first reported case of a CD20-negative extranodal lymphoma involving the colon. Our patient had a favourable response to the CHOP based chemotherapy evidenced by radiological and endoscopic resolution of the disease.

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