COMPUTED TOMOGRAPHY ASSESSMENT OF PULMONARY ASPERGILLOSIS: IMAGING PHENOTYPES AND DIAGNOSTIC CORRELATION IN A MACEDONIAN CLINICAL COHORT

Sonja Nikolova
University Institute of Radiology, Medical Faculty- Skopje, North Macedonia, sonikmk@gmail.com

Abstract: Pulmonary aspergillosis comprises a diverse set of fungal disorders with radiologic features influenced by immune status and pre-existing pulmonary architecture. In clinical scenarios where tuberculosis-related structural damage and chronic immunosuppression coexist, computed tomography (CT) plays a central role in raising early diagnostic suspicion and guiding further evaluation. This article presents a single-centre clinical-imaging analysis of patients with confirmed pulmonary aspergillosis managed at a tertiary radiology institution in North Macedonia, with particular focus on CT phenotypes and their diagnostic relevance. Distinct imaging patterns were observed across the cohort, including intracavitary fungal colonization within chronic post-tuberculous cavities, progressive cavitary and paracavitary changes suggestive of semi-invasive disease, and nodular or halo-type lesions correlating with angioinvasion in immunocompromised individuals. CT-based pattern recognition enabled stratification of cases along a spectrum ranging from saprophytic colonization to invasive fungal infection, facilitating targeted microbiologic testing and interventional procedures. Beyond individual diagnostic utility, these findings highlight the broader significance of local epidemiology, as structurally altered lungs provided a permissive substrate for colonization in the majority of patients. Recognition of such CT phenotypes may improve diagnostic confidence, reduce delays in antifungal therapy, and support multidisciplinary management in regions where fungal disease overlaps with chronic pulmonary pathology.
Keywords: pulmonary aspergillosis, computed tomography, aspergilloma, chronic cavitary disease, invasive fungal infection

1. INTRODUCTION

Pulmonary aspergillosis encompasses a spectrum of fungal lung diseases caused predominantly by *Aspergillus fumigatus*. The clinical and radiologic manifestations vary according to host immune status and the presence of underlying structural lung abnormalities (Davda et al., 2018). In healthy lungs, inhaled conidia are usually cleared without consequence. In contrast, patients with impaired immunity or chronic lung damage may develop colonization or invasive disease, resulting in syndromes that range from allergic hypersensitivity to chronic cavitary and angioinvasive forms (Garg et al., 2022).

High-resolution computed tomography (HRCT) is the imaging modality of choice for evaluating these conditions because of its ability to depict intracavitary soft tissue, parenchymal invasion, bronchiectasis, and pleural complications with high sensitivity (Alexander et al., 2021). Among structural risk factors, post-tuberculous lung disease is recognized as the leading global substrate for chronic pulmonary aspergillosis (CPA), particularly in regions where tuberculosis remains endemic (Garg et al., 2023). Residual cavities, pleural fibrosis, and architectural distortion create a favorable environment for saprophytic fungal growth and chronic cavitary progression.

These factors are especially relevant to Eastern Europe and the Balkans, where tuberculosis remains more prevalent than in Western Europe and where CPA is likely underdiagnosed despite its substantial morbidity. Distinguishing chronic cavitary aspergillosis from post-tuberculous residual disease can be difficult due to overlapping symptoms and imaging findings, underscoring the value of immunologic testing (e.g., *Aspergillus* IgG) and careful CT pattern assessment (Garg et al., 2023; Rønberg et al., 2022).

Radiologically, CPA exhibits consistent patterns linked to host factors: cavitary and pleural-based disease in structurally abnormal but immunocompetent lungs, and nodular or angioinvasive patterns in immunocompromised patients (Aquino et al., 1994). The transition between chronic cavitary and semi-invasive forms—particularly in patients receiving long-term low-dose corticosteroids—highlights the need for CT-based phenotype recognition and multidisciplinary evaluation. Within this context, our Macedonian cohort provides a contemporary regional perspective on CT morphology in pulmonary aspergillosis in a population enriched with post-primary TB sequelae.

2. MATERIALS AND METHODS

A retrospective single-center study was performed at the Institute of Radiology in Skopje, North Macedonia, a tertiary referral hospital with dedicated thoracic imaging services. Patients assessed between January 2022 and December 2025 for suspected fungal lung disease were screened. Electronic medical records and imaging archives identified adults (≥18 years) with a final diagnosis of pulmonary aspergillosis based on HRCT and microbiologic,

serologic, or multidisciplinary confirmation. Exclusion criteria were poor image quality, absent confirmatory data, or incomplete documentation. Ten patients met the inclusion criteria.

Diagnostic classification followed contemporary clinical, radiologic, and microbiologic criteria for pulmonary aspergillosis (Garg et al., 2023). Confirmation was obtained through one or more of the following: *Aspergillus* IgG serology, serum or BAL galactomannan, sputum or BAL fungal culture/PCR, histology or cytology from CT-guided or bronchoscopic sampling, or multidisciplinary consensus when direct confirmation was not feasible. This diagnostic strategy aligns with current guidance for chronic and invasive aspergillosis (Alexander et al., 2021).

All patients underwent volumetric chest CT on multi-detector scanners using institutional HRCT protocols (slice thickness ≤1.5 mm, high-frequency reconstruction kernel, supine end-inspiratory acquisition). Intravenous contrast was administered selectively for suspected complications such as hemoptysis or vascular invasion. HRCT is regarded as the imaging modality of choice for pulmonary fungal infections owing to its sensitivity for detecting nodules, cavities, and intracavitary soft tissue (Alexander et al., 2021).

Imaging evaluation included: (1) structural substrate (post-tuberculous cavities, pleural fibrosis, bronchiectasis), (2) fungal morphology (intracavitary soft tissue, wall thickening, nodules, halo sign, bronchoceles), (3) lobar distribution, and (4) complications (hemoptysis, pleural reaction, vascular findings). CT features were categorized according to established descriptors for pulmonary aspergillosis (Aquino et al., 1994) and chronic pulmonary disease (Davda et al., 2018).

The study complied with institutional ethical standards for retrospective research, and all patient data were anonymized.

3. RESULTS

Ten patients met inclusion criteria (7 males, 3 females; age range 34–72 years; mean age 56 ± 12 years). Structural lung disease was present in 8/10 patients, most commonly residual cavities and pleural fibrosis from prior pulmonary tuberculosis. Two patients had chronic obstructive pulmonary disease (COPD) as an additional comorbidity, and three were receiving systemic corticosteroids at the time of presentation.

The predominant presenting symptoms were chronic cough (7/10), exertional dyspnea (6/10), and hemoptysis (5/10).

Fever was infrequent and observed primarily in immunosuppressed patients (2/10).

Serum *Aspergillus* IgG was positive in 7/10 cases.

Galactomannan testing (serum or bronchoalveolar lavage) yielded positive results in 4/6 tested patients.

Microbiological confirmation via sputum or BAL culture occurred in 5/9 tested patients.

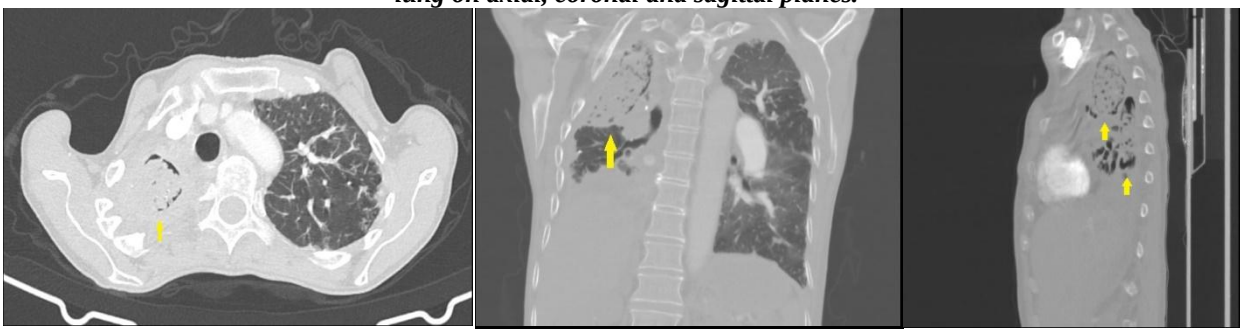
CT-guided aspiration or bronchoscopic biopsy was performed in three cases, all demonstrating fungal elements consistent with *Aspergillus* species.

Four reproducible CT phenotypes were identified:

Saprophytic–Intracavitary Phenotype (n = 4)

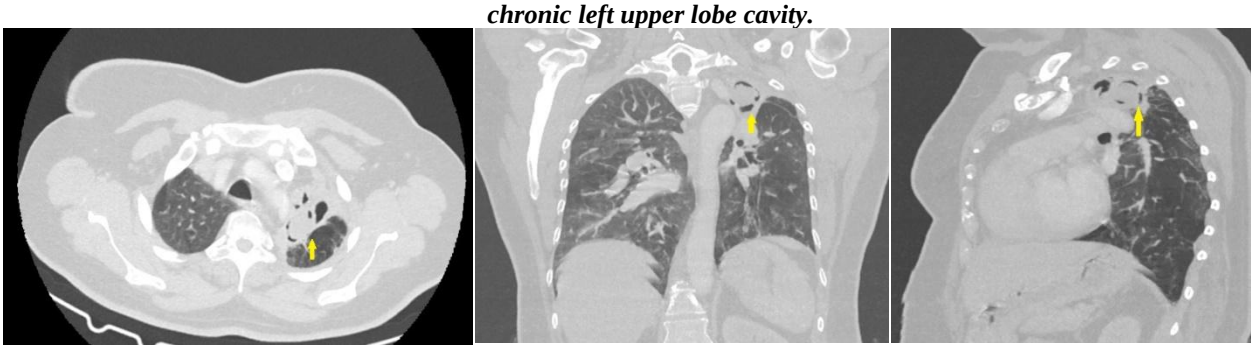
Patients demonstrated thin- or thick-walled cavities containing intracavitary soft-tissue masses consistent with aspergillomas. Dependent intracavitary positioning compatible with Monod's sign was observed in 3/4 cases. Cavities were located predominantly in the upper lobes and corresponded to residual post-tuberculous disease,
Figure 1 and 2.

Figure 1. a-c, Expansile intracavitary aspergillomas within chronic post-tuberculous cavities of the right upper lung on axial, coronal and sagittal planes.



Source: Author

Figure 2. a-c, Axial, coronal, and sagittal CT showing an intracavitary fungus ball with Monod sign in a chronic left upper lobe cavity.



Source: Author

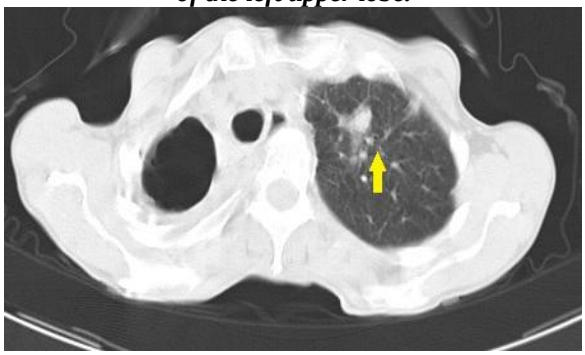
1. Chronic Cavitary / Semi-Invasive Phenotype (n = 3)

Findings included progressive cavity wall thickening, paracavitary consolidation, pleural thickening, and architectural distortion. One steroid-treated patient exhibited more rapid progression. No angioinvasive halo signs were observed in this subgroup.

2. Angioinvasive / Nodular Phenotype (n = 2)

Two immunosuppressed patients exhibited multiple nodules measuring 5–18 mm with ground-glass halo sign, consistent with early angioinvasive disease as described in invasive pulmonary fungal infections (Alexander et al., 2021). One patient demonstrated wedge-shaped infarct-like consolidation, ***Figure 3***.

Figure 3. Axial CT demonstrating a solitary angioinvasive nodule with ground-glass halo in the apical segment of the left upper lobe.

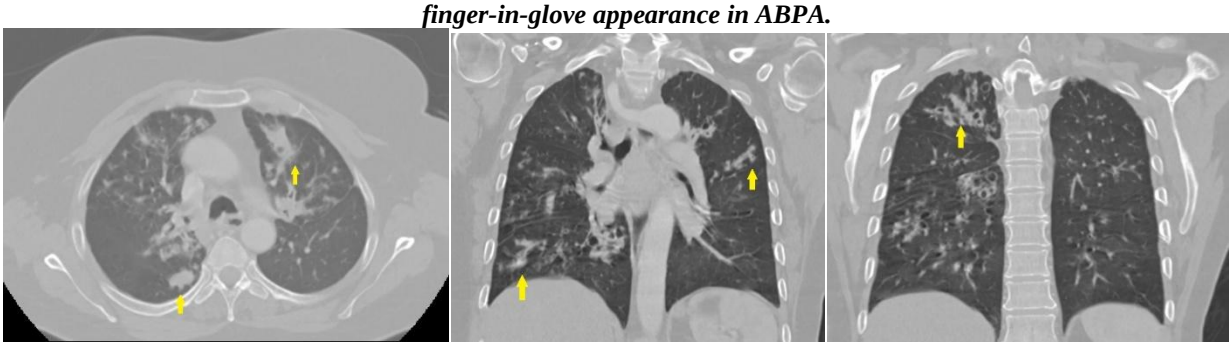


Source: Author

3. Allergic Bronchopulmonary Phenotype (n = 1)

One patient demonstrated branching bronchoceles and segmental bronchial impaction compatible with ABPA, correlating with the described "finger-in-glove" morphology in mucus-filled bronchi (Aquino et al., 1994), ***Figure 4***.

Figure 4. Axial, coronal, and sagittal CT showing branching bronchoceles and segmental mucus impaction with finger-in-glove appearance in ABPA.



Source: Author

CT-guided aspiration or bronchoscopy was performed in four patients without complication. Microbiological or cytologic confirmation was obtained in all sampled cases. Hemoptysis was documented in 5/10 patients but did not result in hemodynamic instability. No patients required emergency surgical intervention.

4. DISCUSSIONS

In this single-center cohort, pulmonary aspergillosis most often manifested as a saprophytic or chronic cavitary process within residual post-tuberculous cavities. This trend reflects the well-recognized relationship between chronic pulmonary aspergillosis (CPA) and structural lung disease in regions with persistent or historical tuberculosis exposure (Madden et al., 2025; Nguyen et al., 2021). Residual cavities and pleural scarring create a ventilated space that supports fungal colonization and may progress to intracavitary mycetomas, chronic cavitary disease, or pleural fibrosis. Our observations align with larger regional data emphasizing TB-related architectural damage as a dominant substrate for CPA.

Radiologically, the CT phenotypes in our cohort mirrored current descriptors in the literature. The saprophytic–intracavitary phenotype demonstrated classical findings, including Monod's sign and pleural thickening, consistent with imaging–pathologic correlation studies (Kang et al., 2002; Barac et al., 2023). In contrast, the chronic cavitary/semi-invasive phenotype showed progressive wall thickening and paracavitary infiltrates, corresponding to the continuum between stable CPA and subacute invasive disease described in immunologically vulnerable groups (Wu et al., 2021). The angioinvasive/nodular phenotype, observed exclusively in immunosuppressed patients, featured halo-type nodules and infarct-like opacities, matching international guidance that identifies the halo sign as an early indicator of invasive fungal infection (Alexander et al., 2021).

These phenotypes carry practical diagnostic implications. The strong association between cavitary disease and prior TB highlights the need to integrate local epidemiology into radiologic assessment, particularly in Eastern Europe. Similarly, identifying halo signs or infarct-like lesions in immunosuppressed individuals should raise suspicion for invasive aspergillosis, in line with radiologic and clinical recommendations (Alexander et al., 2021). The presence of allergic bronchopulmonary aspergillosis (ABPA), although less common in our cohort, underscores the relevance of recognizing bronchoceles, central bronchiectasis, and mucoid impaction—features described in classical radiologic reports (Aquino et al., 1994).

Despite the limited sample size, our experience demonstrates the diagnostic value of CT for stratifying patients along the aspergillosis spectrum. Imaging patterns guided microbiologic and serologic testing and supported a multidisciplinary diagnostic workflow consistent with contemporary CPA guidance (Garg et al., 2023). The notable frequency of hemoptysis further emphasizes CT's role in assessing fungal burden and pleural-based vascular involvement, which may influence clinical decision-making.

This study has limitations, including retrospective single-center design, heterogeneous clinical testing, and limited histopathologic confirmation. Longitudinal imaging and outcome data were not assessed. Nevertheless, these findings offer relevant regional insight into aspergillosis within a TB-endemic environment and reinforce CT as an essential diagnostic tool. Broader multicenter collaboration across the Balkans and Eastern Europe may help define CPA prevalence and refine imaging-based diagnostic criteria specific to structural lung disease.

5. CONCLUSIONS

Pulmonary aspergillosis in our cohort demonstrated distinct and clinically meaningful CT phenotypes that largely reflected the interaction between structural lung disease and host immunity. Saprophytic intracavitary fungal growth was the predominant manifestation, arising almost exclusively within post-tuberculous cavities, while semi-invasive and angioinvasive patterns occurred in patients with varying degrees of immunosuppression. These findings reinforce the central role of high-resolution CT in identifying characteristic morphologic signatures, directing appropriate microbiologic and serologic evaluation, and guiding multidisciplinary care. In regions where tuberculosis remains prevalent, heightened awareness of cavitary substrates and their propensity for fungal colonization is essential to reduce diagnostic delay and mitigate morbidity. Although limited by sample size and retrospective design, this work provides imaging-based insight relevant to local epidemiology and underscores the need for broader regional studies to better define the burden and radiologic spectrum of chronic pulmonary aspergillosis.

REFERENCES

Alexander, B. D., Lamoth, F., Heussel, C. P., Prokop, C. S., Desai, S. R., Morrissey, C. O., & Baddley, J. W. (2021). Guidance on Imaging for Invasive Pulmonary Aspergillosis and Mucormycosis: From the Imaging Working Group for the Revision and Update of the Consensus Definitions of Fungal Disease from the

EORTC/MSGERC. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *72*(Suppl 2), S79–S88. https://doi.org/10.1093/cid/ciaa1855

Aquino, V. R., Nagel, F., Andreolla, H. F., de-Paris, F., Xavier, M. O., Goldani, L. Z., Denning, D. W., & Pasqualotto, A. C. (2012). The performance of real-time PCR, galactomannan, and fungal culture in the diagnosis of invasive aspergillosis in ventilated patients with chronic obstructive pulmonary disease (COPD). *Mycopathologia*, *174*(2), 163–169. https://doi.org/10.1007/s11046-012-9531-1

Barac, A., Vujovic, A., Drazic, A., Stevanovic, G., Paglietti, B., Lukic, K., Stojanovic, M., & Stjepanovic, M. (2023). Diagnosis of Chronic Pulmonary Aspergillosis: Clinical, Radiological or Laboratory?. *Journal of fungi (Basel, Switzerland)*, *9*(11), 1084. https://doi.org/10.3390/jof9111084

Davda, S., Kowa, X. Y., Aziz, Z., Ellis, S., Cheasty, E., Cappocci, S., & Balan, A. (2018). The development of pulmonary aspergillosis and its histologic, clinical, and radiologic manifestations. *Clinical radiology*, *73*(11), 913–921. https://doi.org/10.1016/j.crad.2018.06.017

Garg, M., Bhatia, H., Chandra, T., Debi, U., Sehgal, I. S., Prabhakar, N., Sandhu, M. S., & Agarwal, R. (2022). Imaging Spectrum in Chronic Pulmonary Aspergillosis. *The American journal of tropical medicine and hygiene*, *108*(1), 15–21. https://doi.org/10.4269/ajtmh.22-0366

Garg, A., Bhalla, A. S., Naranje, P., Vyas, S., & Garg, M. (2023). Decoding the Guidelines of Invasive Pulmonary Aspergillosis in Critical Care Setting: Imaging Perspective. *The Indian journal of radiology & imaging*, *33*(3), 382–391. https://doi.org/10.1055/s-0043-57004

Kang, E. Y., Kim, D. H., Woo, O. H., Choi, J. A., Oh, Y. W., & Kim, C. H. (2002). Pulmonary aspergillosis in immunocompetent hosts without underlying lesions of the lung: radiologic and pathologic findings. *AJR. American journal of roentgenology*, *178*(6), 1395–1399. https://doi.org/10.2214/ajr.178.6.1781395

Madden, A. E., Ofori, S. K., Budu, M., Sisay, E., Dooley, B., & Murray, M. B. (2025). A Systematic Review of Chronic Pulmonary Aspergillosis Among Patients Treated for Pulmonary Tuberculosis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *81*(4), e163–e171. https://doi.org/10.1093/cid/ciaf150

Nguyen, N. T. B., Le Ngoc, H., Nguyen, N. V., Dinh, L. V., Nguyen, H. V., Nguyen, H. T., & Denning, D. W. (2021). Chronic Pulmonary Aspergillosis Situation among Post Tuberculosis Patients in Vietnam: An Observational Study. *Journal of fungi (Basel, Switzerland)*, *7*(7), 532. https://doi.org/10.3390/jof7070532

Rønberg, R., Davidsen, J. R., Salzer, H. J. F., Van Braeckel, E., Rosenvinge, F. S., & Laursen, C. B. (2022). Prevalence of Chronic Pulmonary Aspergillosis in Patients Suspected of Chest Malignancy. *Journal of fungi (Basel, Switzerland)*, *8*(3), 297. https://doi.org/10.3390/jof8030297

Wu, J., Zhang, T., Pan, J., Zhang, Q., Lin, X., Chang, L., Chen, Y. C., & Xue, X. (2021). Characteristics of the Computed Tomography Imaging Findings in 72 Patients with Airway-Invasive Pulmonary Aspergillosis. *Medical science monitor : international medical journal of experimental and clinical research*, *27*, e931162. https://doi.org/10.12659/MSM.931162