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CASE REPORT: CLINICAL CASE

Invasive Aspergillosis With Multiple Locations, Mediastinitis, and Cardiac Invasion

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ABSTRACT

A 25-year-old man reporting weight loss and constitutional symptoms was empirically treated for tuberculosis. Following acute seizures, the patient underwent cerebral imaging and was diagnosed with multiple nonischemic cerebral lesions. Thoracic imaging revealed fibrosing mediastinitis infiltrating and obscuring the left atrium and left ventricle. Results of a skin nodule biopsy revealed fungal hyphae, and invasive aspergillosis was finally diagnosed. (JACC Case Rep. 2024;29:102770) © 2024 Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 25-year-old man presented to the emergency department with new-onset multiple episodes of generalized tonic-clonic seizures for the past 24 hours. On clinical examination, he was afebrile and drowsy without focal neurologic deficits. On systemic examination, the patient had multiple subcutaneous nodules in the chest, thighs, and gluteal region.

TAKE-HOME MESSAGES

- Aspergillus infection is rarely responsible for fibrosing mediastinitis.
- Aspergillosis should be suspected when there is involvement of multiple systems, even in young immunocompetent patients.

PAST MEDICAL HISTORY

The patient had a history of significant unintentional weight loss (10 kg in the last 4 months) and fever on and off; mild chest pain was present. Chest radiograph revealed mild cardiomegaly and left-sided pleural effusion without any pulmonary lesions. He had been receiving empirical antitubercular therapy for the past 4 months. Pleural effusion was exudative type, but no microbiologic evidence of tuberculosis was obtained. The patient had not achieved symptomatic relief with earlier treatment.

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

FDG = fluorodeoxyglucose

LA = left atrium

PET = positron emission tomography

DIFFERENTIAL DIAGNOSIS

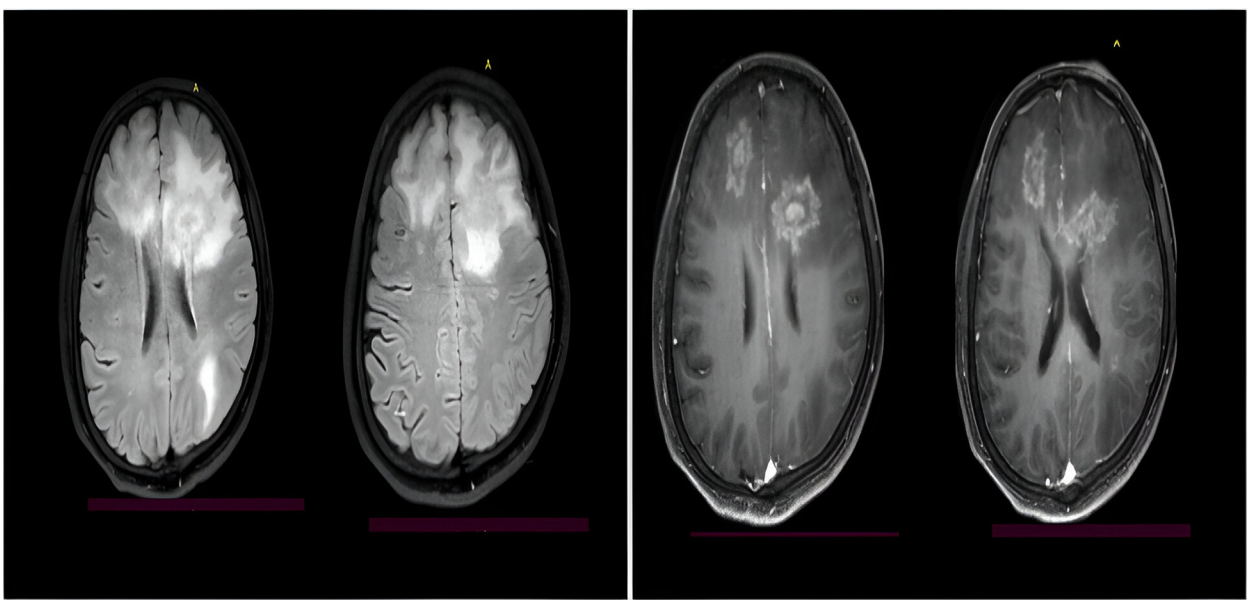
Differential diagnosis may include neuroinfections such as encephalitis or meningoencephalitis, inflammatory disorders (eg, vasculitis, sarcoidosis, IgG4 disease), or neoplastic disease.

INVESTIGATIONS

Computed tomography (CT) imaging of the head revealed nonischemic, multiple hypodense lesions in the bilateral frontal region. Magnetic resonance imaging of the brain showed heterogeneously enhancing lesions in the bilateral frontal and left parietal lobe (Figure 1). An electrocardiogram showed normal sinus rhythm. Transthoracic echocardiogram and transesophageal echocardiogram revealed a large nonpedunculated homogeneous mass lesion infiltrating and obscuring the left atrial appendage and left atrium (LA). No pericardial effusion was noted. Contrast-enhanced CT imaging of the chest and abdomen (Figure 2) revealed an 8.5 × 8 × 5 cm mass in the posterior mediastinum extending into the LA and protruding into its lumen, extending into the base of the left ventricle and encasing the descending thoracic aorta without luminal compromise. The mass was extending into the left lower lobe of the lung causing collapse consolidation, encasing the left inferior pulmonary veins along with pleural thickening and pleural effusion. Mediastinal lymphadenopathy was present. Multiple subcutaneous nodules were noted in subcutaneous planes of the chest and abdomen, with the largest measuring 9 × 6 cm in the right gluteal region. Discrete soft tissue nodules were also noted on the peritoneum.

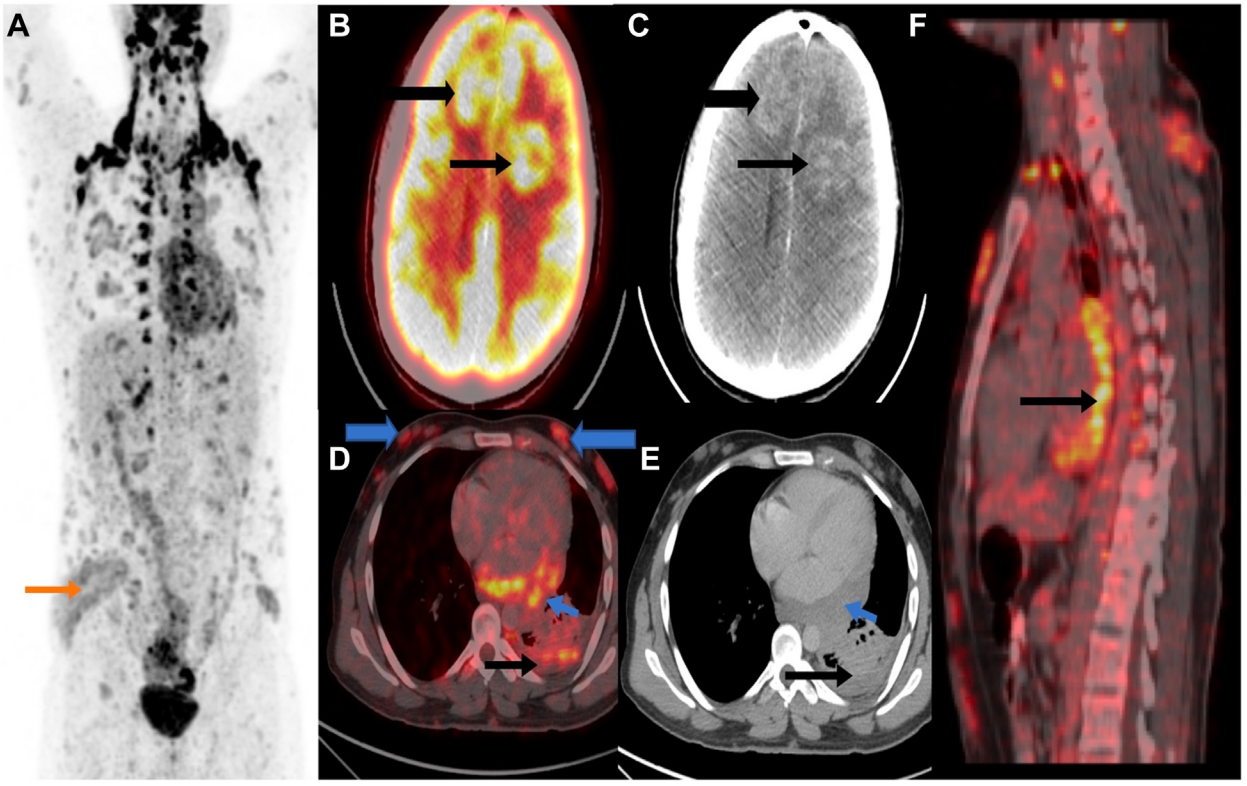
To further characterize the mediastinal mass, thoracic magnetic resonance imaging (Videos 1 and 2) was performed. This revealed a lobulated sheet-like mass with the epicenter in the posterior mediastinum with encroachment into the LA, infiltrating into the base and lateral wall of the left ventricle, encasing the aorta and left pulmonary veins. The lesion was isointense to myocardium, mildly hyperintense to skeletal muscles on T1 turbo spin echo sequences (Figure 3), and exhibited homogeneous post-contrast enhancement T1 turbo spin echo sequences. On T2 short tau inversion recovery sequences, the lesion was hyperintense in signal intensity. Late gadolinium enhancement images exhibited intense enhancement (Figure 4). CT-guided biopsy could not be conducted on the mediastinal mass because it encased major vessels and the heart.

FIGURE 1 Brain MRI Showing Various Lesions



Axial T2 flair (at the level of the lateral ventricle/supraventricular plane) shows edema in the bifrontal white matter and left parieto-occipital area. The postcontrast T1 turbo spin image shows a ring-enhancing lesion with crenated margins in the bilateral frontal location.

FIGURE 2 **FDG and PET Scan Showing Various Lesions**



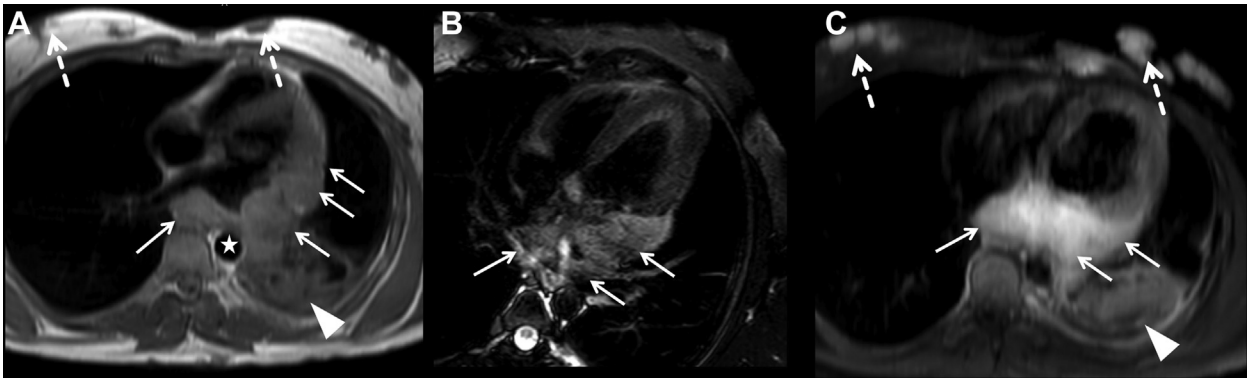
Maximum intensity projection (A) image shows areas of physiological fluorodeoxyglucose (FDG) uptake and brown fat uptake in the bilateral cervical, supraclavicular, and paravertebral regions with multiple FDG avid cutaneous and subcutaneous lesions throughout the body. The arrow in panel A indicates an FDG avid subcutaneous lesion in the right iliac fossa region. Trans-axial fused positron emission tomography (PET)-computed tomography (CT) imaging (B) and CT imaging (C) sections of the brain at the supraventricular level indicate FDG avid ring-enhancing lesions in the bilateral frontal region with perilesional edema. Trans-axial PET/CT (D) and CT (E) sections of the mediastinum below the level of carina (at the level of 4 chambers) indicate an FDG avid sheet like soft tissue mass centered in the posterior mediastinum with frank infiltration of the left atrial posterior wall, as well as encasement of the descending thoracic aorta (the lesion is encircling the aorta making an arc >1,800 [ie, involving >50% of circumference]). Also noted are FDG avid cutaneous and subcutaneous lesions in the chest wall and left-sided pleural effusion and thickening. (F) Sagittal PET/CT image shows the extent of the posterior mediastinal soft tissue mass along the posterior wall of the left atrium abutting the wall of the left atrium anteriorly and descending thoracic posteriorly.

Positron emission tomography (PET)-CT imaging was planned for PET-CT-guided biopsy from another lesion within the body.

Meanwhile, blood investigations revealed hypereosinophilia (eosinophils >12%) with an absolute eosinophil count >1,500/μL. A cerebrospinal fluid work-up was conducted to rule out neuroinfections and malignancy, but results were negative for these conditions. Results of a bone marrow biopsy conducted to rule out malignancy (lymphoma) and infection (bacterial, fungal, parasite) showed only eosinophilia.

PET imaging (Figure 1) revealed a fluorodeoxyglucose (FDG) avid mediastinal mass involving the posterolateral wall of the LA and pericardium and encasing the pulmonary veins. FDG avid, peripherally enhancing, space-occupying lesions were noted in the bilateral frontal and left temporo-occipital

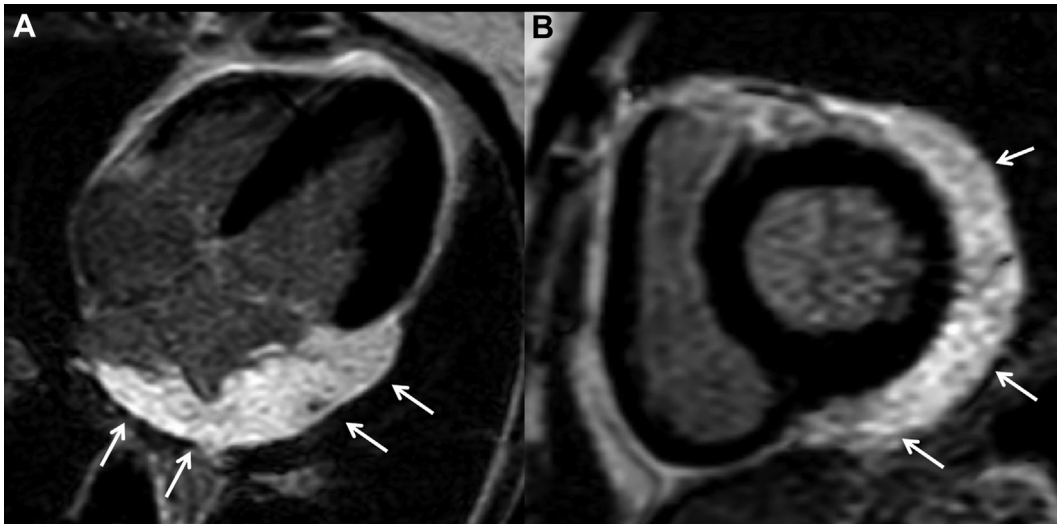
FIGURE 3 Cardiac and Chest MRI Showing Mediastinal and Chest Wall Lesions



(A) Axial T1 turbo spin echo (TSE) image shows a lobulated mass with the epicenter in the posterior mediastinum with encroachment into the left atrium, infiltrating into the base and lateral wall of the left ventricle, encasing the aorta (asterisk) and left pulmonary veins (thin arrows). Note consolidation in the left lower lobe (arrowhead) and multiple soft tissue nodules in subcutaneous nodules in the anterior chest wall (interrupted arrows). (B) The mass shows enhancement on postcontrast T1 TSE image (arrows). (C) Axial T2 short tau inversion recovery images show mass (thin arrows), consolidation (arrowhead), and subcutaneous nodules (dashed arrows) exhibiting hyperintense signal.

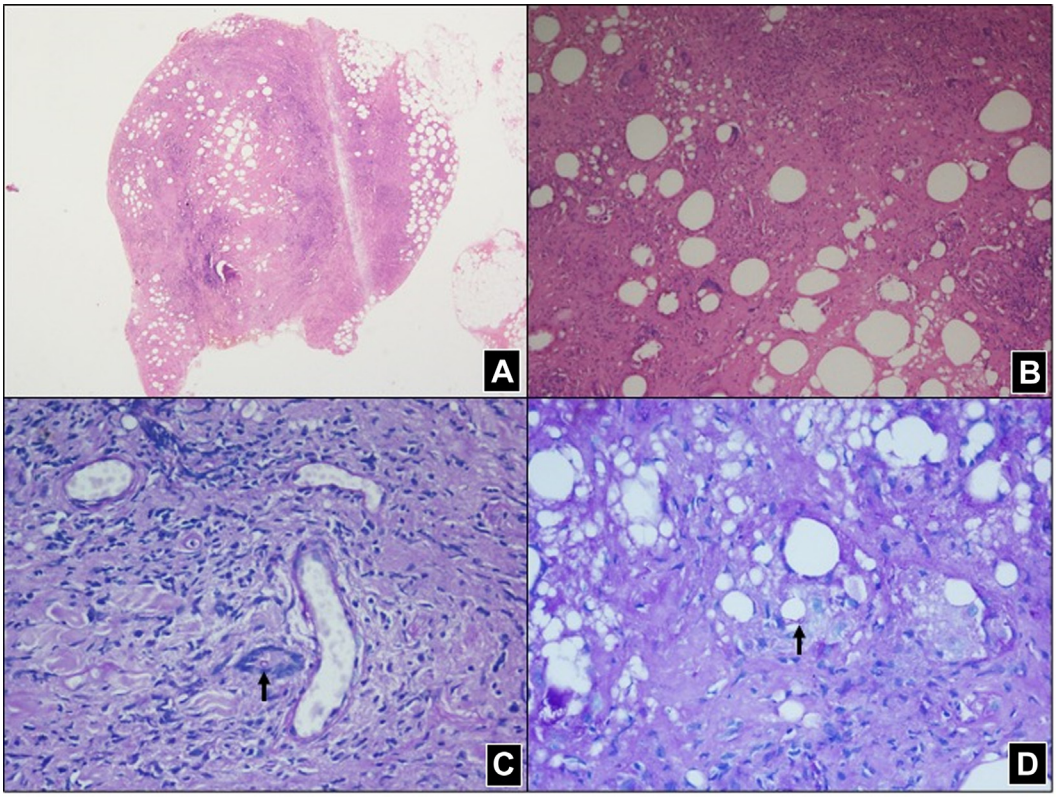
lobes. FDG avid patchy consolidatory changes were noted in the left lower lobe and lymph node. FDG uptake was seen in a soft tissue mass in the right gluteal region. Biopsy results from the right gluteal region showed septate fungal hyphae (Figure 5). Results of beta-D glucan testing were negative; however, the serum galactomannan index was raised significantly. A diagnosis of invasive aspergillosis was made, although polymerase chain reaction was not performed.

FIGURE 4 Cardiac MRI Showing Paracardiac Lesions



Late gadolinium enhancement images in the horizontal axis (A) and basal short-axis (B) indicate the florid-enhancing lesion sparing myocardium (arrows).

FIGURE 5 **Histopathological Microphotographs of Skin Nodules**



Microphotographs of biopsy specimen from right thigh skin nodule show subcutaneous tissue (low-power view, hematoxylin and eosin, ×20) (A) with multiple densely collagenized epithelioid cell granulomas with foreign body type multinucleated giant cells (hematoxylin and eosin, ×200) (B). (C and D) Few fragmented fungal profiles (arrow) are highlighted on periodic acid-Schiff staining (×400).

MANAGEMENT (MEDICAL/INTERVENTIONS)

The patient was given intravenous liposomal amphotericin for 2 weeks and then switched to oral voriconazole for 24 weeks.

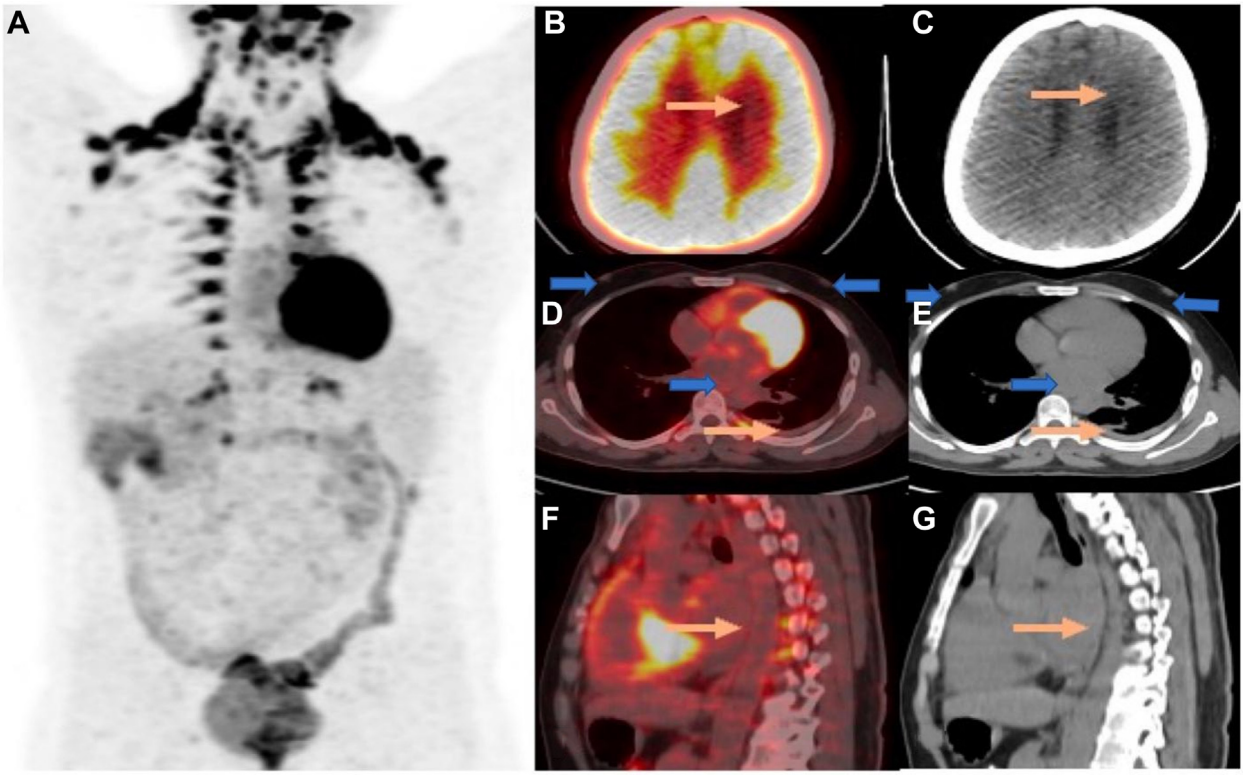
DISCUSSION

Aspergillus fibrosing mediastinitis is an extremely rare condition, and only a few cases have been reported, characterized by fibrous tissue proliferation in the mediastinum producing a mass effect.[1] The causes of fibrosing mediastinitis mostly remain unknown, although many etiologies have been suggested, including infectious causes. Fibrosing mediastinitis has been classified as granulomatous and non-granulomatous by some authors.[2]

Cases of non-granulomatous fibrosing mediastinitis are mostly idiopathic, whereas granulomatous fibrosing mediastinitis cases are mostly secondary to infection, mycobacteria infection being the most common. Aspergillus fibrosing mediastinitis is an extremely rare condition, and only a few cases have been reported in the English literature that fit the diagnostic criteria of fibrosing mediastinitis.[3-11]

Our patient was immunocompetent and did not have a component of Aspergillus bronchopneumonia. In fact, he had Aspergillus pericarditis, with extension into the mediastinum accompanied by a fibrosing inflammatory response, giving rise to Aspergillus fibrosing mediastinitis. He was undergoing treatment for tuberculosis, and because of the broad-spectrum and multiple antibiotics he was administered, a fungal infection might have developed and been

FIGURE 6 Follow-Up Positron Emission Tomography-Computed tomography Reports After Treatment



Follow up (after 12 months of treatment) (A) whole-body positron emission tomography-computed tomography imaging shows complete resolution of previously noted (B and C) brain space occupying lesion (orange arrow), (D and E) skin lesion, subcutaneous nodules (blue arrow), lung consolidation in the left lower lobe (orange arrow) and posterior mediastinal soft tissue mass with significant reduction in pleural effusion and pleural thickening. The same reformatted sagittal positron emission tomography-computed tomography imaging (F and G) shows complete regression of posterior mediastinal mass (orange arrow).

disseminated via the bloodstream to other parts of his body.[12]

Cardiac involvement is usually seen as part of a disseminated systemic fungal infection; however, Aspergillus carditis after surgical intervention, intravenous access, and blood transfusion has also been reported.[10] In our case, the cardiac involvement was more on the left side of the heart, involving the LA and baso-lateral wall of the left ventricle. Whether the infection disseminated into the mediastinum causing a fibrosing reaction from the heart or vice versa can be debated. The antemortem diagnosis of fibrosing mediastinitis is often challenging on imaging, as it could mimic any other mediastinal mass; however, the diagnosis of malignancy is less likely as the lesion was not infiltrating or causing destruction of the adjacent structures. The diagnosis can be established by results of a tissue biopsy or a culture study.[3,13] Serum galactomannan and fungal serology can also provide a clue toward the etiologic diagnosis. The prognosis is usually grave as the diagnosis is often delayed, and death occurs usually as a result of compression of vital mediastinal structures.[1] Because awareness of this condition is low, a high index of suspicion is required to diagnose this condition.

FOLLOW-UP

At the 1-year follow up, the patient's transesophageal echocardiogram showed complete resolution of the LA and left atrial appendage, and PET imaging showed resolution of all lesions in the body

(brain, skin, and mediastinum) (**Figure 6**, Videos 3 and 4). The patient was doing well at the 18-month follow-up.

CONCLUSIONS

Aspergillus infection can be responsible for fibrosing mediastinitis, and this rare disease needs a high index of suspicion and timely diagnosis to have a favorable outcome.

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KEY WORDS aspergillosis, fibrosing mediastinitis, left atrial mass, thoracic magnetic resonance imaging

APPENDIX For supplemental videos, please see the online version of this paper.