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CASE REPORT

Case report: Small cell lung cancer presenting as the "sunray sign" in the chest radiograph and recurrent hemoptysis

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Lung cancer prognosis has not changed in the last few decades due to diagnosis at an advanced stage. The majority of cases with early disease are asymptomatic, and whenever clinical presentations with cough, dyspnea, hemoptysis, or chest pain occur, when these cases have progressed to an advanced stage. Lung cancer tops the list of all causes of cancer-related deaths globally and is ahead of digestive tract malignancies. Small-cell lung cancer (SCLC) has the worst outcome, with survival rates in the range of weeks to months from diagnosis. SCLC is usually manifested as an extensive disease due to its delayed presentation, early metastasis, systemic nature, and poor response to available treatment options. "sunray sign" in chest radiographs is first described in literature and constitutes a hilar mass or radiopacity with inhomogeneous linear opacities spreading toward the periphery like sunrays, which is a marker of interstitial lymphatic involvement due to malignant spread of disease. The "sunray sign" is an indicator of underlying lung malignancy with central airway or main stem bronchus involvement and lymphatic dissemination in linear opacities. In this case report, we have reported a 51-year-old male who presented with cough and hemoptysis with progressive worsening of shortness of breath. Chest X-rays documented round opacities occupying the right hilum with linear opacities emerging toward the periphery in lung parenchyma, showing the typical "sunray sign." Bronchoscopy was done after clinical stabilization and showed endobronchial polypoidal growth in the right main stem bronchus, causing partial occlusion of the bronchial lumen. Endobronchial needle aspiration (EBNA) cytology and forceps-guided (FB) histopathology are suggestive of "small cell histological type" lung malignancy for the "sunray sign" in our case. A high index of suspicion is a must to rule out underlying malignancy, and bronchoscopy is the "gold standard" test in cases with the sunray sign to confirm the diagnosis.

Keywords: sunray sign, chest radiograph, bronchoscopy, EBNA, small-cell carcinoma

Introduction

Lung cancer is the leading cause of cancer-related mortality in both males and females across the globe. Lung cancer has a dismal prognosis in spite of advancements in diagnosis and treatment worldwide due to the advancement of the stage of the disease at diagnosis and the fact that there are very few options left for the management of lung cancer other than palliative care. Overall, 5-years survival in lung cancer patients is only 15%, and that too after all possible measures to tackle the disease with advanced treatment modalities (1).

In India, lung cancer accounts for the greatest number of cancer-related deaths and leads the table ahead of oral, breast, and cervix cancer, although the latter are ahead in the table with a greater number of cases in comparison to lung cancer cases. The rationale for the worst outcome in

terms of survival would be asymptomatic disease in the early stages, and when cases present in outdoor units, they are usually with advanced disease. This issue of delayed diagnosis can be solved with lung cancer screening with a low-dose computed tomography (CT) scan of the thorax, but due to cost constraints, it is not widely used across the globe.

Up to 80% of lung cancer cases are asymptomatic initially when picked up in the early stages, but when the disease is advanced or surgically inoperable, these cases present with cough, hemoptysis, dyspnea, chest pain, and recurrent or non-resolving pneumonia. Importantly, only 10% of lung cancer cases are usually diagnosed incidentally in routine care; this reflects the nature of the disease and the prognosis (2). Small-cell lung cancer (SCLC) is considered an advanced disease at diagnosis due to the high propensity of distant metastases at diagnosis.

Small-cell lung cancer is an aggressive tumor of the neuroendocrine type with a short doubling time, a high growth fraction, and uncontrolled mitosis frequencies, which contribute to an extremely poor prognosis in this histological type (3–5). Usually, it arises from the bronchial luminal epithelium as carcinoma *in situ* and evolves later to full-fledged or advanced cancer in smokers. Thus, cigarette smoking is the most common etiological factor for squamous cell cancer, and nicotine and polycyclic aromatic hydrocarbons (PAH) in tobacco smoke are directly linked to lung cancer in smokers.

Usually, small-cell cancers present with mass lesions, and more than half of the cases have central attenuation due to necrosis and cavitation due to central tumor cell necrosis. Thus, radiologically, a mass lesion up to 4 cm on a chest radiograph and a mass with heterogeneity or cavitation in a chest CT are most commonly documented with this histological type (4). As these types commonly have endobronchial lesions, bronchoscopy is very important to confirm the diagnosis (5).

Cases with a negative tropical workup for lung consolidation, mass, or suspected post-obstructive pneumonia need bronchoscopy (6).

Sunray sign in chest radiograph is first time described in our case in literature. We have documented bronchogenic carcinoma of the small cell histological type. Thus, bronchoscopy is the best diagnostic method in cases with the sunray sign in the chest radiograph.

Case summary

A 51-year-old male, farmer, smoker, normotensive, and non-diabetic, was referred to our center by his family physician for complaints of the following:

1. Dry cough with intermittent yellowish-white sputum for 1 month

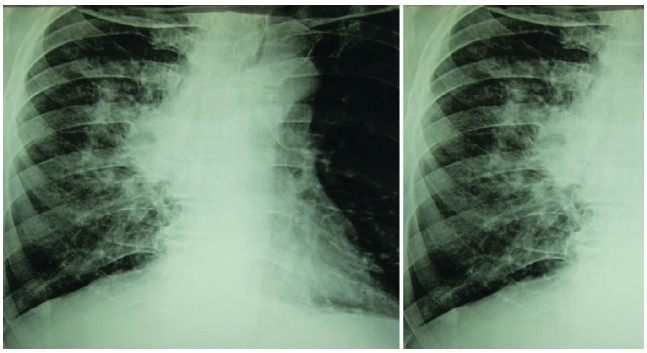

FIGURE 1 | Chest X-ray PA view showing right hilar opacity with linear spreading margins and edges typical of the "sunray sign."

2. Hemoptysis—minimal streaky type associated with yellow-white sputum for 3 weeks, exaggerate with cough, no history of massive hemoptysis
3. Shortness of breath for 2 weeks, grade II
4. Dull, aching retrosternal chest pain, continuous, and more during hemoptysis

No fever in the last month

1. Chronic smoker with smoking index of 30 pack years

Family members said that he was treated with intravenous antibiotics for 7 days by the family physician and showed a poor response to antibiotics and other supportive care during hospitalization. A chest X-ray done by the family physician documented right hilar opacity (**Figure 1**). He was referred by the family physician for hilar opacity, and after careful examination of the chest radiograph, the "Sunray sign" is clearly visible. We have clearly noted the "sunray sign" in the chest radiograph, i.e., the right hilar mass or radiopacity with inhomogeneous linear opacities spreading toward the peripheries like sunrays, which is a marker of interstitial lymphatic involvement due to malignant spread of disease (**Figure 1**).

Clinical examination documented

Well-nourished, moderately built, anxious male; no cyanosis or clubbing.

Heart rate: 98/min, respiratory rate: 24 bpm, blood pressure: 110/60°mmHg.

PsO_2: 96% in room air.

Respiratory system examination revealed normal vesicular breathing and no adventitious breath sounds in the bilateral lung field.

Other systemic examinations were normal.

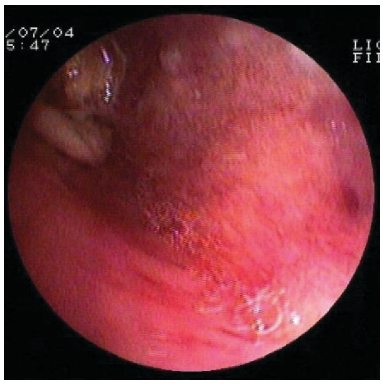

FIGURE 2 | Fiberoptic video-bronchoscopy showing polypoidal multinodular growth in the right main stem bronchus.

Laboratory examination documented as follows

A complete hemogram reported normal blood counts and hemoglobin percentage.

Kidney and liver function tests were normal.

C-reactive protein: 86 mg/L (0–6 mg/L); random blood sugar level: 110 mg%.

LDH: 1,080 IU/L (70–470 IU/L); uric acid: 3.4 mg (3.5–7.5 mg/dL).

Procalcitonin: 0.05 ng/mL (normal).

Viral markers: Human immunodeficiency virus (HIV) I and II negative; Australia antigen: Negative.

Sputum gram stain: gram-positive cocci in chains.

Sputum culture: no growth.

We have decided to further investigate with bronchoscopy due to the absence of fever, minimal hemoptysis, negative procalcitonin and sepsis screen, and importantly, the "sunray sign" in the chest radiograph and the mass lesion in the left upper lobe abutting and infiltrating the left main stem bronchus.

A fiberoptic video-bronchoscopy was done in a bronchoscopy suit with all necessary precautions with topical anesthesia (xylocaine jelly plus spray and xylocaine solution) and documented polypoidal growth in the right main stem bronchus.

Polypoidal multinodular growth in the right main stem bronchus, causing near total occlusion of the lumen. Bronchoscopy was unable to negotiate distal growth. The growth was fleshy and bled on touch, with a yellowish-white slough overlying it (**Figure 2**).

We have performed endobronchial needle aspiration cytology (EBNA) as the first procedure during bronchoscopy due to the presence of slough overgrowth and chances of negative growth and forceps biopsy as the second technique during bronchoscopy.

Endobronchial needle aspiration cytology cytology documented a small-cell histological type of lung malignancy (**Figure 3**).

Histopathology confirmed a small cell histological type of lung cancer (**Figure 4**).

Further immunohistochemistry analysis is documented as follows:

TTF 1: Positive

Synaptophysin: Positive

Neuron-specific enolaseis negative.

Chromogranin A: Positive

CD 56: Positive

An oncologist's opinion was taken for the treatment of small cell cancer, and further assessment in view of chemotherapy and radiotherapy was done. Positron emission tomography (PET) scan was done and shown adrenals and spine metastasis. Due to the central airway tumor's disseminated nature, oncologists decided on palliative chemotherapy and radiation therapy in the oncology department.

Discussion

Sunray sign

"Sunray sign" in a chest radiograph is defined as a mass lesion or radiopacity occupying the hilum on any side of the chest with inhomogeneous linear opacities spreading toward the peripheries like "sunrays," which is a marker of interstitial lymphatic involvement due to malignant spread of disease.

The sunray sign is easily picked up during a routine chest radiology examination. A hilar mass with peripheral linear opacities spreading from margins of opacity is the sunray sign.

Other features in this regard include the following:

1. This is a direct sign of lung malignancy.
2. This is indicative of a central airway tumor.
3. This is an indication for a bronchoscopy workup due to two reasons: one central tumor and the fact that the majority of the cases present with hemoptysis.
4. This is a marker of lymphatic dissemination due to the malignant process.
5. This is an indicator of local spread and needs a PET scan to rule out distant metastasis.
6. The sunray sign indicates positive yield during bronchoscopy due to the endobronchial nature of the disease.
7. "Sunray sign" is documented in the two most common histological types, such as squamous or small cell cancer tumors, due to their propensity to involve the central airways and be labeled as central tumors.
8. Practically inoperable due to its central location and surgically unrespectable due to lymphatic involvement due to the malignant process.

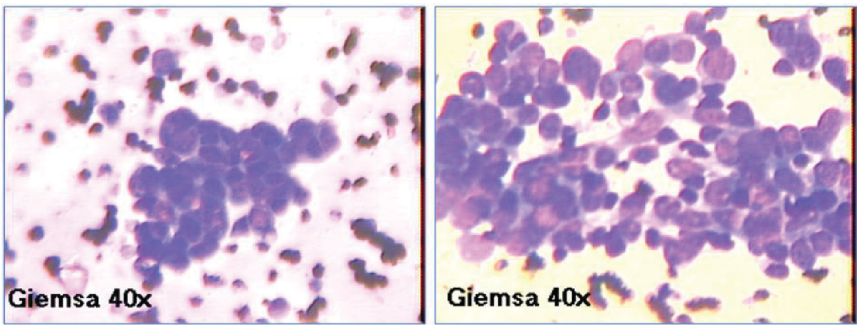

FIGURE 3 | Endobronchial needle aspiration cytology showing the small cell type of lung cancer.

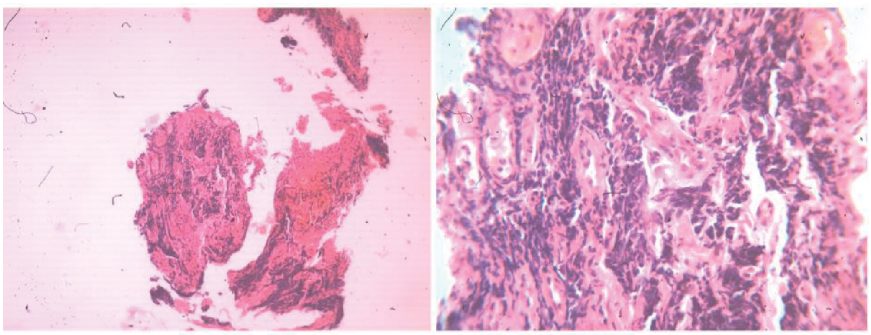

FIGURE 4 | Histopathology shows the small cell type of lung cancer as the histological type.

9. Exclusively documented in lung malignancies only. There are no other causes, such as benign lesions or infective or inflammatory causes, for the sunray sign.

We have decided to further investigate with bronchoscopy due to absence of fever, minimal hemoptysis, poor response to antibiotics, negative procalcitonin, and importantly bulging fissure sign in chest radiograph (7). We have performed EBNA as the first procedure during bronchoscopy due to the presence of slough overgrowth and chances of negative growth, and forceps biopsy as the second technique during bronchoscopy. Similarly, in our published study, we document the additional role of EBNA in endobronchial lesions over other conventional diagnostic techniques (CDTs) such as forceps biopsy and bronchial wash in diagnosing lung cancer during bronchoscopy and report a significant yield difference with the inclusion of EBNA (8).

Authors have mentioned that EBNA is complementary to CDTs, and importantly, in a few cases with endobronchial lesions, only EBNA samples showed a positive yield. Thus, EBNA increases the diagnostic sensitivity of bronchoscopy. Authors have observed the importance of the rapid onsite evaluation (ROSE) facility for EBNA samples to increase diagnostic yield, decrease need for repeat bronchoscopy, and ensure that these samples are adequate for immunohistochemistry analysis whenever required (9).

Authors have observed the importance of EBNA in endobronchial lesions in the presence of slough overgrowth and the chances of a negative yield with conventional forceps biopsy due to superficial necrosis. The EBNA sampling method will take deeper samples due to needle insertion in mass lesions, and the yield is better as compared to forceps biopsy, thus decreasing the need for repeat procedures if only forceps biopsy is used. They have mentioned the safety of the EBNA procedure and the negligible chances of bronchoscopy damage with adequate training (9).

Authors have mentioned the added value of EBNA in cases of fleshy vascular growth in endobronchial growth where bleedings risk during procedure is high with conventional forceps biopsy and chances of an inadequate procedure are high if only forceps biopsy is used. In these cases, EBNA is safe, and the chances of profuse bleeding are less. EBNA samples are comparable with histopathology, and in a few cases, cytology patterns will help to differentiate squamous cell carcinoma from adenocarcinoma in poorly differentiated non-small cell carcinoma, whereas EBNA samples will give clear-cut cytology typing of either squamous cell or adenocarcinoma types of non-small cell lung cancer, as in our case (10). EBNA samples can be processed for immunohistochemistry, and the results are comparable to those of histopathology (9, 10).

Small-cell lung cancer is relatively less common, documented in 13–15% of lung malignancies, and exclusively observed in smokers. SCLC has the worst outcome due to its nature of distant metastases and poor response to chemotherapy and radiotherapy. SCLCs are very aggressive malignancies in all lung histological types and considered tumors with a dismal prognosis due to their high growth rate,

shorter doubling time, and early development of metastatic disease in comparison to other types of NSCLC (11).

Mostly, cases with SCLC present with advanced disease and PET CT has documented very crucial role exact staging of disease. In SCLC, it is very unlikely to have isolated endobronchial growth due to the small cell histological type without distant metastasis. Like in squamous cell NSCLC, SCLC also involves the central airways, and the majority of these cases have hilar or perihilar growth with moderate to large mediastinal lymphadenopathy.

Many times, SCLC cases present with distal disease and lung lesions were picked up during routine assessment for the search of the primary source of metastatic disease. Previously, SCLC has been divided into limited and extensive disease according to the presence or absence of dilatant metastases. This classification of limited and extensive was used for treatment planning, predicting the outcome, and analyzing the prognosis.

A tumor along with its nodal disease confined to one hemithorax that could be covered in a single radiation field was classified as a limited disease. Extensive disease included extrapulmonary involvement and distal metastasis, while cases with paraneoplastic syndromes, which are the most common presentation in SCLC, are not extensive disease. Currently, TNM staging is used for the staging of SCLC as well as other histological types.

Treatment planning, grading of prognosis, and analyzing outcomes would depend on and be best predicted with previous staging as limited and advanced disease as compared to the widely used TNM staging, especially in SCLC (12). Immunohistochemistry workup of neuroendocrine markers has documented importance in predicting response to treatment and survival in SCLC cases (13). Synaptophysin has a very strong correlation with survival, i.e., tumors expressing more synaptophysin have better survival, and cases with synaptophysin-negative tumors need further analysis for an assessment of their poor prognosis.

TTF-1 expression has a positive correlation with performance status in these cases, and TTF-1-negative cases usually show a poor response to available treatment options. This phenotyping according to TTF-1 and synaptophysin would help with treatment planning in most of the cases, assessing response, and predicting the final outcome (13).

In the present case report, we have documented constitutional symptoms such as cough, hemoptysis, and shortness of breath with the absence of fever, and a negative sepsis screening panel has given a clue to work for a non-infective cause for the sunray sign. With interventional pulmonology, the fiberoptic videobronchoscopy technique has given a diagnostic clue as to lung malignancy. EBNA has been an important bronchoscopy-guided method apart from forceps biopsy for confirming the diagnosis.

Key learning points from this case report are the following

1. "Sunray sign" in a chest radiograph is a hilar mass or radiopacity with inhomogeneous linear opacities spreading toward the periphery like sunrays, which is a marker of interstitial lymphatic involvement due to malignant spread of disease.
2. The "Sunray sign" is a direct sign of underlying lung malignancy and documented in the two most common histological types, such as squamous or small cell cancer tumors, due to their propensity to involve the central airways and be labeled "central tumors."
3. The majority of cases with the sunray sign present with hemoptysis, which is a marker of a central airway tumor with endobronchial involvement.
4. Bronchoscopy is the gold standard test to diagnose endobronchial pathology rather than high-resolution computed tomography (HRCT) thorax. It should be done to rule out the exact cause of the sunray sign.
5. Various bronchoscopy-guided techniques are available, and the sequence of techniques usually depends upon the choice and expertise of the operator during the procedure. EBNA is underutilized over forceps biopsy in endobronchial lesions due to a lack of training and a fear of bronchoscope damage during EBNA procedures.
6. Forceps biopsy is considered the gold standard test in endobronchial lesions due to the larger sample size and adequacy of specimens for further analysis, such as immunohistochemistry. EBNA has overtaken these concepts and become the first test during bronchoscopy in endobronchial lesions with superficial necrosis or slough over lesion, blood clot over lesion, or crush artifacts resulting during biopsy samplings, especially with serrated-edge forceps during bronchoscopy.
7. "Sunray sign" will be documented in squamous cell lung cancer, or SCLC. In search of published literature, this will be our first case involving the "sunray sign" in lung malignancy.
8. The "Sunray sign" is easily picked up during a routine chest radiology examination. Family physicians and general physicians' training is a must for most common radiological signs of lung malignancy, including the sunray sign, to prevent delay in diagnosis and have a successful treatment outcome.

Author contributions

All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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