Primary Clear Cell Carcinoma of Lung Presented with Generalized Lymphadenopathy Mimicking Lymphoma

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Abstract
Primary Clear cell carcinoma of lung with distant metastasis is a rare tumour. Here is a case of 45 year old male presented with gradual onset dyspnoea, low grade fever and weight loss. Radiologically patient had hilar and parahilar lesion at posterior mediastinum with mild changes of chronic obstructive pulmonary disease with right supraclavicular, peripancreatic and celiac axis lymph nodes enlargement. Fine needle aspiration from lymph node followed by excision biopsy was done. For further localization Fibre optic Bronchoscopy was done which is followed by bronchial wash cytology and transbronchial needle aspiration and bronchial biopsy. Correlating all above diagnostic modalities diagnosis of metastatic clear cell adenocarcinoma of lung was made which is further supported by Immunohistochemistry.

Introduction
Clear cell adenocarcinoma is an extremely rare lung tumor composed predominantly or exclusively of clear cells. All lung carcinomas with greater than 50% of clear cells despite the presence of focal glandular or squamous differentiation are presently grouped as clear cell carcinoma. Histopathologically, this tumor must be differentiated from metastatic renal cell carcinoma, benign sugar tumor of the lung, predominant squamous mucoepidermoid carcinoma, and myoepithelial tumor. Immunohistochemical staining of tumor cells facilitates the differential diagnosis of these entities. Because of the low metastatic potential of these lesions and their rarity of recurrence, the role of chemotherapy for these lesions is dubious.

Case Report
A 45 years old male farmer presented with gradual onset, progressively increasing shortness of breath, occasional blood tinged sputum around four to five episode per week, low grade fever, significant loss of appetite and weight loss of around 8 kg since six month. He denied any history of hoarseness, dysphagia, voice disorder and backache. General examination revealed pallor and soft, bilateral multiple cervical lymph nodes of which maximum size was 4 cm× 3 cm without any evidence of clubbing, limb edema, and cyanosis or dilated veins.

Complete blood count showed hemoglobin of 10.8 gm% with mild leucopenia and normal platelet count. Peripheral smear for Cell Morphology is apparently negative for any precursor of hematological malignancy. Complete biochemical renal analysis did not reveal any abnormality. Several Enzymes level were found to be impaired like Serum lactate dehydrogenase-21,400 unit and Serum Alkaline phosphatase- 340 IU. X-ray chest showed hilar and parahilar shadow in posterior mediastinum with changes of chronic bronchitis. Ultrasonography of Abdomen showed generalized lymphadenopathy in the form of peripancreatic, celiac and aorto and porto caval axis without any mass lesion in kidney or any affection to liver and gastro intestinal tract. CT- scan neck region showed enlarged lymph node – 16 × 26 mm in right supraclavicular region. CT – scan of thorax up to adrenal show moderately enhancing large hypodense mass with lobular outline predominant in posterior mediastinum inferior to carina, indenting and displacing the

Fig. 1: CT scan abdominal section showing extensive lymphadenopathy
left atrium and pulmonary vein anteriorly. Mass measured approximately 80× 66 mm extending along parabronchial regions bilaterally in aorta pulmonary window, aortocaval region and paracaval region. Considering lymphadenopathy clinically lymphoma was strongly suspected (Figure 1).

Fine needle aspiration of lymph node, Trans bronchial needle aspiration and bronchial wash were done. On Light Microscopy Fine needle aspiration of lymph node showed clusters of cells with pleomorphism forming glandular pattern with palisading of nuclei in hemorrhagic background suggesting metastatic lesion from adenocarcinoma of lung. Fibre Optic Bronchoscopic mediated Transbronchial needle aspiration smears showed normal bronchial lining cells with few atypical cells. Bronchial wash fluid showed few atypical cells.

Histopathology of lymph node biopsy, Haemotoxylin and Eosin stained section showed total effacement of lymph node architecture, cell borders were distinct and cytoplasm was watery clear or foamy and at places faintly eosinophilic granular. Nuclei were round with open chromatin pattern, Moderate number of mitosis were seen. No stratification or keratinization and no intercellular bridges were seen (Figure 2).

Histopathology of Transbronchial needle aspiration showed malignant epithelial cells along vascular core (Figure 3) while that of Bronchoscopic biopsy showed hyperplastic bronchial lining and disrupted at places with sub mucosal tissue showing infiltration of inflammatory cells. Many atypical cells with clear or granular cytoplasm with marked nuclear pleomorphism, variation. Some cells were binucleated. The cell arrangements were lobular and trabecular placed along vascular channels. At places cells formed palisades pattern at periphery of clusters. Periodic acid Schiff stained with diastase were negative and without diastase is positive (Figure 4). So, final diagnosis offered was clear cell adenocarcinoma of lung excluding metastasis from renal cell carcinoma.

For further Immuno-histochemistry was done which showed CK7, CK, EMA were positive and CD-10, TTF-1 were negative which strongly suggest the diagnosis. Moreover these cells were negative for the marker of renal cell carcinoma, the thyroid transcription factor-1 expressed by alveolar pneumocytes, and the neuroendocrine markers chromogranin and synaptophysin.

Discussion

Lung cancer is currently the most frequently diagnosed major cancer and the most common cause of cancer mortality in males worldwide. Clear cell carcinoma of the lung is defined by the World Health Organization as “an anaplastic large cell tumour forming nests and clusters and sheets of cells with large vesicular nuclei and abundant clear or foamy cytoplasm which may or may not contain glycogen”. No mucin is present and this category does not include squamous cell carcinoma or adenocarcinoma with clear cells. The resemblance of such tumours to carcinoma of kidney may give rise to diagnostic problems.

In 1955, Walter and Pyrce first drew attention to carcinoma of the lung composed predominantly or entirely of clear cells. In 1980, the existence of tumour as a distinct subtype was questioned by Katzenstein et al who reviewed 348 consecutive cases of pulmonary carcinoma and found 15 that contained over 50% clear cells.
Primary carcinoma of lung with clear cell change, secondary renal adenocarcinoma and clear cell adenoma of lung (sugar tumour) show similar histological structure and contain cytoplasmic glycogen. The distribution between these tumours, which is important in relation to their management and prognosis, may be impossible in small biopsies where the availability of tissue permits multiple sections should be examined for evidence of mucus secretion and squamous differentiation. Clear cell tumours have been described in patients with tuberous sclerosis in association with lymphangiomatomatosism and microndular pneumocyte hyperplasia. Some suggest they are part spectrum of so called perivascular epithelioid cell tumours (PEComas).

The development and implementation of Immunohistochemical (IHC) methods have revolutionized the practice of diagnostic pathology. IHC is now a days great help to differentiate the various origin of tumour. IHC shows most clear cell to be strongly positive with melanoma antigen, HMB45, NSE, Synaptophysin and CD57. It also help to differentiate it from the clear cell carcinoma of kidney which can metastasize to lung, as tumour of kidney has positivity for Vimentin and CD10 and negativity for CEA, CD15 and BerEP4.

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References