# Diffuse Large B-Cell Lymphoma in Obese: How Physical Examination Unlocked the Mystery

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**Abstract**

Although difficult to perform a good physical examination in morbidly obese patient, it can still be very valuable like in our patient in whom biopsy of deep lymph nodes seen was benign but superficial lymph node excisional biopsy found due to good physical exam diagnosed diffuse large B-cell lymphoma.

*Title*: Diffuse Large B-Cell Lymphoma in Obese: How Physical Examination Unlocked the Mystery

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*Abstract:*

Although difficult to perform a good physical examination in morbidly obese patient, it can still be very valuable like in our patient in whom biopsy of deep lymph nodes seen was benign but superficial lymph node excisional biopsy found due to good physical exam diagnosed diffuse large B-cell lymphoma.

*Keywords:* Diffuse large B-cell lymphoma, physical exam, supra-clavicular lymph node

*Key message:*

Bedside thorough physical examination in an inexpensive and valuable diagnostic tool. Superficial lymph node excision biopsy is one of the best methods to diagnosed diffuse large B-cell lymphoma.

*Manuscript text*

**Introduction:**

Diffuse large B-cell lymphoma is a non-Hodgkin lymphoma (NHL) and constitute about a third of all NHL lymphomas. It arises from a mature B cell. Patients usually present with rapidly enlarging symptomatic mass. They can also have "B" symptoms such as fever, weight loss and night sweats. Evaluation is best made by excisional tissue biopsy such as superficial lymph nodes. Diagnosis can sometimes be challenging when no superficial lymphadenopathy is seen. Herein, we present a case of rapidly enlarging symptomatic lung masses with extensive workup including mediastinal lymph node biopsy which was negative for DLBCL. Initially, PET scan did not show any superficial lymphadenopathy. Eventually, thorough physical examination helped in unveiling the diagnosis by excision biopsy of superficial lymph nodes.

**Presentation:**

51-year-old morbidly obese female (BMI 47.8 kg/m2) with history of type-2 diabetes mellitus and polycystic ovarian syndrome presented with chest tightness, wheezing, dyspnea, dry cough and low-grade fever in November 2019. She had no history of tobacco or alcohol use. Her examination at that time revealed no obvious abnormality. No palpable lymphadenopathy. Laboratory indices were within normal limits except white cell count of 13,000/μL with absolute neutrophil count of 11,000/μL (normal range [NR], 1600-7700/μL) and absolute lymphocyte count (ALC) of 1120/μL (NR, 1300-3200/μL). Computed tomography (CT) demonstrated bilateral pulmonary masses with diffuse bilateral hilar and mediastinal adenopathy, and mild splenomegaly. (Figure 1A) Lung mass on right side measured 4x4 cm and left side 3x3 cm. Serum calcium, vitamin D and angiotensin converting enzyme levels were within normal limits. CT guided needle biopsy of left hilar mass and mediastinal lymph node returned negative for malignancy. Flow cytometry of biopsy specimen showed normal lymphoid cell population. Lung parenchyma showed dense fibro-collagenous tissue with focal alveolar plugs (Masson bodies). She was empirically treated for pneumonia and was discharged home.

In February 2020, she presented for a follow-up PET-CT scan which showed hypermetabolic bilateral lung masses with standardized metabolic activity (SUV) of 11.8. (Figure 1B, 1C) Multiple mediastinal lymph nodes were hypermetabolic with a left para-tracheal lymph node measuring SUV of 5.1. Previously biopsied lymph node was noted to have an SUV of 1.4 only, thus explaining possibility of obtaining biopsy from an unaffected lymph node. Endobronchial ultrasound guided needle biopsy of mediastinal lymph node and left lung mass was then performed which again returned negative for malignancy. At that time, she was started on prednisone 20 mg per day for presumed sarcoidosis.

In May 2020, she presented again with worsening of similar symptoms. Repeat CT scan of Chest showed increase in size of the lung masses with left measuring 5x5 cm and right mass measuring 6x6 cm. (Figure 1D, 1E) Due to persistent concern of malignancy, patient was prepared for open mediastinal lymph node and lung mass biopsy under general anesthesia. She developed hypoxemia and respiratory arrest during the procedure. She was successfully resuscitated, and the procedure was aborted. She was eventually discharged home with no plans to reattempt biopsy due to high risk of peri-operative mortality.

In July 2020, she had dyspnea and hypoxemia with saturations of 87% on baseline 2 liters of supplemental oxygen. She reported night sweats and a weight loss of 28 pounds in the past one and a half months. On examination, her respiratory rate was 29/minute with oxygen saturations 95% on 5 L. She appeared in mild respiratory distress. Bilateral wheezing was heard. Laboratory tests showed hyperglycemia with blood sugar 450 mg/dL (NR, 70-99 mg/dL) and hyperkalemia of 5.8 mmol/L (NR, 3.5-5.1 mmol/L). White cell count was elevated at 14,000/μL with neutrophilia and low ALC of 570/μL. C-reactive protein 14.86 mg/dL (normal <0.5 mg/dL). Levofloxacin was started for presumed pneumonia. She tested negative for SARS-Cov-2 virus. Repeat chest CT scan showed enlarging pulmonary and hilar masses bilaterally with

moderate splenomegaly and mesenteric lymphadenopathy. Mediastinal adenopathy appeared worsened with right para-tracheal lymph node conglomerate measuring 4.6 x 4.5 cm.

Differential diagnosis is still broad in a patient with multiple negative biopsies. The suspicion of malignancy was still high due to new presentation of unintentional weight loss, night sweats and increasing size of lung and hilar masses. Primary lung cancer, lymphoma, mediastinal tumor, and fungal infections were all in the differentials. Infectious workup including blood cultures, urine cultures, sputum cultures were negative. Microbial cell-free DNA test was also negative for any pathogens in the serum.1 Two days after admission, on a careful bedside examination by third year medical student, supraclavicular lymphadenopathy was noticed. Neck CT confirmed multiple superficial and deep left neck cervical lymph nodes with largest measuring 1.9 x 1.5 cm. (Figure 1F) General surgery team performed an excisional lymph node biopsy under local anesthesia. Biopsy showed presence of diffuse large B-cell lymphoma (DLBCL) with cells positive for CD20, CD21, CD30 and PAX-5. (Figure 2) Immunohistochemistry demonstrated dual expression for BCL2 and MYC proteins. Fluorescence in situ hybridization (FISH) studies on the biopsy specimen confirmed rearrangement of BCL6. No rearrangement of MYC or BCL2 and no fusion of MYC and IGH was observed. Bone marrow biopsy did not reveal lymphomatous involvement. Final diagnosis was confirmed to be stage 4, DLBCL, non-germinal center B-cell type. Our patient received 6 cycles of R-CHOP regimen and tolerated it well with minor complications of grade 2 peripheral neuropathy and transient immune thrombocytopenic purpura. Follow up PET-CT scan showed significant reduction in hyper-metabolic activity in the hilar regions and right upper lobe mass area.

**Discussion:**

DLBCL is a non-Hodgkin lymphoma (NHL) and constitute about a third of all NHL lymphomas.[2],[3] DLBCL is further divided into two categories - germinal cell or non-germinal center type which has prognostic implications but not therapeutic.[4] Presentation at stage 3 or 4 at the time of diagnosis is commonly seen.[4] In morbidly obese patients with thick neck, lymph node examination is significantly challenging whether axillary, inguinal, or cervical nodes. Subcutaneous fatty tissue nodules are common in obese patients which frequently puzzles clinicians. Careful examination in our patient revealed lymph nodes in the neck which eventually proved to be the diagnostic clue and unveiled the whole disease process. As her PET-CT was negative for supraclavicular lymphadenopathy 5 months ago, it is likely that our patient developed this recently. The superficial lymphadenopathy was the cornerstone in reaching to the final diagnosis in our case. Another important fact to remember is the relative ease of obtaining superficial lymph node biopsy and preferably performing excisional lymph node biopsy when lymphoma is suspected.[4] A simple but effective examination technique by medical student proved immensely beneficial from patient care standpoint in our case. Due to high peri-procedural risk in morbidly obese patients, a surgical biopsy of lung masses under general anesthesia can be challenging. Recommended first line therapy is R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, Vincristine, and prednisone).[4] Benign residual masses after treatment completion are common. Prognosis is poor without treatment, but cure rate is as high as 90% in treated patients.[5]Our patient went into cardiac arrest during mediastinal biopsy, where procedure had to be aborted and confirmative diagnosis was delayed. In future, authors recommend, focus should also be paid in developing improved protocols to attain mediastinal biopsy in morbidly obese patients who are at high risk for peri-procedural complications.

**Conclusion:**

Physical exam in morbidly obese patients is difficult. Procedure related complications are higher in morbidly obese population due to baseline compromised respiratory status which can be associated with obstructive sleep apnea or obesity hypoventilation syndrome. Empiric diagnosis when not responding to treatment should be questioned and further workup to pursue alternate diagnosis should continue until a definite diagnosis is confirmed. A careful and thorough bedside physical examination can prevent physicians from ordering extensive unnecessary testing saving significant healthcare resources.

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*Figure legends*

**Figure 1.** A. CT scan of the chest from November 2019 showing bilateral lung masses (red arrow); B,C. PET-CT scan from February 2020 showing hypermetabolic bilateral lung masses; D,E. CT scan of the chest from May 2020 showing enlarging bilateral lung masses; F. CT scan of the neck from July 2020 showing left supraclavicular and anterior cervical lymphadenopathy (yellow arrow).

**Figure 2.** Left supraclavicular lymph node excision biopsy specimen histologic sections. Hematoxylin and Eosin (H&E) stain reveal solid sheets of atypical lymphoid infiltrate consisting of large atypical lymphoid cells with scattered mitoses and frequent apoptosis. (Panel A, low resolution; Panel B, high resolution); The atypical lymphoid cells are positive for CD20 (Panel C) and PAX-5 (Panel D).