August 2019 Imaging Case of the Month: A 51-Year-Old Man with a Headache

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Clinical History: A 51-year-old previously healthy man presented with complaints of increasing headache frequency and severity. The patient noted headaches in the past, but that the frequency of these headaches, which he referred to as “migraines,” had been increasing in recent months. The patient does note some auras with the headaches.

The patient reported a history of pneumonia in the past, but denied recurrent pneumonias. The only medication the patient takes was ibuprofen, for his headaches; he denied allergies. The patient’s past surgical history was remarkable only for a right inguinal hernia repair, a right Achilles tendon injury repair, and surgical removal of a palpable left thigh mass, ultimately shown to represent scar tissue. The patient smoked 1-8 cigarettes / day for 35 years, quitting one year earlier.

The patient’s physical examination was remarkable for obesity (BMI= 30.4). His vital signs were within the normal range. A few reddish rounded spots were noted on his lower lip, but no other abnormalities were noted at physical examination.

Basic laboratory data, including a complete blood count, electrolyte panel, B12 and folate levels, a C-reactive protein level, and liver function studies were all within the normal range. Mild hypercholesterolemia was noted. An electrocardiogram revealed normal findings. As part of a routine office visit, frontal and lateral chest radiography (Figure 1) was performed.

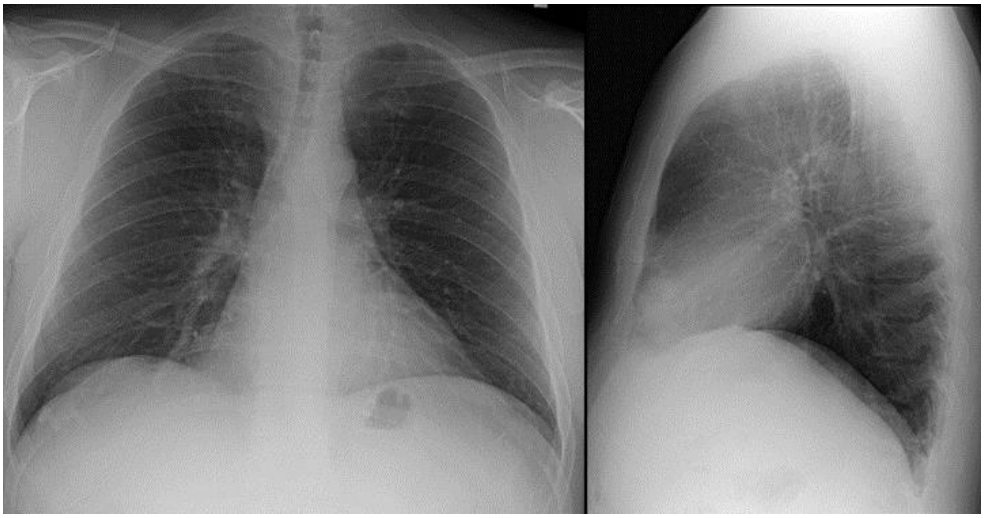

Figure 1. Frontal and lateral chest radiography

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

1. The chest radiograph shows circumscribed nodular opacities
2. The chest radiograph shows multifocal nodular pulmonary consolidation
3. The chest radiograph shows multiple, bilateral cavitary nodules
4. The chest radiograph shows multiple, bilateral small circumscribed nodules
5. The chest radiograph shows nodular interstitial thickening

Correct!
1. The chest radiograph shows circumscribed nodular opacities

Frontal and lateral chest radiography shows a normal heart size. Lung volumes appear normal and no linear or reticular opacities to suggest interstitial lung disease is seen, nor is there consolidation. No pleural abnormality is present. A circumscribed opacity is present in the lateral right lung on the frontal projection, seen in the caudal substernal region on the lateral study. A second circumscribed opacity may be present in the medial right cardiophrenic angle region on the frontal projection.).

Which of the following courses of action is the ***most appropriate next step*** for the management of this patient?

1. ^{18}FDG-PET scanning
2. Bronchoscopy with transbronchial biopsy
3. Comparison to prior thoracic imaging studies
4. Percutaneous transthoracic fine needle aspiration biopsy
5. Thoracic MRI

Correct!
3. Comparison to prior thoracic imaging studies

Among the choices listed, comparison to prior studies is typically the first approach when abnormalities are detected at chest radiography. Indeed, as a general rule, whenever chest imaging studies show an abnormality, if comparison images are available, they should be reviewed. When such comparison studies show stable findings, a less aggressive posture regarding the evaluation of the imaging abnormalities may be possible, and, occasionally, imaging abnormalities may be entirely dismissed as benign when long-term stability is demonstrated. Thoracic CT would clearly be an appropriate choice for further evaluation of this patient's chest radiographic abnormalities, but thoracic CT was not offered as one of the choices for the question. Thoracic MRI was offered as one choice to the answer to this question, but thoracic MRI is not the best answer because the abnormalities at chest radiography appear to reside within the lung, and thoracic MRI is not the best modality for evaluation of the lung parenchyma. ^{18}FDG-PET scanning is premature that this point, and the results of ^{18}FDG-PET are unlikely to alter the approach to the chest radiographic findings given the size and morphology of the opacities seen at chest radiography- if the nodules are metabolically active, they will likely be characterized by thoracic CT, and the same will occur if little metabolic activity is seen within these nodules. Furthermore, ^{18}FDG-PET scanning for nodule assessment is typically employed for patients in whom the nodules are found to be indeterminate and morphologically non-specific following thoracic CT characterization. Finally, tissue sampling procedures- both bronchoscopy with transbronchial biopsy and percutaneous transthoracic needle biopsy- are premature at this point.

The patient underwent brain MRI for the evaluation of his headaches, which showed multifocal sinus opacification, but no abnormalities of the brain parenchyma or meninges were seen. A frontal chest radiograph from 4 years earlier (not shown) was located for comparison, which showed that the nodules seen at presentation chest radiography (Figure 1) were unchanged in both size and morphology.

Regarding the presentation chest radiograph (Figure 1), which of the following statements is ***most accurate***?

1. The nodules at chest radiography are associated with a tubular configuration
2. The nodules at chest radiography are associated with gas trapping
3. The nodules at chest radiography are likely pleural in location
4. The nodules at chest radiography are spiculated
5. The nodules at chest radiography show calcification

Correct!

1. The nodules at chest radiography are associated with a tubular configuration

The nodules seen on the presentation chest radiograph have *sharply circumscribed* margins where the margins are visualized (see the lateral projection of Figure 1 in particular); the margins are not spiculated. There is no clear evidence of increased attenuation within the nodules to suggest the presence of calcium within the opacities. The nodules show *acute angles* where they contact the pleural surface- this morphology is been seen for the right middle lobe nodule on the lateral projection of Figure 1, where the anterior margin of the lesion can be seen to approach the posterior cortex of the sternum. In general, when a parenchymal opacity forms an *acute angle* with the pleural surface, a *parenchymal location*, as opposed to an *extraparenchymal location* (such as a pleural or chest wall location), is favored. This contrasts with the *obtuse angle* typically formed between a lesion and the adjacent chest wall when the lesion resides in an *extraparenchymal* position. The nodules are located peripherally- the right middle lobe lesion is even frankly subpleural- and hence gas trapping, which would manifest with hyperlucency peripheral to the nodule- is not seen. The nodules, particularly the right middle lobe lesion, are associated with a faintly visualized tubular morphology- see Figure 2.

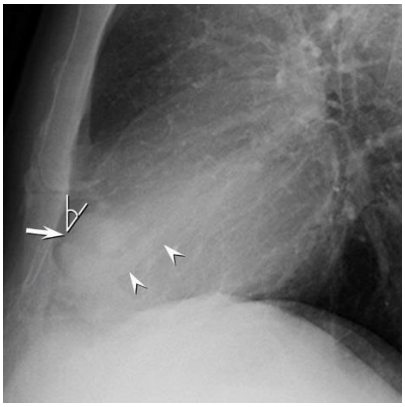

Figure 2. Detail image of the lateral chest radiograph shown in Figure 1 shows the circumscribed subpleural right middle lobe nodule (arrow); note how nearly the entire circumference of the nodule is visualized, and that the anterior margin of the lesion makes an acute angle (see angle) with the pleural surface / anterior chest wall, typical of a lesion located within the lung parenchyma. A faintly visualized tubular opacity (arrowheads) is seen extending towards the nodule.

Which of the following courses of action is the ***most appropriate next step*** for the management of this patient?

1. ^{18}F-Fluciclovine scanning
2. ^{68}Ga-Dotatate scanning
3. Bronchoscopy with transbronchial biopsy
4. CT pulmonary angiography
5. Enhanced thoracic MRI

Correct!
4. CT pulmonary angiography

Enhanced thoracic MRI is useful for cardiovascular disease assessment, the evaluation of chest wall masses, and characterization of mediastinal masses, but the rather poor signal typical of the pulmonary parenchyma at MRI renders this modality less suitable than CT for pulmonary nodule evaluation, as discussed previously. ^{68}Ga-Dotatate scanning is usually employed for neuroendocrine malignancy detection and staging, which may ultimately prove useful in this patient should that diagnosis be established, but that diagnosis is probably unlikely given the morphology of the pulmonary lesions seen at chest radiography. ^{18}F-Fluciclovine (anti-1-amino-3-18F-fluorocyclobutane-1-carboxylic acid) scanning is an amino acid tracer used for the detection of recurrent prostatic malignancy, typically after therapy when elevated prostatic specific antigen levels are detected. This tracer has the ability to image prostatic malignancy because prostatic malignancies are associated with over-expression of several amino acid transporter systems, and has advantages over ^{18}FDG-PET scanning for prostatic carcinoma detection because hormone-naïve prostate carcinomas are often associated with low glucose metabolism and the ^{18}F-Fluciclovine tracer has lower urinary excretion compared with the ^{18}FDG-PET tracer (which allows improved visualization of pelvic organs, such as the prostate gland). Bronchoscopy with transbronchial biopsy may prove necessary during the course of this patient's evaluation, but is premature at this point; typically this procedure is more rewarding following characterization of pulmonary opacities with CT scanning. CT scanning, in this case with a CT pulmonary angiogram protocol, is the correct choice.

The patient subsequently underwent thoracic CT pulmonary angiography (Figure 3) for further characterization of the pulmonary nodule seen at chest radiography.

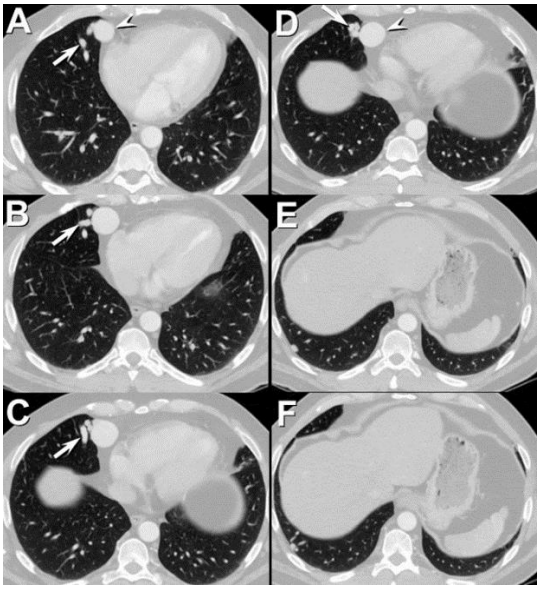

Figure 3. Axial enhanced thoracic CT performed using a CT pulmonary angiography protocol.

Regarding the thoracic CT, which of the following statements is ***most accurate***?

1. The thoracic CT shows that the nodule seen at presentation chest radiography is associated with vessels
2. The thoracic CT shows that the nodule seen at presentation chest radiography is associated with cystic change
3. The thoracic CT shows that the nodule seen at presentation chest radiography displays the “reverse halo” or “atoll” sign
4. The thoracic CT The thoracic CT shows that the nodule seen at presentation chest radiography is associated with a surrounding ground-glass opacity “halo”
5. The thoracic CT The thoracic CT shows that the nodule seen at presentation chest radiography is cavitary

Correct!

1. The thoracic CT shows that the nodule seen at presentation chest radiography is associated with vessels

The right middle lobe nodule seen at chest radiography is seen to be circumscribed and avidly enhancing at CT, and is closely associated with enhancing vasculature. The enhancing nodule does not show internal cavitation, nor is there surrounding ground-glass opacity to suggest that the “ground-glass opacity halo” sign (an imaging feature commonly associated with hemorrhagic lesions, such as angio-invasive fungal infections in immunocompromised hosts or metastatic lesions from highly vascular tumors) is present. The nodule shows homogeneous enhancement- the “reverse halo” or “atoll” sign, which presents as an incomplete or complete ring of consolidation surrounding ground-glass opacity, is not evident. No evidence of cystic change within the right middle lobe is seen.

Regarding the assessment of the thoracic CT findings, which of ***the following is most accurate***?

1. The imaging appearance of the lesion is consistent pulmonary malignancy
2. The imaging appearance of the lesion is consistent with a pulmonary artery aneurysm
3. The imaging appearance of the lesion is consistent with allergic bronchopulmonary aspergillosis
4. The imaging appearance of the lesion is consistent with an arteriovenous malformation
5. The imaging appearance of the lesion is non-specific and not diagnostic of any particular disorder

Correct!
4. The imaging appearance of the lesion is consistent with an arteriovenous malformation

The imaging appearance of the right middle lesion is diagnostic of pulmonary arteriovenous malformation. When a tubular opacity is seen at chest radiography, either abnormal vessels (arteries, as part of arteriovenous malformations, or, even more rarely, veins, in the context of a pulmonary varix or anomalous pulmonary venous drainage) or dilated, impacted bronchi should be considered as possibilities accounting for the tubular morphology. When dilated, impacted bronchi are present, bronchiectasis with impaction, as could occur in the context of allergic bronchopulmonary aspergillosis, should be considered. However, the airways in this patient are completely normal; therefore, no evidence of allergic bronchopulmonary aspergillosis is present. The large associated vessels and intense enhancement of the nodule are inconsistent with pulmonary malignancy, either primary or metastatic, even when considering vascular tumors, such as carcinoid tumor, glomus tumor, or vascular metastases, such as renal cell carcinoma, choriocarcinoma, and melanoma. Pulmonary artery aneurysm should be a consideration when an intensely enhancing nodule associated with vessels is detected at CT, but aneurysms present as either fusiform or saccular dilations of a pulmonary artery, rather than an intensely enhancing nodule associated with an enlarged artery, apparently “fed” by that enlarged artery. Furthermore, pulmonary artery aneurysms do not connect directly to dilated pulmonary veins.

At this point, which of the following represents the ***correct diagnosis*** for this patient?

1. Behçet syndrome
2. Hughes-Stovin syndrome
3. Hypogenetic lung syndrome
4. Sporadic pulmonary arteriovenous malformation
5. None of the above

Correct!
5. None of the above

Both Hughes-Stovin and Behçet syndrome are associated with pulmonary artery aneurysms (the former representing the combination of pulmonary artery or bronchial artery aneurysms and thrombophlebitis, and the latter representing a vasculitis presenting with oral and genital ulcers, arthritis, dermatologic manifestations, and posterior uveitis, in addition to pulmonary artery aneurysms); neither of these disorders is associated with pulmonary arteriovenous malformations. The hypogenetic lung syndrome is known by a number of other designations, including pulmonary venolobar syndrome and the "scimitar" syndrome. This disorder consists of the combination a hypoplastic thorax (typically the right thorax), often with dextroposition of the heart towards the most commonly affected right thorax, anomalous pulmonary venous drainage, and a hypoplastic (again usually) right pulmonary artery; pulmonary arteriovenous malformations are not a feature of this condition. While the lesion detected at chest radiography does indeed represent an arteriovenous malformation, the diagnosis of a sporadic, or isolated, arteriovenous malformation is not correct as illustrated in Figure 4.

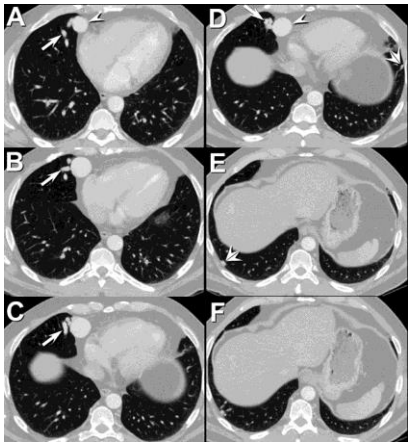

Figure 4. Axial enhanced thoracic CT performed using a CT pulmonary angiography protocol shows that the medial right middle lobe lesion is an avidly enhancing pulmonary nodule (arrowhead). The tubular opacity seen in association with the nodule at chest radiography (Figures 1 and 2) is seen to reflect a large, enhancing pulmonary vessel (arrows). A second smaller nodule and third even smaller nodule (double arrowheads) are present in the subpleural region of the right lower lobe and left anterior base, respectively; these nodules are as also associated with enlarged vessels.

Which of the following is ***NOT associated*** with this patient's diagnosis?

1. Asymptomatic hypoxemia
2. Left-to-right shunting of blood
3. Mutations in endoglin
4. Orthodeoxia
5. Stroke

Correct!
2. Left-to-right shunting of blood

Pulmonary arteriovenous malformations in the context of hereditary hemorrhagic telangiectasia (HHT, also referred to as Osler-Weber-Rendu disease, or OWR) are often associated with mutations in endoglin, *ACVLI*/ALK1, or *Smad4*. Hypoxemia in patients with HHT may be the result of right-to-left shunting, and may even be present even when such patients are completely asymptomatic. Strokes may occur in patients with HHT owing to right-to-left shunting producing cerebral embolization. Orthodeoxia- a decrease in blood oxygenation in the standing position compared with the supine position- occurs in patients with pulmonary arteriovenous malformations owing to the basal predominance of the vascular lesions, which leads to increased shunting when upright and reduction in perfusion of the arteriovenous malformations when lying supine. Pulmonary arteriovenous malformations are associated with right-to-left, *not* left-to-right, shunting of blood.

Which of the following courses of action is the ***NOT an appropriate next step*** for the management of this patient?

1. Antibiotic prophylaxis for minor procedures associated with transient bacteremia
2. Assess for shunting with an echocardiographic bubble study
3. Bronchoscopy with fluoroscopically-guided transbronchial biopsy of the right middle lobe lesion
4. Catheter pulmonary angiography with embolization
5. Fecal occult blood testing

Correct!
3. Bronchoscopy with fluoroscopically-guided transbronchial biopsy of the right middle lobe lesion

Biopsy, either performed via bronchoscopy with transbronchial biopsy or percutaneous transthoracic needle biopsy, is *clearly contraindicated* and could potentially precipitate catastrophic hemorrhage. Furthermore, the imaging appearance of the pulmonary lesions alone is diagnostic of arteriovenous malformation and tissue sampling of the lesions by any means is unnecessary. Testing for occult gastrointestinal bleeding is appropriate to screen for potential gastrointestinal vascular lesions. Antibiotic prophylaxis when minor procedures associated with transient bacteremia, such as dental procedures, are performed is important to reduce the risk of paradoxical embolization resulting brain abscess. Assessing for shunt with an echocardiographic bubble study is a reasonable non-invasive means by which to demonstrate the presence of right-to-left shunting. Finally, the definitive treatment for pulmonary arteriovenous malformations of sufficient size or when right-to-left shunting is apparent is catheter pulmonary angiography with embolization.

The patient's room air oxygen saturation was 94%. Testing for occult gastrointestinal hemorrhage was unrevealing, and no evidence of anemia was noted on a complete blood count. Tiny vascular malformations were noted in the liver on a CT of the abdomen and pelvis, but no large malformations were evident. Echocardiography did not show evidence for pulmonary hypertension (a finding that portends an increased risk of arteriovenous malformation rupture), but the bubble study was positive for right-to-left shunting. The patient subsequently underwent catheter pulmonary angiography with coil embolization of the two largest arteriovenous malformations- the right middle lobe (Figure 5) and right lower lobe- without incident.

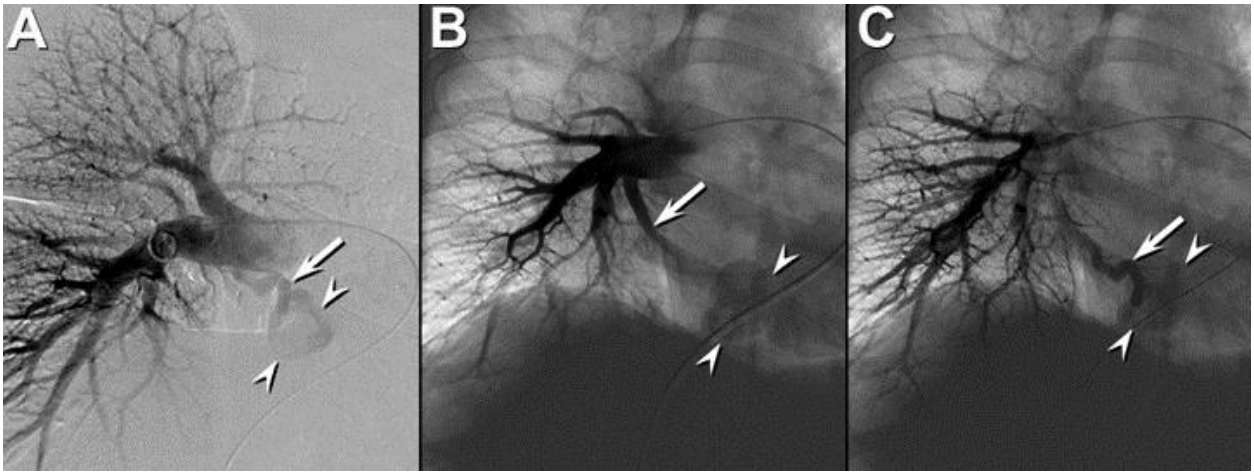

Figure 5. Catheter pulmonary angiography during coil occlusion of an arteriovenous malformation. Injection of the right pulmonary artery shows opacification of the "feeding" artery (arrows) to the large right middle lobe pulmonary arteriovenous malformation nidus (arrowheads); this vessel proximally (approximately at the level of the arrow in B) measured 6.7 mm.

Over the next year, the patient's migraines improved and serial CT pulmonary angiography assessment of the arteriovenous malformations (Figure 6) showed progressive reduction in both size and degree of enhancement of the embolically treated arteriovenous malformations and their associated feeding arteries in both the right middle and right lower lobes.

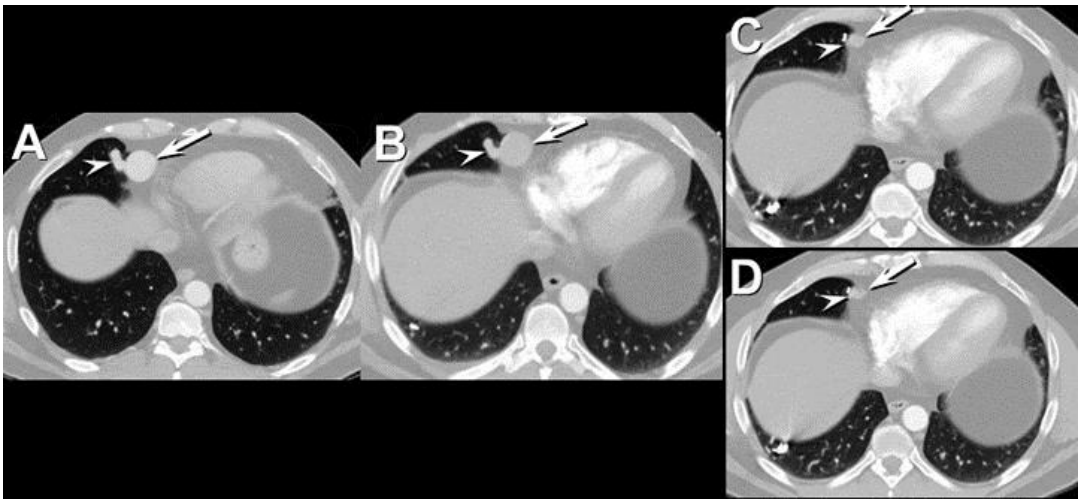

Figure 6. Axial enhanced thoracic CT performed using a CT pulmonary angiography protocol at presentation (A), 2 months following coil embolization of the two largest arteriovenous malformations (B), and 10 months following coil embolization of the two largest arteriovenous malformations (C and D) shows that the initially intensely enhancing vascular nidus (arrow in A) displays diminished enhancement 2 months after treatment (arrow in B) and no longer enhances and is markedly decreased in size 10 months following endovascular therapy (arrows in C and D). The large feeding artery is visible prior to therapy (arrowhead in A), shows somewhat diminished enhancement 2 months following endovascular therapy (arrowhead in B), and significantly involutes 10 months following endovascular therapy (arrowheads in C and D). The coils used to treat the smaller right lower lobe arteriovenous malformation are visible in B-D.

Diagnosis: Arteriovenous malformations in the context of hereditary hemorrhagic telangiectasia.

References

1. Shovlin CL. Pulmonary arteriovenous malformations. Am J Respir Crit Care Med. 2014;190(11):1217-28.[CrossRef] [PubMed]
2. Gossage JR, Kanj G. Pulmonary arteriovenous malformations. A state of the art review. Am J Respir Crit Care Med. 1998;158(2):643-61. [CrossRef] [PubMed]
3. Cartin-Ceba R, Swanson KL, Krowka MJ. Pulmonary arteriovenous malformations. Chest. 2013;144(3):1033-44. [CrossRef] [PubMed]
4. Circo S and Gossage JR. Pulmonary vascular complications of hereditary hemorrhagic telangiectasia. Curr Opin Pul Med. 2014;20:421-8. [CrossRef] [PubMed]