

Fireworks sign: a CT feature of active pulmonary tuberculosis

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Abstract

Background: Imaging manifestations of active pulmonary tuberculosis (APTb) on CT described in previous studies did not cover a variety of imaging appearances of bronchogenic spread of pulmonary tuberculosis (PTb) and could overlap with many other diseases.

Purpose: To propose a CT imaging sign—"fireworks sign" to demonstrate the bronchogenic spread of active pulmonary tuberculosis and correlate with histopathology.

Methods: A total of 679 patients with confirmed PTb were enrolled in this study. The histological proof of APTb was obtained by means of sputum smear in 429 patients, bronchoalveolar lavage in 167 patients, biopsy or surgical histopathology in 83 patients. The clinical and imaging data were retrospectively reviewed. The "fireworks sign" on CT which was a focal conglomeration (clusters) of multiple nodules could be classified into three patterns: pistil pattern (consolidation or more nodules in the central region and fewer nodules in the peripheral region), dandelion pattern (fewer nodules in the central region and more nodules in the peripheral region) and peony pattern (nodules evenly distributed in the affected region). Imaging assessment included the pattern, number, site of fireworks sign and other associated imaging features. The histopathological comparison of fireworks sign was also performed in the biopsy or surgical specimens.

Results: A total of 180 lesions with fireworks sign were found in 106 patients (106/679, 15.6%), including 71 pistil patterns, 21 dandelion patterns and 88 peony patterns, respectively. More than two patterns of fireworks sign presented in 68 patients. Histopathological proof was achieved in 83 patients and the fireworks sign was composed of centrilobular nodules which corresponded pathologically to caseous necrotic granulomas in bronchioles and alveolar ducts. Single lobe, multiple lobes of unilateral lung, and bilateral lungs involvement was presented in 66.0% (70/106), 6.6% (7/106), and 27.4% of patients (29/106), respectively. The fireworks sign decreased in density or turned into ground-glass opacity during or after anti-tuberculosis treatment in 34 patients in a series of follow-up CT scans. Other imaging features including tree-in-bud sign (21.7%), consolidation (18%), cavity (24%), bronchiectasis (21.7%), pleural effusion (2.8%), pneumothorax (1.9%), pleural thickening (35.9%) and mediastinal lymph node enlargement (13.2%) were also found.

Conclusion: The fireworks sign is a CT feature of bronchogenic dissemination of active pulmonary tuberculosis and histopathologically corresponds to a conglomeration of caseous necrotic granulomas in the bronchiole and alveolar ducts.

Key Results

The "fireworks sign" on CT is a focal conglomeration (clusters) of multiple centrilobular nodules dispersing around the bronchus or bronchiole just like an appearance of fireworks show. Pathologically, the centrilobular nodules in fireworks sign correspond to caseous necrotic granulomas in the bronchioles

and alveolar ducts. According to the accumulation patterns of centrilobular nodules, fireworks sign could be classified as pistil pattern, dandelion pattern and peony pattern.

Introduction

Tuberculosis, the second leading cause of infectious disease death following Acquired Immunodeficiency Syndrome (AIDS)¹, is a chronic granulomatous infection characterized by caseation necrosis. According to *Global Tuberculosis Report 2016*, there were estimated 10.4 million new pulmonary tuberculosis (PTB) cases in the world, and China was listed as one of the countries with a high incidence of PTB². As a chronic infectious disease, PTB is a major problem to be prevented and controlled in China. The early diagnosis and standardized treatment of PTB, especially for those highly contagious active PTB (APTB), are critical for disease control and management. The diagnosis of APTB is a comprehensive procedure involving clinical manifestations, bacteriology, imaging and other auxiliary examinations. Imaging examination is of great value in the diagnosis of APTB. The WHO has recommendations for the role of chest radiography but has not recommended CT as part of the role for diagnosis and management of PTB^{3,4}. Although the conventional chest radiography is considered as the preferred and main method for detection of PTB, there are still some limitations such as misdiagnosis caused by low spatial resolution, low specificity, and overlapping of imaging findings of various diseases. In recent years, CT, especially high resolution CT (HRCT) has played an increasingly important role in the diagnosis of PTB, assessment of its activity and post-treatment follow-up and has been a preferred imaging method for screening and diagnosis of PTB^{3,4}.

Imaging manifestations of APTB on CT have been well described in previous studies, including consolidation, tree-in-bud sign, centrilobular nodules, cavitation, and lymph node necrosis⁴⁻⁷. "Galaxy sign", "rosette sign", and "reversed halo sign" have also been proposed as CT manifestations of APTB⁸⁻¹³. Unfortunately, these imaging signs did not cover a variety of imaging appearances of bronchogenic spread of APTB and could overlap with many diseases, such as cryptogenic organizing pneumonia (COP), sarcoidosis, pulmonary lymphomatoid granulomatosis, invasive pulmonary fungal infections¹⁴⁻¹⁷ and so forth. Thus, the aim of this study was to propose a new CT feature "fireworks sign" to comprehensively describe the bronchogenic spread of APTB and may be more conducive to identify APTB on CT.

Materials And Methods

Patient Population

This study was approved by the Medical Ethical Management Committee of our institutional review board. As a retrospective study, the requirement for patients' informed consent was waived in accordance with the International Committee of medical science organizations (CIOMS) guidelines. A total of 2283 consecutive patients who underwent chest CT examination from 2014 to 2019 was retrieved in Picture

Archiving and Communication Systems (PACS) with the keywords of “tuberculosis”, “pulmonary tuberculosis” and “active pulmonary tuberculosis”. Their clinical and image data were analyzed and patients with confirmed PTB were finally enrolled in this retrospective study. The diagnosis of APTB was in accordance with the “Diagnostic Standards for Tuberculosis in China (WS 288-2017)”¹⁸ and WHO consolidated guidelines on tuberculosis³ and confirmed by sputum smear, bronchoalveolar lavage, biopsy or surgical histopathology. The exclusion criteria included: (1) without bacteriological or histopathological confirmation; (2) previous treatment with anti-tuberculosis drug; (3) loss to follow-up. Finally, 679 patients with confirmed APTB were enrolled in this study (Figure 1).

CT Examinations

All patients underwent chest CT examination in a supine position with arms raising. Chest CT scans were performed using Philips Brilliance 256 iCT or Siemens Cardiac 64-slice spiral CT scanners during deep end-inspiration. Scan was performed using the following parameters: 120 kV and automatic mA, 5.0-mm slice thickness for scan and 1.0 mm for reconstruction. In addition, 83 patients received contrast examination: CT scan started at 25-30s (arterial phase) and 60-65s (venous phase) after injection of 70-90 ml of non-ionic iodinated contrast agent (iohexol, 300 mgI/ml) through antecubital venous access at a rate of 3.5 ml/s.

Imaging Assessment

All original thin-slice images were reviewed by two experienced thoracic radiologists (with 20 years and 10 years of thoracic imaging experience, respectively) using both lung (width, 1600 HU; level, -600 HU) and mediastinal (width, 350 HU; level, 35 HU) window settings.

The definition of “fireworks sign” was a focal conglomeration (clusters) of multiple centrilobular nodules, dispersing around the bronchus or bronchiole just like an appearance of fireworks show. According to accumulation patterns of centrilobular nodules, fireworks sign was classified into three patterns: pistil pattern (consolidation or more nodules in the central region and fewer nodules in the peripheral region), dandelion pattern (fewer nodules in the central region and more nodules in the peripheral region) and peony pattern (nodules evenly distributed in the affected region) (Figure 2). Imaging assessment included: (1) patterns of fireworks sign: pistil pattern, dandelion pattern, and peony pattern; (2) sites of fireworks sign: the right upper lobe, right middle lobe, right lower lobe, left upper lobe and left lower lobe; (3) the number of fireworks sign; (4) other associated imaging features: including tree-in-bud sign, consolidation, cavity, bronchiectasis, pleural effusion, pneumothorax, pleural thickening and mediastinal lymphadenopathy. A consensus was reached by consultation with another radiologist (with 30 years of thoracic imaging experience) if there was disagreement.

Bacteriological and Histopathological Analysis

Ziehl-Neelsen (Z-N) staining was used to detect acid-fast bacilli (AFB) for microscopic analysis of sputum smear and bronchoalveolar lavage liquid¹⁹. Diagnosis for active tuberculosis (TB) was confirmed by

detection of AFB twice or mycobacterium tuberculosis complex bacilli was found in sputum culture.

Lung specimens for light microscopy were fixed by immersion in 10% neutral buffered formalin for 24–48 h, dehydrated in a graded isopropanol series and embedded in paraffin wax. Paraffin sections of 4 µm thickness were stained with haematoxylin and eosin (H&E) stain and examined using an Olympus BX51TF light microscope (Olympus Corporation, Tokyo, Japan). H&E-stained sections of the lung tissue were examined for multi-nucleated giant cells and other granulomatous inflammatory findings compatible with tuberculosis²⁰.

Results

Patient Demography

A total of 679 patients (448 men and 231 women) with mean age of 45.2 ± 17.3 years (range, 12 to 80 years) with confirmed APTB were enrolled in this study. Of 679 patients, 365 patients were with tuberculosis-related symptoms (such as fever, cough, hemoptysis, chest pain, and etc.) and 314 patients had no respiratory symptoms. In addition, 57 patients had a history of diabetes, 23 patients had a history of tuberculosis, 13 patients had rheumatoid arthritis, nine patients had a steroid therapy history, six patients had nephrotic syndrome, one had systemic lymphadenopathy (Table 1). The bacteriological or histological proof of APTB was obtained by means of sputum smear (N=429), bronchoalveolar lavage (N=167), biopsy or surgical specimens (N=83).

Imaging Interpretations

A total of 180 lesions with fireworks sign were found in 106 patients (106/679, 15.6%): pistil pattern in 71 patients, dandelion pattern in 21 patients, peony pattern in 88 patients, and single firework in 38 patients, more than two different patterns in 68 patients (Figure 3). The right upper lobe involvement was found in 62 patients (58.5%), the right middle lobe involvement in 16 patients (15.1%), the right lower lobe involvement in 30 patients (28.3%), the left upper lobe involvement in 41 patients (38.7%), and the left lower lobe involvement in 25 patients (23.6%). Single lobe involvement was presented in 66.0% of patients (70/106), multiple lobes of unilateral lung involvement in 6.6% of patients (7/106), and bilateral lungs involvement in 27.4% of patients (29/106).

Simultaneously, other imaging features including tree-in-bud sign (23 patients), consolidation (19), cavity (25, single cavity in 13 patients and multiple cavities in 12 patients), bronchiectasis (23), pleural effusion (3), pneumothorax (2), pleural thickening (38) and mediastinal lymph node enlargement (14) were also found (Table 2).

In 34 patients with a series of CT scans during 3-14 months follow-up, the density of small centrilobular nodules within fireworks sign decreased, the margin became blurred and ground-glass opacity appeared after anti-tuberculosis treatment (Figure 4).

Histopathological Correlation

Biopsy was performed in 59 patients and surgical resection in 24 patients. Acid-fast stain was positive in 61 patients and negative in 22 patients. The nodules within fireworks sign pathologically presented as caseous necrotic granulomas in bronchioles and alveolar ducts (Figure 5). Caseous necrosis was also detected in removed mediastinal lymph nodes in two patients.

Discussion

Many CT findings including centrilobular nodules, consolidation, cavitation, poorly defined opacity, ground-glass opacity, bronchial or bronchiolar wall thickening, pleural effusion, lymph node necrosis with ring-like enhancement have been described as imaging features of APTB in previous studies⁴⁻⁷. In accordance with the pathophysiological characteristics of the dissemination along the bronchus of tuberculosis, lesions composed of multiple micronodules with or without coalescence in and around small airways had been considered as a characteristic feature of early APTB⁵. Therefore, bronchogenic spread lesion characterized with centrilobular micronodules and tree-in-bud sign are the most common imaging findings, which could be present in 87% of pre-treatment cases²¹⁻²⁴. However, these radiological manifestations just reflect a spectrum of endo- and peribronchiolar disorders and can be found in many lung diseases^{25,26}. Moreover, with the decreasing globally overall incidence of PTB and increasing incidence of diabetes, immunodeficiency and immunosuppressive diseases, the incidence of atypical manifestations of tuberculosis is increasing. Several unusual HRCT aspects involved the coalescence of small nodules such as “galaxy sign”, “cluster sign”, “rosette sign”, and “reversed halo sign” have also been used to describe the bronchogenic dissemination of APTB^{6-10,27,28}, leading to confusion on the diagnosis and differential diagnosis of APTB.

In this study, however, although the varied imaging features could be presented, we find that the distribution patterns of centrilobular nodules through bronchogenic spread in APTB are similar to the different effects of fireworks show in celebration ceremony. Therefore, we put forward the “fireworks sign”, including pistil pattern, dandelion pattern and peony pattern, to provide a clear and quick explanation of these associated radiological patterns. Compared to other imaging findings reported, we believe that the “fireworks sign” is more conducive to summarize the varied coalescence patterns of APTB. In our study, fireworks sign presented in 15.6% of patients with APTB and the location of fireworks sign was also consistent with the previously reported prone sites of tuberculosis (upper lobe and lower lobe)^{22,23}. Unilateral involvement presented in 72.6% of cases. The other radiological imaging features including tree-in-bud sign, consolidation, cavity, bronchiectasis, pleural effusion, pneumothorax, pleural thickening, mediastinal lymph node enlargement presented in 21.7%, 18%, 24%, 21.7%, 2.8%, 1.9%, 35.9%, and 13.2% of patients, respectively, which can also increase the confidence of fireworks sign in the diagnosis of APTB.

In addition, due attention should be paid to single fireworks sign, especially for the case with pistil pattern and peony pattern which is easy to be interpreted as a ground-glass nodule and be misdiagnosed as lung

adenocarcinoma. Two cases with single fireworks sign in this study had been resected as lung adenocarcinoma (Fig. 4). Moreover, after anti-tuberculosis medication, the density of fireworks sign decreased, the margin of centrilobular nodules became blurred and ground-glass opacity appeared, the fireworks sign in this period also could be interpreted as lung adenocarcinoma. Therefore, a series of CT images are very important to prevent the misdiagnosis. Moreover, the improvement of lesions (fireworks sign) after anti-tuberculous treatment also favored the diagnosis of APTB^{3,9}.

It is worth noting that only 53.8% of patients (365/679) in our study showed tuberculosis related symptoms, indicating that clinical symptoms are not reliable. Thus, correct recognition of radiological manifestations is crucial for radiologists and clinicians to preclude the spread of tuberculosis, especially for those patients lack of typical clinical symptoms.

Clusters of micronodules seen on radiographs with tuberculosis has been proven to be histological correlation with the presence of lesions in the airways and caseous material in both bronchioles and alveolar ducts²⁹. Yeh et al. and Heo et al. also found the clusters of nodules represented the peribronchovascular nodules, which was a significant finding in APTB^{10,24}. In this study, the centrilobular nodules in the fireworks sign histopathologically also corresponded to caseous necrotic granulomas in biopsy or surgical specimens, which was the pathological characteristics of bronchogenic spread of postprimary or reinfection type of tuberculosis^{5,29}. In addition, vessels could be found in the center of some fireworks signs, especially for those lesions with dandelion pattern showed in Fig. 4, this may indicated the bronchial dissemination of APTB as the accompanying of pulmonary artery and bronchus.

There were some limitations of this study. First, there was selection bias in this study. We searched the patients in PACS who were diagnosed tuberculosis by CT, therefore, some cases with APTB which were misdiagnosed by CT might be lost. Second, the proportion of fireworks sign in those cases that initially were suspected tuberculosis on CT but eventually not were not discussed. Because our institution receives a large number of chest CT examinations every year (more than 180,000 cases per year), as a retrospective study, it is unrealistic to trace the clinical and imaging data of each patient, therefore, only clinically confirmed APTB was included in this study to retrospectively assess the clinical scenario and image features. Third, we did not discuss whether the fireworks sign could be present in other diseases. Further prospective studies should be carried out to include other infectious and noninfectious diseases to evaluate the specificity, sensitivity and accuracy of fireworks sign.

In conclusion, the fireworks sign proposed in this study is a CT feature of bronchogenic dissemination of active pulmonary tuberculosis and histopathologically corresponds to the conglomeration of caseous necrotic granulomas in the bronchioles and alveolar ducts.

Abbreviations

PTB: pulmonary tuberculosis; APTB: active pulmonary tuberculosis

Declarations

Funding:

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Author contribution:

Guarantors of integrity of entire study, R.F., J.P., S.Z.; study design, all authors; data acquisition and interpretation, all authors; manuscript drafting and revision, R.F., J.P., S.Z.; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, R.F., J.P., X.J., X.T.; clinical studies, all authors; statistical analysis, R.F., J.P.; and manuscript editing, X.Z., S.Z.

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Tables

Table 1. Summary of Demographic Characteristics

Characteristics	No. of patient (N=679)
Age	
Max age	80
Min age	12
Mean age	45.2±17.3
Sex	
Male	448
Female	231
Clinical Characteristics	
<i>Tuberculosis-related symptoms</i>	365
Fever	51
Cough	173
Expectoration	83
Hemoptysis	38
Chest pain	45
Emaciation	32
Lymphadenopathy	13
Other respiratory symptoms	102
<i>Asymptomatic</i>	314
Diagnosis method	
Sputum smear	429
Bronchoalveolar lavage	167
Biopsy or surgical histopathology	83

Table 2. CT characteristics of fireworks sign

CT characteristics	Number	Percentage
Pattern of fireworks sign (N=180)		
Pistil pattern	71	39.4%
Dandelion pattern	21	14%
Penoy pattern	88	51%
Location		
The right upper lobe	62	58.5%
The right middle lobe	16	15.1%
The right lower lobe	30	28.3%
The left upper lobe	41	38.7%
The left lower lobe	25	23.6%
Involvement of fireworks sign		
single lobe	70	66%
multiple lobes of unilateral lung	7	6.6%
bilateral lung involvement	29	27.4%
Associated findings		
tree-in-bud sign	23	21.7%
consolidation	19	18%
cavity	25	24%
bronchiectasis	23	21.7%
pleural effusion	3	2.8%
pneumothorax	2	1.9%
pleural thickening	38	35.9%
mediastinal lymphadenopathy	14	13.2%

Figures

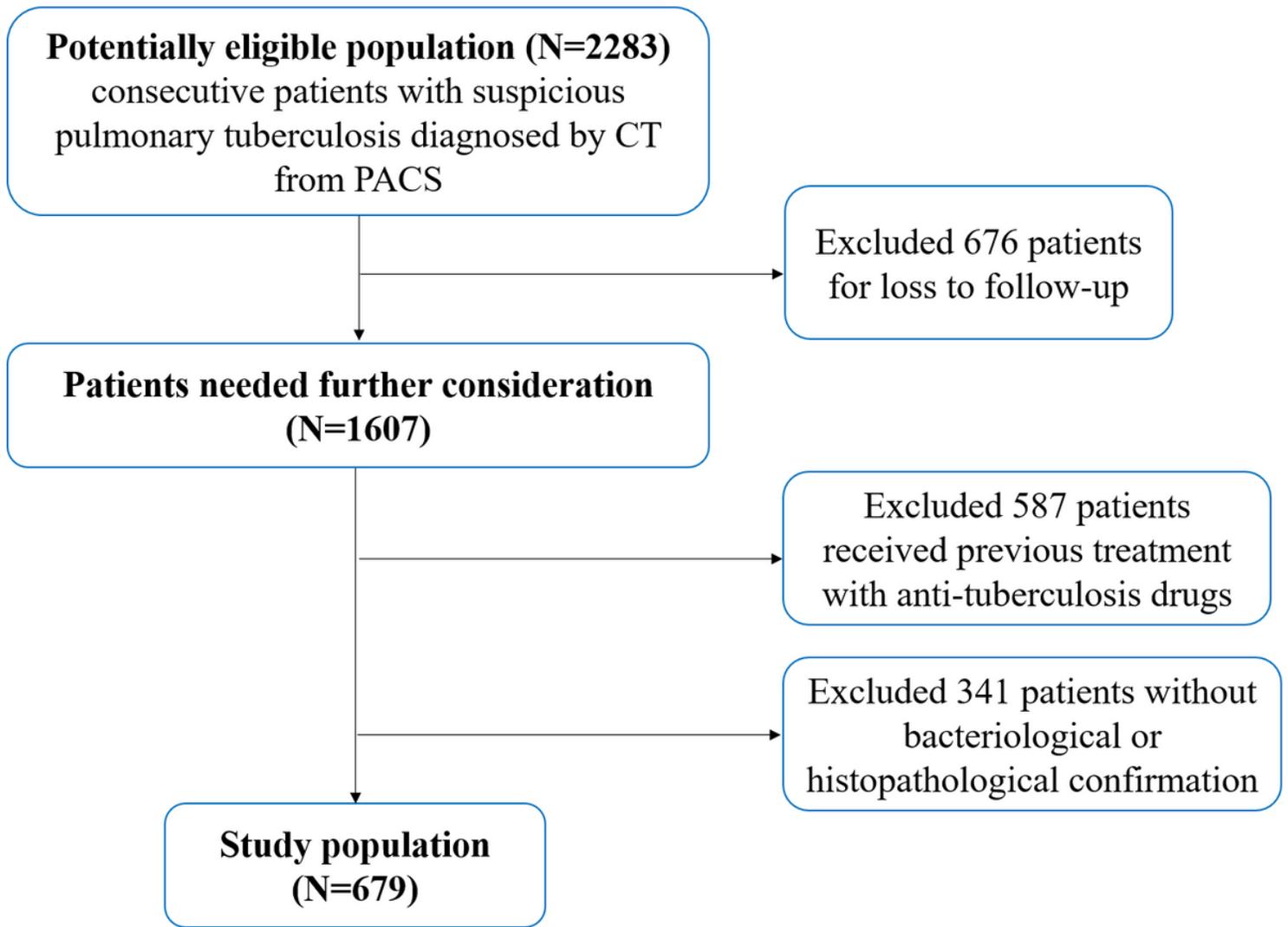


Figure 1

Flowchart of patient selection. PACS=picture archiving and communication systems.

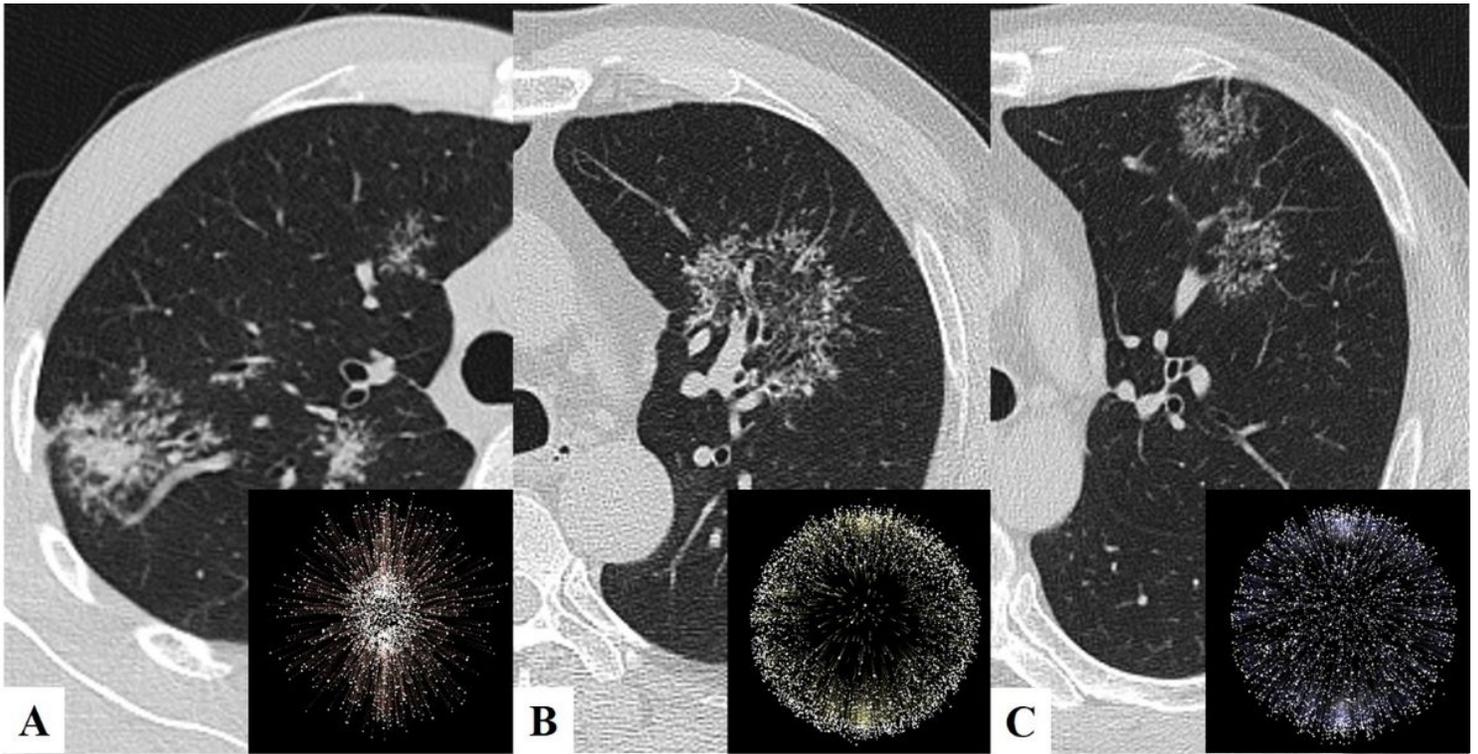


Figure 2

Three patterns of fireworks sign in pulmonary tuberculosis (color picture in the right lower corner is a schematic diagram of the corresponding pattern of fireworks sign). (A) Pistil pattern of fireworks sign: A lesion containing multiple nodules with more coalescent nodules in the central region and fewer nodules in the peripheral region presents in the right upper lobe of a 56-year-old male patient with APTB. This imaging feature is similar to the “pistil” effect in fireworks glossary, which contains centre sphere of stars in a spherical burst shell surrounded with an outer sphere of stars. (B) Dandelion pattern: In contrast to “pistil pattern” in Figure A, a lesion consisting of fewer nodules in the central region and more nodules in the peripheral region presents in the left upper lobe of a 34-year-old female patient with APTB, looks like a dandelion with petals falling off in the air. (C) Peony pattern: Two lesions containing multiple micronodules with a homogenous distribution in the left upper lobe of a 47-year-old male patient with APTB, is similar to the most commonly seen shell type in fireworks glossary “peony”, which looks like a spherical break of colored stars.

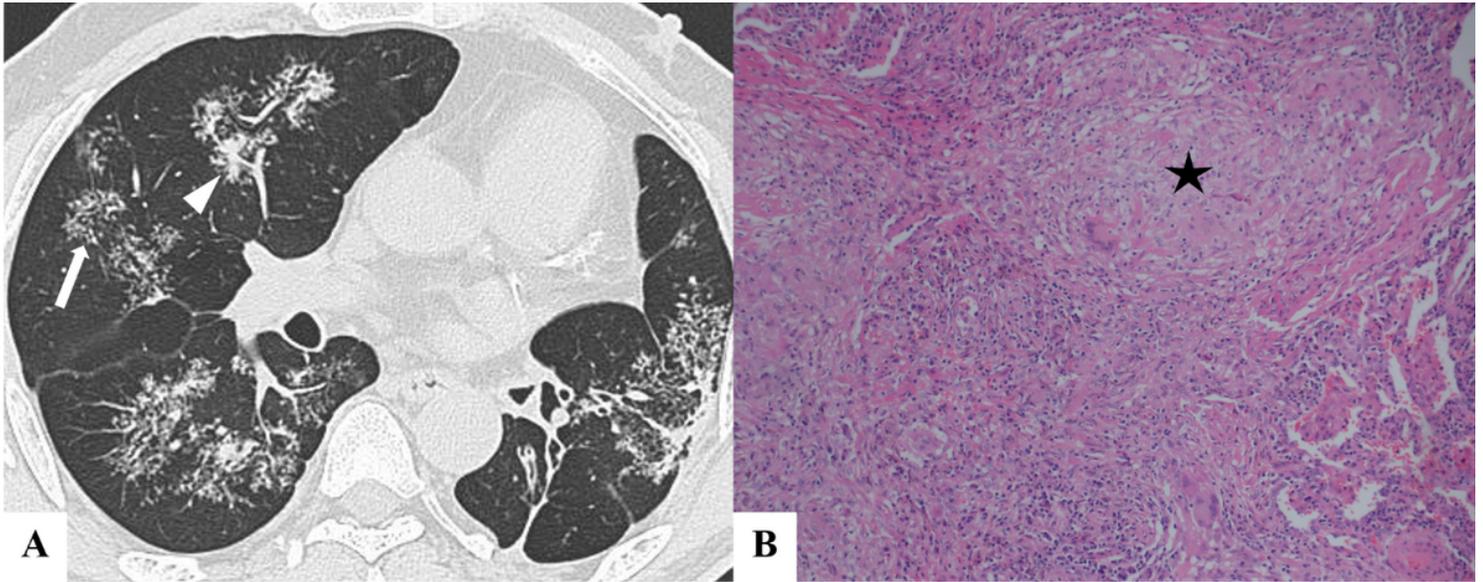


Figure 3

(A) Peony pattern (arrow) and pistil pattern (arrowhead) of fireworks sign in right upper lobe are detected in a 56-year-old male patient. (B) Biopsy specimen shows interstitial fibrous tissue hyperplasia, hyaline degeneration, caseous granulomas (☐) and multinucleated giant cells, which is consistent with the diagnosis of tuberculosis (HE, x40).

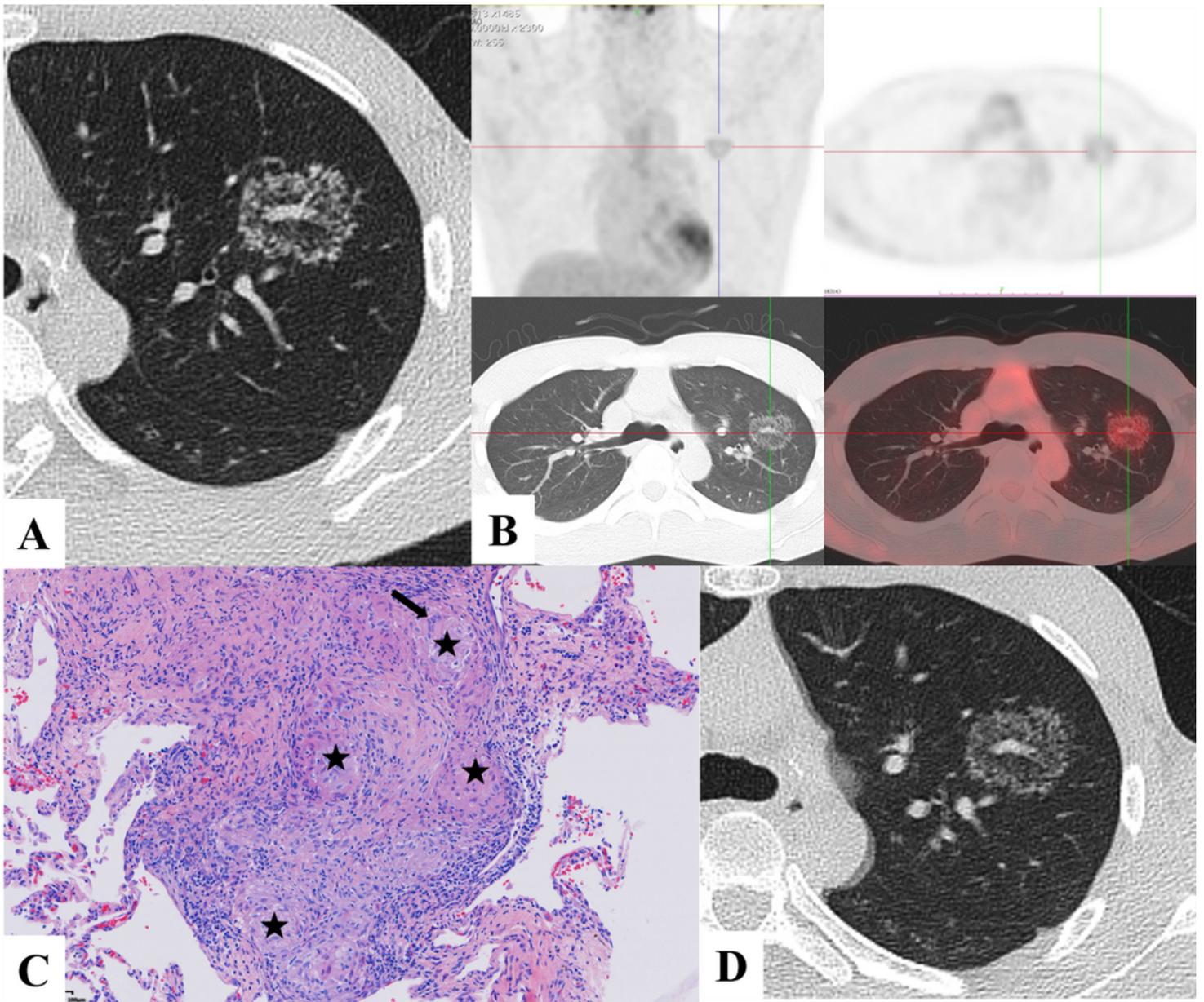


Figure 4

(A) A single fireworks sign with a dandelion pattern in the apical-posterior segment of the left upper lobe is detected in a 20-year-old male patient. (B) The lesion shows increased radioactivity with a SUVmax value of 2.3 on PET-CT. (C) Multiple granulomas (★) and multinucleated macrophages (arrow) are found in the lung biopsy specimen (HE, x20). Acid-fast staining shows positive and PAS staining negative, the diagnosis of tuberculosis is considered. (D) After 30 days of antituberculosis treatment, the follow-up CT shows absorption of some peripheral micronodules and appearance of ground-glass opacity, which could be misdiagnosed as lung adenocarcinoma.

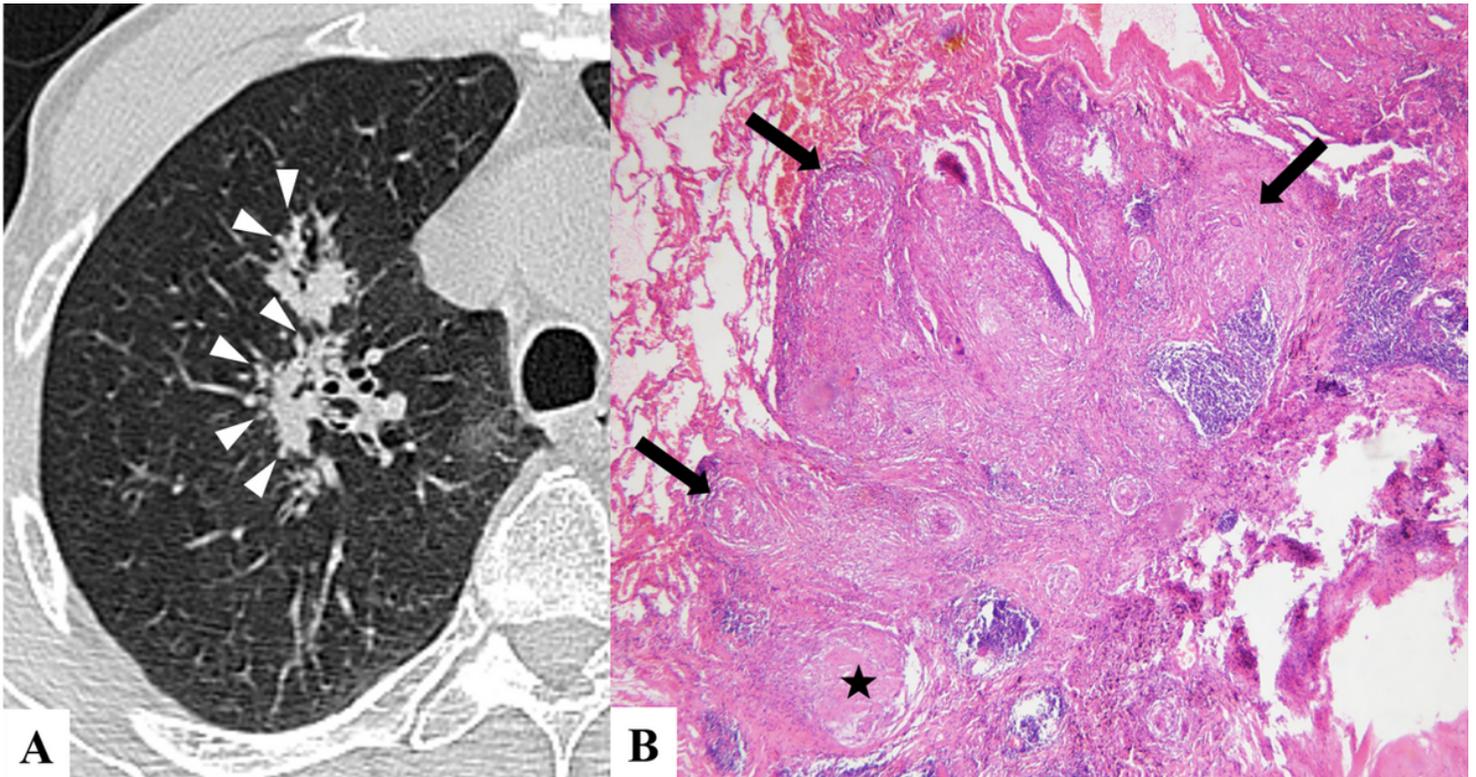


Figure 5

(A) The peony pattern of fireworks sign is demonstrated in the posterior segment of the upper lobe of the right lung in a 65-year-old male patient. (B) The micronodules in the peripheral region (arrowhead in Figure A) corresponds to granulomas (arrow) and unstained necrotic areas (★) in resected specimen (HE, x40).