DOI: 10.7860/JCDR/2021/48758.15292

Case Report

Oncology Section

Hepatoid Adenocarcinoma of Lung Presenting as Unknown Primary with Cervical Lymphadenopathy: A Rare Case Report

GANDHAVALLI ANUSHA[1], BALA VENKAT SUBRAMANIAN[2], PRANABANDHU DAS[3], TC KALAWAT[4], ARUNA K PRAYAGA[5]

ABSTRACT

Hepatoid adenocarcinoma is a rare Alpha Fetoprotein (AFP) producing extrahepatic malignant tumour commonly seen in the stomach but can also arise from the ovary, endometrium lung. It is a rare type of adenocarcinoma with hepatocyte like histological differentiation and occurs outside the liver. In the lung, it is often presented as a bulky tumour, highly malignant, and associated with a poor prognosis. Early diagnosis and appropriate treatment options can result in long term survival. Here, authors reported a case of 58-year-old male patient, with no history of smoking presented as an Unknown Primary (UKP) with cervical and mediastinal lymphadenopathy which was later diagnosed histopathologically and confirmed by Immunohistochemistry (IHC) as Hepatoid Adenocarcinoma Lung (HAL) without any lesion in the lung on Computed Tomography (CT) chest. The serum AFP levels were normal. It expressed IHC markers Cytokeratin (CK7), CDX-2, Hep Par1 positivity, Thyroid Transcription Factor 1 (TTF-1) cytoplasmic positivity, and abnormally raised serum Carcinoembryonic Antigen (CEA). The patient was treated with definitive lower neck and mediastinal irradiation followed by adjuvant chemotherapy with five cycles of three weekly pemetrexed and carboplatin. Post treatment the serum CEA levels are decreasing and attained clinically complete response. The patient was in a close follow-up. To date, the review of literature about HAL didn't showed any case presented as UKP with neck nodes without any lesion in the lung. The purpose of this case report was to present a new case of HAL with nodal metastasis, its unique histological findings, and its approach to diagnosis and treatment.

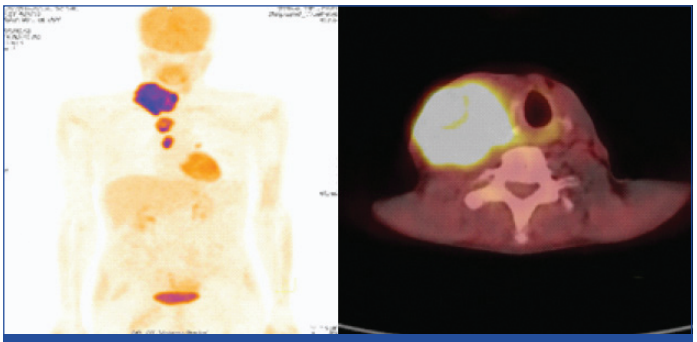
Keywords: Carcinoma lung, Hepatoid histology, Immunohistochemistry, Neck nodes, Positron emission tomography imaging

CASE REPORT

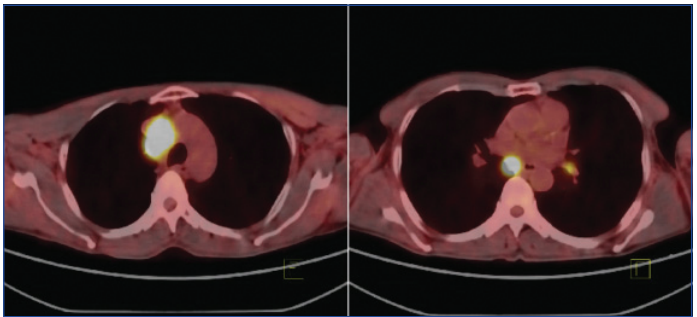
A 58-year-old male presented with right-sided neck swelling of two months duration to the Radiotherapy Outpatient Department (OPD). The patient was a non smoker, known hypertensive (on regular medication) and no other medical co-morbidities were reported. On clinical examination, approximately 6×6 cm firm to hard non tender swelling at level III and right supraclavicular region apparently fixed to underlying structures was seen.

Biopsy from the supraclavicular node showed metastatic adenocarcinomatous deposits. Immunohistochemistry (IHC) showed Cytokeratin (CK7) positive, CK20 negative, and Thyroid Transcription Factor 1 (TTF-1) positive. The CEA was abnormally raised (7103 ng/mL). Serum Alpha Fetoprotein (AFP) 5 ng/mL and Serum Prostate Specific Antigen (PSA) was 15 ng/mL which was within normal limits. On colonoscopy, rectum and colon showed normal mucosa. Indirect laryngoscopy of oropharynx, hypopharynx and larynx revealed no abnormal lesions.

On the Contrast Enhanced Computed Tomography (CECT) chest including neck, lung parenchyma, and pleural space were normal and there were enlarged lymph nodes at the right upper and lower paratracheal, aortopulmonary, subcarinal regions largest measuring 2.5×1.7 cm at the right upper paratracheal region. Normal thyroid gland and thyroid function tests were within normal limits. As the CEA levels were abnormally elevated and TTF-1 was cytoplasmic positive it was considered that primary origin from the lung. Hence, the patient was offered three cycles of three weekly paclitaxel and carboplatin chemotherapy following which the right cervical nodal mass progressed in size clinically and he developed obstructive symptoms like dysphagia to solids and dyspnoea. He was then referred to the Radiotherapy Department for an opinion regarding radiotherapy. On whole body Fluorodeoxyglucose-Positron Emission Tomography and Computed Tomography (FDG-PET/CT) to rule out metastatic disease and to assess post chemotherapy response that showed right-side level III, IV conglomerate lymphadenopathy [Table/Fig-1] and enlarged right upper and lower paratracheal, subcarinal lymph nodes [Table/Fig-2].

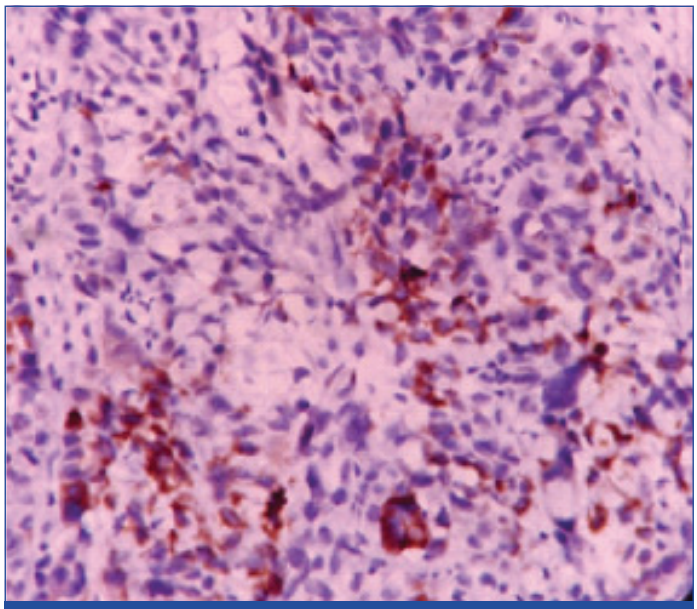


[Table/Fig-1]: Intensely increased fluorodeoxyglucose concentration noted in right level III and IV conglomerate lymph nodal mass with central necrosis measuring 6.2×8.1 cm with maximum standardised uptake value (SUV max) of 19.7.

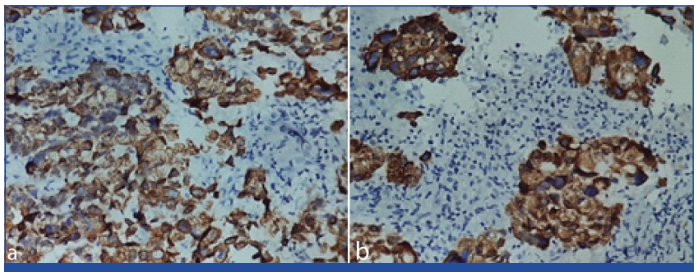


[Table/Fig-2]: Intensely increased fluorodeoxyglucose concentration noted at Right upper and lower paratracheal, subcarinal lymphnodes largest measuring 3.8×2.9 cm at right upper paratracheal region maximum standardised uptake value (SUV max) of 12.3.

Tracheostomy was performed because of stridor from obstruction due to nodal mass. As TTF-1 cytoplasmic positivity was an unusual occurrence unlike TTF-1 nuclear positivity in carcinoma lung and thyroid, multidisciplinary tumour board opinion was sought which suggested other IHC panels to rule out hepatoid variant of adenocarcinoma lung. Various IHC panels were undertaken that revealed TTF-1 cytoplasmic positivity [Table/Fig-3]. Hepatocyte Paraffin 1 (Hep Par1) positive, and CDX2 positive [Table/Fig-4a,b]. Napsin A expression and calcitonin was negative. Therefore, the diagnosis of hepatoid variant of adenocarcinoma lung was finally conferred.



[Table/Fig-3]: Immunohistochemistry (IHC) showing Thyroid Transcription Factor 1 (TTF-1) marker cytoplasmic positivity with 100X magnification.



[Table/Fig-4]: a) Immunohistochemistry (IHC) showing positivity for Hepatocyte Paraffin 1 (Hep Par1) (400X); b) Immunohistochemistry (IHC) showing positivity for CDX-2 (400X).

As there was no visible mass in the lung, patient was treated with definitive nodal irradiation with 66Gy in 33 fractions followed by five cycles of adjuvant three weekly pemetrexed and carboplatin chemotherapy. After six months, post radiotherapy, patient had achieved complete clinical response and better quality of life and symptomatically relieved.

DISCUSSION

Carcinoma of UKP is a heterogeneous group of tumours that present as metastatic deposits with no identified tumour at the primary site of origin. The UKP with cervical lymphadenopathy most commonly represents a primary in the head and neck region. But the involvement of lower deep cervical lymph nodes, mediastinal lymphnodes, and adenocarcinoma histology commonly associated with infraclavicular primary like lung or breast primary [1,2]. A 50-70% of UKP cases are adenocarcinomas, 20-30% poorly differentiated, 5-8% squamous cell carcinomas, and 2-3% undifferentiated type histology [3]. After a detailed workup by panendoscopy, Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) neck, abdomen/Positron Emission Tomography and Computed Tomography (PET-CT) Scans, and biopsy from the lymph nodes followed by IHC play an important role in diagnosing the primary site of origin and histological variant. The mainstay of management of a non metastatic UKP with neck nodes is surgical lymphnode dissection followed by adjuvant radiotherapy if indicated. If the disease is unresectable or in case of medical inoperability, definitive bilateral neck nodal irradiation with or without concurrent chemotherapy is the treatment of choice. Systemic chemotherapy is suggested in the case of locoregionally advanced tumours and metastatic cases [2]. An empirical platin and/or taxane based systemic chemotherapy is considered routinely which results in a poor outcome. But if a complete work-up with IHCs was done, it can able to tell the site of origin, then site specific chemotherapy can be given which results in better response and improved prognosis [3]. The IHC positive for TTF-1 and Napsin A is confirmative for adenocarcinoma lung. The Hep Par1 is the marker for hepatoid variance. Herein, authors report a case of a 58-year-old male patient who presented with cervical lymphadenopathy of UKP the diagnosis of which was finally confirmed as HAL having a possible occult primary in the lung.

Hepatoid adenocarcinoma is a rare AFP producing aggressive tumour most commonly arising from the stomach (63%) [4]. It can be detected in extrahepatic regions like the ovary, lung, endometrium, cervix, pancreas, and urinary bladder. The incidence in lung is 5% and uncommon is the extrahepatic site after the ovary which is 10%. The HAL is associated with a male predilection [4]. It is often presented with lymphadenopathy or distant metastasis at the initial presentation and associated with a poor prognosis [5]. The HAL histologically resembles hepatocellular carcinoma metastasised to the lung. The distinguishing characters between the two are mainly IHC. The HAL expresses tumour markers like CK7, Hepatocyte Paraffin 1 (Hep Par1), TTF-1, and CDX2 with elevated serum CEA levels [5,6]. Even though HAL is an AFP producing tumour, AFP expression is not a requisite for the clinical diagnosis of HAL [7]. Common clinical presentation of HAL is a large solitary lung tumour [5] but in the present case, there is no lesion in the lung and presented with lower cervical and mediastinal lymphadenopathy which is the rarest presentation. For solid lung tumours, surgical resection is the first treatment of choice [5]. But as there is no lesion in the lung, the present case was treated with empirical systemic chemotherapy at first which did not respond to treatment and became progressive. Later the patient was treated with radical neck irradiation which resulted in a near complete response followed by adjuvant chemotherapy as per IHC studies and achieved complete response.

CONCLUSION(S)

In the diagnosis of adenocarcinoma lung with cytoplasmic TTF-1 positivity, the possibility of HAL should be considered and IHC like Hep Par1 and CDX2 should be considered as a priority to confirm the diagnosis before proceeding to treat such an unusual neoplasm with curative intent.

REFERENCES

[1] Krishnamurthy A. Metastatic adenocarcinoma of unknown primary presenting with cervical lymphadenopathy: A diagnostic challenge. J Can Res The. 2017;13(3):599.
[2] Calabrese L, Jereczek-Fossa B, Jassem J, Rocca A, Bruschini R, Orecchia R, et al. Diagnosis and management of neck metastases from an unknown primary. Acta Otorhinolaryngol Ital. 2005;25(1):02-12.
[3] De Miguel AC, Cid RP, Trufero JM, Bernad IP, Urquizu LC, Cubero JH, et al. Gene expression profiling and its use in adenocarcinomas of unknown primary origin: A case report. Oncology letters. 2015;10(4):2657-61.
[4] Wang F, Weng Y, Geng J, Zhu J, Mi B, Zhou X, et al. A rare case of hepatoid adenocarcinoma in the lung and literature review: Case report. Curr Chall Thorac Surg; 2020;2:30. Available at: https://ccts.amegroups.com/article/view/36761/pdf.
[5] Grossman K, Beasley MB, Braman SS. Hepatoid adenocarcinoma of the lung: Review of a rare form of lung cancer. Respiratory Medicine. 2016;119:175-79.

[6] Haninger DM, Kloecker GH, Bousamra Ii M, Nowacki MR, Slone SP. Hepatoid adenocarcinoma of the lung: Report of five cases and review of the literature. Mod Pathol. 2014;27(4):535-42.

[7] Yang K, Jiang H, Li Q. Primary pulmonary hepatoid adenocarcinoma: A case report and review of the literature. Medicine (Baltimore). 2019;98(14):e15053.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Radiation Oncology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.
2. Professor, Department of Radiation Oncology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.
3. Associate Professor, Department of Radiation Oncology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.
4. Professor, Department of Nuclear Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.
5. Professor, Department of Pathology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Pranabandhu Das,
Associate Professor, Department of Radiation Oncology, Sri Venkateswara Institute of Medical Sciences University Cancer Centre, Tirupati-517507, Andhra Pradesh, India.
E-mail: daspranabandhu@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 08, 2021
- Manual Googling: Jun 16, 2021
- iThenticate Software: Jul 31, 2021 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Feb 06, 2021**
Date of Peer Review: **Mar 17, 2021**
Date of Acceptance: **Jun 18, 2021**
Date of Publishing: **Aug 01, 2021**