Original Article

Imaging findings of multislice computed tomography in 21 patients with airway invasive pulmonary aspergillosis

Xiaoqiong Ni[1#], Rui Yu[1#], Jinpeng Hou[1], Yang Ya[1], Guohua Fan[1], Zhengrong Chen[2]

[1]Department of Radiology, The Second Affiliated Hospital of Soochow University, Suzhou, China; [2]Department of General Surgery, The Second Affiliated Hospital of Soochow University, Suzhou, China

Contributions: (I) Conception and design: X Ni, R Yu, Z Chen, G Fan; (II) Administrative support: X Ni, J Hou, Y Ya; (III) Provision of study materials or patients: R Yu, J Hou, Y Ya; (IV) Collection and assembly of data: X Ni, R Yu, Z Chen, G Fan; (V) Data analysis and interpretation: X Ni, R Yu, Z Chen, G Fan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Guohua Fan, PhD. Department of Radiology, The Second Affiliated Hospital of Soochow University, 1055 Sanxiang Road, Suzhou 215004, China. Email: fangh22@126.com; Zhengrong Chen, MD. Department of General Surgery, The Second Affiliated Hospital of Soochow University, 1055 Sanxiang Road, Suzhou 215004, China. Email: chen_zhengrong@126.com.

Background: Airway invasive aspergillosis (AWIA) poses a diagnostic challenge due to its nonspecific clinical manifestations. This study aimed to characterize the imaging findings of AWIA and explore the clinical characteristics that facilitate the diagnosis of AWIA.

Methods: A retrospective analysis was conducted on 21 patients clinically and pathologically diagnosed with AWIA. All subjects underwent chest multislice computed tomography (MSCT) scans, and their clinical data were collected. The computed tomography (CT) features were evaluated, and 17 patients received the follow-up of MSCT in our hospital.

Results: The high-frequency CT signs with an incidence of ≥60% included lobar and segmental bronchial lumen stenosis and wall thickening, patchy peribronchial consolidation, tree-in-bud sign, nodules (>5 mm), bronchioles wall thickening and lumen expansion. The low-frequency signs with an incidence of <40% included trachea or left/right main bronchial wall thickening, lobar and segmental bronchiectasis and wall thickening, ground-glass opacity, cavity, and pleural effusion. The inter-reader agreement for CT features was substantial (kappa =0.78). Additionally, we observed that clinical symptom improvement did not always correspond with immediate improvement in CT imaging findings during the early stages of treatment.

Conclusions: The presence of specific high-frequency CT features in patients with underlying risk factors should prompt consideration of AWIA. Early recognition of these CT patterns may facilitate timely diagnosis and treatment, potentially improving patient outcomes.

Keywords: Airway invasive aspergillosis (AWIA); multislice computed tomography (MSCT); imaging manifestations; diagnosis

Submitted May 21, 2024. Accepted for publication Dec 20, 2024. Published online Feb 21, 2025.
doi: 10.21037/jtd-24-843
View this article at: https://dx.doi.org/10.21037/jtd-24-843

Introduction

Invasive pulmonary aspergillosis (IPA) is the most dangerous form of pulmonary aspergillosis infection, with a high mortality rate, particularly in patients who are immunocompromised. IPA can be divided into angio-IPA and airway invasive aspergillosis (AWIA) (1,2). Previous studies have reported that the two forms may represent successive phases of IPA, and the rate of progression to angio-IPA varies with different immune states of patients (3,4). Ledoux *et al.* (5) reported that patients with IPA who had severe neutropenia may quickly develop the angio-invasive pattern, even within several hours. However, in patients with IPA who

did not have neutropenia, the phase of AWIA may persist for several days. By inhibiting the synthesis of fungal cell walls, antifungal drugs prevent fungal growth and reproduction, thereby achieving antifungal effects. As a special type of IPA, AWIA is characterized by direct invasion of the airway by *Aspergillus*, which may lead to serious consequences, such as airway obstruction and respiratory failure. Therefore, early identification of AWIA is crucial for timely intervention. If the possibility of AWIA is not considered promptly, treatment may be delayed, increasing the patient's risk of disease deterioration and death. Early recognition of AWIA and the prompt use of antifungal drugs may prevent the exacerbation of IPA and improve prognosis.

The clinical diagnosis of AWIA poses a challenge, given that its symptoms and signs may closely resemble those of other pulmonary infections. Currently, the gold standard to diagnose AWIA depends on endobronchial mucosal biopsies, with the diagnosis based on the presence of *Aspergillus* organisms deep into the basement membrane, causing pseudomembrane (6,7). However, the fact that this method demands high cooperation from patients and is invasive has limited its wide clinical usage, particularly in patients with poor cardiorespiratory fitness. As a non-invasive examination method, multislice computed tomography (MSCT) can visualize the chest structure clearly through excellent tissue and spatial resolution.

To the best of our knowledge, there is limited literature concerning the computed tomography (CT) findings of AWIA for imaging physicians. This study aimed to review clinical data and CT findings of 21 cases of AWIA in our hospital and identify clinical characteristics that can facilitate the diagnosis of AWIA. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-843/rc).

Highlight box

Key findings

- High-frequency computed tomography (CT) signs of airway invasive aspergillosis (AWIA) include bronchial lumen stenosis, peribronchial consolidation, and nodules >5 mm.
- Clinical improvement may precede radiological improvement in AWIA cases.

What is known and what is new?

- AWIA typically affects immunocompromised patients.
- CT imaging is crucial for diagnosis.
- AWIA can occur in previously healthy individuals.
- Specific combinations of CT features can suggest AWIA diagnosis.

What is the implication, and what should change now?

- Clinicians should maintain high suspicion for AWIA even in patients without classic risk factors.
- Early recognition of characteristic CT patterns may facilitate timely diagnosis and treatment.

Methods

Patient enrolment

Patients who were admitted to the hospital between January 2010 and August 2022 and were clinically diagnosed with AWIA and underwent CT scans of the chest were enrolled. The inclusion criteria were as follows: (I) all patients underwent bronchoscopy and were diagnosed with AWIA based on endobronchial mucosal biopsies [the discovery of *Aspergillus* hyphae in pathological examination of bronchial mucosal tissue biopsy specimens, which can help to diagnose AWIA, and a positive galactomannan (GM) test of bronchoalveolar lavage fluid or sputum culture with a threshold of 0.5 μg/L]; (II) to ensure better consistency, all patients underwent chest CT scans within 1 week before bronchoscopy; and (III) patients did not use antifungal drugs before the initial CT scans. The exclusion criteria were as follows: patients who were diagnosed with other types of pulmonary aspergillosis, including saprophytic aspergillosis (aspergilloma), chronic pulmonary aspergillosis, allergic bronchopulmonary aspergillosis and angio-invasive aspergillosis according to the criteria of the European Cancer/Mycological Research Group (8). The study was approved by the institutional review board of The Second Affiliated Hospital of Soochow University [No. EC-AF(SQ)-14/20230101] and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The requirement for informed consent was waived. Ultimately, 21 patients were enrolled for further analysis. Patients were treated with antifungal drugs, primarily voriconazole, with some cases receiving amphotericin B or caspofungin as alternatives or in combination therapy.

CT image acquisition

To exclude the impact of a single piece of equipment, the chest CT examinations were performed using 64-channel multi-detector-row CT units, using either a GE Discovery CT750 HD CT scanner (GE Healthcare, Chicago, IL, USA) or a GE Light Speed CT scanner (GE Healthcare).

The CT scanning parameters were as follows: 120 kV tube voltage; 360 mA tube current; 0.6 s tube rotation time; 512×512 matrix; scan field of view, large body; and 1–5 mm section thickness. To make the scanning thickness unified and reduce observation errors, all CT images were reconstructed using a 0.625 mm slice thickness. Scans were viewed at standard mediastinal windows (window level, 35 HU; width, 450 HU) and lung windows (window level, –600 HU; width, 1,200 HU). The images were transmitted and processed in Digital Imaging and Communications in Medicine format and assessed by two radiologists (with 8 and 10 years of experience in chest image interpretation) independently, and conclusions were reached by consensus.

Data collection

Clinical data were obtained from medical records of patients. The number, distribution and characteristics of lesions in each CT image were recorded.

Typical CT morphological manifestations

The primary CT morphological manifestations observed in the patients included the following: (I) thickening of the trachea or left/right main bronchial walls; (II) bronchial lumen stenosis with wall thickening involving the lobar and segmental bronchi; (III) bronchiectasis with wall thickening involving the lobar and segmental bronchi; (IV) patchy peribronchial consolidation; (V) tree-in-bud sign; (VI) lumen expansion and wall thickening involving the bronchioles; (VII) pulmonary nodules >5 mm, most of which were located near the bronchus and bronchus containing air found inside the nodules; (VIII) cavity, all of which were thick-walled, with patchy/line-like shadows seen in the cavity; (IX) ground-glass opacity surrounding the patchy consolidation or nodules; and (X) pleural effusion (*Figures 1-3*).

Typical clinical factors

Referring to previous research, 10 typical factors were defined as follows: by including past medical history, such as (I) chronic lung disease, (II) diabetes, (III) immunocompromised disease treated with glucocorticoids therapy, (IV) patients in an intensive care unit (ICU) setting, (V) previous influenza infection; and clinical features such as (I) cough, (II) shortness of breath and dyspnea, (III) fever, (IV) chest pain, (V) chest discomfort.

The above 10 CT morphological manifestations were observed in the initial MSCT images of all the enrolled patients. These were followed up, and the CT manifestations were recorded for the appropriate patients.

Statistical analysis

The clinical concomitant diseases, clinical symptoms, and CT features were analyzed using percentage statistics. The inter-reader agreement for CT features was assessed using Cohen's kappa statistic. Logistic regression analysis was performed to evaluate the association between initial CT findings and worsening of CT patterns at follow-up. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and a P value <0.05 was considered statistically significant.

Results

Patients clinical data

Between January 2010 and August 2022, a total of 21 patients were retrospectively enrolled in this study according to the inclusion and exclusion criteria (*Tables 1,2*), as shown in the patient selection flow diagram (*Figure 4*). The study included 8 women and 13 men, aged 27–75 years, with an average age of 57.95±14.71 years. Among all the patients, 18 had various underlying diseases, including chronic lung disease (n=9, 42.86%), diabetes (n=6, 28.57%), immunocompromised disease treated with glucocorticoids therapy (n=2, 9.52%), patients in an ICU setting (n=2, 9.52%, including trauma and duodenal perforation) and previous influenza infection (n=2, 9.52%). Three patients (14.29%) were previously healthy, including two with long-term exposure to paint or dust and one with foreign matter aspiration. Chronic lung disease was the most common underlying condition. The main clinical manifestations of the patients were cough (n=19, 90.48%), shortness of breath and dyspnea (n=9, 42.86%), fever (n=6, 28.57%), chest pain (n=3, 14.29%) and chest discomfort (n=3, 14.29%). Cough was the most typical symptom.

Patients imaging data

The lesions exhibited a diffuse distribution in both lungs in 17 patients. In four patients, the lesions were confined to one lobe of the right lung. *Table 1* shows the incidence rate of 10 morphological manifestations of AWIA. High-

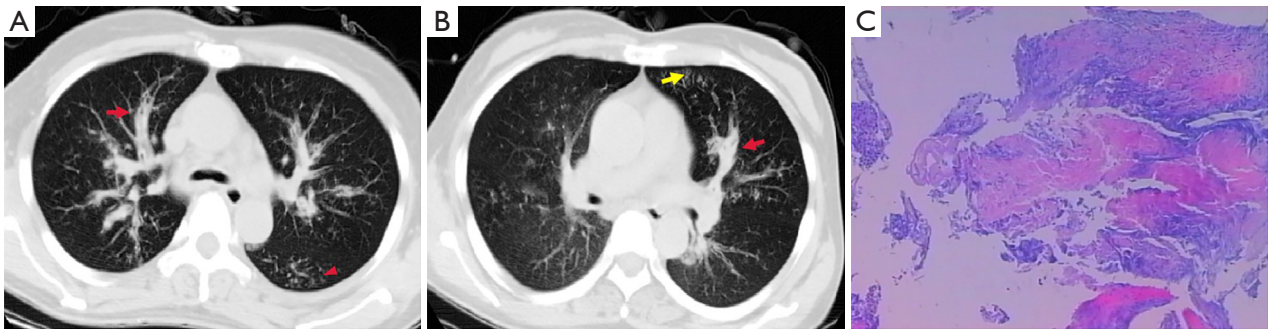

Figure 1 A 47-year-old woman had wracking cough, sputum, chest pain and fever, and she had been previously in good health. (A,B) Axial CT scans showed lumen stenosis and wall thickening involving lobar and segmental bronchial (red arrows), clusters of nodules, with some opacities appearing as "tree-in-bud" (red arrowhead). The yellow arrow indicates an example of bronchiolar wall thickening, defined as visible bronchiolar walls with a thickness greater than 0.5 mm on high-resolution CT images. (C) Histopathological examination of the bronchoscopic biopsy specimen showed chronic inflammation associated with infiltration of fungal hyphae on hematoxylin-eosin staining (×4). CT, computed tomography.

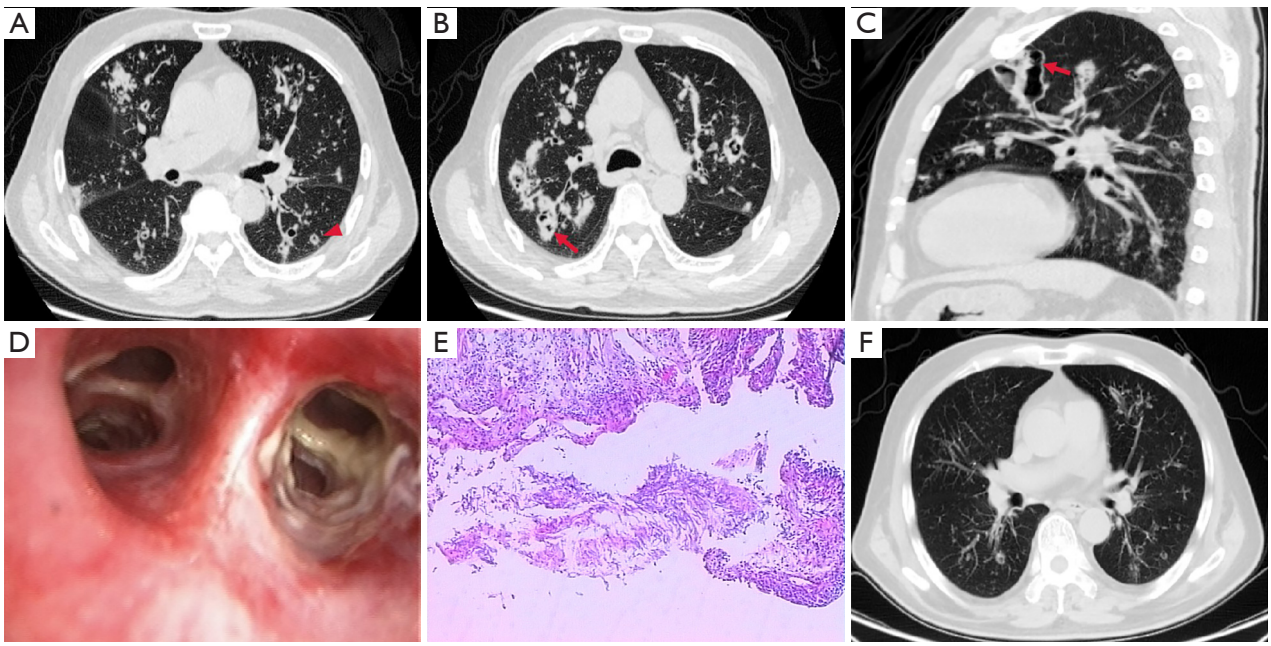

Figure 2 A 61-year-old man had diabetes and long-term exposure to paint. Axial (A,B) and sagittal (C) CT scans showed patchy peribronchial consolidation, bronchiectasis with wall thickening involved the lobar and segmental bronchi (arrows) and cavity (arrowhead). (D) The bronchoscopy showed that bronchial wall in the segmental bronchus was covered by pus-like exudates. (E) Histopathological examination of the bronchoscopic biopsy specimen showed chronic inflammation associated with infiltration of *Aspergillus* on hematoxylin-eosin staining (×4). (F) Axial CT scans showed lesions were significantly absorbed after 2 weeks of voriconazole treatment. CT, computed tomography.

frequency signs were defined as those with an incidence of ≥60%, while low-frequency signs were defined as those with an incidence of <40%. The highest-frequency signs included lobar and segmental bronchial lumen stenosis and wall thickening, patchy peribronchial consolidation, and nodules (>5 mm), the incidence of which were all 71.43%.

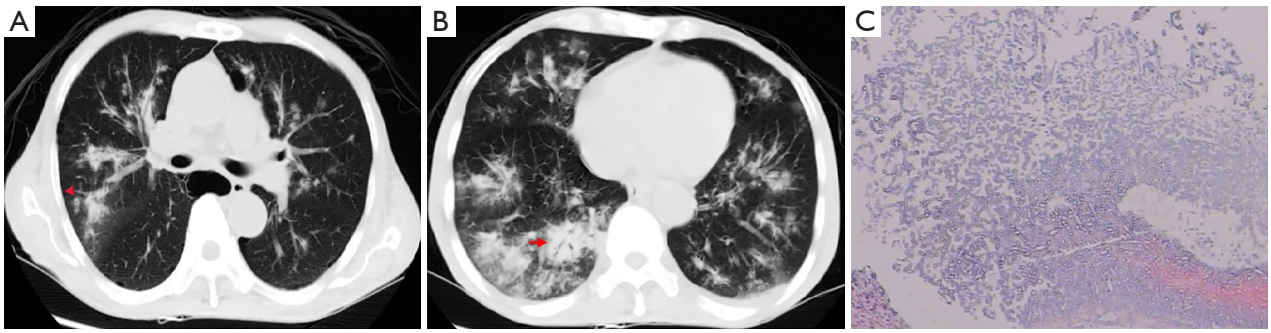

Figure 3 A 59-year-old man had diabetes and COPD with cough and shortness of breath and dyspnea. (A,B) Axial CT scans showed nodules (arrowhead) and patchy peribronchial consolidation (arrow). (C) Histopathological examination of the bronchoscopic biopsy specimen showed *Aspergillus* on hematoxylin-eosin staining (×10). COPD, chronic obstructive pulmonary disease; CT, computed tomography.

Table 1 The incidence rate of CT manifestations of AWIA

CT manifestations	Number	Incidence rate (%) (n=21)
Trachea or left/right main bronchial wall thickening	1	4.76
Lobar and segmental bronchial lumen stenosis and wall thickening	15	71.43
Lobar and segmental bronchiectasis and wall thickening	4	19.05
Patchy peribronchial consolidation	15	71.43
Tree-in-bud sign	14	66.67
Nodules (>5 mm)	15	71.43
Bronchioles wall thickening and lumen expansion	14	66.67
Ground-glass opacity	8	38.10
Cavity	7	33.33
Pleural effusion	5	23.81

CT, computed tomography; AWIA, airway invasive aspergillosis.

The second-highest-frequency indicators were tree-in-bud sign and bronchioles wall thickening, with an incidence of 66.67%. All other CT morphological manifestations were considered low-frequency signs. Bronchiolar wall thickening was defined as visible bronchiolar walls with a thickness greater than 0.5 mm on high-resolution CT images (*Figure 1*).

Outcome after treatment

After treatment with voriconazole and other antifungal drugs in all patients with AWIA, 17 patients received the follow-up of MSCT in the hospital. Six of them had clinical symptoms that were milder than before; however, the imaging showed that the lesions were more progressive than before, or new lesions appeared while the original lesions were absorbed. In addition, three patients with cavities were found to have collapsed cavities, which, after MSCT review, were found to have transformed into solid nodules. The inter-reader agreement for CT features was substantial, with a kappa value of 0.78 (95% CI: 0.70–0.86). Analysis of baseline CT signs and follow-up outcomes revealed that patients with extensive tree-in-bud opacities at initial presentation were more likely to show worsening CT patterns at follow-up (OR =2.5; 95% CI: 1.2–5.1; P=0.02).

Discussion

This study provides valuable insights into the CT features of AWIA in a cohort of 21 patients. Our findings

Table 2 The CT time of initial symptom and post-treatment follow-up

Patients No./sex/age (years)	Past medical history	Clinical symptoms	Initial CT scan time	Predominnant CT findings	Source of diagnosis	Treatment	Post-treatment follow-up
1/M/59	Diabetes, COPD	Cough, shortness of breath and dyspnea	2 weeks	Peribronchial consolidation, bronchial lumen stenosis and wall thickening, nodules	Histopathology	Voriconazole	4 weeks/symptoms improved and CT findings progressed
2/F/73	Duodenal perforation	Cough, fever	9 days	Nodules	Sputum culture	Caspofungin	2 weeks/symptoms improved and CT findings progressed
3/F/47	None	Cough, fever, chest pain	10 days	Peribronchial consolidation, bronchial lumen stenosis and wall thickening, nodules	Histopathology	Voriconazole, amphotericin	7 weeks/symptoms improved and CT findings progressed
4/F/27	None	Cough, chest pain, shortness of breath and dyspnea	4 weeks	Nodules, tree-in-bud sign, ground-glass opacity	BALF GM positive	Voriconazole	3 weeks/uniformly improved
5/F/44	Diabetes	Cough, fever	3 weeks	Peribronchial consolidation, bronchial lumen stenosis and wall thickening, nodules	Histopathology	Voriconazole	2 years/uniformly improved
6/F/63	None	Foreign matter aspiration	1 week	Peribronchial consolidation, bronchial lumen stenosis and wall thickening, nodules	Histopathology	–	None
7/M/72	COPD	Cough, shortness of breath and dyspnea	3 weeks	Cavity, peribronchial consolidation, tree-in-bud sign	BALF GM positive	Voriconazole	2 weeks/uniformly improved
8/M/61	Diabetes	Cough, shortness of breath and dyspnea	2 weeks	Cavity, bronchioles wall thickening and lumen expansion	Histopathology	Voriconazole	2 weeks/uniformly improved
9/M/74	Diabetes, COPD	Cough, shortness of breath and dyspnea	6 months	Trachea or main bronchial wall thickening, peribronchial consolidation	Histopathology	Voriconazole	None
10/M/75	Diabetes, COPD	Cough, shortness of breath and dyspnea, chest discomfort	4 weeks	Bronchial lumen stenosis and wall thickening, cavity, nodules	Sputum culture	Voriconazole	4 weeks/uniformly improved
11/M/70	Diabetes	Cough	2 weeks	Bronchiectasis and wall thickening, bronchioles wall thickening and lumen expansion	BALF GM positive	Voriconazole	6 weeks/the same as before
12/M/32	Previous influenza infection	Cough, shortness of breath and dyspnea, chest discomfort	2 days	Nodules, bronchioles wall thickening and lumen expansion	BALF GM positive	Voriconazole	2 weeks/symptoms improved and CT findings progressed

Table 2 (*continued*)

Table 2 (*continued*)

Patients No./sex/age (years)	Past medical history	Clinical symptoms	Initial CT scan time	Predominnant CT findings	Source of diagnosis	Treatment	Post-treatment follow-up
13/F/40	Old tuberculosis	Cough	3 months	Nodules, tree-in-bud sign, bronchioles wall thickening and lumen expansion	BALF GM positive	Voriconazole	4 months/symptoms improved and CT findings progressed
14/F/59	Lung cancer	Cough	1 week	Bronchial lumen stenosis and wall thickening, tree-in-bud sign	BALF GM positive	Voriconazole	5 weeks/symptoms improved and CT findings progressed
15/M/74	Sicca syndrome	Cough, shortness of breath and dyspnea	2 weeks	Nodules, ground-glass opacity	Sputum culture	Voriconazole	None
16/M/56	Trauma	Fever	1 week	Bronchioles wall thickening and lumen expansion, nodules, cavity	Histopathology	Voriconazole	None
17/M/37	Previous influenza infection	Cough, fever, chest pain	1 week	Bronchioles wall thickening and lumen expansion, nodules, cavity	BALF GM positive	Voriconazole	4 weeks/uniformly improved
18/M/65	Bronchiectasis	Cough	2 weeks	Peribronchial consolidation, bronchial lumen stenosis and wall thickening	BALF GM positive	Voriconazole	5 months/uniformly improved
19/F/65	Previous influenza infection	Cough	4 weeks	Peribronchial consolidation, bronchial lumen stenosis and wall thickening	BALF GM positive	Voriconazole	1 weeks/ uniformly improved
20/M/68	COPD	Cough, fever, chest discomfort	2 weeks	Cavity, peribronchial consolidation	BALF GM positive	Voriconazole	2 weeks/uniformly improved
21/M/56	SLE, COPD	Cough, shortness of breath and dyspnea	2 weeks	Bronchial lumen stenosis and wall thickening, peribronchial consolidation	BALF GM positive	Voriconazole	8 months/uniformly improved

Initial CT scan time, time interval between symptom occurrence and CT examination; post-treatment follow-up, the time interval between initial CT and follow-up CT. CT, computed tomography; M, male; COPD, chronic obstructive pulmonary disease; F, female; BALF, bronchoalveolar lavage fluid; GM, galactomannan; SLE, systemic lupus erythematosus.

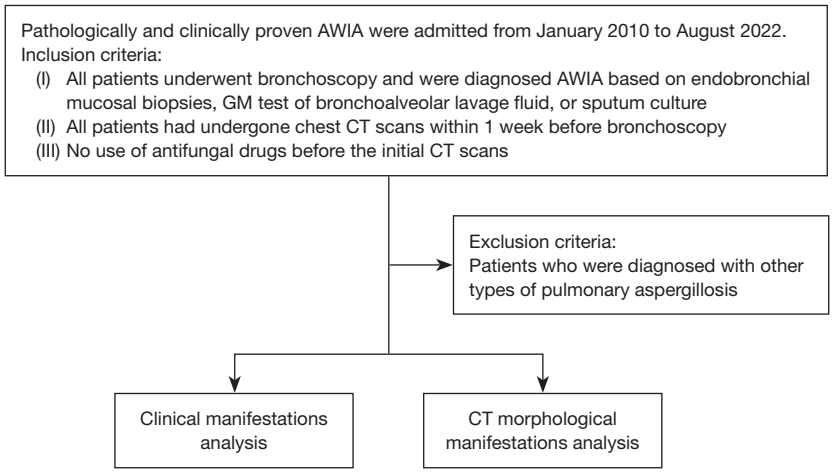

Figure 4 Flow diagram of the patient selection process. AWIA, airway invasive aspergillosis; GM, galactomannan; CT, computed tomography.

highlight several key CT patterns that may aid in the early recognition and diagnosis of AWIA. The most frequent CT features observed were lobar and segmental bronchial lumen stenosis with wall thickening, patchy peribronchial consolidation, and nodules >5 mm, each occurring in >70% of cases. Additionally, tree-in-bud sign and bronchiolar wall thickening were present in two-thirds of patients. These high-frequency signs, especially when occurring in combination, should raise suspicion of AWIA, particularly in patients with underlying risk factors, such as chronic lung disease or diabetes. Importantly, our study also revealed that AWIA can occur in patients without classic immunocompromising conditions, expanding the potential patient population at risk for this infection.

It has been widely documented that immunodeficiency is a classic risk factor and pre-requisite for IPA, encompassing conditions such as neutropenia, stem-cell transplantation, and solid-organ transplantation (9). Recently, conditions unrelated to the patient's immune status, such as chronic obstructive pulmonary disease, diabetes, and pre-influenza infection, have also gained recognition as risk factors for IPA (10-12). This aligns with our study's findings, indicating that the most prevalent risk factor is chronic lung disease, followed by diabetes. The reasons for the results may be that patients have ciliated dysfunction of airway epithelial cells in chronic lung disease and malnutrition and decreased immunity in diabetes (13).

In our study, 19 patients experienced the symptom of cough (n=19, 90.48%), which is the most typical symptom in our results. Generally, cough is highly related to factors such as airway inflammation, injury, secretion accumulation, and airway spasm; therefore, it is regarded as one of the most typical symptoms of chronic lung disease. It was followed by shortness of breath and dyspnea (n=9, 42.86%), chest pain and chest discomfort were also common. Although not entirely consistent with previous studies (14,15), all common clinical manifestations were airway-responsive changes, which may be related to *Aspergillus* invasion to the airway basement membrane leading to airway irritation spasm.

Comparing our findings with previous studies, we found some similarities and differences in the frequencies of CT features. Wu *et al.* (14) conducted a larger study with 72 patients with AWIA, categorizing the imaging findings into different types. They reported bronchial wall thickening in early type II cases, which occurred in 4.2% of their patients, whereas we observed this feature more frequently (71.43% of our cases). The tree-in-bud sign, which Wu *et al.* associated with their Type III category (25.0% of cases), was more common in our study (66.67%). Interestingly, Wu *et al.* found bronchiectasis (their type IIa) in 37.5% of patients, whereas in our study, bronchiectasis was less common, occurring in only 19.05% of patients. They also reported consolidation around the bronchus (type IIb) in 30.6% of cases, which is lower than our observation of peribronchial consolidation (71.43%). These differences may be attributed to variations in patient populations, disease stages at the time of imaging or the specific classification system used. Additionally, our study focused on individual CT features rather than categorizing patients into distinct types, which may account

for some of the discrepancies in reported frequencies. These comparisons highlight the need for standardized reporting of CT features in AWIA to facilitate more direct comparisons across studies. Furthermore, depending on the clinical type, AWIA can be divided into three forms: acute tracheobronchitis, bronchiolitis, and bronchopneumonia (2). The tracheobronchitis usually presented bronchial wall thickening with lumen stenosis; when the *Aspergillus* invaded the full-thickness of the bronchus and involved the adjacent lung parenchyma, bronchopneumonia would present as patchy peribronchial consolidation (6). Occasionally, bronchiectasis would occur because of increasing mucus secretion stimulated by *Aspergillus* proteases in the airways (16), which accounted for 19.05% in our study. The bronchiolitis usually presented a tree-in-bud sign corresponding to the bronchiolar walls thickening with mucus and *Aspergillus* hyphae in the lumen pathologically (17). If impacted mucus is expelled or invaded in the bronchiole, CT depicts lumen expansion and wall thickening involving the bronchioles and nodules, respectively.

In this study, ground-glass opacity and cavities were infrequently observed, constituting 38.10% and 33.33%, respectively. The study elucidated that these cavities exhibited a thick wall with patchy/line-like septal shadows. The pathological explanation is that with the recovery of the disease, the hyphae in the solid nodules were partially broken and coagulated; necrotic substances were then excluded with the barrier of hyphae, leading to patchy/line-like septal shadows in the cavity. Ground-glass opacity around nodules was facilitated by the proximity between bronchi and arteries and caused perinodular alveolar hemorrhage (18). The imaging manifestations mentioned above may reflect the invasion and destruction processes of *Aspergillus* in the airway, as well as the inflammatory response of surrounding tissues to infection. Identifying and interpreting these imaging features can help doctors in identifying and interpreting these CT features and diagnosing and evaluating IPA of the airways.

In this study, we employed MSCT to acquire imaging manifestations of AWIA. The high spatial resolution of MSCT enables a more precise representation of the morphology and structure of the examined area, helping doctors determine the type and extent of the disease more accurately. This not only improves diagnostic accuracy but also provides more targeted guidance for treatment. Furthermore, MSCT is a non-invasive imaging method, posing no trauma, pain, or danger to patients. It can also perform multi-phase scans to observe dynamic changes in lesions, providing comprehensive information for disease diagnosis and treatment. Although MSCT is an advantaged imaging technique, we still need to emphasize that the imaging manifestations of AWIA were not specific, and the above imaging signs can also be seen in other diseases, such as tuberculosis. However, tuberculosis infection has relatively favored sites, which are the apical posterior segment of the upper lobe and the dorsal segment of the lower lobe, and it has lesions of different stages simultaneously. In addition, extensive peribronchial consolidation with dilated segmental or subsegmental bronchi is not a common finding (19). In this study, we also found an interesting phenomenon; after 17 cases were treated with antifungal drugs, in six cases with relief of clinical manifestations, MSCT revealed a progressive lesion or a new lesion while the original lesion was absorbed and reduced, but all the patients eventually showed better imaging performance than before. The reasons for the variability of treatment response may be as follows: (I) the follow-up time was not fixed; (II) the antifungal drugs used by patients were not exactly the same, and different individuals have different reactions to the drugs; and (III) there were also differences in the concentration of pathogens in the patient's body and the immune system's resistance to *Aspergillus*. Our observations suggest that clinical improvement may precede radiological improvement in some AWIA cases. However, given our small sample size and variable follow-up times, further research is needed to establish definitive guidelines for treatment duration based on clinical and radiological responses.

Some limitations of this study should be noted. First, because this was a retrospective study from a single center with a small sample size, and airway invasive aspergillosis is a rare infectious disease, some cases of AWIA were not entirely pathologically confirmed but partially clinically proven with the notable symptoms, such as severe cough with chest pain. Further multicenter studies are needed to enlarge the sample size. Second, the study spanned a long time, and CT scan equipment and scan layer thickness were not identical in all patients. Third, no control group of angio-invasive aspergillosis was established in our study.

In conclusion, our study demonstrates that the risk factors for AWIA were not confined to classically immunocompromised patients. The presence of one or more high-frequency CT signs—including lobar and segmental bronchial lumen stenosis with wall thickening, patchy peribronchial consolidation, nodules >5 mm, tree-

in-bud sign, and bronchiolar wall thickening—should raise suspicion of AWIA, particularly in patients with underlying diseases. However, it is important to note that while underlying conditions are common in patients with AWIA, they were not a prerequisite for diagnosis. In our study, 3 patients (14.3%) had no significant medical history, indicating that AWIA can occur in previously healthy individuals.

When these characteristic CT features are observed, especially in combination, clinicians should consider AWIA as a differential diagnosis. Early consideration of this possibility may lead to prompt initiation of diagnostic procedures, such as bronchoscopy or GM testing, and timely antifungal therapy when indicated. This approach could potentially prevent the exacerbation of IPA and improve patient outcomes.

Our findings underscore the importance of maintaining a high index of suspicion for AWIA, even in patients without classic risk factors, and highlight the value of CT imaging in guiding clinical decision-making. Further, research with larger, prospective studies is needed to validate these findings and to develop more precise diagnostic criteria for AWIA based on CT features.

Conclusions

This study demonstrates that AWIA can occur in patients without classic immunocompromising conditions. The presence of characteristic high-frequency CT features—including bronchial lumen stenosis, peribronchial consolidation, nodules >5 mm, tree-in-bud sign, and bronchiolar wall thickening—should raise clinical suspicion for AWIA. Early recognition of these imaging patterns, particularly in combination, may facilitate timely diagnosis and treatment. Further prospective studies are needed to validate these findings and develop more precise diagnostic criteria.

Acknowledgments

We would like to thank Brandon D for his help in polishing our paper.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-843/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-843/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-843/prf

Funding: The work was financially supported by the Pre-Research Fund Project for Young Employees of The Second Affiliated Hospital of Soochoow University (No. SDFEYJC2236) and the Jiangsu Research Hospital Society Infection Imaging Research Special Fund Project (No. GY202308).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-843/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of The Second Affiliated Hospital of Soochow University [No. EC-AF(SQ)-14/20230101]. The requirement for informed consent was waived.

References

1. Yanagawa N, Sakai F, Doki N, et al. CT of invasive pulmonary aspergillosis (IPA) in cases with hematologic malignancy: Comparison of CT features in the group classified by the severity of neutropenia and underlying disease. Eur J Radiol 2020;131:109042.
2. Moldoveanu B, Gearhart AM, Jalil BA, et al. Pulmonary Aspergillosis: Spectrum of Disease. Am J Med Sci 2021;361:411-9.

3. Liu Z, Li Y, Tian X, et al. Airway-invasion-associated pulmonary computed tomography presentations characteristic of invasive pulmonary Aspergillosis in non-immunocompromised adults: a National Multicenter Retrospective Survey in China. Respir Res 2020;21:173.
4. Nucci M. Is Early Invasive Pulmonary Aspergillosis Coming of Age? Clin Infect Dis 2020;70:347.
5. Ledoux MP, Guffroy B, Nivoix Y, et al. Invasive Pulmonary Aspergillosis. Semin Respir Crit Care Med 2020;41:80-98.
6. Sousa C, Pasini RA, Pasqualotto A, et al. Imaging Findings in Aspergillosis: From Head to Toe. Mycopathologia 2023;188:623-41.
7. Nyga R, Maizel J, Nseir S, et al. Invasive Tracheobronchial Aspergillosis in Critically Ill Patients with Severe Influenza. A Clinical Trial. Am J Respir Crit Care Med 2020;202:708-16.
8. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis 2020;71:1367-76.
9. Vélez Pintado M, Camiro-Zúñiga A, Aguilar Soto M, et al. COVID-19-associated invasive pulmonary aspergillosis in a tertiary care center in Mexico City. Med Mycol 2021;59:828-33.
10. Mir T, Uddin M, Khalil A, et al. Mortality outcomes associated with invasive aspergillosis among acute exacerbation of chronic obstructive pulmonary disease patient population. Respir Med 2022;191:106720.
11. Ghanaat F, Tayek JA. Weight loss and diabetes are new risk factors for the development of invasive aspergillosis infection in non-immunocompromized humans. Clin Pract (Lond) 2017;14:296-301.
12. Schauwvlieghe AFAD, Rijnders BJA, Philips N, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. Lancet Respir Med 2018;6:782-92.
13. Bulpa P, Duplaquet F, Dimopoulos G, et al. Invasive Pulmonary Aspergillosis in Chronic Obstructive Pulmonary Disease Exacerbations. Semin Respir Crit Care Med 2020;41:851-61.
14. Wu J, Zhang T, Pan J, et al. Characteristics of the Computed Tomography Imaging Findings in 72 Patients with Airway-Invasive Pulmonary Aspergillosis. Med Sci Monit 2021;27:e931162.
15. Kanaujia R, Singh S, Rudramurthy SM. Aspergillosis: an Update on Clinical Spectrum, Diagnostic Schemes, and Management. Curr Fungal Infect Rep 2023. [Epub ahead of print]. doi: 10.1007/s12281-023-00461-5.
16. Jaggi TK, Ter SK, Mac Aogáin M, et al. Aspergillus-Associated Endophenotypes in Bronchiectasis. Semin Respir Crit Care Med 2021;42:556-66.
17. Russo A, Tiseo G, Falcone M, et al. Pulmonary Aspergillosis: An Evolving Challenge for Diagnosis and Treatment. Infect Dis Ther 2020;9:511-24.
18. Casutt A, Couchepin J, Brunel AS, et al. High prevalence of peribronchial focal lesions of airway invasive aspergillosis in hematological cancer patients with prolonged neutropenia. Br J Radiol 2020;93:20190693.
19. Kim JH, Lee HL, Kim L, et al. Airway centered invasive pulmonary aspergillosis in an immunocompetent patient: case report and literature review. J Thorac Dis 2016;8:E250-4.

Cite this article as: Ni X, Yu R, Hou J, Ya Y, Fan G, Chen Z. Imaging findings of multislice computed tomography in 21 patients with airway invasive pulmonary aspergillosis. J Thorac Dis 2025;17(2):887-897. doi: 10.21037/jtd-24-843