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May 2024 Imaging Case of the Month: Nothing Is Guaranteed

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Clinical History: A 68-year-old man with mantle cell lymphoma diagnosed 5 years earlier presents with weight loss and abdominal distension. HIs lymphoma presented as lymphadenopathy in the neck, chest, and abdomen (Figure 1A), the diagnosis established by percutaneous needle biopsy of enlarged lymph nodes in the neck (Figure 1B); the lymph nodes showed CD5 positivity.

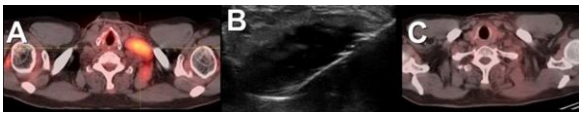

Figure 1. (A) Axial ^{18}FDG – PET scan shows intense tracer uptake within left supraclavicular lymphadenopathy. (B) Percutaneous fine needle aspiration biopsy of the left supraclavicular lymphadenopathy. (C) Axial ^{18}FDG – PET scan 3 month after diagnosis following hyper-CVAD therapy shows resolution of the tracer-avid left supraclavicular lymphadenopathy. To view Figure 1 in a new, separate window. click here.

Peripheral flow cytometry revealed leukemic involvement as well. The patient underwent hyper-CVAD therapy (cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride [aka, Adriamycin], and dexamethasone), with rituximab, with a good response (Figure 1C). Radiotherapy was also performed for the left neck and supraclavicular lymphadenopathy.

PMH, SH, FH: The patient's past medical history was otherwise unremarkable and he had no previous surgical history. The patient had no known allergies and denied alcohol use. He was former smoker, having quit at a young age.

Physical Exam: The patient's physical examination showed a blood pressure of 130 / 76 mmHg, pulse rate 67 / min, respiration rate of 16/min, and a temperature of 36.3° C. His pulmonary and cardiovascular examination was unremarkable, and his musculoskeletal examination did not disclose any abnormalities, and he was neurologically intact.

Laboratory Evaluation: A complete blood count showed a normal white blood cell count at 5.1 x 10^9/L (normal, 3.4 – 9.6 x 10^9/L), with a normal absolute neutrophil count of 2.8 x 10^9/L (normal, 1.4 – 6.6 x 10^9/L). His hemoglobin and hematocrit values were mildly decreased at 13.2 gm/dL

(normal, 13.5 – 17.5 gm/dL) and 38.7% (normal, 38.8 – 50%). The platelet count was normal at 196 x 10^9/L (normal, 149 – 375 x 10^9/L). The patient's serum chemistries and liver function studies were normal aside from an elevated lactate dehydrogenase level at 745 U/L (normal, 122-222 U/L). A urinary drug toxicity screen was negative, and coagulation parameters were normal. SARS-CoV-2 PCR testing was negative. Thyroid stimulating hormone level was within the normal range. Frontal and lateral chest radiography (Figure 2) was performed.

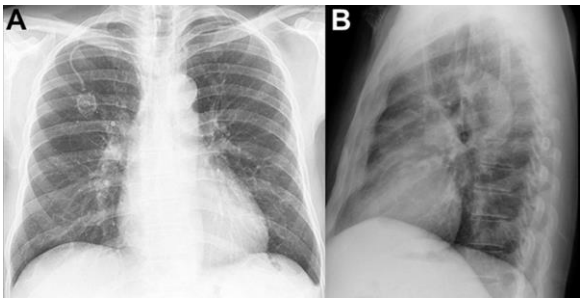

Figure 2. Frontal (A) and lateral (B) chest radiography at presentation. To view Figure 2 in a new, separate window click here.

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

1. Frontal chest radiography shows normal findings
2. Frontal chest radiography shows the "dense hilum" sign
3. Frontal chest radiography shows mediastinal lymphadenopathy
4. Frontal chest radiography shows pleural effusion
5. Frontal chest radiography shows numerous small nodules

Correct!
2. Frontal chest radiography shows the "dense hilum" sign

The frontal chest radiograph shows a relatively dense appearing right hilum compared to the left hilum.

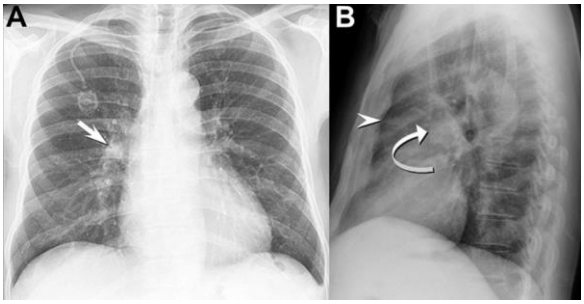

Figure 3. Frontal (A) and lateral (B) chest radiography at presentation shows a "dense hilum" on the right side (arrow)- note how the right hilum appears somewhat "dense" compared to the left hilum on the frontal projection (A). This finding results from abnormal opacity residing within, or overlying, the right hilum. The lateral projection (B) shows an oblong opacity (arrowhead) in the anterior segment of the right upper lobe; this opacity residents at the level of the right hilum (curved arrow) and is responsible for producing the "dense hilum" appearance on the frontal projection. To view Figure 3 in a new, separate window click here.

Which of the following is the ***most appropriate course of action*** to address the abnormal findings at chest radiography.

1. ^{18}FDG – PET scan
2. Enhanced chest CT
3. Unenhanced chest MRI
4. Robotic bronchoscopy
5. Comparison to prior chest imaging studies

Correct!
5. Comparison to prior chest imaging studies

When an abnormal lung opacity, particularly an indeterminate solitary pulmonary nodule, is encountered at chest imaging studies, in nearly all circumstances comparison to prior imaging studies to assess for stability should be the first step in evaluation. While additional imaging studies are often helpful for determining further management, if an opacity shows long-term stability when

compared to remote prior studies, as a rule, the evaluation approach can be tempered as the likelihood of an aggressive lesion is low. Furthermore, interventional approaches are usually not appropriate until an opacity has been thoroughly characterized with non-invasive approaches.

Prior chest radiography from over 2 years earlier was obtained for comparison (Figure 4).

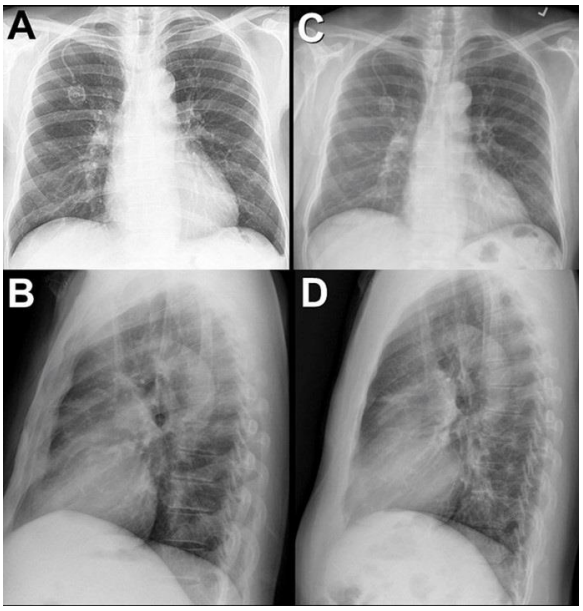

Figure 4. Frontal (A) and lateral (B) chest radiography at presentation compared to over 2 years earlier (C and D). To view Figure 4 in a new, separate window click here.

Which of the following statements regarding the comparison between the current and previous chest radiographs ***is most accurate***?

1. Comparison with previous chest radiography shows ***stable findings***
2. Comparison with previous chest radiography shows ***progressive enlargement*** of the anterior segment right upper lobe nodule
3. Frontal chest radiography shows the anterior segment right upper lobe nodule is ***new***
4. Frontal chest radiography shows the anterior segment right upper lobe nodule has ***decreased in size***
5. Frontal chest radiography shows indeterminate findings and is therefore ***non-contributory***

Correct!
1. Comparison with previous chest radiography shows stable findings

The comparison between the presentation chest radiograph and the chest radiograph 2 years earlier shows stable findings- the "dense" right hilum and oblong opacity in the anterior segment of the right upper lobe visible on the lateral projection appear relatively unchanged.

Based on the imaging data thus far, which of the following statements is ***most accurate***?

1. The relative stability of the nodule for 2 years provides ***no*** useful management information
2. The relative stability of the nodule for 2 years indicates the lesion is ***unequivocally benign***
3. The relative stability of the nodule for 2 years provides a ***strong indicator*** the lesion is benign
4. The relative stability of the nodule for 2 years indicates the lesion is of ***no clinical significance***
5. None of the above

Correct!
3. The relative stability of the nodule for 2 years provides a strong indicator the lesion is benign

The "2-year stability rule" at chest radiography suggests that a nodule, when shown to be stable (e.g., no growth or change in size) is a strong, reliable indicator that the

nodule is benign. Note that this rule has been challenged, particularly with the increasing recognition of slow-growing adenocarcinomas following the advent of lung cancer screening with CT, and hence the rule is not absolute. Nevertheless, such slow-growing adenocarcinomas often show subsolid (ground-glass) attenuation, as opposed to solid attenuation, and nodules with subsolid morphology are often not even visible at chest radiography. Note that the stability of a nodule for 2 years at chest radiography, while suggesting that a nodule is very likely benign, does not guarantee that the nodule is of no clinical significance. For example, an arteriovenous malformation (AVM) may present at chest radiography as an indeterminate nodule, and lack of change in size of an AVM over a 2-year period would not allow one to assume the lesion is of no clinical significance.

Prior outside imaging performed as part of the patient's lymphoma treatment monitoring was obtained for comparison to the current imaging (Figure 5).

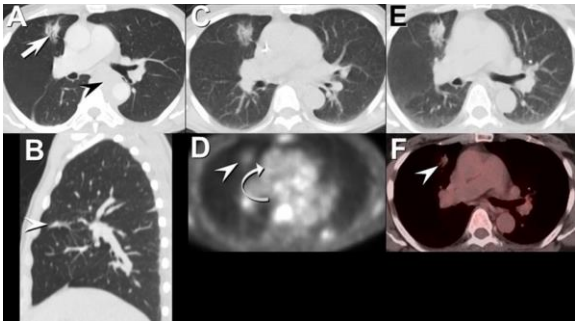

Figure 5. (A) Axial enhanced CT from nearly 5 years earlier at the time of the patient's presentation with lymphoma shows poorly defined nodule (arrow) in the right upper lobe accounting for the chest radiographic abnormality. Note the lymphadenopathy abutting the descending thoracic aorta (black arrowhead). (B) Sagittal CT reconstruction shows the nodule (white arrowhead) has an oblong morphology, which correlates with the appearance at lateral chest radiography. (C and D) Axial 18FDG – PET scan (C, CT attenuation correction image, D, 18FDG image) several months after lymphoma treatment was initiated has uptake (arrowhead) equal to, or slightly less than, mediastinal blood pool (curved arrow), which is typical for a nonaggressive lesion. (E and F) Axial 18FDG – PET scan (C, CT attenuation correction image, D, 18FDG fused image) 2 years after lymphoma diagnosis shows no evidence of significant tracer uptake within the lesion. To view Figure 5 in a new, separate window click here.

Which of the following statements regarding the comparison between the current and previous chest imaging studies ***is most accurate***?

1. The anterior segment right upper lobe nodule appears ***stable*** compared to priors
2. The anterior segment right upper lobe nodule has shown ***clear growth*** compared to priors
3. The anterior segment right upper lobe nodule is ***metabolically active***
4. The anterior segment right upper lobe nodule shows ***calcification***
5. The anterior segment right upper lobe nodule is associated with ***satellite nodules***

Correct!
1. The anterior segment right upper lobe nodule appears *stable* compared to priors

The anterior segment right upper lobe nodule shows no clear evidence of growth over the 2-year period between the initial staging chest CT and the repeat staging ^{18}FDG – PET scan. The nodule shows no clear evidence of significant metabolic activity, with the visualized tracer uptake equal to, or slightly less than, mediastinal blood pool activity at the first post-therapy ^{18}FDG – PET scan, and no metabolic activity at repeat staging ^{18}FDG – PET scan 2 years later. There is no evidence of calcification

within the nodule, and there are no adjacent satellite nodules.).
Outside imaging with ^{18}FDG – PET 2 years after the patient's initial lymphoma diagnosis performed as part of the patient's lymphoma treatment monitoring (Figure 6) was performed.

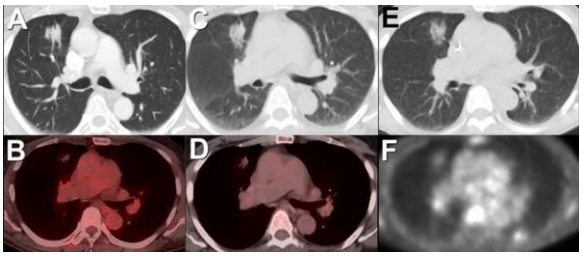

Figure 6. (A and B) Axial ^{18}FDG – PET scan chest portion of whole-body PET shown] (A, CT attenuation correction image, B, ^{18}FDG fused image) again shows the anterior segment right upper lobe nodule. (C and D) Axial ^{18}FDG – PET scan (C, CT attenuation correction image, D, ^{18}FDG fused image) 2 years after initial lymphoma diagnosis for comparison. (E and F) First restaging axial ^{18}FDG – PET scan (C, CT attenuation correction image, D, ^{18}FDG image), several months after lymphoma treatment was initiated, presented for comparison. To view Figure 6 in a new, separate window click here.

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

1. ^{18}FDG – PET scan shows multiple foci of metabolically active lymphoid tissue
2. ^{18}FDG – PET scan shows ***increasing metabolic activity*** within the anterior segment right upper lobe nodule
3. ^{18}FDG – PET scan shows ***decreasing nodularity*** within the anterior segment right upper lobe nodule
4. ^{18}FDG – PET scan shows ***recurrence*** of the metabolically active mediastinal and left supraclavicular lymphadenopathy
5. None of one of the above

Correct!

1. ^{18}FDG – PET scan shows multiple foci of metabolically active lymphoid tissue

The anterior segment right upper lobe nodular opacity again does not show metabolic activity greater than mediastinal blood pool background, and no evidence of recurrent metabolic activity in the mediastinum or left supraclavicular zone- the sites of presentation of the patient's original lymphoproliferative disorder in the thorax- is present. The ^{18}FDG – PET scan shows multiple foci of metabolically active lymphoid tissue, particularly in the bilateral peribronchial regions; these foci of tracer activity have been present and stable over a number of years.

Five years after the initial lymphoma diagnosis, a new p53 mutation was discovered and the patient underwent repeat ^{18}FDG – PET scan (Figure 7) and enhanced CT.

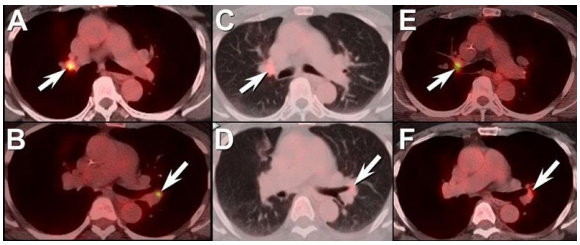

Figure 7. Axial ^{18}FDG – PET performed 5 years after initial lymphoma diagnosis shows continued metabolic activity in the bilateral peribronchial regions as well as elevated tracer utilization in the left pelvis, the later suggesting recurrent lymphoma. The right upper lobe anterior segment nodule shows metabolic activity that does not exceed mediastinal blood pool. To view Figure 7 in a new, separate window click here.

The repeat ^{18}FDG – PET is compared with the prior ^{18}FDG – PET studies in Figure 8.

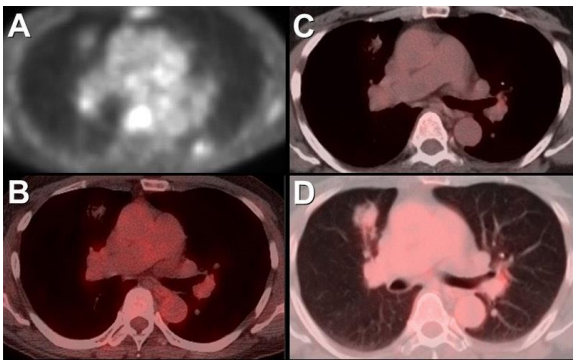

Figure 8. Comparison of anterior segment nodule tracer uptake over time. (A) ^{18}FDG – PET scan at initial lymphoma diagnosis. (B) ^{18}FDG – PET scan at restaging 1 year after initial lymphoma diagnosis. (C) ^{18}FDG – PET scan at restaging 2 years after initial lymphoma diagnosis. (D) ^{18}FDG – PET scan at restaging nearly 5 years following initial lymphoma diagnosis. The anterior segment right upper lobe nodule does not show tracer accumulation greater than mediastinal blood pool at any time point. To view Figure 8 in a new, separate window click here.

Which of the following represents ***an appropriate interpretation*** for the repeat ^{18}FDG – PET scan (Figure 7) and the comparison to previous ^{18}FDG – PET studies (Figure 8)?

1. ^{18}FDG – PET scan shows *multiple foci* of metabolically active lymph node enlargement
2. ^{18}FDG – PET scan shows *increasing metabolic activity* within the anterior segment right upper lobe nodule
3. ^{18}FDG – PET scan shows metabolically active bilateral peribronchial lymph nodes
4. ^{18}FDG – PET scan shows recurrence of the metabolically active mediastinal and left supraclavicular lymphadenopathy
5. More than one of the above

Correct!
5. More than one of the above

No significant tracer uptake is seen in the mediastinum or left supraclavicular zone, which was the patient's site of lymphoma originally (Figure 1A). Bilateral peribronchial lymph node tracer utilization is again evident and has been present on previous examinations, unchanged. The anterior segment right upper lobe nodule again shows metabolic activity not exceeding mediastinal blood pool.

The repeat ^{18}FDG – PET scan shows foci of metabolic activity in the left pelvis within enlarged iliac lymph nodes, consistent with lymphoma recurrence (highlighted in Figure 9).

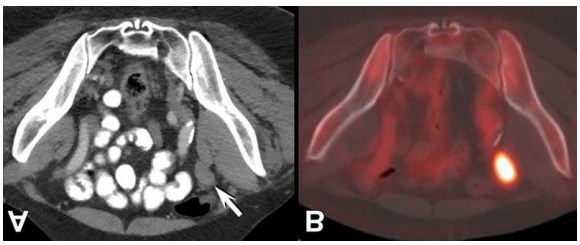

Figure 9. (A) Enhanced CT (A) and (B) axial 18FDG – PET scan at lymphoma recurrence 5 years following initial diagnosis shows left metabolically active external iliac lymphadenopathy (arrow). To view Figure 9 in a new, separate window click here.

The current thoracic ^{18}FDG – PET (Figure 7) is compared to previous cross-sectional imaging studies (Figure 10).

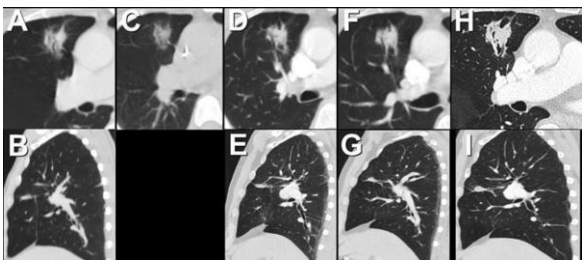

Figure 10. Comparison of anterior segment nodule size over time. (A and B) Axial (A)

and (B) sagittal CT at initial diagnosis of lymphoma nearly 5 years earlier. (C) Axial CT attenuation correction image from ^{18}FDG – PET scan obtained 3 months following initiation of therapy. (D and E) Axial (D) and (E) sagittal CT at restaging 3 years after lymphoma diagnosis (no tracer uptake was seen within the nodule around this time at ^{18}FDG – PET). (F and G) Axial (F) and (F) sagittal CT at restaging 4 years after lymphoma diagnosis (no tracer uptake was seen within the nodule around this time at ^{18}FDG – PET). (H and I) Axial (H) and (I) sagittal CT at restaging nearly 5 years after lymphoma diagnosis (no tracer uptake was seen within the nodule around this time at ^{18}FDG – PET). To view Figure 10 in a new, separate window click here.

Regarding the comparison of the repeat ^{18}FDG – PET (shown in Figure 7) with previous cross-sectional imaging studies (Figure 10) is ***most accurate***?

1. Comparison of the repeat ^{18}FDG – PET scan to previous cross-sectional studies shows ***no change*** in the anterior segment right upper lobe nodule
2. Comparison of the repeat ^{18}FDG – PET scan to previous cross-sectional studies shows ***increasing nodularity*** within the anterior segment right upper lobe nodule
3. Comparison of the repeat ^{18}FDG – PET scan to previous cross-sectional studies shows anterior segment right upper lobe nodule has ***developed cavitation***
4. Comparison of the repeat ^{18}FDG – PET scan to previous cross-sectional studies shows the anterior segment right upper lobe nodule has ***decreased*** in size
5. None of the above

Correct!
2. Comparison of the repeat ^{18}FDG – PET scan to previous cross-sectional studies shows *increasing nodularity* within the anterior segment right upper lobe nodule

Comparing the current ^{18}FDG – PET scan with previous cross-sectional studies suggests that the anterior segment right upper lobe nodule is developing increasing nodularity along its medial aspect. The application of volumetric analysis tended to corroborate this impression. The nodule still does not show significantly elevated tracer accumulation. There is no evidence of cavitation.

Following multiple cycles of hyper-CVAD therapy that had now failed, new approaches to lymphoma therapy were discussed with the patient, including CAR (chimeric antigen receptor) T therapy and BTK inhibitor therapy (interferes with B-cell signaling). The patient was considered not a candidate for stem cell transplant. Therapy with ibrutinib (tyrosine kinase inhibitor) was initiated. The patient was lost to follow up for 2 years, but re-presented 2 years later (7 years following his initial lymphoma diagnosis). New approaches to therapy, given the failure on hyper-CVAD therapy, were again discussed. Repeat ^{18}FDG – PET scan was performed (Figures 11).

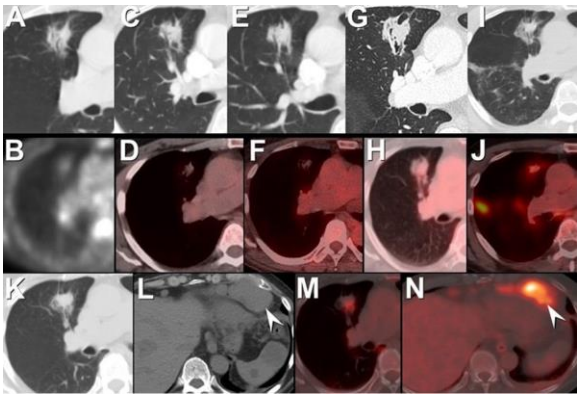

Figure 11. Comparison of anterior segment nodule size and metabolic activity over time. (A and B) Axial CT attenuation correction image (A) and ^{18}FDG (B) image at initial diagnosis of lymphoma. (C and D) Axial CT attenuation correction image (C) and ^{18}FDG image (D) obtained 2 years following initiation of therapy. (E and F) Axial CT

attenuation correction image (E) and ^{18}FDG image (F) obtained 3 years following initiation of therapy. (G and H) Axial CT attenuation correction image (G) and ^{18}FDG image (H) obtained 5 years following initiation of therapy. (I and J) Axial CT attenuation correction image (I) and ^{18}FDG image (J) at restaging 7 years after initial lymphoma diagnosis. (K-N) Axial CT attenuation correction images (K and L) and ^{18}FDG images (M and N) at restaging 8 years after initial lymphoma diagnosis. To view Figure 11 in a new, separate window click here.

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

1. ^{18}FDG – PET shows widespread nodal hypermetabolic activity suggesting recurrent lymphoma
2. ^{18}FDG – PET shows enlargement of the anterior segment right upper lobe nodule
3. ^{18}FDG – PET shows metabolic activity with the anterior segment right upper lobe nodule
4. ^{18}FDG – PET shows widespread pulmonary tracer activity
5. More than of the above

Correct!
5. More than of the above

The repeat ^{18}FDG – PET scan now shows widespread metabolic activity traceable to areas of curvilinear consolidation and ground-glass opacity in the lung parenchyma, but no tracer uptake within enlarged lymph nodes to suggest recurrent lymphoma is seen. Bilateral peribronchial hypermetabolism within non-pathologically enlarged lymph nodes is again present and has been seen on multiple prior studies. The anterior segment right upper lobe nodular opacity, with solid nodularity along its medial aspect, is at least similar in size, arguably slightly increased compared to more remote priors, but now clearly shows tracer uptake that now exceeds background mediastinal blood pool activity.

Which of the following represents ***the most appropriate next step*** for the evaluation of this patient?

1. Pulmonary medicine consultation for bronchoscopy
2. Percutaneous transthoracic needle biopsy
3. Thoracic surgery consultation
4. Serologic assessment for fungal infection
5. More than one of the above

Correct!
5. More than one of the above

Given the slow increase in size and increasingly apparent metabolic active with the nodule, a diagnosis must be established. There are a number of methods by which a diagnosis may be obtained, including bronchoscopic biopsy, percutaneous transthoracic needle biopsy, and even surgical resection. Surgical resection is probably overly aggressive, but thoracic surgical consultation is certainly appropriate.

Which of the following represents the ***least likely diagnosis*** for the anterior segment right upper lobe opacity?

1. Bronchogenic carcinoma
2. Hamartoma
3. Carcinoid tumor
4. Pulmonary lymphoma
5. Coccioidomycosis

Correct!
2. Hamartoma

The slow increase in size and metabolic activity within the anterior segment right upper lobe nodule is inconsistent with pulmonary hamartoma, nor is there fat within the lesion to suggest this diagnosis. The other choices are certainly possibilities. Pulmonary lymphoma is probably less likely as a

diagnosis since the nodule's behavior appears discrepant from the behavior of the lymphadenopathy known to reflect lymphoma, but that possibility is difficult to exclude on the basis of imaging alone. Coccioidomycosis serology was unrevealing. Pulmonary medicine was consulted and robotic bronchoscopy (Figure 12) was performed and the diagnosis of adenocarcinoma was established.

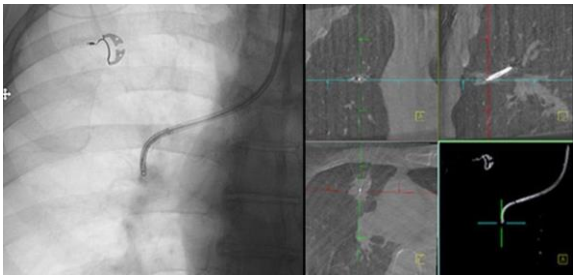

Figure 12. Robotic bronchoscopic biopsy of the anterior segment right upper lobe nodule. The patient subsequently underwent right upper lobe resection and lymph node dissection which showed a 2.2 cm acinar predominant adenocarcinoma with no lymph node metastases. Spread through the air spaces and visceral pleural invasion were noted. Mixed dust deposition was also found in the lung parenchyma and resected lymph nodes. To view Figure 12 in a new, separate window click here.

Diagnosis: Slow growing adenocarcinoma, initially non-^{18}FDG – PET avid, possibly related to previous scar

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