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Case report

Expecting the unexpected – Primary mediastinal large B cell lymphoma presenting as huge lung parenchymal mass

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ABSTRACT

The first possibility considered in the etiology of large lung masses is neoplastic lesions. The differential diagnoses of these masses include bronchogenic carcinoma, pulmonary sarcoma, primitive neuroectodermal tumor etc. Primary or secondary pulmonary parenchymal lymphomas presenting as large mass is distinctly rare. We share the case of a young lady who presented with a large left lung mass almost entirely replacing the left lung parenchyma, with associated intrathoracic lymphadenopathy. On evaluation she was proved to have primary mediastinal large B-cell lymphoma. Treatment with an aggressive chemotherapy regimen led to complete remission of the parenchymal and nodal disease. The uncommon radiological presentation and the excellent therapeutic response despite huge tumor load merit clinical attention.

1. Introduction

A lung mass is defined as a well circumscribed fairly rounded lung parenchymal lesion greater that 3 cm in the greatest dimension. Although the etiology of lung masses is many and varied, lung carcinoma is a frequent and concerning possibility. The probability of the lesion being malignant increases with increasing size, although some benign lesions can reach large size. Although uncommon, malignant pulmonary parenchymal lymphoproliferative diseases can present as nodules and masses.

Lung parenchymal involvement by lymphoma can be primary or, much more commonly, secondary [1,2]. Primary pulmonary lymphomas account for 0.5% of primary malignancies involving the lung. The malignant lymphoproliferative disorders that can have primary pulmonary origin include extranodal marginal zone lymphoma of MALT origin (MALT lymphoma), diffuse large B-cell lymphoma (DLBCL), lymphomatoid granulomatosis etc. While primary involvement is uncommon, secondary parenchymal involvement is encountered much more frequently. Non-Hodgkin lymphoma (NHL) is encountered more frequently in this fashion and accounts for 80–90% of all cases with secondary lung involvement. Almost 50% of these patients have intrathoracic involvement detectable at first visit itself. Lung involvement occurs in 24% of NHL [3]. Primary mediastinal large B-cell lymphoma (PMLBCL) is a less frequently encountered, but not rare, clinicopathological entity. It has been assigned as a distinct entity in the updated WHO classification of Lymphoid Malignancies [4]. Involved patients are typically young ladies with disease origin in the mediastinum. Features of local invasion are conspicuous.

Primary or secondary lung parenchymal involvement by lymphomatous process presenting as large mass (>10 cm) is distinctly rare. PMLBCL usually presents as an anterior mediastinal lesion. We report the case of a young lady who presented with a large left lung mass, thoracic and cervical adenopathy, chest wall invasion and pleural involvement who on evaluation had a final diagnosis of PMLBCL. Despite the extensive tumor bulk, she responded well to aggressive chemotherapy and remains disease free.

1.1. Case report

A 24 year old lady with no comorbid illnesses presented to us with 12 kg weight loss and dry cough of 4 month duration. She also had fever, progressive shortness of breath and bilateral knee pain of 1 month duration. In the wake of the current covid 19 pandemic, she chose not to physically attend hospitals and took symptomatic medications based on telemedicine consultations. Worsening symptoms forced her to seek medical care and she attended the emergency department of our hospital. On admission she was febrile, dyspnoeic and tachypneic. Physical evaluation revealed a breathless patient with a respiratory rate of 24/

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minute and moderate work of breathing. Breath sounds were absent in the entire left hemithorax with stony dull note on finger percussion. She was hypoxic with a room air oxygen saturation of 94% measured by finger oximetry. Neck examination detected bilateral firm supraclavicular lymphadenopathy and lower limb eczematous lesions were made out. She had no organomegaly and higher mental functions were normal. No past history of tuberculosis or contact history was present. Her menstrual cycles were regular.

A posteroanterior Chest radiograph taken at admission revealed a uniformly opaque left hemithorax with contralateral mediastinal shift (Fig. 1). After stabilization and collection of blood samples she was sent for CT evaluation of thorax. CT images revealed a huge heterogeneously enhancing soft tissue density mass lesion occupying the entire left hemithorax (Fig. 2a and b). Except for a small patch of aerated lung in the left lower lobe, the left lung was not separately delineated. Enlarged nodes were seen in the perivascular, subcarinal, supraclavicular and left axillary regions. Extra thoracic extension of the mass lesion into the anterior chest wall and left breast was noted. Small left pleural effusion and minimal pericardial effusion was seen with nodular deposits. (Fig. 3 a and b). Focal erosion of left anterior 3rd rib was made out (Fig. 4). Peripheral blood smear revealed microcytic hypochromic anemia with neutrophilic leucocytosis and mild lymphocytopenia. Renal, liver and thyroid functions were normal. Serum LDH level was elevated.

Based on the history and imaging findings a malignant etiology was highly probable and the differentials entertained were bronchogenic carcinoma (with mediastinal lymph node spread and chest wall invasion), lymphoma with parenchymal and pleural involvement, Askins tumor, pulmonary sarcoma, primitive neuroectodermal tumor, germ cell tumor like teratoma etc. She subsequently underwent trucut biopsy from the right supraclavicular nodes and the left lung mass. Core biopsy samples revealed sheets of medium to large sized lymphoid cells containing abundant pale cytoplasm with round to ovoid vesicular nuclei and nucleoli. (Fig. 4a). Scattered mitotic figures and foci of necrosis were noted. The neoplastic cells were separated into compartments by fibrous tissue. Scattered small lymphocytes and small clusters of histiocytes were also seen. The neoplastic cells were diffusely positive for CD20 (Fig. 4b and c). They were also positive for CD23, MUM1 (50%), CD10 (80%) and BCL2 (70%). They were focally positive for CD30 and were negative for CD3, CD15, CMYC and BCL6. Patchy positivity for EBV – LMP1 was seen. A final pathological diagnosis of Primary mediastinal large B - cell lymphoma was made. CSF evaluation was negative for lymphomatous involvement. Bone marrow aspiration and biopsy showed no evidence of bone marrow involvement by lymphomatous process.A CT done for staging purposes revealed no infradiaphragmatic disease.

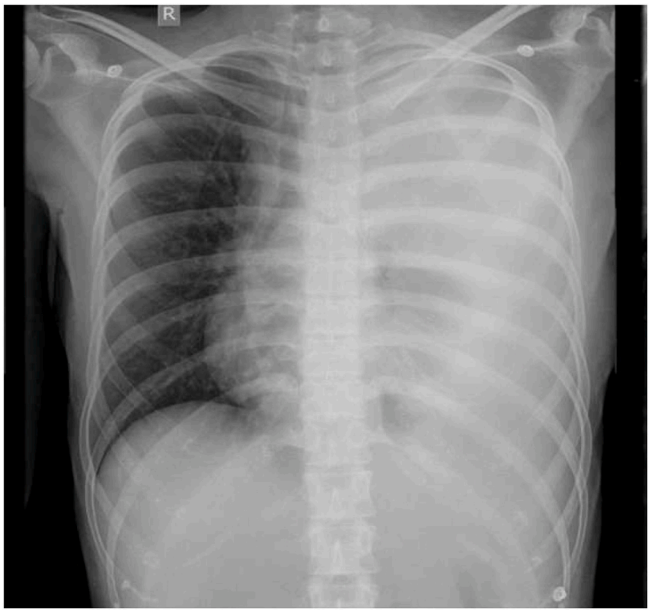

Fig. 1. Chest x ray (PA view): Near total homogenous opacification of the left hemithorax. Mediastinal shift to right side is noted.

The patient and family were counselled in detail about the diagnosis and she was initiated on R – DA - EPOCH chemotherapy protocol and CNS prophylaxis with intrathecal methotrexate. In view of the current COVID -19 pandemic and critical clinical nature, ovum preservation was deferred after discussing with family and she was started on monthly Leuprolide injection during the time of chemotherapy for 4–6 months. She had excellent clinical improvement with resolution of fever and dyspnoea. Serial chest radiographs and interim CT revealed significant resolution of thoracic disease (Figs. 5b and 6) with only residual soft tissue thickening remaining in the mediastinum. The remaining lesions were FDG non-avid representing metabolically quiescent residual lymphoma.

2. Discussion

A pulmonary mass lesion is radiologically defined as a well circumscribed intraparenchymal rounded lesion greater than or equal to 3 cm in greatest dimension [5]. A variety of benign and malignant diseases can present with parenchymal nodules or masses, although the possibility of malignancy increases with increasing lesion size [6]. In carcinoma lung, the staging increases as the lesion size increases and is associated with worse prognosis [7]. Large lung masses (>10 cm in size) are usually neoplastic in etiology although a some benign lesions [8–10] can grow up to this size. The usual differentials of large neoplastic lung masses include bronchogenic carcinoma, sarcomas, primitive neuroectodermal tumours, blastomas, metastatic lesions, lymphomas etc [11, 12].

PMLBCL is an uncommon tumor that accounts for 2–3% of all NHL [13]and 6%–10% of all Diffuse Large Cell Lymphoma [14]. Excellent reviews of the entity are available [15]. PMLBCL normally presents as a large conglomerate rapidly growing lesion in the anterior mediastinum. Local compressive symptoms including superior vena cava syndrome make the patient seek clinical attention in most cases. The rapid growth and compressive symptoms result in relatively early presentation and detection, so that at diagnosis, most patients (around 80%) have stage I or 2 disease. The duration of symptoms is almost always less than 3 months. The mediastinal lesion is typically bulky, being over 10 cm in about 70–80% of patient. Infiltration of surrounding tissues including the lung, chest wall, pleura, and pericardium is a prominent feature. Pleural or pericardial effusions are noted in around 30% of cases. Breast oedema is common. Although the lesion has early local infiltration, distant spread is seldom seen at presentation. Evidence of metastasis to marrow or cerebrospinal fluid involvement is uncommon. Elevated LDH levels are observed in 70%–80% of cases.

An anterior mediastinal mass is the classical imaging finding, better appreciated and delineated in CT scans of the neck and thorax than a plain radiograph. Posterior mediastinal or subcarinal masses are encountered less commonly [16]. Pleural or pericardial effusions can occur and pericardial effusions are markers of poor prognosis in PMLBCL [17]. Acute pancreatitis due to pancreatic involvement of PMLBCL has been described rarely [18]. The conglomerate lymph node lesions have areas of low-attenuation in CT, indicating variable degrees of hemorrhage, necrosis, or cystic degeneration [19]. FDG PET/CT after initial diagnosis is useful to identify extra mediastinal distant spread and disease staging [20]. On completion of treatment regimen, persistent findings are often present and difficult to differentiate from active disease. FDG PET is valuable in distinguishing fibrotic tissue or necrosis from active tumor [21].

The diagnosis is made by the morphological and immunohistochemical features of a biopsy specimen. The notable features of PMLBCL are a diffuse proliferation of medium to large B-cells in the background

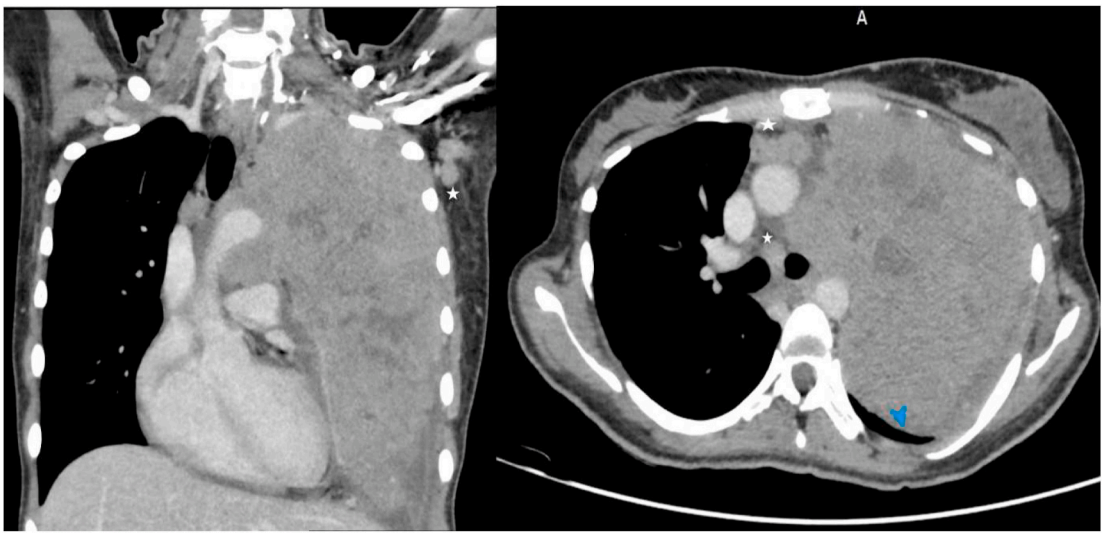

Fig. 2. (a, b): Post contrast CT thorax images in coronal and axial sections. Heterogeneously enhancing mass lesion replacing the left lung. A small patch of aerated left lower lobe was noted (blue arrow).Enlarged perivascular, subcarinal and left axillary nodes seen (white stars).

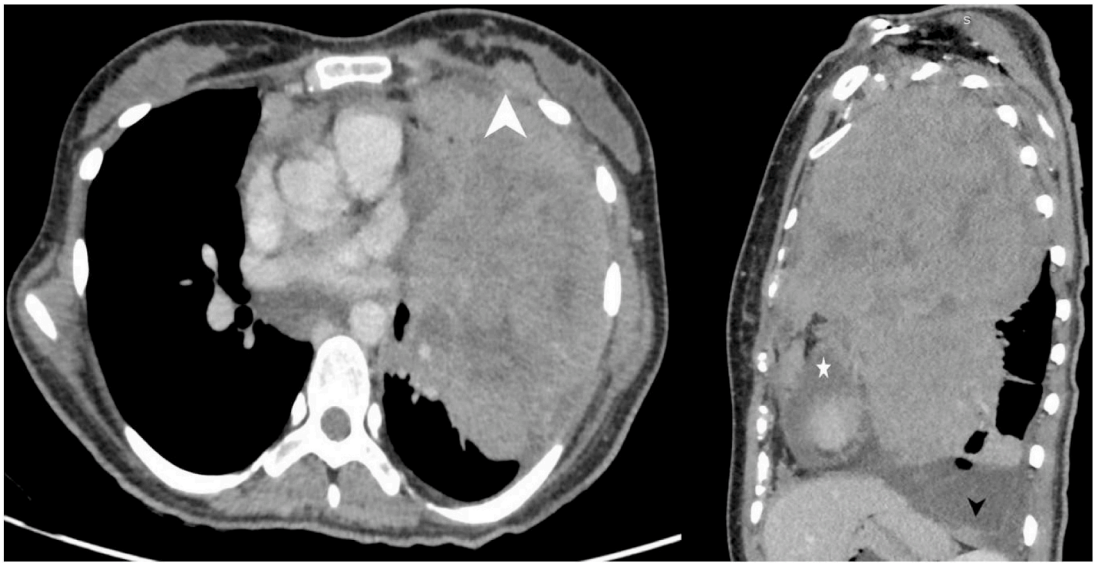

Fig. 3. (a, b): Post contrast CT thorax images in axial and sagittal sections. Extra thoracic extension into left breast seen (White arrow head). Pericardial (star) and pleural effusion with deposits noted (Back arrowhead).

of considerable sclerosis. The sclerotic reaction is visible as thin strands of reticulin fibres surrounding groups of neoplastic cells. Neoplastic cells have polymorphic nuclei and a wide rim of cytoplasm which is clear or slightly basophilic. In > 50% of cases, there are conspicuous collagen bands that give a sense of compartmentalisation. PMLBCL expresses B-cell-related antigens such as CD19, CD20, CD22, CD79a, PAX5 and CD45. CD30 staining is prominent in approximately 80% of cases, although staining is faint and less homogeneous than in classic Hodgkin Lymphoma (cHL) and anaplastic large cell lymphoma (ALCL). Neoplastic cells exhibit BCL2 (55–80%) and CD23 (70%), whereas the expression of BCL6 is less constant (45–100%). CD10 is usually negative (8–32%) and CD15 is present very occasionally. MAL protein positivity is documented in about 70% of cases. EBV positivity is unusual in PMLBCL, adding uniqueness to the present case.

PMLBCL being an uncommon entity, there has been a paucity of prospective trials to establish the best treatment regimen. Although individual institutional protococols vary, a rituximab and anthracycline–containing regimen is preferred in most centers. Dose-intensive regimens obviating the need for radiation have been increasingly investigated in the last decade. Avoiding the need for radiation is particularly handy, considering remote consequences, including breast cancer and cardiovascular disease. A phase 2 trial of DA-EPOCH-R (dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, rituximab) without radiation was recently undertaken in PMBCL. 5-Year EFS of 93% was observed among 51 patients [22]. Yet another multicenter retrospective study of DA-EPOCH-R observed a 3-year EFS of 87% in 118 adults [23]. Considering the superior clinical end points with DA-EPOCH-R, many hospitals have adopted this as the standard of care for PMBCL; prospective multicenter studies are encouraged to replicate and consolidate these results.

3. Conclusion

We describe the case of a young lady in her third decade who presented with a large left sided lung mass with pleural effusion, pericardial effusion, mediastinal adenopathy and chest wall invasion which on

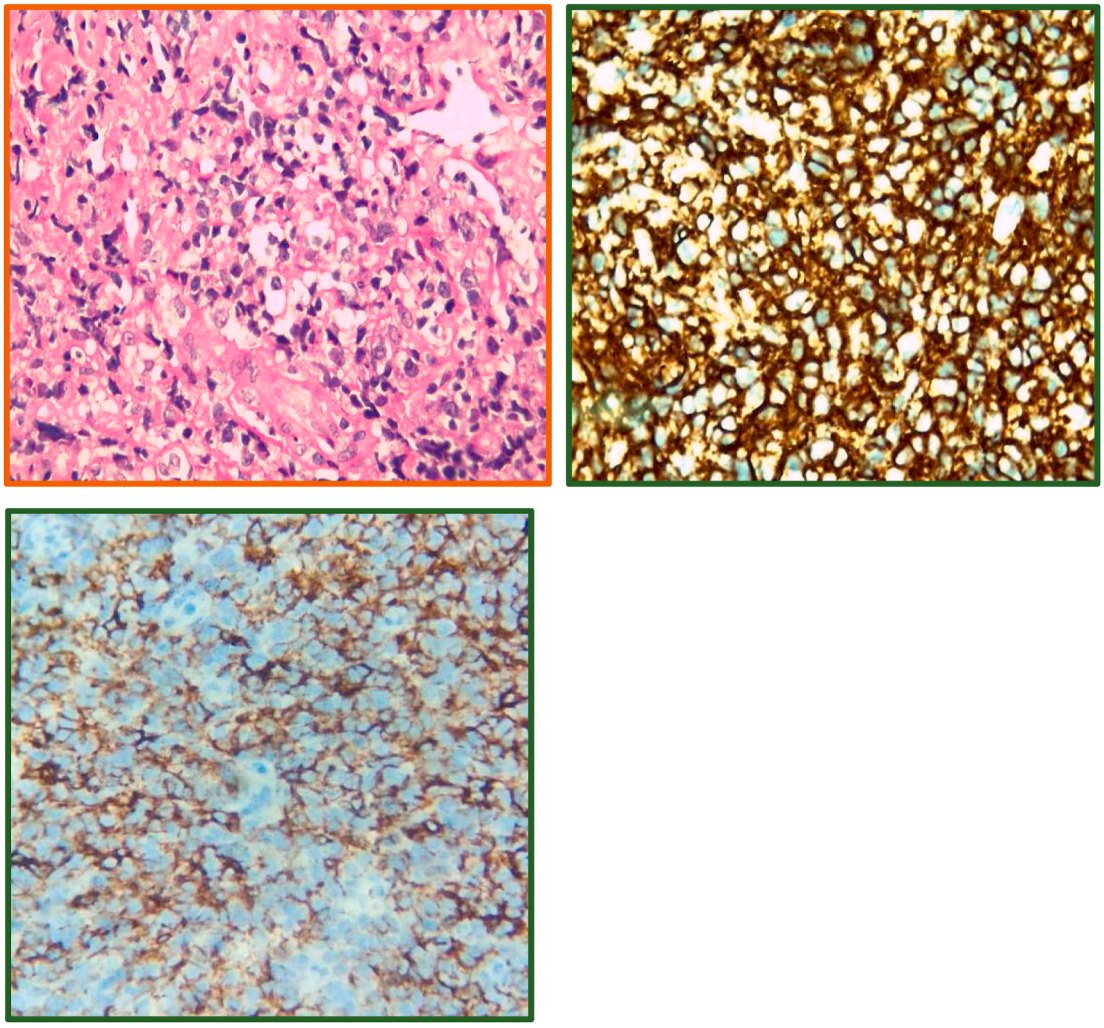

Fig. 4. a, b and c – Histopathology images of the biopsy specimen from left lung. (a - H&E stain high power showing sheets of medium to large sized lymphoid cells with abundant pale cytoplasm, round to ovoid vesicular nuclei with nucleoli. Neoplastic cells separated into compartments by fibrous tissue; b – Immunohistochemistry with CD 20 positivity; c – Immunohistochemistry with CD 23 positivity).

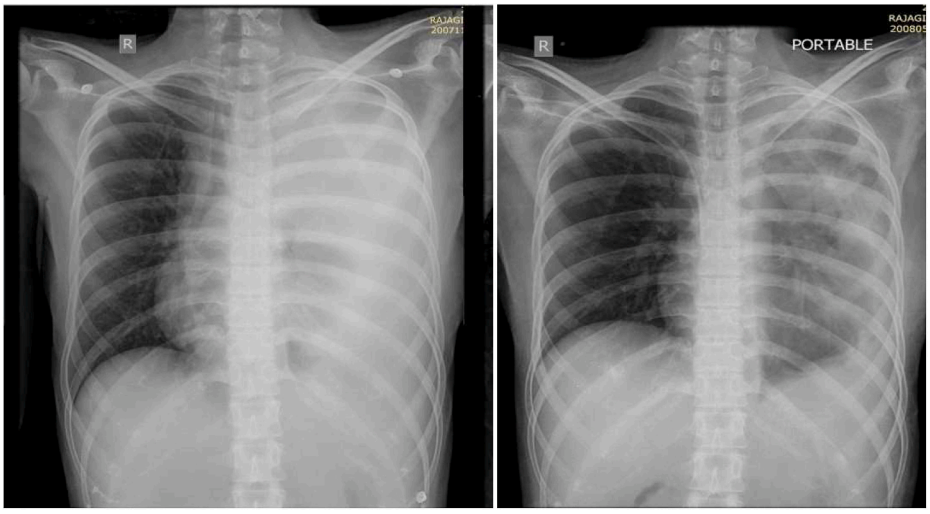

Fig. 5. a and b. Chest x ray at presentation compared with that after 3 cycles of chemotherapy show partial clearance of the mass lesion from the left hemithorax with increase in lung aeration.

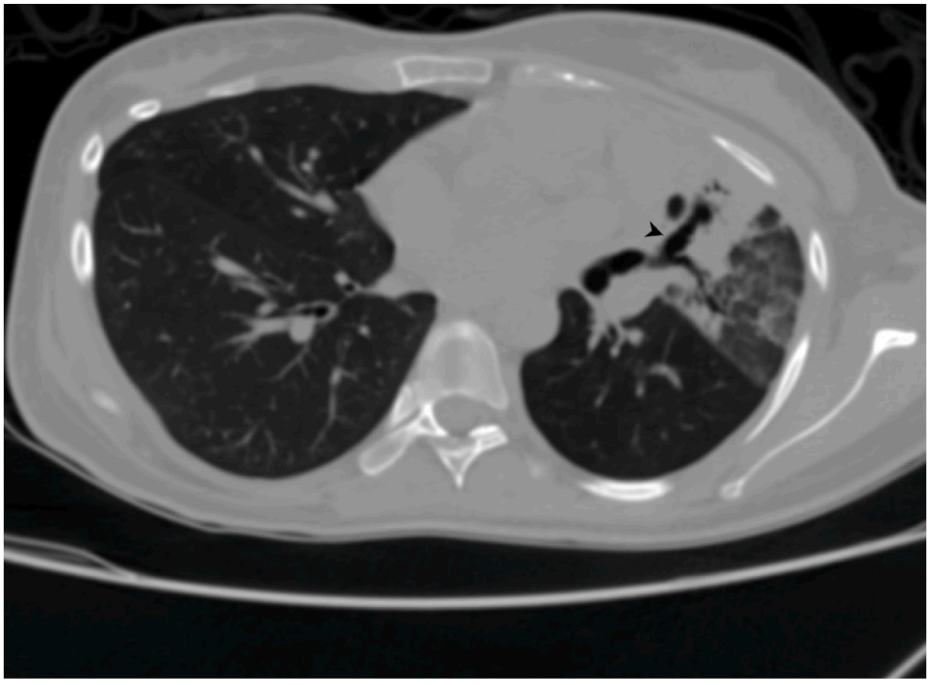

Fig. 6. Limited CT sections taken during the course of treatment showing areas of traction bronchiectasis (black arrow head), cicatricial atelectasis and minimal persisting residual disease.

biopsy and pathological evaluation was diagnosed to be PMLBCL. Positivity for EBV is unusual in PMLBCL, but was noted in our case. She had an excellent response to R-DA-EPOCH regimen based chemotherapy with complete remission of the disease. The case is noteworthy due to the rare radiological presentation as a huge lung mass and chest wall invasion. The excellent response to therapy despite bulky disease also deserves attention. Finally, the delay in treatment seeking behaviour of patients imposed by fear about Covid 19 is distressing from a clinical stand point.

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