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## December 2022 Pulmonary Case of the Month: New Therapy for Mediastinal Disease

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### *History of Present Illness*

A 43-year-old woman complained of persistent cough over 1 year with mild increasing dyspnea on exertion. She denied fever, sweats or weight loss. She had noted fatigue and dry cough, as well as shortness of breath, particularly when supine.

### *Past Medical History (PMH), Social History (SH), Family History (FH)*

- An outside bronchoscopy done in 2019 with washings and biopsy showing only some non-specific inflammation
- Life-long nonsmoker
- Not on any chronic medications
- Had only lived in Arizona, although has travelled in other states
- There is no significant family history

### *Physical Examination*

- Prominent vascularity on anterior chest

What should be *done at this time?*

1. Chest X-ray
2. Obtain old x-rays
3. Pulmonary function testing
4. Serology for coccidioidomycosis

5. All of the above

**Correct!**

**5. All of the above**

We hope you got this one right. When “All of the above” is one of the choices, it is often, although not always, the correct answer. The cause of her cough and dyspnea is not apparent so some baseline information needs to be obtained. We found an old thoracic CT scan near the time of her bronchoscopy which is below (Figure 1).

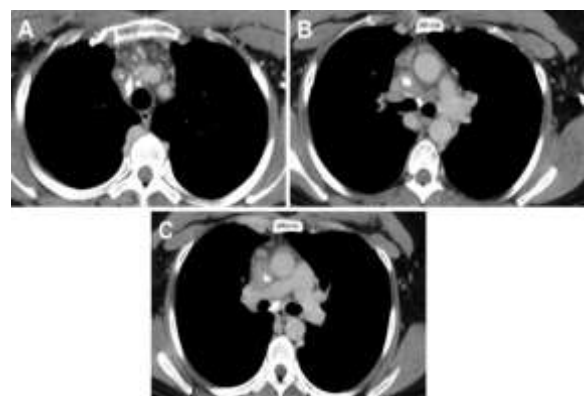


Figure 1. Representative images in soft tissue windows from the thoracic CT scan done in 2019. To view Figure 1 in a separate enlarged window, click [here](#).

Her pulmonary function testing showed a FVC 85% predicted, FEV1 89% predicted, and a Dlco 112% predicted. Her chest x-ray showed mediastinal calcifications but was otherwise negative. The serology for coccidioidomycosis (Valley Fever) was negative.

Which of the following is/are *true*?

1. Thoracic CT scan shows mediastinal calcification and obliteration of the superior vena cava
2. Thoracic CT shows a large aortic aneurysm
3. Pulmonary function testing is normal
4. 1 and 3
5. All of the above

**Correct!**  
**4. 1 and 3**

We warned you that “All of the above” was usually, although not always true. The thoracic CT scan shows mediastinal calcification along with obliteration of the superior vena cava.

What should be *done at this time*?

1. Repeat the thoracic CT scan
2. Repeat bronchoscopy
3. Histoplasmosis serology
4. 1 and 3
5. All of the above

**Correct!**  
**4. 1 and 3**

Repeat bronchoscopy might be necessary although it is premature at this time. Histoplasmosis is a common cause of mediastinal calcifications in the Midwest where she had traveled but the serology was negative. The repeat thoracic CT scan is shown in Figure 2.

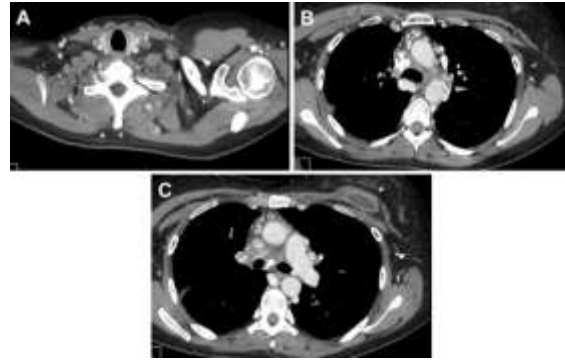


Figure 2. Representative images from the repeat thoracic CT scan in soft tissue windows. To view Figure 2 in a separate enlarged window, click [here](#).

The interpretation of the CT scan was “Infiltrative soft tissue resulting in occlusion of the central brachiocephalic veins with internal areas of calcification. The soft tissue lesion is obliterating the superior vena cava. Multiple collateral venous channels within the anterior mediastinum and upper chest wall are noted. Portions of the right upper lobe pulmonary veins appear narrowed. Distal periaortic venous collaterals via the azygous and hemiazygos systems are noted”.

Because of the mediastinal masses, a positron emission tomography CT scan (PET/CT) was ordered (Figure 3).

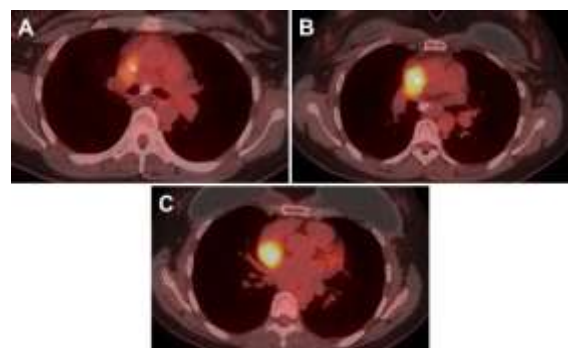


Figure 3. Representative images from thoracic PET/CT scan. To view Figure 3 in a separate enlarged window, click [here](#).

The PET/CT was interpreted as showing “In the right paratracheal mediastinum there is an approximately 4.9 x 3.8 x 2.8

hypermetabolic mass with maximum SUV of 8.1. The mass is compressing the SVC and superior border of the right atrium. The lesion has enlarged slightly since 4/26/2019”.

What is the ***most likely diagnosis?***

1. Castleman’s disease
2. Fibrosing mediastinitis
3. Hodgkin’s disease/lymphoma
4. Metastatic cancer to the mediastinum
5. Sarcoidosis

**Correct!**

## 2. Fibrosing mediastinitis

All the disorders listed as choices can be associated with hypermetabolic masses in the mediastinum (1). Metastatic cancer is usually unilateral and rapidly progressive. Metastatic disease, Hodgkin’s disease or lymphoma would be expected to rapidly progress and not have the slow progression observed in our present patient. Clinical and radiologic features of fibrosing mediastinitis and selected diffuse mediastinal diseases are shown in Table 1.

Table 1. Fibrosing mediastinitis and differential diagnoses of non-neoplastic diffuse mediastinal diseases (1).

	Castleman’s Disease	Fibrosing Mediastinitis	Hodgkin’s Disease/Lymphoma	Sarcoidosis
<b>Clinical Features</b>	Fluid retention	Superior vena cava syndrome	+/- Palpable lymphadenopathy +/- hepatosplenomegaly	50% asymptomatic Dry eyes Erythema nodosum Parotid enlargement
<b>X-ray Features</b>	Mediastinal masses Displacement of adjacent structures Ipsilateral pleural effusion Pericardial reaction	Focal/calcified paratracheal, subcarinal or hilar mass => Widening of the mediastinum Distortion and obliteration of lines	Mediastinal widening Retrosternal filling Hilar enlargement	Mediastinal widening Mass effect Hilar lymphadenopathy Nodal and lung calcifications Reticulonodular opacities Lung fibrosis Traction bronchiectasis
<b>CT Features</b>	Solitary or multicentric Infiltrative mediastinal mass Arborizing calcifications Intense homogeneous enhancement and washout Lymph nodes Central/nodular nodules	Focal/calcified paratracheal, subcarinal or hilar mass => Superior vena cava syndrome	Superior vena cava syndrome Lymphadenopathy, including internal mammary, axillary Pericardial, pleural (unilateral) effusion Calcification (post-treatment) Pulmonary nodule Mass-like consolidation	Lymphadenopathy Perilymphatic nodules Abnormalities of upper/mid lung distribution Lung fibrosis

To view Table 1 in a separate enlarged window, click [here](#).

The present patient’s disease is consistent with fibrosing mediastinitis which is the most likely diagnosis. Fibrosing mediastinitis, also known as sclerosing mediastinitis, is a

condition related to an abnormal immunologic reaction that results in the proliferation of fibro-inflammatory tissue in the mediastinum and/or hila. It leads to a variable constriction of systemic veins, pulmonary arteries and veins, the airways and/or the esophagus, with a morbidity related to location and extent of fibrosis. The pleura, pericardium, and coronary arteries may also be involved.

The most common form of fibrosing mediastinitis is the focal or granulomatous subtype of fibrosing mediastinitis, mainly due to histoplasmosis (less frequently tuberculosis), and other fungal or inflammatory conditions. This form usually manifests as a localized, calcified mass in the paratracheal or subcarinal regions of the mediastinum or in the pulmonary hila, commonly responsible for a superior vena cava syndrome. Diagnosis can be made based on imaging findings, preventing the need for tissue sampling.

There is also a diffuse or non-granulomatous subtype of fibrosing mediastinitis which accounts for about 10 to 20% of cases. It may be idiopathic or can originate in association with autoimmune disorders, methysergide exposure, or prior radiation exposure. Fibrosing mediastinitis has been reported as an unusual mediastinal manifestation of IgG4-related disease. The diagnosis requires a comprehensive evaluation for other disease manifestations, including Riedel’s thyroiditis, retroperitoneal fibrosis, sclerosing cholangitis, or autoimmune pancreatitis, which may precede and/or suggest the diagnosis.

In addition to IgG4 disease, some disorders, such as Erdheim-Chester disease, must be suspected in case of multisystemic involvement. This rare, non-inherited, non-Langerhans form of histiocytosis, commonly with a BRAF mutation, is characterized by xanthomatous infiltration of the involved tissues with foamy histiocytes surrounded by

fibrosis, and appears with heterogeneous systemic manifestations.

Castleman's disease is a very rare heterogeneous cluster of disorders, with distinct unicentric and multicentric subtypes. Subsequently, the fundamental roles of human herpesvirus-8 (HHV-8) and interleukin-6 (IL-6) has been identified in a significant proportion of cases.

Which of the following medications has been reported to result in ***dramatic improvement*** in patients with fibrosing mediastinitis?

1. Azathioprine
2. Corticosteroids
3. Cyclosporin
4. Itraconazole
5. Rituximab

**Correct!**  
**5. Rituximab**

There is no standard therapy for fibrosing mediastinitis. Antifungals, prednisone, tamoxifen, non-steroid anti-inflammatory medications such as indomethacin, and immunosuppressants such as azathioprine or cyclosporin have all been tried and have either proven disappointing or have limited data available about their effectiveness (2). Physicians at the Mayo Clinic have now treated almost 30 patients with metabolically active (confirmed by PET-CT), progressive fibrosing mediastinitis with rituximab. Disease progression was almost universally halted, 67% of patients improved symptomatically and the noncalcified areas decreased on average by 41% (3-5). The present patient was treated with 2 courses of rituximab and her PET/CT scan was repeated (Figure 4).

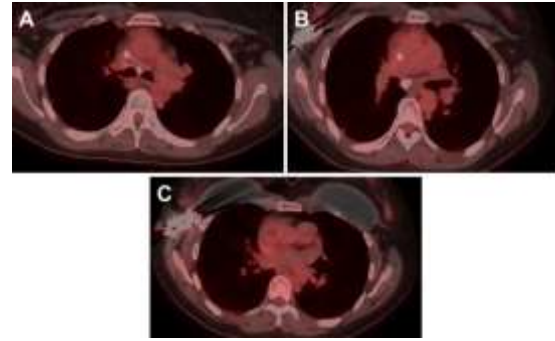


Figure 4. Repeat thoracic PET/CT scan after 2 courses of rituximab. To view Figure 4 in a separate enlarged window, click [here](#).

Her PET/CT scan showed improvement compared to the one done about 7 months earlier. She was symptomatically improved and is being followed.

### ***References***

1. Tabotta F, Ferretti GR, Prosch H, *et al*. Imaging features and differential diagnoses of non-neoplastic diffuse mediastinal diseases. *Insights Imaging*. 2020 Oct 15;11(1):111. [[CrossRef](#)] [[PubMed](#)]
2. National Organization for Rare Disorders. Fibrosing Mediastinitis. 2021. Available at: <https://rarediseases.org/rare-diseases/fibrosing-mediastinitis/> (accessed 11/24/22).
3. Westerly BD, Johnson GB, Maldonado F, Utz JP, Specks U, Peikert T. Targeting B lymphocytes in progressive fibrosing mediastinitis. *Am J Respir Crit Care Med*. 2014 Nov 1;190(9):1069-71. [[CrossRef](#)] [[PubMed](#)]
4. Mirza S, Specks U, Keogh K, Peikert T. Rituximab in the management of complicated fibrosing mediastinitis: the Mayo Clinic experience. *Am J Resp Crit Care Med* 2017;195:A7121.
5. Mayo Clinic. Management of fibrosing mediastinitis. 2019. Available at: <https://www.mayoclinic.org/medical-professionals/pulmonary->

[medicine/news/management-of-fibrosing-mediastinitis/mac-20471676](#) (accessed 11/24/22).