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A Rare CD30+ Follicular B-Cell Lymphoma in a Female Child with Pulmonary Tuberculosis (PTB): A Case Report

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Abstract

Background

Follicular lymphoma (FL) occurs in Tanzania but its CD30+ subtype is undocumented yet. Targeted immunotherapy for CD30+ Hodgkin lymphoma (HL) is available and consequently, its immunoreactivity in some non-Hodgkin lymphoma (NHL) may imply additional therapeutic benefit. Concomitant tuberculosis (TB) is rare but may have similar presentation.

Case Summary

A 13-year-old female with recurrent, progressive left cervical lymphadenopathy was initially biopsied at Kilimanjaro Christian Medical Center (KCMC), diagnosed as undifferentiated carcinoma and pulmonary tuberculosis (PTB) and referred to Muhimbili National Hospital (MNH) where CD30+ follicular lymphoma was diagnosed and transferred to Ocean Road Cancer Institute (ORCI).

Discussion

This case, was associated with abundant CD45+, CD20+, CD30+ and CD3- neoplastic cells including Sputum positive PTB.

Conclusion and recommendation

This CD30+ NHL is amenable to additional specific immunotherapy. Routine CD30 immunohistochemistry is recommended and concomitant TB be ruled-out.

Keywords: *Follicular lymphoma, CD30 positive, Immunotherapy, Pulmonary TB.*

Introduction

Follicular lymphoma (FL) is not uncommon in Tanzania but its CD30 positive subtype is not yet documented within the country as well as in Africa (1-4). However, targeted immunotherapeutic agents for the treatment of relapsed/refractory CD30-positive Hodgkin lymphoma (HL) and anaplastic large cell lymphoma (ALCL) are currently available and their extended use to other lymphomas may be beneficial (5, 6). Follicular lymphomas may be elusive when it comes to routine histological diagnosis alone, as there are lesions which may mimic it including follicular hyperplasia (FH), classic HL nodular sclerosis (CHLNS) subtype and Nodular lymphocyte predominant HL (NLPHL) which need to be distinguished from it may be complicated when FL is also CD30+ (3, 4). However, the later may also benefit from anti-CD30 therapy. Furthermore, tuberculosis (TB) is known to be associated with an increased

risk of lymphoma (both HL and NHL) but this is not yet documented from Tanzania (7-9). Here we present a case of NHL which was also CD30+ as well as positive for pulmonary TB (PTB).

Case Presentation

Herein we report a retrospective case of recurrent CD30+ follicular lymphoma (FL) of the neck in a 13 years old female African child.

Clinical information: Progressive left lateral neck swelling since September 2013. Consulted Meru District Hospital where she was diagnosed with smear positive TB and started on anti-TB. One month later, she was referred to the KCMC as the swelling was progressively increasing and ulcerating. The neck mass was excised (de-bulked) at KCMC one month after that. The specimen was sent for histopathology and diagnosis of undifferentiated carcinoma was entertained. However, there was a rapid recurrence after excision and about 6 weeks afterwards, she was referred to the MNH for further management.

On examination (O/E):

General examination: sick looking, pale and wasted.

Locally: Fungating and ulcerating tumor of left lateral neck, 7cm diameter, easily bleeding on touch and it was tender. However, there was no lymphadenopathy elsewhere.

Other systems: Upper aero-digestive and head and neck regions were examined and reported as normal, chest x-ray was normal, abdominal US was normal, FBP: anaemia (Hb 6.3g/dl) but HIV status was unknown.

A tentative clinical diagnosis of a primary malignant tumor on left lateral neck (either a lymphoma or a carcinoma) was made. An open biopsy of the neck mass was performed at MNH and reviewed by an experienced Pathologist/Lymphomatologist (the author-AM) [Figure 1] and the Provisional Anatomical Diagnosis (PAD) of FL was entertained including the following Differential Diagnoses: Anaplastic Large Cell Lymphoma (ALCL) due to the presence of large cells; Rhabdomyosarcoma (RMS) due to large cells with sometimes abundant cytoplasm; and Hodgkin lymphoma (HL) this was entertained also because of the age group and clinical presentation of a localized cervical lymphadenopathy in a 13-year-old juvenile.

Further investigations were requested and done. Histochemistry for: Periodic Acid-Schiff (PAS) staining to rule out Rhabdomyosarcoma was negative. Immunohistochemistry (IHC) for: CD45 to confirm that this was a lymphoid neoplasm and results showed strongly positive reaction in all tumour cells (not shown); CD45 to confirm or rule out a lymphoma which was strongly positive in all tumour cells (not shown); CD3 to rule out a T-cell lymphoma which was

negative in the neoplastic follicles but positive only in infiltrating T-cells in Figure 2A; CD20 to rule out a B-cell lymphoma which was strongly positive in all tumour cells in Figure 2: B & C implying a B-cell tumour. CD30 to rule out a Hodgkin lymphoma which was strongly positive in all tumour cells in Figure 3: A, B & C implying a CD30+ B-cell tumour.

Due to logistical constraints, Alk-1 was not done since lesion was already positive to CD45, CD20 and CD30 and a definitive anatomical diagnosis of a B-cell neoplasm could be reached. Also, Myogenin was not done because the lesion was negative to PAS thus ruling out rhabdomyosarcoma.

In Summary

A 13 years old female with recurrent, progressive, painless, ulcerative and fungating left cervical lymphadenopathy. Initial biopsy KCMC: undifferentiated carcinoma, de-bulking surgery done with rapid recurrence of the lesion and the patient referred to MNH, biopsy repeated showing large-cell follicular neoplasm and immunohistochemistry was done.

A definitive histopathological diagnosis of a CD30+ Follicular B-Cell/Large-cell Lymphoma was reached and patient was immediately sent to ORCI for further management.

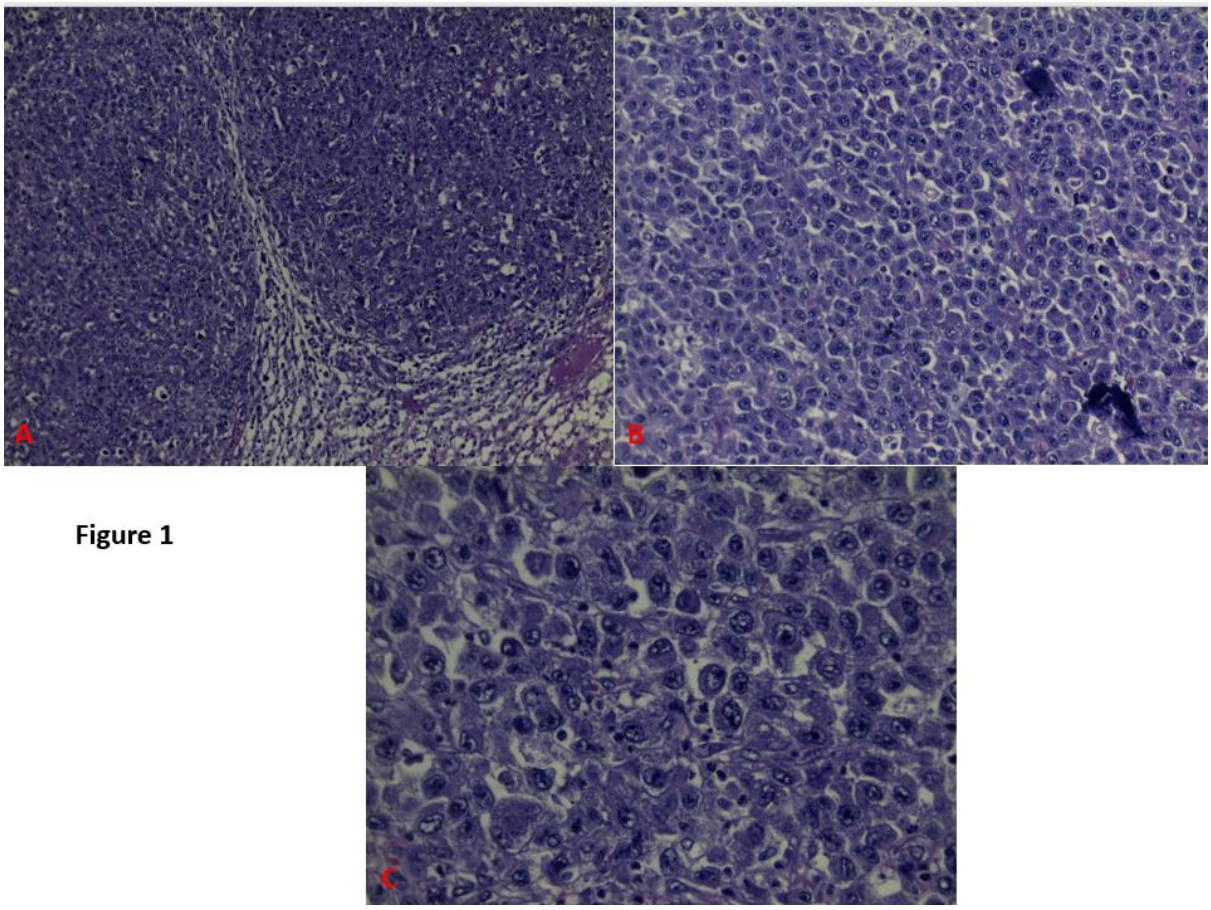

Figure 1

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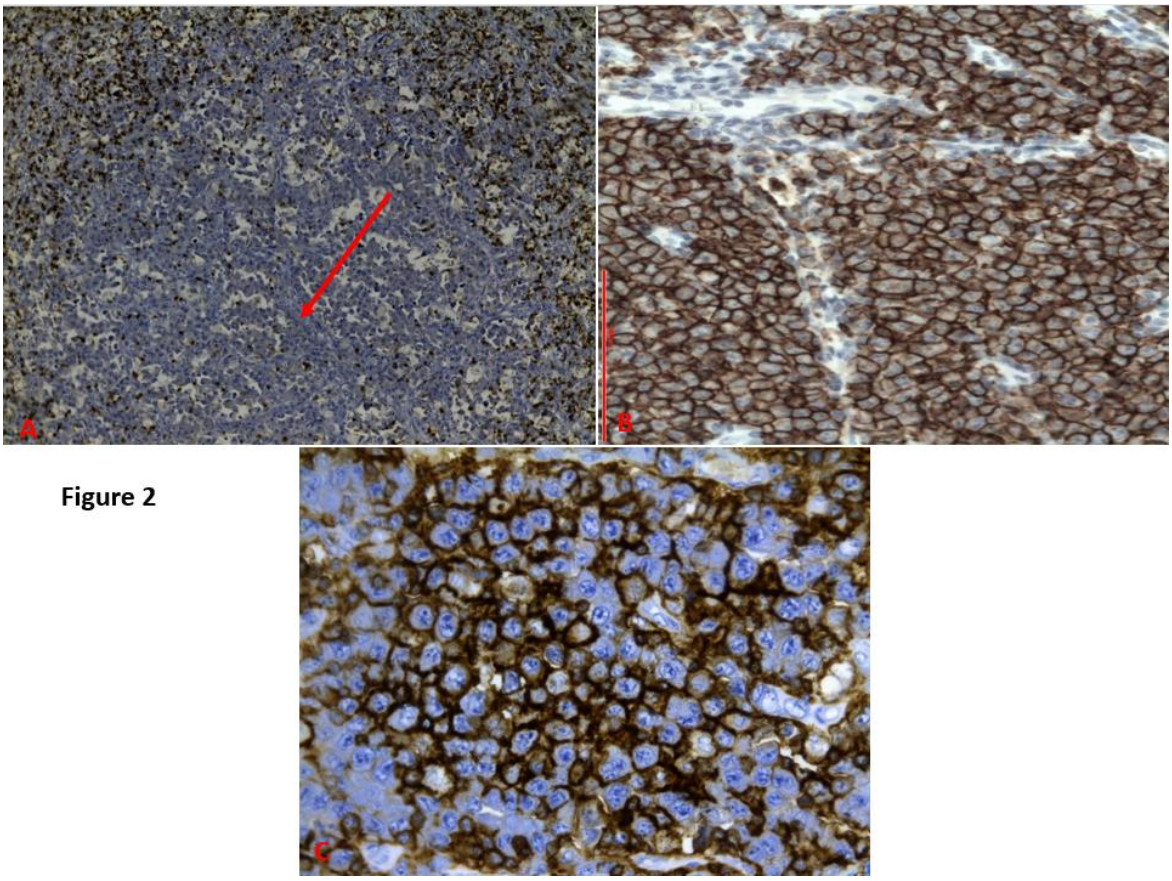

Figure 2

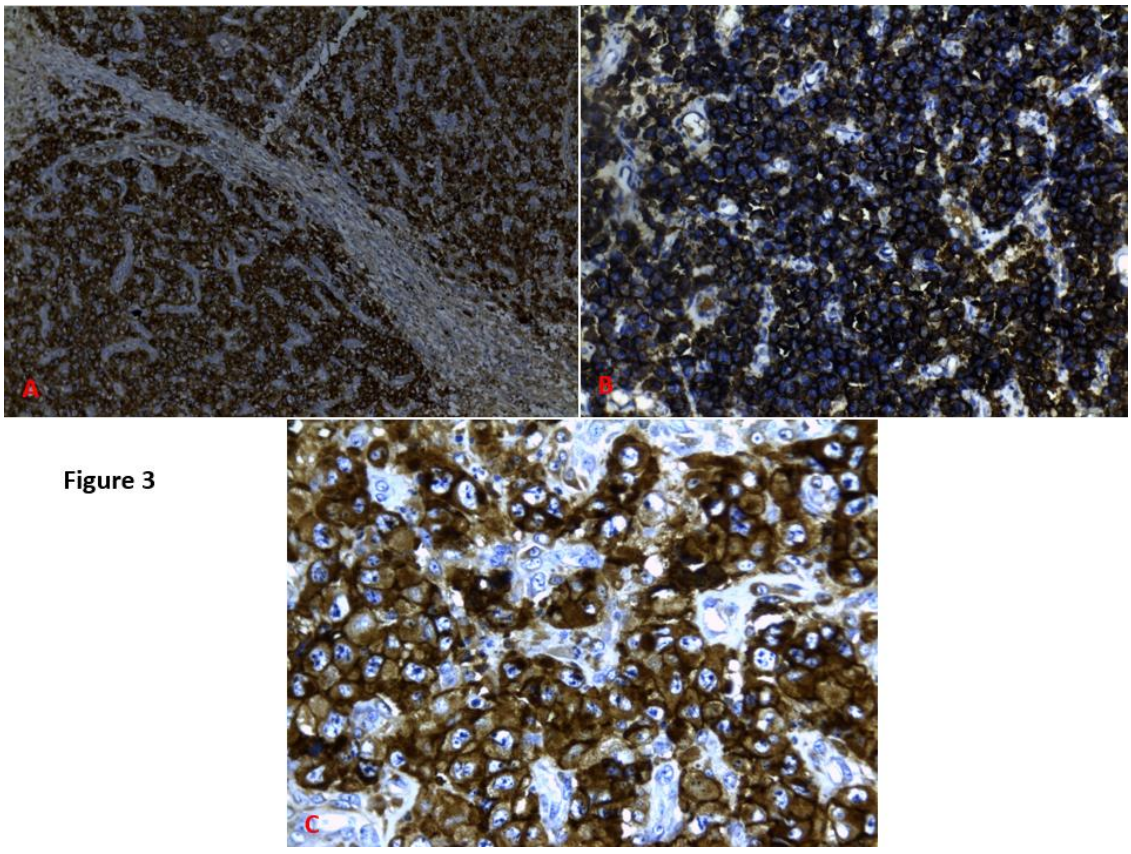

Figure 3

Discussion

Malignant lymphomas are divided broadly into two groups; Hodgkin (HL) and non-Hodgkin (NHL) respectively.(3, 4) Immunohistologically, Reed-Sternberg cells (RSC) and variants are CD30+ and NHL particularly B-cell lymphomas which do lack RSC, should have been CD30 negative.(3, 4) However, this is not the case in reality as several NHL may be CD30+ (CD30 rich non-Hodgkin lymphoma) which does not make lymphoma diagnosis easier. However, since the FDA approved brentuximab vedotin and other drugs including conjugates, as targeted immunotherapeutic agents for the treatment of relapsed/refractory CD30+ HL and anaplastic large cell lymphoma (ALCL), CD30 immunoreactivity of some NHL means they can also benefit from these novel therapies.

The following relevant positive findings enabled reaching the diagnosis:
A recurrent, progressive, painless, ulcerative and fungating left cervical lymphadenopathy in a female juvenile. This should have been the peak age for HL but the lesion was CD20 positive and CD30 was diffusely positive in the whole lesion contrary to few neoplastic Hodgkin cells in HL.
CD45 (LCA): Diffusely and strongly positive; granular membranous cytoplasmic staining in all tumour cells.
CD20: Diffusely and strongly positive; granular membranous cytoplasmic staining in all tumour cells.
CD30: Diffusely and strongly positive; pan- cytoplasmic staining in all tumour cells.
CD3: Negative in tumour cells in follicles but positive in infiltrating T-cells (ITLs).

The final diagnosis was CD30+ FL. Nevertheless, the following differential diagnoses should also be considered:
CD30+ Anaplastic large cell lymphoma (ALCL) but this was positive to CD20 (usually ALCL are negative); NSCHL but this was positive to CD20 (usually Classic HL are negative); NLPHL but this was CD30+ (usually NLPHL are negative); FL on transit to DLBCL this is a possible diagnosis as well; and a CD30+ DLBCL is counteracted by the follicular pattern. The Pathogenesis of CD30+ FL includes t(14;18) in BCL-2 over-expression leading to immortalization and translocations of BCL-6 at 3q27 can also be involved.

Treatment options:

Localized disease, can be cured by local irradiation; but this patient had a local recurrence.

However, clinical trial results released in June 2012 show that bendamustine, first developed in East Germany in the 1960s, more than doubled disease progression-free survival given alongside rituximab. The combination also left patients with fewer side effects than the older treatment [a five drugs combination: rituximab, cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine and prednisone, collectively called R-CHOP].

The FDA approved brentuximab vedotin as well as its chemotherapeutic conjugates as targeted agents for the treatment of relapsed/refractory CD30-positive HL and ALCL (6) and these have emerged as potent, clinically active, and well-tolerated targeted agents for the management of relapsed/refractory CD30-positive malignant lymphomas. Furthermore, anti-CD30 Chimeric Antigen Receptor T-cells as well as anti PD-1 antibody therapy are also beneficial in CD30 positive lymphomas.(5, 6) These treatments should be included in the algorithm of the management of CD30+ lymphoid neoplasms.

However, treatment with high-dose therapy (HDT) and autologous hematopoietic peripheral stem cell transplantation (AHSCT) show the same curative potential in patients with follicular large-cell lymphoma (FLCL) who relapse, as it does in patients with DLBCL who relapse. The good news is that both these later treatment modalities are currently available in Tanzania and specifically at MNH although not when this patient was being managed. Unfortunately, patient was lost to follow-up as she went back upcountry.

Furthermore, comprehensive co-morbidities investigations and treatment is necessary. In this particular patient a con-current sputum positive pulmonary tuberculosis (PTB) could have masked or delayed the diagnosis of the lymphoma, considering that TB may present with lymphadenopathy as well as constitutional symptoms that are similar to lymphoma “B-symptoms”; but also, lymphoma-associated (cell-mediated) immunosuppression may increase the risk for concomitant TB.(8-10) TB appears to have a pathogenetic association with lymphomagenesis. A large recent prospective cohort study of young and middle-aged adults shows that history of TB infection is associated with increased risk of lymphoma independent of other risk factors including age, sex, body mass index (BMI) and lifestyle choices.(7)

Conclusion

This CD30 positivity in a B-cell NHL allows the addition of anti-CD30 immunotherapy besides available treatment modalities. Thus, a rare lymphoid neoplasm as well as the presence of co-morbidities including TB should be ruled out in cases of recurrent/refractory cervical lymphadenopathy. Routine screening of NHL for CD30 expression may offer increased treatment success through precision medicine, however, routine immunohistochemistry must

be established first. Moreover, further research is needed to clarify the association of tuberculosis with lymphomagenesis. This is the first time a CD30+ non-Hodgkin lymphoma including a PTB comorbidity are reported from Tanzania.

Ethical Considerations

This case report does not contain any patient identifiers and neither does it show picture(s) of any patient. Confidentiality has been strictly adhered to. Only de-identified information is presented for the benefit of the medical fraternity and community at large.

Author's Contributions

AM made the histopathological including histochemical and immunohistochemical diagnoses, collected the patient's clinical information, conceived the case report, drafted manuscript, made all figures and microphotographs, footnotes, corresponded with editors, performed reviews, all corrections and proofreading.

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