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## February 2024 Imaging Case of the Month: Connecting Some Unusual Dots

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**Clinical History:** A 37-year-old woman presents with abdominal pain, tongue and throat swelling, and intermittent shortness of breath and dyspnea on exertion. She also notes some pain on swallowing.

The patient's past medical history was largely unremarkable. Her one prior surgery included cholecystectomy for cholelithiasis, and she was not taking any prescription medications.

The patient is a lifelong non-smoker, her only reported allergy due to medications containing sulfa, and she drinks alcohol only socially and denied illicit drug use.

**Laboratory:** A complete blood count showed a normal white blood cell count at  $9.7 \times 10^9/L$  (normal,  $3.4 - 9.6 \times 10^9/L$ ), with an elevated absolute neutrophil count of  $8.18 \times 10^9/L$  (normal,  $1.4 - 6.6 \times 10^9/L$ ); the percent distribution of lymphocytes, monocytes, and eosinophils was normal. Her hemoglobin and hematocrit values were 15 gm/dL (normal, 13.2 - 16.6 gm/dL) and 46% (normal, 34.9 - 44.5%). The platelet count was normal at  $220 \times 10^9/L$  (normal,  $149 - 375 \times 10^9/L$ ). The patient's serum chemistries and liver function studies were normal, including an albumin level at 4.3 gm/dL (normal, 3.5 - 5 gm/dL). SARS-CoV-2 PCR testing was negative. The erythrocyte sedimentation rate was normal at 6 mm/hr (normal, 0-29 mm/hr), although her C-

reactive protein was mildly elevated at 4.8 mg/L (normal, <2 mg/L).

**Radiology:** Frontal chest radiography (Figure 1) was performed.



Figure 1. Frontal chest radiography at presentation shows normal heart size, clear lungs, and no pleural abnormality. Click [here](#) to view Figure 1 in a separate, enlarged window.

Which of the following statements regarding this chest radiograph *is accurate*?

1. Frontal chest radiography shows normal findings
2. Frontal chest radiography shows mild cardiomegaly

3. Frontal chest radiography shows mediastinal lymphadenopathy
4. Frontal chest radiography shows pleural effusion
5. Frontal chest radiography shows numerous small nodules

**Correct!**

**1. Frontal chest radiography shows normal findings**

The heart size is normal and the lungs appear clear. No pleural abnormality is seen. No evidence of lymphadenopathy is noted. The patient's physical examination showed a blood pressure of 132 / 82 mmHg, pulse rate 92 / min, respiration rate of 12 / min, and a temperature of 37.1° C. The patient is mildly obese. Her pulmonary and cardiovascular examination was unremarkable, and her musculoskeletal examination did not disclose any abnormalities. She was neurologically intact. Mild tenderness was elicited with palpation over the right lower quadrant and fullness with detected on pelvic examination in the right adnexal region. The patient's skin examination showed deep, eroded ulcers on both inferior sides of her tongue (Figure 2) as well as stellate scars in her posterior pharynx.



Figure 2. Image of the patient's tongue shows deep ulcerations along the inferior aspect of the tongue. Click [here](#) to view Figure 2 in a separate, enlarged window.

Similar lesions were seen on the labia and stellate erosions and ulcerations were found on the labia.

Based on the information thus far, which of the following *is the most appropriate course of action?*

1. Swab of the oral and genital lesions for infections
2. Enhanced CT abdomen and pelvis
3. Brain MRI
4. Dermatological consultation
5. More than one of the above

**Correct!**

**5. More than one of the above**

Given the skin and mucosal lesions, dermatological consultation is appropriate. The patient's complaint of abdominal pain and the detection of right adnexal fullness indicate the need for cross sectional imaging, which could be conducted with CT, ultrasound, or MRI. The presence of oral and genital ulcers makes evaluation for an infectious etiology for these findings appropriate, and dermatological consultation for characterization of these lesions to narrow the differential diagnostic considerations would be helpful. There is no indication for brain MRI at this point.

The patient underwent enhanced CT of the abdomen and pelvis (Figure 3).

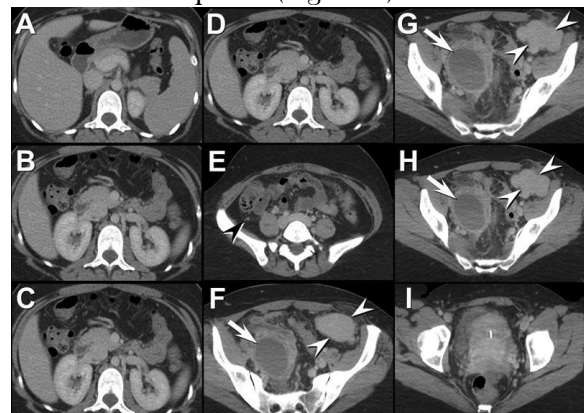


Figure 3. Representative images from axial enhanced abdominal CT scan. Click [here](#) to view Figure 3 in a separate, enlarged window.

Which of the following represents *an appropriate interpretation* for this examination?

1. Enhanced abdominal-pelvic CT shows findings of appendicitis
2. Enhanced abdominal-pelvic CT shows a right adnexal cystic mass
3. Enhanced abdominal-pelvic CT shows normal findings
4. Enhanced abdominal-pelvic CT shows a solid mass in the left pelvis
5. Enhanced abdominal-pelvic CT shows more than one of the above findings

**Correct!**

**5. Enhanced abdominal-pelvic CT shows more than one of the above findings**

The axial enhanced CT of the abdomen and pelvis shows a large cystic mass centered in the right adnexal region, accounting for the patient's palpable fullness at pelvic examination. The right adnexal region also appears inflamed, with surrounding fat infiltration. A solid lesion is seen in the left pelvis, remote from the right adnexal process. The appendix was discretely visualized and appeared normal, excluding appendicitis. The patient returned to her previous institution and was lost to follow up, but she re-presented 2 years later, again complaining of the ulcers on her tongue as well as mild intermittent shortness of breath and dyspnea on exertion, again with painful swallowing. She felt a palpable lump in her left groin as well. The patient again underwent enhanced CT of the abdomen and pelvis (Figure 4).

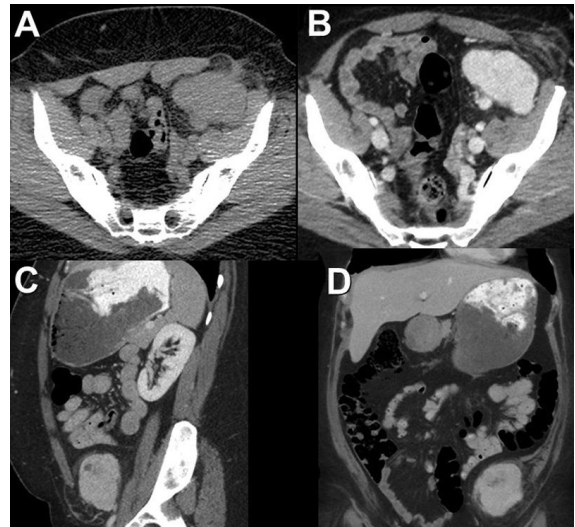


Figure 4. Axial unenhanced (A) and enhanced axial (B), sagittal (C), and coronal (D) images 2 years after presentation. Click [here](#) to view Figure 4 in a separate, enlarged window.

Which of the following represents an appropriate interpretation for this examination?

1. CT of the abdomen and pelvis shows only postsurgical changes
2. CT of the abdomen and pelvis shows right adnexal inflammation
3. CT of the abdomen and pelvis shows a left pelvic mass
4. CT of the abdomen and pelvis shows multifocal lymphadenopathy
5. CT of the abdomen and pelvis shows none of the above

**Correct!**

**3. CT of the abdomen and pelvis shows a left pelvic mass**

The CT of the abdomen and pelvis, performed in unenhanced and enhanced phases, shows resolution of the right adnexal process seen two years earlier, but reveals a strongly enhancing left pelvic mass in approximately the same location as the study performed two years earlier (Figure 3). Based on the findings at the repeat CT abdomen and pelvis, the patient underwent <sup>18</sup>FDG - PET scan (Figure 5).



Figure 5. Coronal <sup>18</sup>F-FDG-PET scan. Click [here](#) to view Figure 5 in a separate, enlarged window.

Which of the following represents an appropriate interpretation for this examination?

1. <sup>18</sup>F-FDG - PET shows widespread nodal hypermetabolic activity
2. <sup>18</sup>F-FDG - PET shows hypermetabolic activity in the right adnexal region
3. <sup>18</sup>F-FDG - PET is non-diagnostic, probably owing to improper fasting
4. <sup>18</sup>F-FDG - PET shows hypermetabolic activity within the left pelvic mass

5. <sup>18</sup>F-FDG - PET shows mild hypermetabolic activity traceable to the colon, reflecting nonspecific uptake

**Correct!**

**4. <sup>18</sup>F-FDG - PET shows hypermetabolic activity within the left pelvic mass**

<sup>18</sup>F-FDG - PET shows no right adnexal metabolic activity, but intense tracer utilization in the left pelvic mass is present. No other significant FDG avid foci are seen.). The patient's outside surgical records were located, which showed that the right adnexal mass seen at presentation cross sectional imaging 2 years earlier (Figure 3) reflected a hemorrhagic cyst resulting from endometriosis. The left pelvic mass was also resected and a diagnosis established. Which of the following is most consistent with the appearance of the patient's pelvic mass?

1. Hemorrhagic right ovarian cyst
2. Lymphoma
3. Castleman disease
4. Sarcoma
5. Solitary fibrous tumor

**Correct!**

**3. Castleman disease**

The left pelvic mass shows intense enhancement, reflecting hypervascularity, which is typical of Castleman disease (also known as angiofollicular hyperplasia). The presence of the enhancement excludes a cyst, including hemorrhagic cyst- such lesions should not show such profound diffuse enhancement. Lymphoma is a consideration, but such intense enhancement is atypical, and no other enlarged lymph nodes are seen. Sarcoma is always a consideration for an isolated pelvic mass, but such intense enhancement is atypical. Furthermore, sarcomas can be aggressive, but this lesion has not spread either locally or distantly in 2 years, apparently only recurring in the same location following surgical resection. Solitary fibrous tumor is also a remote consideration, given the rarity of this lesion (particularly

outside the thorax), but again, intense contrast enhancement is atypical. Additional differential diagnostic considerations, not provided as answer options, should include neuroendocrine malignancy and metastatic disease from hypervascular tumors such as melanoma and renal cell carcinoma.

The outside surgical resection records showed the left pelvic mass to represent the hyaline vascular variant Castleman disease, unicentric.

Based on the information thus far, which of the following represents **the *most appropriate next step*** for the patient's management?

1. Autoimmune antibody testing
2. Pulmonary function testing
3. Bronchoscopy with biopsy
4. Dermatologic consultation
5. More than one of the above

**Correct!**

**5. More than one of the above**

Castleman disease may be associated with various paraneoplastic syndromes and hence further investigation is warranted, including testing for autoimmune antibodies, particularly in light of some of the patient's complaints that are seemingly unrelated to the pelvic mass. Repeat dermatologic consultation to establish an etiology for the oral and genital ulcers is appropriate.

Pulmonary function testing is reasonable given the patient's complaint of dyspnea on exertion and the rare association of Castleman disease with obstructive airway disease. However, bronchoscopic intervention is premature at this point.

The patient was seen by a dermatologist who again noted the ulcerating lesions on the patient's tongue and labia. Biopsy of the labia was performed- the results showed slight acanthosis with spongiosis and eosinophils within the epidermis, as well as a lymphohistiocytic infiltrate in the papillary epidermis with a vacuolar interface reaction and occasional eosinophils and plasma cells. The results were interpreted as consistent

with paraneoplastic pemphigus.

Autoantibody testing showed primate esophagus IgG antibody positive (normal, negative), basement membrane IgG antibody negative, cell surface antibody IgG positive at 1:320 (normal, negative), primate split skin IgG negative, bullous pemphigoid 180 S = 5.06 U (normal, <9 U), bullous pemphigoid 230 S = 5.28 (normal, <9 U), desmoglein 1 = 2.51 U (normal, <14 U), and desmoglein = 2.32 U (normal, <9 U). A repeat complete blood count and serum chemistries were within normal limits, and a urinalysis was unremarkable. Serum vascular endothelial growth factor measurement = 31 pg/mL (normal, 31 - 86 pg/mL).

Which of the following represents **the *most appropriate next step*** for the patient's management?

1. High-resolution chest CT
2. Pulmonary function testing
3. Oncology consultation
4. Surgical consultation
5. All of the above

**Correct!**

**5. All of the above**

The constellation of findings thus far indicate that paraneoplastic pemphigus is responsible for the oral and genital ulcerations and is associated with surgically proven, and now presumably recurrent, hyaline vascular Castleman disease. The concurrence of these entities may be associated with other conditions, notably obstructive pulmonary disease. Therefore, pulmonary function testing and chest imaging are appropriate. Surgical consultation for removal of the recurrent pelvic mass is appropriate, and the tissue sampling and autoantibody testing results, in the context of pathologically proven Castleman disease, raise the possibility of *paraneoplastic autoimmune multiorgan syndrome* (PAMS), suggesting the oncological consultation would be of benefit also.

The patient underwent high-resolution chest CT (Figures 6 and 7).

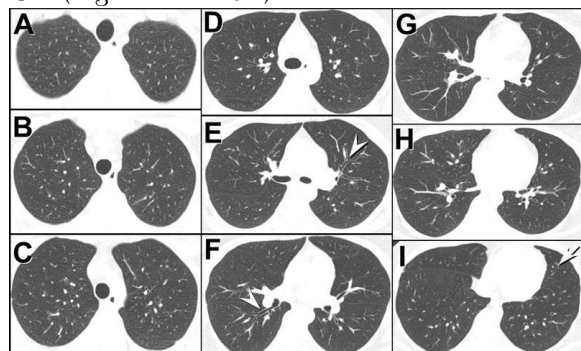


Figure 6. Axial unenhanced inspiratory HRCT images through the upper (A-C), mid (D-F) and lower (G-I) lungs. Click [here](#) to view Figure 6 in a separate, enlarged window. Click [here](#) to view a video of Figure 6.

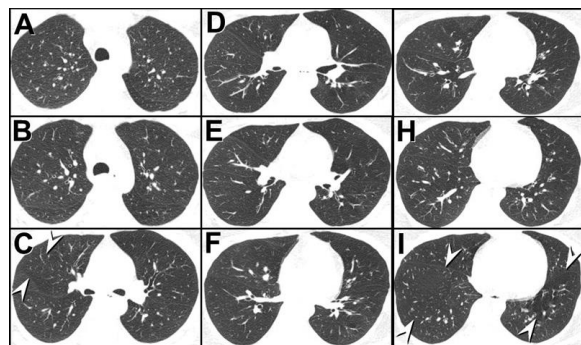


Figure 7. Axial unenhanced post-expiratory HRCT images through the upper (A-C), mid (D-F) and lower (G-I) lungs. Click [here](#) to view Figure 7 in a separate, enlarged window. Click [here](#) to view a video of Figure 7.

Which of the following represents an appropriate interpretation for this examination?

1. High-resolution chest CT shows normal findings
2. High-resolution chest CT shows lymphadenopathy
3. High-resolution chest CT shows numerous small nodules
4. High-resolution chest CT shows patchy multifocal ground-glass opacity
5. High-resolution chest CT shows features of airflow obstruction

**Correct!**

### 5. High-resolution chest CT shows features of airflow obstruction

HRCT shows multifocal questionable central airway thickening as well as bilateral inhomogeneous lung opacity with some accentuation on post-expiratory imaging, suggesting possible gas trapping. These features are subtle and not entirely convincing, but they are not normal, and suggest some element of air flow obstruction. No significant nodules are present nor is ground-glass opacity.

Oncology was consulted and considered high-dose corticosteroid therapy (that patient had been treated similar elsewhere and noted improvement in symptoms, but symptoms recurred following taper), but deferred steroid therapy given the planned surgical resection of the pelvic mass. Consideration for additional therapies, including rituximab and siltuximab (anti-IL6 antibody, although serum IL-6 antibodies were checked and found to be in the normal range) were discussed but deferred pending surgery. Pulmonary function testing showed a forced vital capacity (FVC) of 2.84L (81% predicted), a forced expiratory volume in the first second of exhalation (FEV<sub>1</sub>) of 2.35L (82% predicted), forced expiratory flow rate<sub>25-75%</sub> = 2.39 L/sec (78% predicted), and DLCO = 98% predicted. The results were interpreted as showing mild obstruction. General surgery was also consulted, intravenous immunoglobulin administered preoperatively, and the left pelvic mass was uneventfully resected later in the same month. The pathological analysis confirmed unicentric hyaline vascular variant Castleman disease.

The patient recovered well after her pelvic surgery. Her incision was healing appropriately at post-surgical follow up one month later. During this post-operative visit, bilateral wheezing was noted. The patient said she had sick contacts at home and the wheezing was ascribed to a presumed viral

illness. At her follow up oncology appointment 2 weeks later, dapsone was initiated (*Pneumocystis jirovecii* prophylaxis) and 40 mg prednisone daily was begun, subsequently increased to 60 mg daily. The patient's follow up <sup>18</sup>FDG - PET scan (Figure 8) showed only post-operative change at the surgical resection site.

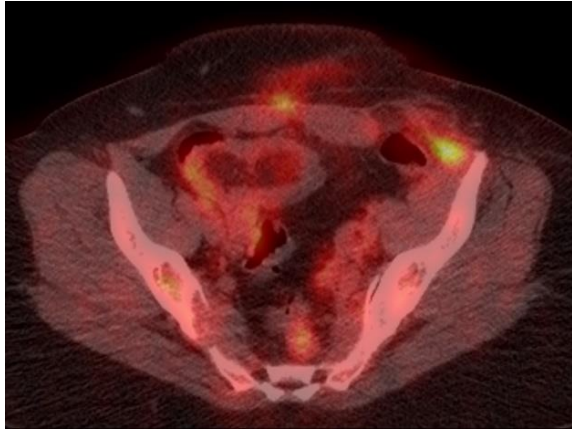


Figure 8. Axial <sup>18</sup>FDG-PET image one month following surgery shows nodular foci of hypermetabolism related to the recent post-operative state; no residual disease is evident. Click [here](#) to view Figure 8 in a separate, enlarged window.

Which of the following represents **the most appropriate next step** for the patient's management?

1. Pulmonary medicine consultation
2. Pelvic MRI
3. Increase prednisone to 80 mg daily
4. Begin Rituximab therapy
5. More than one of the above

**Correct!**

**5. More than one of the above**

Given that the surgical resection was complete and uneventful, and the post-operative <sup>18</sup>FDG - PET scan showed no residual disease, pelvic MRI is not indicated. The current prednisone dose is probably sufficient [the patient noted improvement in the oral and genital ulcers], and any adjustments in this medication would be best conducted after further observation of the

effectiveness of the current dose. Pulmonary medicine consultation is appropriate given the persistent wheezing and abnormal pulmonary function testing performed preoperatively. Rituximab therapy is appropriate for treatment of the patient's pemphigus associated with Castleman disease.

Pulmonary medicine was consulted nearly 3 months post-operatively. Pulmonary function tests were repeated, showing a FVC of 2.21L (63% predicted), a forced expiratory volume in the first second of exhalation (FEV<sub>1</sub>) of 1.08L (37% predicted), and forced expiratory flow rate<sub>25-75%</sub> = 0.45 L/sec (14% predicted). Repeat high-resolution chest CT (Figures 9 and 10) was performed.

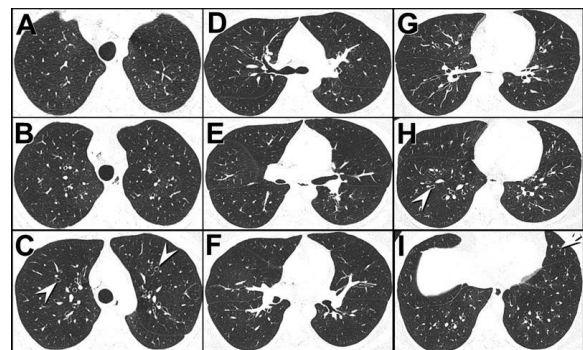


Figure 9. Axial unenhanced inspiratory HRCT images through the upper (A-C), mid (D-F) and lower (G-I) lungs. Click [here](#) to view Figure 9 in a separate, enlarged window. Click [here](#) to view a video of Figure 9.

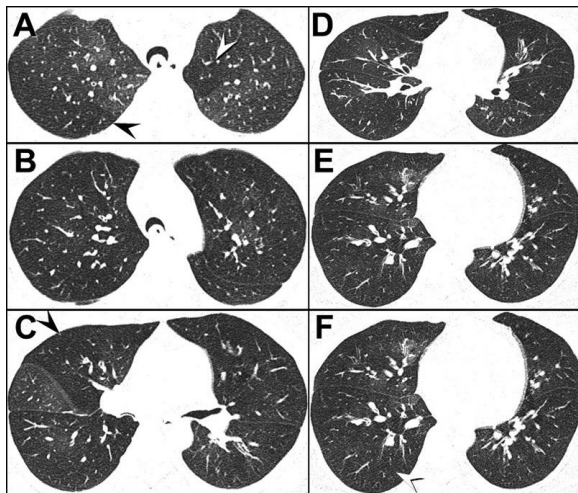


Figure 10. Axial unenhanced post-expiratory HRCT images through the upper (A and B), mid (C and D) and lower (E and F) lungs. Click [here](#) to view Figure 10 in a separate, enlarged window. Click [here](#) to view a video of Figure 10.

Which of the following represents *the most appropriate description* of the CT scan pattern?

1. High-resolution chest CT shows normal findings
2. High-resolution chest CT shows lymphadenopathy
3. High-resolution chest CT shows numerous small nodules
4. High-resolution chest CT shows patchy multifocal ground-glass opacity
5. High-resolution chest CT shows features of airflow obstruction

**Correct!**

**5. High-resolution chest CT shows features of airflow obstruction**

Repeat high-resolution chest CT shows bilateral inspiratory inhomogeneous lung attenuation with accentuation of this pattern on post-expiratory imaging, suggesting gas trapping. Central airway thickening is present and may have become more conspicuous compared to the study nearly 3 months earlier (Figures 6 and 7). No nodules or

lymphadenopathy are evident, and there is no evidence of ground-glass opacity.

Based on available information this far, which of the following is the *best working diagnosis*?

1. Opportunistic infection
2. Lymphocytic interstitial pneumonia
3. Bronchiolitis obliterans
4. Medication - induced organizing pneumonia
5. Increased pressure edema

**Correct**

**3. Bronchiolitis obliterans**

While opportunistic infections may present in various fashions, usually infiltrative abnormalities, such as ground-glass opacity, consolidation, and/or nodules, are present, and these findings are conspicuously lacking. Lymphocytic interstitial pneumonia may also present with various pulmonary manifestations, commonly randomly distributed thin-walled cysts; such are also lacking in this case. Medication-induced pulmonary injury, as an organizing pneumonia pattern, presents with patchy, non-segmental, multifocal peripheral and peribronchial consolidation and/or ground-glass-opacity; again, these findings are absent. Rather, the CT findings suggest obstructive pulmonary disease. Increased pressure edema would manifest with smooth interlobular septal thickening, possibly with pleural effusion, and neither of these findings are seen.

The patient presented to the emergency room with hypoxic respiratory failure 5 months after her surgery, and tested positive for influenza A. She eventually recovered, and was started on additional medications for her obstructive airway disease, including azithromycin, rosuvastatin, montelukast, Spiriva, a bronchodilator, and steroid inhalers, for which she was intermittently non-compliant. Attempts to taper her corticosteroid therapy resulted in worsening



respiratory symptoms as well as return of the oral and genital ulcers. She has remained in remission from her Castleman disease for over 5 years and, while her respiratory function declined rapidly over the ensuing months following her surgery (just over one year after surgery, FVC = 2.06L (57% predicted), forced expiratory volume in the first second of exhalation (FEV<sub>1</sub>) = 0.63L (21% predicted), and forced expiratory flow rate<sub>25-75%</sub> = 0.26 L/sec (8% predicted), her pulmonary function has remained relatively stable since. Chest CT performed just over 4 years after initial diagnosis (Figure 11) showed more well-developed features of bronchiolitis obliterans.

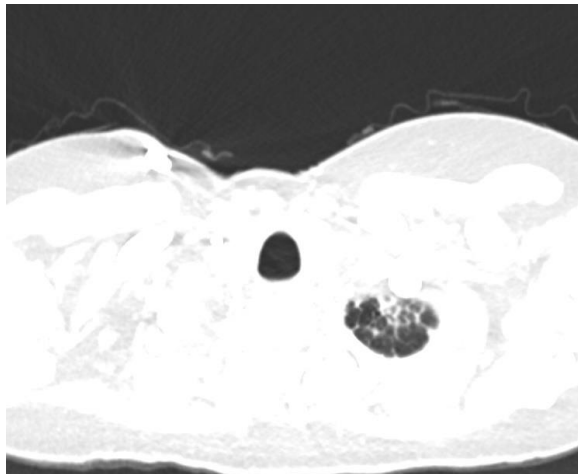


Figure 11. Video of axial unenhanced chest inspiratory CT. Click [here](#) to view Figure 11 in a separate, enlarged window.

The patient is alive more than 5 years after her initial diagnosis and has been evaluated for potential lung transplantation.

**Diagnosis:** Bronchiolitis obliterans associated with paraneoplastic pemphigus and Castleman disease

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