DOI: 10.7860/JCDR/2023/60366.17712

Case Series

Internal Medicine Section

Lung to Lung Cannon Ball Metastases: A Case Series on Primary Lung Malignancy

GOVIND SINGH RAJAWAT[1], MANOJ MEENA[2], AASHISH KUMAR SINGH[3], ARUN DUTT SHARMA[4], DEEPAK SUTHWAL[5]

ABSTRACT

Cannon ball metastases refer to large, well circumscribed, round pulmonary nodules like cannon balls that are scattered over both lungs, being a classical presentation of haematogenous tumour spread.Cannon ball pulmonary metastases are typically seen in the patients with choriocarcinoma or renal cell carcinoma. Rarely, pulmonary metastases with the same appearance may be secondary from prostate cancer, synovial sarcoma, endometrial carcinoma or haepatocellular carcinoma.The present case series is about six patients diagnosed with cannon ball metastases which occurred from primary lung carcinoma. Out of these six cases, three were of small cell carcinoma, two of squamous cell carcinoma and one of adenocarcinoma.The histopathology of all the cases was established by biopsy from the tumour site and appropriate treatment was started in the form of chemotherapy and radiotherapy as needed. Clinicians must investigate thoroughly for primary origin of cannon ball metastasis, though rare but lung cancer can present as this kind of metastasis.

Keywords: Choriocarcinoma, Chemotherapy, Lung cancer, Radiotherapy

INTRODUCTION

Lung cancer is the leading cause of mortality worldwide and according to 2018 Global Cancer Observatory (GLOBACON) report, lung cancer affected about 2.1 million persons (11.6% of all cancers) and caused 1.8 million deaths (which comprised 18.4% of all cancer related deaths; around 67,795 new cases of lung cancer have been reported from India which accounts for around 5.9% of all types of cancers [1].Adenocarcinona is the most common histopathological subtype followed by squamous cell carcinoma and small cell carcinoma being the least prevalent among all [2]. Lung to lung metastases may be associated with primary malignancy within the lung or may be of an extra pulmonary origin. A prompt follow-up of such patients by pathology, tumour markers and Contrast Enhanced Computerised Tomography (CECT) is suggested to clarify the origin of metastasis and early initiation of treatment.

CASE SERIES

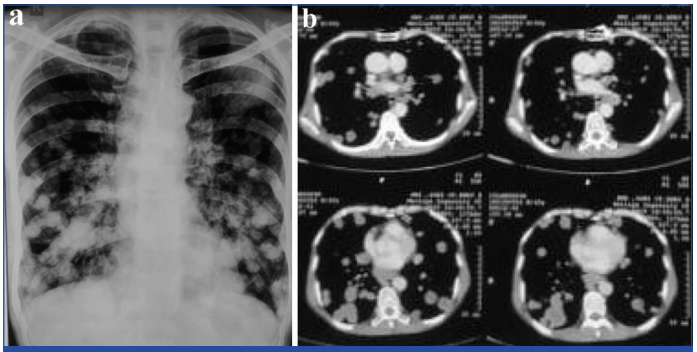
Case 1

A 63-year-old male presented with complaints of bilateral diffuse chest pain for four months, shortness of breath and low-grade fever for three months, dry cough for two months with loss of appetite and loss of weight for one month. He was an active smoker, with 40 packs per year [Table/Fig-1]. Physical examination revealed clubbing, reduced chest movements on right infrascapular area, dull note on percussion and reduced breath sound on auscultation were present in this area.

Age/sex	Smoking status	Mode of diagnosis	Type of malignancy	IHC markers
63/M	Present	CT Guided Biopsy	Small cell carcinoma	TTF,Ki-67 positive
46/M	Present	CT Guided Biopsy	Squamous cell carcinoma	P-40,P-63,CK 5/6
40/F	No	Bronchoscopy	Adenocarcinoma	Napsin-A, TTF-1, CK-7
65/M	Present	CT Guided Biopsy	Small cell carcinoma	TTF-1, Ki-67
60/M	Present	CT Guided Biopsy	Squamous cell carcinoma	P-40,P-63,CK 5/6
55/M	Present	CT Guided Biopsy	Small cell carcinoma	TTF-1, Ki-67

[Table/Fig-1]: Demograpic profile,mode of diagnosis,morphological subtype and immunohistochemistry (IHC) of case reports.

Chest X-ray Posterior-anterior (PA) view showed multiple round opacities of various sizes scattered in both lungs [Table/Fig-2a]. Routine blood investigations were normal. CECT chest showed multiple round opacities in bilateral lung fields along with enlarged mediastinal lymph nodes [Table/Fig-2b]. CECT abdomen showed liver metastasis and Magnetic Resonance Imaging (MRI) brain was normal. Computed Tomography (CT) guided biopsy of right lower lobe lung nodule revealed small cell carcinoma and Immunohistochemistry (IHC) study marker were positive for Thyroid transcription factor 1 (TTF-1), Ki-67, Keratin and negative for Napsin-A, Chromogranin, these finding suggested primary of lung origin in stage IV-B and chemotherapy was started.Patient completed six cycles of chemotherapy with trivial radiological improvements in size of metastasis thereafter, he was referred to radiotherapy for further palliative management.

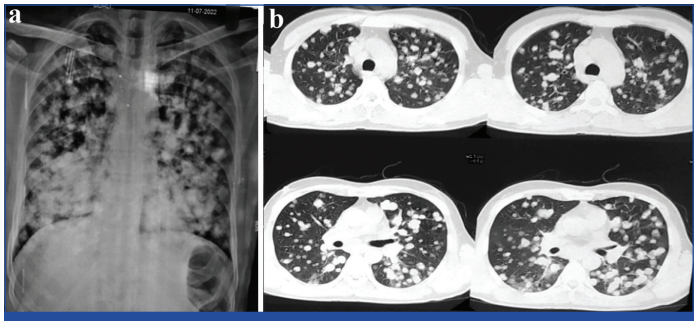


[Table/Fig-2]: a) showing a chest X-ray PA view with multiple round opacities in bilateral lung fields; b) showing a CECT thorax with multiple enlarged mediastinal lymphnodes with bilateral round cannon ball opacities and a heterogenous lung mass lesion in posterior segment of right upper lobe. (Images from left to right)

Case 2

A 46-year-old male presented with complaints of bilateral diffuse chest pain for six months, shortness of breath and low-grade fever for six months, dry cough for four and half months with loss of appetite and loss of weight for four months. He was an active smoker, with 40 packs per year. Physical examination revealed clubbing.

Chest X-ray PA view showed multiple round opacities of various sizes scattered throughout in both lung fields [Table/Fig-3a]. Routine blood investigations were normal. CECT chest showed multiple round opacities in bilateral lung fields along with enlarged mediastinal lymph nodes [Table/Fig-3b]. CECT abdomen and MRI brain was normal. CT guided biopsy of right lower lobe lung nodule revealed non small cell carcinoma and IHC study marker were positive for Tumor protein (p), p40, Cytokeratin (CK) 5/6 and negative for Napsin-A, TTF-1, CK7,alphafetoprotein, Beta Human Chorionic Gonadotropin (hCG), and Central Electricity Authority (CEA). This finding suggested primary of squamous cell carcinoma of lung origin in stage IV-A and chemotherapy was started.The patient had an episode of fatal massive haemoptysis after second chemotherapy and he succumbed to death following this episode.



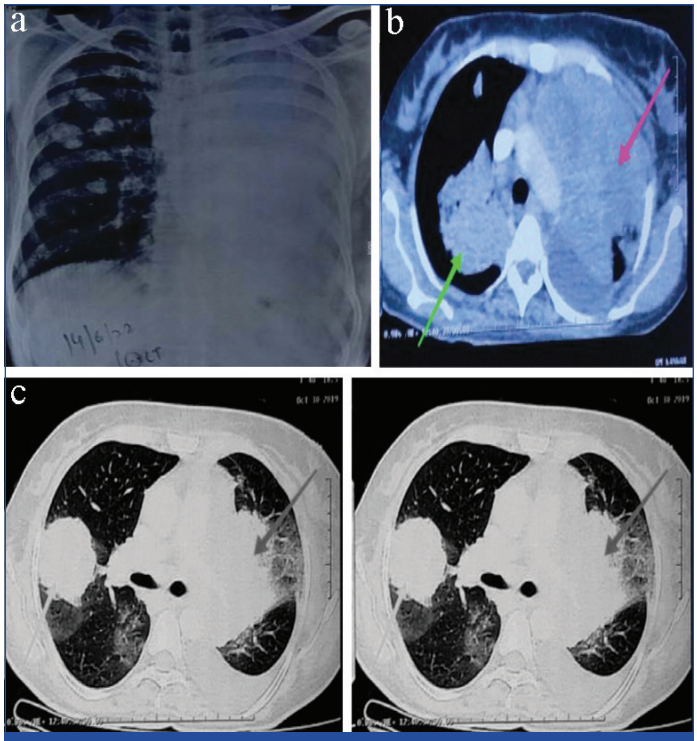
[Table/Fig-3]: a) Showing a chest X-ray PA view having a heterogenous mass lesion in right lower lung with multiple round opacities scattered in bilateral lungs; b) Showing a lung window of CECT thorax having multiple round cannon ball secondaries in both lung fields. (Images from left to right)

Case 3

A 40-year-old female,presented with complaints of shortness of breath for four months, cough with expectoration for three and half months, low-grade fever for three months, loss of weight and loss of appetite for three months, pain abdomen for two months on right hypochondria and flank.She was known to have People Living with Human Immunodeficiency Virus (PLHIV) and was a diagnosed case of pulmonary tuberculosis with ongoing anti retroviral and antitubercular therapy, but did not show any improvement despite of adequate and regular treatment. On examination, clubbing was present, chest movements reduced on left-side and markedly diminished breath sounds on left-side. On abdominal examination, there was no tenderness, no rigidity/haepatosplenomegaly/free fluid. Routine blood investigations were normal and sputum smear Acid-fast Bacillus (AFB), Cartridge Based Nucleic Acid Amplification Test (CBNAAT) was negative.

Chest X-ray showed left hilar mass with right lung nodules [Table/Fig-4a]. CECT chest showed large mass in left upper lobe along with bronchial cut-off and left moderate pleural effusion [Table/Fig-4b]. Multiple round nodules (cannon balls) were present in both lungs suggestive of metastasis [Table/Fig-4c]. Enlarged mediastinal lymph nodes were present. Thoracocentesis revealed haemorrhagic pleural fluid, which was lymphocytic, exudative with low Adenosine Deaminase (ADA) and negative for cytology. CECT abdomen showed mass in left adrenal and enlarged lymph nodes in right pelvic region. MRI brain was normal. Bronchoscopy was done and biopsy from mass in left main bronchus revealed Adenocarcinoma. IHC study marker was positive for Napsin-A, TTF-1, CK7 and negative for thyroglobulin, revealed primary of lung origin in stage IV-B and chemotherapy was started. Estimated Glomerular Filtration Rate (EGFR) mutation was positive in this case.

Intercostal chest tube drainage and talc pleurodesis was done in this patient as the pleural effusion was recurrent.The patient survived for 16 months and completed six chemotherapies of paclitaxel and carboplatinand was on oral EGFR inhibitor in the form of oral gefitinib after completion of chemotherapy.



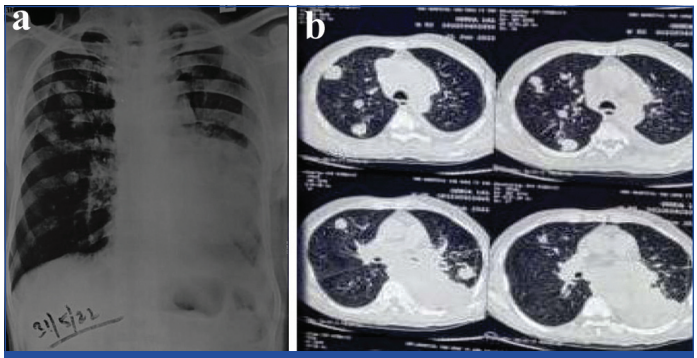
[Table/Fig-4]: a) Showing left lung mass with right lung nodules; b) Showing mass in left upper lobe with a bronchial cut-off sign with moderate leftpleural effusion; c) Showing lung window of CECT thoraxhaving a left hilar mass with cannol ball metastasis in right upper and mid lung zones.

Case 4

A 65-year-old male presented with complaints of cough with expectoration for six months, left-sided chest pain, loss of appetite and loss of weight for five months, shortness of breath for three months. He was active smoker with 60 packs per year and farmer by occupation.

On examination, clubbing and palpable left-sided supraclavicular lymph node was found. On respiratory system examination chest movements were reduced on left-side along with a dull note on percussion and diminished breath sounds on left-side.

Chest X-ray PA view showed large homogenous mass in left mid and lower lung along with rounded opacities in right upper and mid zone [Table/Fig-5a]. Routine blood investigations were normal. CECT chest showed left lower lobe mass compressing left upper lobe bronchus along with bronchial cut-off sign [Table/Fig-5b]. On right-side multiple round opacities/cannon balls was seen in all lobes of right lung. CECT abdomen showed metastasis in liver. MRI brain was normal. Fine Needle Aspiration Cytology (FNAC) from supraclavicular lymph node and CT guided biopsy of left lower lobe mass both revealed small cell carcinoma and IHC study marker was positive for TTF-1, Ki-67, Keratin and negative for Napsin-A, Chromogranin which was suggestive of primary of lung origin in stage IV-B and chemotherapy was started.



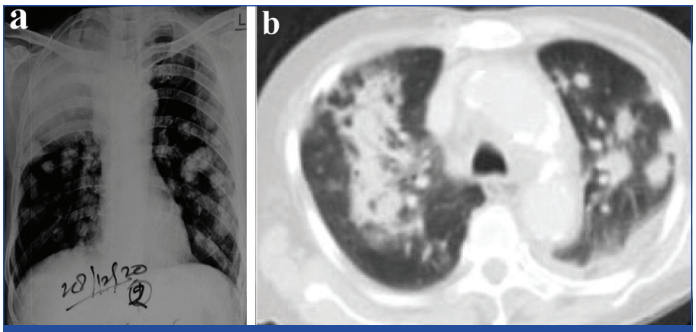
[Table/Fig-5]: a) Showing a homogenous opacity in left lower and mid lung zones; b) Showing a mediastinal window with multiple cannon ball opacities in both lung fields.

The patient developed multiple episodes of malena after 3rd chemotherapy with etoposide and carboplatin and subsequently he developed oral thrush and gingivitis. Haematological parameters showed severe anaemia and thrombocytopenia. He died after three months of initial presentation.

Case 5

A 60-year-old male presented with complaints of right-sided chest pain for five months, loss of appetite and loss of weight for four months, shortness of breath for two and half months and dry cough for two months. He was an active smoker with 40 pack per years and farmer by occupation. On examination clubbing was present; trachea was shifted towards left-side, decreased chest movements and vocal fremitus on right-side.

Chest X-ray showed multiple round opacities in both lungs along with a large homogeneous opacity in right upper and midlung [Table/Fig-6a]. CECT chest showed a large mass in right upper lobe with intrinsic necrotic areas and multiple round nodules in both lungs along with multiple enlarged mediastinal lymph nodes [Table/Fig-6b]. CECT abdomen and MRI brain was normal. Positron Emission Tomography (PET) scan revealed lesions only in lung and mediastinum. CT guided biopsy of right upper lobe mass revealed squamous cell carcinoma and IHC study marker positive for p63, p40, ck5/6 and negative for Napsin-A, TTF-1, ck7 suggested primary of lung. Lung cancer stage was B and patient was started on treatment in the form of chemotherapy.



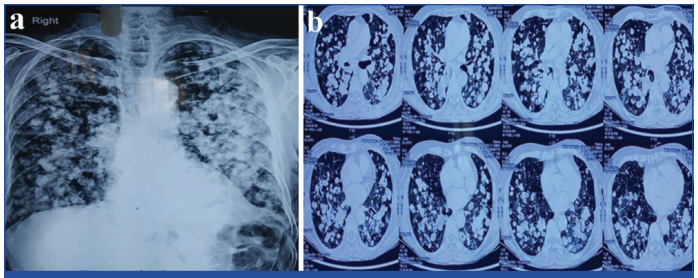
[Table/Fig-6]: a) Showing a homogenous opacity in right upper and mid lung with multiple cannon ball secondaries in left lung; b) showing a lung window revealing amass lesion in right upper lung with cannon ball metastasis in left upper lung.

Despite transient relief, after 2nd chemotherapy, the patient developed lung abscess and metastasis also increased in number and size before the next cycle.The patient went to hospital and did not turn up further.

Case 6

A 55-year-old male ex-smoker,driver by occupation, presented with complaints of central chest pain for four months, low grade fever for two months, loss of appetite and loss of weight for two months,cough with blood-tinged expectoration for one months and shortness of breath for 20 days. On examination, clubbing was present, chest movements reduced on right-side along with dull note on percussion. There was a decreased intensity of breath sound on right-side.

Chest X-ray PA view showed multiple round opacities of various sizes scattered throughout in both lung fields [Table/Fig-7a]. CECT chest showed multiple round opacities in bilateral lung fields of various sizes (cannon balls) along with enlarged mediastinal lymph nodes in both lungs [Table/Fig-7b]. CT guided biopsy of left lower lobe lung nodule revealed small cell carcinoma. IHC study marker was positive for TTF-1, Ki-67, and Keratin and negative for Napsin-A, Chromogranin, which revealed primary of lung origin. MRI brain and CECT whole abdomen revealed no abnormality at this stage. Lung cancer stage was IV-B and chemotherapy was started.



[Table/Fig-7]: a) showing multiple round shadows distributed in bilateral lung fields; b) showing mediastinal window of a CECT thorax showing a mass in left lower lung with diffuse bilateral cannon ball secondaries.

The patient responded well to a couple of chemotherapy cycles but he developed hospital-acquired *Klebsiella* pneumonia after the second cycle and developed intractable vomiting. He was managed with appropriate antibiotics and antiemetics in the form of substance p inhibitors.He completed five chemotherapy cycles. MRI brain was done due to persistent complaints of vertigo and headache which showed brain metastasis.Thereafter,he was advised radiotherapy for palliative management.

Demography and IHC of patients is shown [Table/Fig-1].

DISCUSSION

Multiple pulmonary nodules in the chest X-ray have multiple causes, including metastases (cannon-ball secondaries), various infections, immunological diseases, and arteriovenous malformations. Pulmonary metastasis is seen in 20-54% of the extra thoracic malignancies [3]. They usually represent a disseminated malignancy and indicate a poor prognosis although rarely few cases with favourable outcome have been reported [4,5]. Metastases with cannon ball appearance are classically from renal cell carcinoma or choriocarcinoma, and less commonly from an alternative primary tumour,such as prostate malignancy, synovial sarcoma, or endometrial carcinoma [6]. This case series had both the primary lesion and metastasis within the lung parenchyma and this makes it unique and a very rare presentation.

Neoplasms with rich vascular supply draining directly into the systemic venous system often present in this fashion.Pulmonary metastasis is usually asymptomatic in 90 percent of the cases [7]. Six cases of lung to lung cannon ball metastasis have been described in this case series.Out of six cases three were small cell carcinoma, two were squamous cell carcinoma and one was adenocarcinoma. History of significant smoking was present in all cases of squamous and small cell carcinoma. Smoking is already a well-known risk factor responsible for lung carcinogenesis [8]. In heavy smokers with chest radiograph showing cannon ball metastasis, they can originate from primary in the lung parenchyma as well as any other extra-pulmonary organs. All patients were managed with chemotherapy, palliative management and radiation therapy wherever required. One case has a positive EGFR mutation which was managed on oralchemotherapy with EGFR inhibitor and showed the best survival among all the cases we reported.

One similar case report was reported by He CH and Su YJ where a 62-year-old non-smoker male presented with complaints of back pain and weight loss since one month [9]. CECT thorax revealed lung to lung cannon ball metastasis.Biopsy of lung mass revealed adenocarcinoma. TTF-1 and CK7 was positive on IHC. This patient had vertebral metastasis also and survived for three months postchemotherapy. In this case series,one patientwas diagnosed with adenocarcinoma, he completed all six chemotherapies and survived for around 16 months and had the best survival among all cases reported.Probable explanation for a good survival was absence of brain metastasis and EGFR positivity in this case. Patients with small cell carcinoma have the least survival and rapid radiological deterioration [10]. It was the most aggressive form of all reported cases and is consistent

with recent guidelines which also conclude that small cell lung cancers has the highest frequency of extra thoracic metastasis [10]. Out of six cases reported, five had a staging of IV-B and one case of IV-A. Mean survival in such cases is less than a year [11].The exact survival could not be traced in this case series exact assome of them did not turn upfor further treatment. The main regimen for treatment of lung carcinoma cases with local or distant metastasis is platinum-based doublet chemotherapy with oral EGFR and tyrosine kinase inhibitors. Palliative treatment in the form of radiation therapy and management ofadverse effects of chemotherapy is also an important part of management of such cases. Further work-up by assessing cytopathology, IHC markers and CECT should be done to establish the origin of metastasis and decide the course of treatment [12].

This case series emphasises on certain noteworthy things firstly, it depicts a rare behaviour of lung cancer both radiologically and clinically as manifestation of both primary and secondaries in the same organ is an unusual presentation in context to lung carcinoma.Secondly, smoking was the single most important risk factor noted in most of the cases,thus, creating awareness regarding hazardous effects of smoking and running clinics for smoking cessation is a very important non pharmacological task which can significantly cut down the incidence of all varieties of lung cancers.

CONCLUSION(S)

Most of the time presence of cannon ball metastases indicates an advance stage of malignancy and represents poor survival. Clinicians should not deprive such advanced cases from the chemotherapy regimen as we have seen that despite being stage IV-B,some cases have responded well to chemotherapy and other supportive regimen in the form of radiotherapy and targeted therapy. Clinicians must investigate thoroughly for primary origin of cannon ball metastasis though rare but lung malignancy can present as this kind of metastasis also.

REFERENCES

[1] Bray F, Ferlay J, Soerjomataram I, Seigel RL, Torre LA, Jemal A. Global cancer statistics 2018. GLOBACON estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer J Clin. 2018;68:394-424.
[2] Mohan A, Garg A, Gupta A, Sahu S, Choudhari C, Vasistha V, et al. Clinical profile of lung cancer in North India. A 10-year analysis of 1862 patients from a tertiaty care center. Lung India. 2020;37:190-97.
[3] Agarwal R, Mukhopadhyay J, Lahiri D, Biswas A, Maity P. Cannon-ball pulmonary metastases as a presenting feature of stomach cancer. Lung India. 2015;32(3):300-02. Doi: 10.4103/0970-2113.156264.
[4] Kurian A, Lee J, Born A. Born urothelial bladder cancer with cavitary lung metastases.Can Respir J. 2011;18(3):e46-47.
[5] Gan Z, Lin S, Han K, Shen Z, Yao Y, Min D. Bilateral spontaneous pneumothorax in an osteosarcoma patient with pulmonary metastases: A case report. Oncol Lett. 2016;11(2):1179-80.
[6] Kshatriya R, Patel V, Chaudhari S, Patel P, Prajapati D, Khara N, et al. Cannon ball appearance on radiology in a middle-aged diabetic female. Lung India. 2016;33:562-68.
[7] Cavitating pulmonary metastases from a renal cell carcinoma- PubMed [Internet]. [cited 2021 Jun 9]. https://pubmed.ncbi.nlm.nih.gov/32431800/.
[8] Furrukh M.Tobacco smoking and lung cancer.Sultan QaboosUniv Med J.2013;13(3):345-58.
[9] He CH, Su YJ. Lung to lung cannonball metastasis. Am J Med Sci. 2020;359(2):133-34.
[10] NCCN.National comprehensive cancer network. https://www.nccn.org. (last accessed on 23rd November 2022).
[11] Wang X, Wang Z, Pan J, Lu Z-Y, Xu-D, Zhang H-J, et al. Patterns of extrathoracic metastases in different histological types of lung cancer. Front Oncol. 2020;10:715.
[12] Cavitating pulmonary metastases from a renal cell carcinoma.PubMed(internet). [cited 2021 jun 9]. https://pubmed.ncbi.nlm.nih.gov/32431800.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Institute of Respiratory Diseases, Sawai Mann Singh Medical College, Jaipur, Rajasthan, India.
2. Associate Professor, Department of Institute of Respiratory Diseases, Sawai Mann Singh Medical College, Jaipur, Rajasthan, India.
3. Associate Professor, Department of Institute of Respiratory Diseases, Sawai Mann Singh Medical College, Jaipur, Rajasthan, India.
4. Junior Specialist, Department of Institute of Respiratory Diseases, Sawai Mann Singh Medical College, Jaipur, Rajasthan, India.
5. Junior Resident, Department of Institute of Respiratory Diseases, Sawai Mann Singh Medical College, Jaipur, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Arun Dutt Sharma,
1 H 383, Indira Gandhi Nagar, Jagatpura, Jaipur-302017, Rajasthan, India.
E-mail: drarundutt@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 23, 2022
- Manual Googling: Nov 23, 2022
- iThenticate Software: Dec 08, 2022 (14%)

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. Yes

Date of Submission: **Sep 21, 2022**
Date of Peer Review: **Nov 08, 2022**
Date of Acceptance: **Dec 24, 2022**
Date of Publishing: **Apr 01, 2023**