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Case Report

A Rare Manifestation of Hodgkin's Lymphoma- a Presentation as an Extensive Granulomatous Disease

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ABSTRACT

The author reports a 24 years old female, presented with newly detected lump in her left breast, left upper limb edema and abdominal distension. She was diagnosed with TB lymphadenitis in view of caseating granuloma in FNAC which was performed in the initial hospital and was initiated on Anti tuberculosis treatment. After the intensive phase of Anti tuberculosis treatment, she developed drug induced hepatitis, hence ATT was stopped. In spite of adjusting dose modified ATT, her liver function deteriorated with worsening of clinical symptoms. Further evaluation showed extensive granulomatous lesions in the breast, multiple lymph nodes, liver and spleen. A new excision lymph node biopsy of lymph node revealed Nodular lymphocyte predominant Hodgkin's lymphoma. Immunohistochemistry revealed positivity for CD20, PAX-5, OCT-2 and negative for CD3, CD15. Whole body PET CT showed multiple hypo dense nodules in liver and spleen, mediastinal and costal pleural deposits and soft tissue density nodules in left breast, left Latissimus dorsi, multiple skeletal sites suggestive metabolically active extra nodal lymphomatous deposits. She was treated with chemotherapy and she showed an excellent response.

Keywords: Hodgkin's lymphoma, breast and hepatic involvement

INTRODUCTION

Hodgkin's lymphoma is hematological malignancy which arises from the B lymphocytes. Histologically, it is characterized by the presence of Reed-Sternberg cells and/or its variants. However Hodgkin's lymphoma can present as granulomatous lesion with the formation of epithelioid cell granuloma in rare cases. This can mislead clinicians, especially in areas endemic for other diseases such as Tuberculosis, and result in unnecessary treatment. Fine needle aspiration biopsy is not the ideal method of diagnosing this disease. Lymphoma of breast is very rare and it constitutes only 1.7-2.2% of extra nodal lymphomas and 0.4-0.5% of breast malignancies. [(1, 2)] Hepatic involvement with acute liver failure in Hodgkin's lymphoma is extremely rare and it usually occurs in advanced stages of the disease. Hence in most cases, diagnosis was made at autopsy. [(3)] The present case describes an atypical presentation of lymphoma in the form of

granulomatous lesion in the breast, liver, spleen, pleura and lymph nodes which was initially misdiagnosed as disseminated tuberculosis.

CASE REPORT

In March 2019, a 24 years old married female, presented to our institution with complaints of newly detected lump in her left breast since 20 days and left upper limb oedema, abdominal distension and bilateral pedal oedema since 10 days. Initially she noticed a lump in her left breast 20 days back and it was not associated with pain, nipple discharge or retraction. After 10 days, she started noticing swelling of her left upper limb which was not associated with pain/discoloration / raised temperature. She also developed abdominal distension along with bilateral pedal oedema. There was associated dyspnoea, weight loss and nausea. She had normal menstrual cycles. There was no significant family history or travel history.

She had a background history of axillary lymphadenopathy which was diagnosed to be tuberculous lymphadenitis from outside hospital in July 2018 in view of caseating granuloma in FNAC. So she was initiated on Anti tuberculosis treatment (ATT) from August 2018 with which she gained weight, although there was no significant reduction in the size of the lymph nodes. However, after the intensive phase she developed hepatitis which was attributed to ATT and it was stopped. She was referred to Department of Gastro medicine of our institution where she was restarted on modified ATT after stabilizing the liver function. But despite multiple attempts to introduce a full regime of modified ATT, she experienced worsening of liver function each time. Hence she was initiated on modified ATT with Ethambutol and Levofloxacin. On modified ATT she developed new breast lesion. Thus she was referred to the Department of Internal Medicine for re-evaluation.She had a history of polyarthralgia 2 years back involving bilateral shoulder joint, ankle joint and inter phalangeal joint with morning stiffness and swelling which was treated with azathioprine/ sulfasalazine for 1 year, after she stopped the medications on her own.

On physical examination, she had pallor, bilateral pitting pedal edema, few lymph nodes in supraclavicular area and a large firm matted lymph node measuring 5x 6 x 3 cm in axillary area. Breast examination revealed well defined hard mobile lump of 3 cm. She had reduced air entry bilaterally with bilateral basal crackles, distended abdomen with shifting dullness and mild splenomegaly.

Initial blood investigations showed thrombocytopenia, direct hyperbilirubinemia, hypoalbuminemia, transaminitis, prolonged PT INR and elevated LDH. Details of laboratory results are given in table 1. Chest x-ray showed bilateral pleural effusion. Ultrasound breast showed bilateral extensive lymphadenopathy involving the cervical and axillary region with hypo echoic solid mass with circumscribed margins in the left breast of 2.7x1.3x 2.7cm.Trucut biopsy taken from the left breast was showing lobulocentric and interlobular stroma granulomatous inflammation which was suggestive of tuberculous mastitis. However biopsy sample sent for AFB smear, Genexpert and AFB culture were negative. Ultrasound abdomen showed coarse echo texture of liver with minimal surface irregularities and few iso - hypo echoic lesion in right lobe of liver, spleen was enlarged with multiple scattered hypo echoic lesion, moderate ascites and bilateral minimal pleural effusion.

The clinical presentation of generalized lymphadenopathy with multiple lesions in the liver and spleen with serositis along with radiological and histological evidence of TB initially made us consider the possibilities of partially treated Disseminated Tuberculosis versus multi-drug resistant TB. She was started on IV Amikacin and continued on Ethambutol along with Levofloxacin.

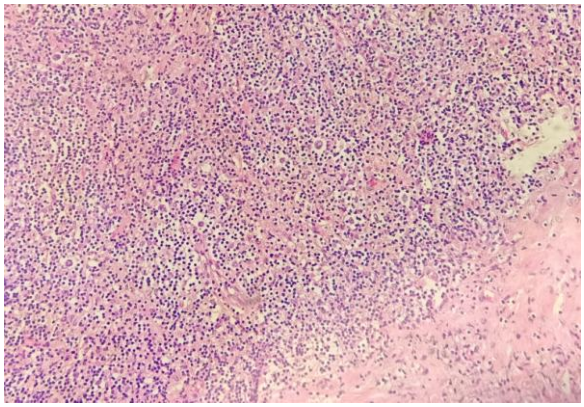
However, she deteriorated with development of fever and dyspnea. Ultrasound guided ascitic tapping showed transudative picture with a low ADA and protein which was against TB. Samples sent for AFB smear, gene expert and AFB culture were negative. Other possibilities considered were sarcoidosis and Carcinoma Breast presenting as granulomatous lesion. Considering the gender, age and background history of polyarthralgia, autoimmune etiology was also considered. Workup done for the same was negative. Over the following days as her counts continued to fall with worsening pancytopenia, LFT and PT INR, it was decided to go ahead with excision biopsy of lymph node. Cytology report of lymph node biopsy revealed Nodular lymphocyte predominant Hodgkin's lymphoma which was confirmed with IHC (positive for CD20, PAX-5, OCT-2, some cells were weakly positive for CD30; negative for CD3, CD15)

A PET CT scan was done for staging which suggested metabolically active extra nodal lymphomatous deposits - stage IV disease involving liver, spleen and bone. Her family wanted to continue further treatment from nearby hospital due to personal reasons. Hence, she was discharged and started on R-CHOP in the outside hospital.

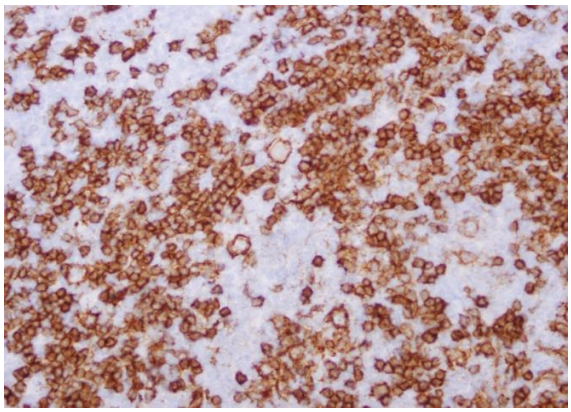
LAB INVESTIGATIONS

Table No: 1

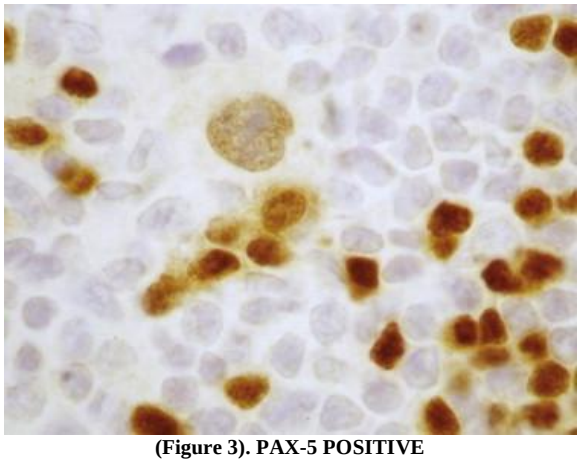
Lab	Reference Range (Unit)	
WBC-Blood	4.0 - 10.0 (K/uL)	6.1
NEU-Blood	60.0 - 80.0 (%)	61
LYM - Blood	20.0 - 40.0 (%)	30.3
MONO -Blood	2.0 - 10.0 (%)	8
EOS-Blood	1.0 - 8.0 (%)	0.2
BASO-Blood	0.0 - 2.0 (%)	0.5
RBC-COUNT-Blood	3.8 - 4.8 (M/uL)	4.17
HGB-Blood	12.0 - 15.0 (g/dl)	12.1
HCT-Blood	36.0 - 46.0 (%)	36.4
MCV-Blood	88.0 - 101.0 (fL)	87.3
MCH-Blood	27.0 - 32.0 (pg)	29
MCHC-Blood	18.0 - 48.0 (g/dl)	33.2
RDW-Blood	11.6 - 14.8 (%)	23.3
PLT-COUNT-Blood	150.0 - 400.0 (K/uL)	111
MPV-Blood	6.8 - 10.0 (fL)	10.5
Bilirubin Total -Serum	0.0 - 1.1 (mg/dl)	3.02
Bilirubin Direct - Serum	0.0 - 0.2 (mg/dl)	1.65
Protein, total-serum	6.4 - 8.3 (g/dl)	4.6
Albumin; serum	3.5 - 5.2 (g/dl)	3.1
Globulin	2.5 - 4.0 (g/dl)	1.59
AST (SGOT) - serum	0.0 - 32.0 (IU/L)	72.6
ALT [SGPT]-serum	0.0 - 33.0 (IU/L)	39.8
ALP[Alkaline Phosphatase]-serum	0.0 - 105.0 (IU/L)	191.0
PT[Prothrombin Time with INR]-Plasma		26.50/14.0/2.21
Urea - Serum	15.0 - 40.0 (mg/dl)	14.4
Creatinine;-Serum	0.0 - 0.9 (mg/dl)	0.79
CRP (C-reactive protein) (Ultrasensitive)	0.0 - 1.0 (mg/L)	6.1
ESR [Erythrocyte Sedimentation-Blood	8.0 - 20.0 (mm/hr)	5
LDH [Lactate dehydrogenase]-Serum	0.0 - 247.0 (U/L)	309
Ferritin -Serum	15.0 - 150.0 (ng/ml)	774.40
Triglycerides -Serum		106.6
Fibrinogen		151.8
Cell count, misc. fluids		TC:-89 Cells/mm3
Pleural fluid ADA		2.9
Pleural fluid LDH		27
Pleural fluid Protien		0.61
Coombs test direct		Negative
Coombs test indirect		Negative
Anti CCP	0.0 - 17.0 (U/ml)	<7
ACE	16.0 - 85.0 (U/L)	103.30
ANA Screen (IFA)		Negative
Anti HCV - Emergency Screen		0.04 : Non-reactive
HBs Ag Test - Emergency Screen		0.23 : Non-reactive
HIV - Emergency Screen		0.16 : Non-reactive



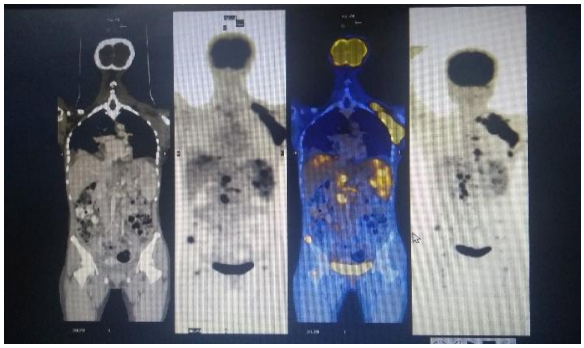
(Figure 1). Excision Biopsy of lymph node showing large atypical cells, fibrotic bands in lymphocyte background



(Figure 2).CD 20 POSITIVE



(Figure 3). PAX-5 POSITIVE



(Figure 4).WHOLE BODY PET CT showing FDG uptake in multiple supra and infra diaphragmatic lymph nodes, liver and spleen, left breast & left latissimus dorsi

DISCUSSION

Granulomatous lesions and lymphadenopathy are a common clinical problem leading to difficult diagnoses and sometimes incorrect treatment putting the patient at risk of adverse drug reactions and delayed diagnoses. In our case the young lady was initially diagnosed to have a tuberculous lymphadenitis which was treated with ATT. The basis for starting ATT was due to the clinical picture and FNAC of lymph node showing caseous granulomatous lesion with tuberculosis being one of the most common etiologies for the same. However, she did not respond in that her lymphadenopathy continued to persist and she started developing complications of ATT. After completion of intensive phase she developed transaminitis which did not respond adequately even on stopping ATT and starting her on modified regimes. Retrospectively it is possible that the transaminitis was due to the lymphomatous infiltration of the liver. Her subsequent deterioration in clinical condition with worsening lymphadenopathy while on modified ATT with the development of cytopenias and breast mass made us consider alternate diagnoses. Once again the trucut biopsy of the breast mass revealed a granulomatous inflammation pattern and was reported as highly consistent with the possibility of tuberculosis. However, her cultures and gene expert sent from the tissue samples were negative. Development of multiple site effusions while on modified ATT with persistent breast mass and raised liver enzymes prompted us to search for an alternate explanation. Sarcoidosis and fungal infections were also considered in the differentials but KOH smears of the samples were negative for fungal hyphae and serum ACE levels were only mildly elevated. Since granulomatous lesion due to any etiology can cause elevation of the ACE levels, we did not want to start steroids without a definite explanation for the symptoms. Moreover, sarcoid liver and

effusion presenting as sarcoid are rare entities. Pleural fluid study was suggestive of a transudative pattern in contrast to what was expected in disseminated tuberculosis. As the suspicion of the possibility of a non tuberculous cause for the lymphadenopathy was high we went ahead with the option of lymph node biopsy which eventually revealed the Hodgkin's lymphoma via IHC confirmation. This case report is being published as the presentation of Hodgkin's lymphoma as a granulomatous lesions in the breast, liver and axillary and cervical lymph nodes is very rare.

Hodgkin's disease presenting as epithelioid granuloma has been reported previously in literature. But such cases are very rare. Hodgkin's disease is usually confined to the lymph nodes. [(4)] Extra nodal involvement is much less common in Hodgkin's disease than in non-Hodgkin's disease. [(4)] Hepatic involvement is seen in 6-20% of patients. It usually has diffuse involvement, discrete nodular lesions being present only in 10% cases. [(4)] Hodgkin's disease of the liver almost invariably associated with disease of spleen. Nodular liver disease are characteristically hypo echoic at ultrasound and CT. [(4)] Hodgkin's lymphoma is rarely found in the breast. Mammary involvement is often the result of direct extension from axillary or mediastinal lymph nodes [(5,6)] a part of regional disease with discontinuous axillary node involvement [(7,8)] or a manifestation of systemic disease. [(9)] Wood and Coltman reviewed 354 reported cases of extra nodal Hodgkin's lymphoma published prior to 1973, and found 8 cases that also involved in the breast. [(10)] About 13% of the cases have pleural involvement in the form of pleural effusions. [(11)] The present case describes the involvement of lymph nodes, breast, liver, spleen and pleura.

CONCLUSION

The presentation of granulomatous disease in an endemic region is commonly accepted as diagnosis of Tuberculosis, especially in resource poor settings. However, the possibility of alternative diagnosis must always remain in clinician's mind, especially if microbiological confirmation is not obtained. Thereforeit's always better to go ahead with an excision biopsy rather than FNAC or core biopsy.

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