

Case Series: Mediastinal Mass Misdiagnosed As Extra Pulmonary Tuberculosis.

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Abstract: Lymphoma is a malignant disorder which is arising from cells of the lymphoid tissue. It commonly presents with lymphadenopathy and constitutional symptoms of fever, weight loss and night sweats. However, atypical presentations like extra nodal involvement can also be there. With regard to the varied clinical picture, especially in HIV-positive patients, symptoms may mimic other diseases, particularly tuberculosis (TB).

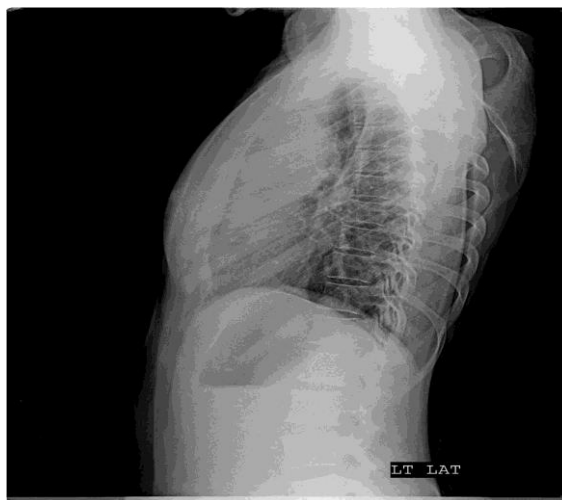
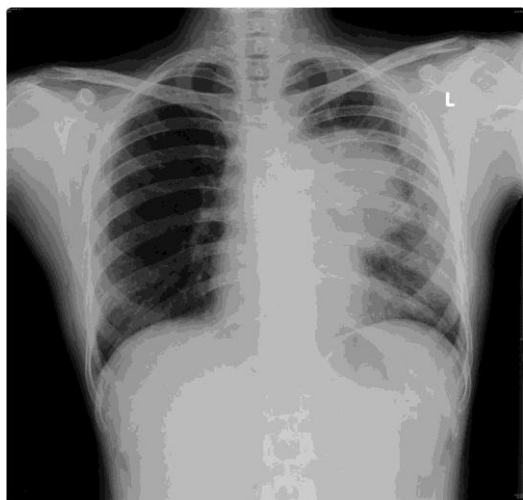
Three cases of non-Hodgkin's lymphoma (NHL) which were initially misdiagnosed as extrapulmonary TB are presented here. They both were initially treated with Antitubercular treatment (ATT) from other health care setups with no remission of symptoms. Clinical examination and investigations revealed mediastinal masses in these cases, on further biopsy and immunohistochemistry, diagnosis of Non Hodgkin's lymphoma was made.

Case 1 History

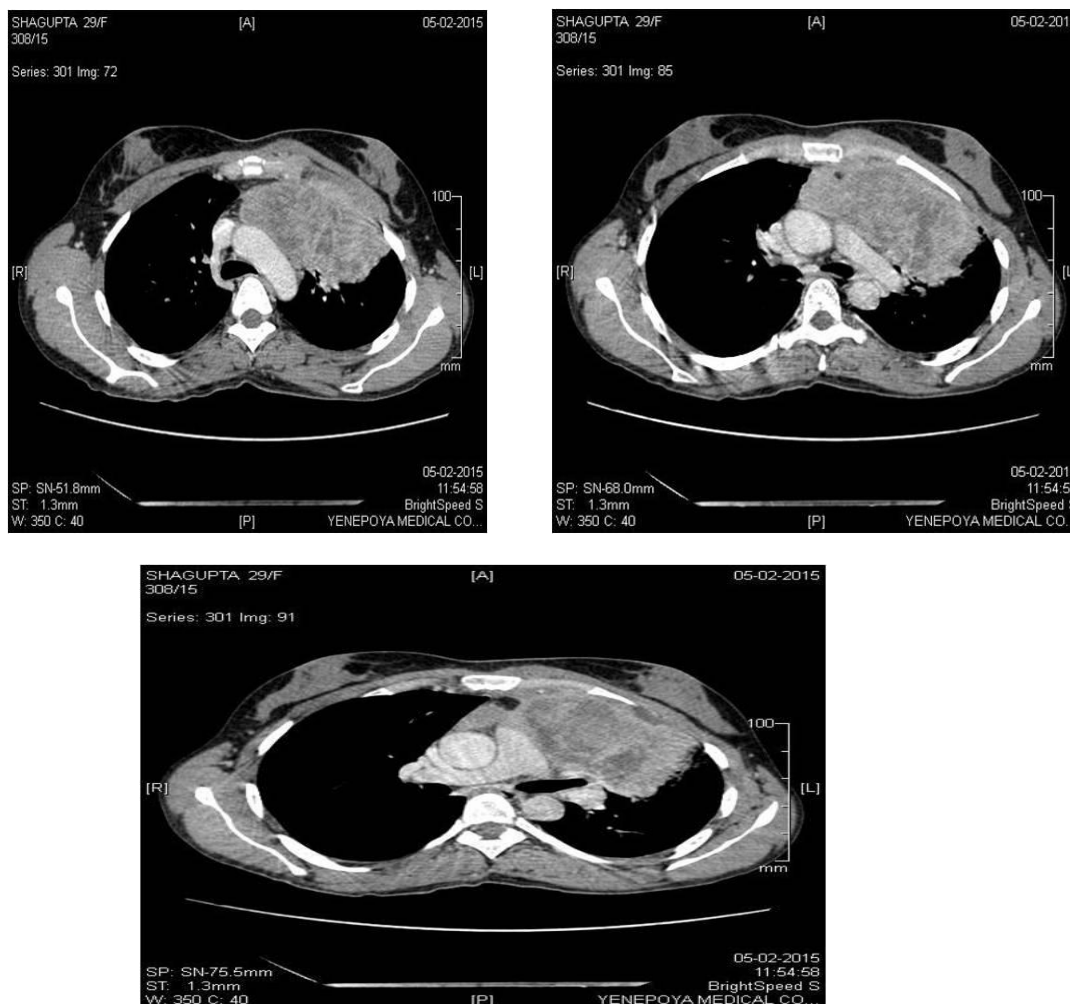
A 29 year old female presented with cough with expectoration, chest pain, low grade fever and weight loss of 7- 8 months duration. Patient was evaluated at a centre elsewhere and was started on ATT private regimen which she took for 5 months.

Physical Examination & Investigations

- Clinical examination showed solitary hard tender swelling of 2x2 cm over the parasternal area in the left 2nd intercostal space. Dullness was noted in the left mammary, inframammary and axillary areas with reduced breath sounds in the same areas.
- Routine blood investigations and sputum examination were unremarkable except for the raised total leukocyte count with neutrophilia.
- A chest X-ray showed homogenous well defined opacity in left perihilar area, with hilum overlay sign positive on the left side. The lesions had progressed when compared with previous xrays.
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- Ultrasound abdomen was normal.
- A computed tomography scan of the thorax revealed heterogeneously enhancing mass lesion in the anterior mediastinum extending from anterior mediastinum into posterior chest wall abutting manubrium sterni and posteriorly abutting the arch of aorta and pulmonary trunk. The lesion in mediastinum was seen abutting the pericardial sac on the left side suggestive of a malignant deposit.



- Bronchoscopy showed patent airways with normal mucosa overlying them.No endobronchial lesion was seen.
- CT guided FNAC showed features of germ cell tumour or a lymphoma.
- CT guided biopsy was planned and showed predominantly medium to large lymphoid like population with background dispersed small cells. Large cells had scant cytoplasm and nucleus appeared hyperchromatic with irregular nuclear outline and inconspicuous nucleoli.
- Immunohistochemistry studies with PanCK, CD45, CD20, CD30, CD3 was done , which showed large cells negative for cytokeratin and positive for CD45.CD3 showed scattered small cell positivity.CD20 and CD30 showed strong positivity in the large tumour cells.

Diagnosis:

A diagnosis of diffuse large B cell lymphoma was made.

Treatment Plan

Patient was started on Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone

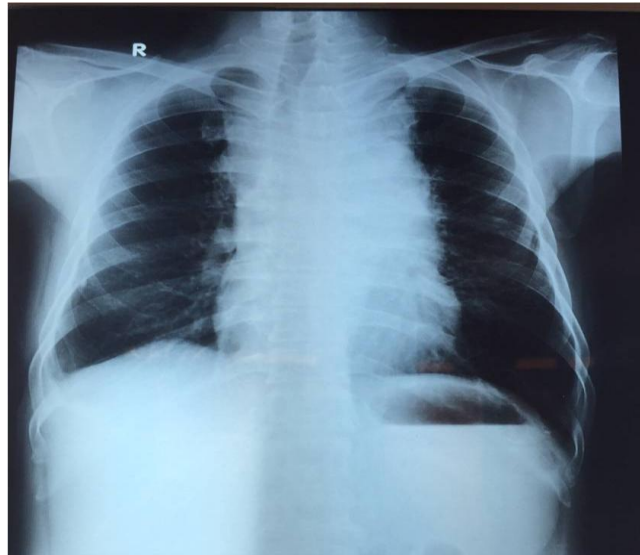
Case 2

History

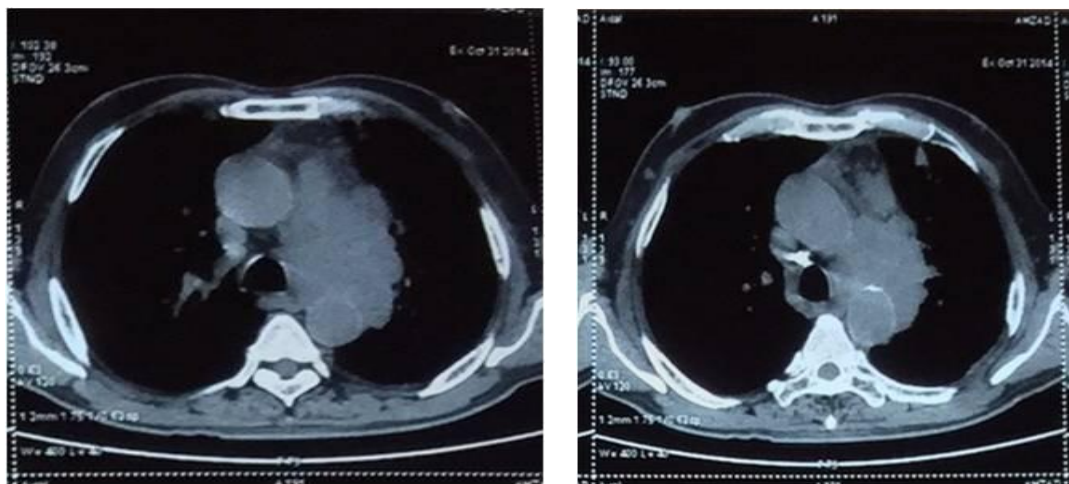
A 59 year old man presented with cough with expectoration and hemoptysis , chest pain, dyspnea , low grade fever , weight loss, loss of appetite and hoarseness of voice of 3- 4 months duration. He was a smoker , but now stopped.He is a known case of Type 2 diabetes mellitus and is on oral hypoglycemic drugs .He was diagnosed as sputum negative pulmonary tuberculosis and started on CAT 1 Private regimen from other centre, with no remission of symptoms.

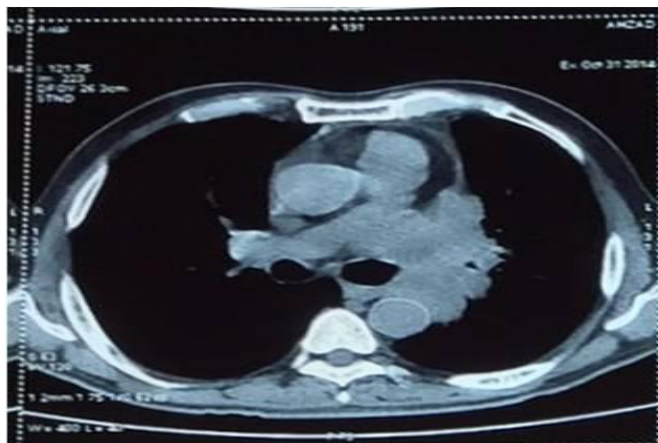
Physical Examination & Investigations

- General physical examination including vitals were normal except for a level 1b group of 2x2 cm firm hard lymph node. Respiratory system examination revealed diffuse crepitations and rhonchi. Abdominal examination were within normal limits.
- Sputum examination and routine blood investigations were normal .
- Chest X-ray showed widening of the upper mediastinum with hilar prominence and hilum overlay sign negative on the left side. Cervicothoracic sign was positive on left side.
- CT Thorax showed an ill defined heterogenous lesion in prevascular space, left hila, precarinal and para aortic region with significant post contrast enhancement, which was suggestive of either a tubercular or neoplastic lymphadenopathy. Calcified right hilar lymphadenopathy was also seen.



The CT features were suggestive of tubercular or neoplastic lymphadenopathy.





- USG abdomen, pelvis and scrotal region was done to rule out testicular involvement and was normal.
- Bronchoscopy showed patent airways with normal mucosa overlying them. No endobronchial lesion was seen.
- CT guided FNAC showed sheets of large lymphoid cells with scant cytoplasm, hyperchromatic nucleus and predominant nucleoli in some. Many mature lymphocytes were seen mixed with larger cells, which were features suggestive of Non Hodgkins Lymphoma.
- Bone marrow aspiration biopsy showed no malignant cells.
- Patient was also planned for CT guided biopsy of mediastinal mass. But it was not done due to worsening of patients general condition

Diagnosis:

Finally, the patient was diagnosed as a case of non hodgkins lymphoma .

Treatment Plan

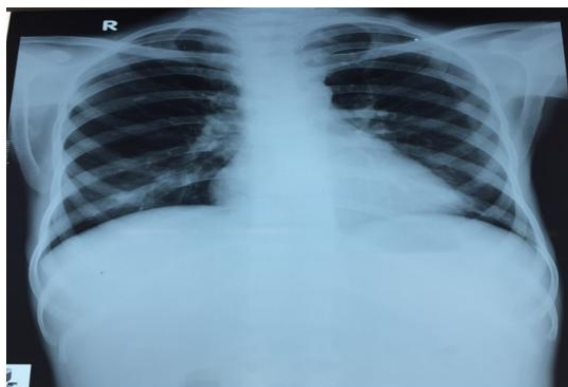
- Patient was started on Cyclophosphamide, Vincristine, Doxorubicin and Prednisolone (CHOP regimen) and was in good health at follow up.

Case 3

A 27 year old female presented with cough with expectoration, breathlessness, low grade fever, loss of appetite, loss of weight, periorbital swelling and generalized lymphadenopathy of 7- 8 months duration. Patient was evaluated at a centre elsewhere and was diagnosed with TB lymphadenopathy and was started on ATT private regimen which she took for 5 months.

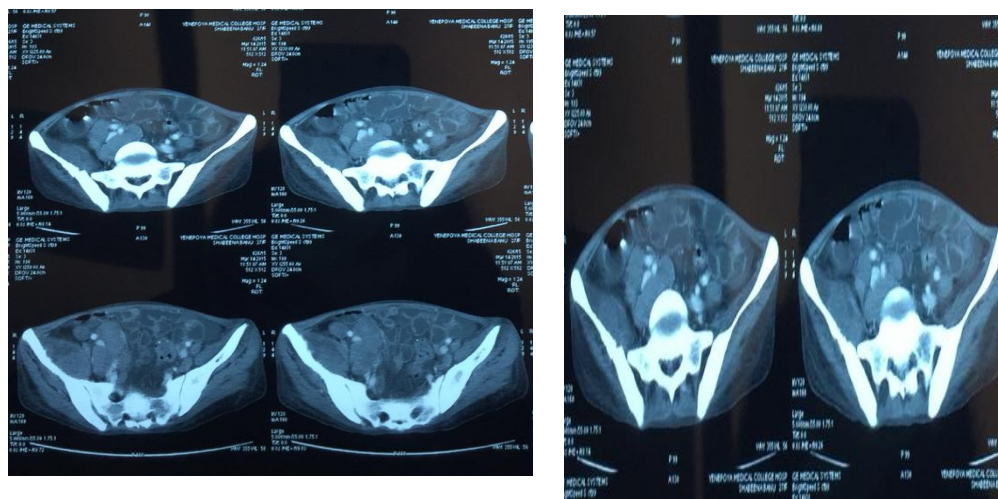
Physical Examination & Investigations

- Clinical examination showed multiple lymph nodes over cervical and over left inguinal area. Chest examination appeared to be normal.
- Routine blood investigations showed anemia with neutrophilia and elevated LDH.
- Peripheral blood smear showed mild normocytic normochromic anemia.
- Sputum examination - normal
- Chest X-ray appeared to be normal



- USG abdomen showed few enlarged mesenteric lymph nodes in lower abdomen, mild ascites, mild splenomegaly and cystitis.

- A computed tomography scan of the thorax and abdomen revealed enlarged lymph nodes in retroperitoneal region, right iliac and right inguino-femoral region with central necrotic area and in the lower jugular, right upper and lower pretracheal, precarinal and right hilar regions- residual disease. Collection extending along the iliopsoas muscle with periosteal reaction of iliac bone. Splenomegaly, mild ascites.



- Bronchoscopy showed patent airways with normal mucosa overlying them.No endobronchial lesion was seen.
- CT guided FNAC was suggestive of germ cell tumour or lymphoma.
- CT guided biopsy showed total effacement of lymph node architecture. The node is replaced by diffuse sheets and nodules of large to intermediate cells. The individual cells had enlarged nuclei, occasional binucleate cells with prominent eosinophilic nucleoli were also seen. Few cells had moderate to abundant cytoplasm. Areas of geographic necrosis were also seen.
- Immunohistochemistry report: Large cells were positive for CD-30 and LCA negative for cytokeratin, CD-20 & S-100. Interspersed population of CD-3 positive cells also seen.

Diagnosis:

A diagnosis of Anaplastic large T-cell lymphoma was made.

Treatment Plan

Patient was started on Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone

I. Discussion

Non-Hodgkin's lymphoma (NHL) consists of a diverse group of malignant neoplasms variously derived from B cell progenitors, T cell progenitors, mature B cells, mature T cells, or (rarely) natural killer cells. It is a disease of old age usually between 60-80 years with 5% cases showing mediastinal involvement¹.

The incidence of Non-Hodgkin's lymphoma is more than Hodgkin's lymphoma with a male predominance. The incidence of B-cell Non-Hodgkin's lymphoma is about 80-85% and that of the T-cell is 15-20%¹. In 2010, an estimated 65,540 new cases of NHL were diagnosed and 20,210 patients died of the disease². NHL is the sixth leading site of new cancer diagnoses among men and women, accounting for 4% of new cancer cases and 4% of cancer-related deaths². The different staging includes, Stage I with involvement of single LN region (I) or extra lymphatic site (IAE), Stage II: Two or more LN regions involved (II) or an extra lymphatic site and lymph node regions on the same side of diaphragm. Stage III: Involvement of lymph node regions on both sides of diaphragm, with (IIIE) or without (III) localized extra lymphatic involvement or involvement of the spleen (IIS) or both (IISE). Stage IV: Involvement outside LN areas (Liver, bone marrow)³.

Painless lymphadenopathy, often cervical region is the most common presentation. Hepatosplenomegaly is another finding. Extranodal involvement includes Intestinal lymphoma (abdominal pain, anemia, dysphagia); CNS (headache, cranial nerve palsies, spinal cord compression); skin; testis; thyroid; lung; bone marrow (low grade) and pancytopenia⁴.

Systemic symptoms include sweating, weight loss and itching. Metabolic complications are hyperuricemia, hypercalcemia, renal failure. Compression syndrome: gut obstruction, ascites and SVC obstruction⁵.

Clinical / Working Formulation classification of Non-Hodgkin's lymphoma are low grade, intermediate grade and high grade⁶. Low grade Non-Hodgkin's lymphoma has low proliferation, indolent

course, absence of symptoms and not curable. High grade Non-Hodgkin's lymphoma has high proliferation, rapid, fatal course if untreated, with manifestation of symptoms and potentially curable.

Etiology cannot be attributed to a single cause. Chromosomal translocations: t(14, 18), infections like viral (EBV, HTLV, HHV-8, HIV), bacterial (H. Pylori - Gastric lymphoma), immunological like congenital immunodeficiency, HIV, organ transplantation all play a role⁷.

Laboratory evaluation includes Complete blood counts, Liver function tests, Uric acid, Calcium, Serum protein electrophoresis, Serum β -microglobulin, Serum lactate dehydrogenase, Chest Xray, CT scan of abdomen, pelvis, & chest, Bone marrow biopsy, Biopsy and immunohistochemistry, Lumbar puncture in lymphoblastic, Burkitts and diffuse large B cell lymphoma with positive marrow biopsy, gallium scan (SPECT) or PET scan in large cell lymphoma¹.

Management of low grade NHL, when asymptomatic requires no treatment. For Stage 1 localised disease radiotherapy is required. Chemotherapy is the mainstay of treatment for intermediate or high grade lymphomas. The main regimen includes CHOP which includes - Cyclophosphamide, Doxorubicin Hydrochloride, Vincristine and Prednisolone, given every 3 weeks, for at least 6 cycles^{8,9}.

For Chlorambucil, Initial response is good, but it has got repeated relapses with a median survival of 6-10 yrs. Another drug is Fludarabine, 2-CdA (Chlorodeoxyadenosine) and monoclonal antibody Rituximab is widely used now a days. In case of high risk cases with poor prognostic factors or relapse, high dose chemotherapy combined with autologous bone marrow transplantation or stem cell transplantation is indicated. With CNS involvement or leukemic relapse, treatment similar to acute lymphocytic leukaemia is given^{8,9,1}.

Prognosis of Non Hodgkin's lymphoma varies according to the severity of the disease. Low grade lymphoma has a median survival period of 10 yrs. Increasing age, advanced stage, concomitant disease, raised LDH, T-cell phenotype are all poor prognostic indicators in high grade Non Hodgkin's lymphoma.

II. Conclusion:

The present cases highlight the importance of ascertaining tissue diagnosis rather than instituting empirical anti TB treatment. Nodal involvement of lymphoma could be misleading as extrapulmonary TB especially for TB endemic setup, hence if patient is not improving with antitubercular medication alternative diagnosis should be ruled out before considering as non responding or drug resistant case.

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