July 2015 Imaging Case of the Month

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Clinical History: A 40-year-old woman with a history of left breast malignancy diagnosed 11 years earlier, initially treated with lumpectomy, radiation, and chemotherapy (doxorubicin, cyclophosphamide, paclitaxel, followed by Herceptin), later treated with mastectomy following recurrence 2 years after diagnosis, presented with a several month history of upper respiratory infectious symptoms, including congestion, productive cough, and rhinorrhea. The patient also complained of some fatigue, although she was still active; she denied shortness of breath initially, but claimed that increasing breathlessness had developed more recently, limiting her exercise tolerance. The patient denied gastrointestinal, gynecological, musculoskeletal, or neurological complaints and no weight loss had occurred.

On admission to the hospital, her white blood cell count was mildly elevated at 14×10^9 cells/L, with anemia as well (hemoglobin / hematocrit= 10 gm/dL / 28%, respectively). Her platelet count was also borderline decreased at 183×10^9 cells/L. Electrolyte and liver panels showed normal values.

A frontal chest radiograph (Figure 1) was performed.

Figure 1. Frontal (A) and lateral (B) chest radiography.

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

1. The frontal chest radiograph shows abnormal mediastinal contours
2. The frontal chest radiograph shows basal predominant fibrotic abnormalities
3. The frontal chest radiograph shows large lung volumes with a cystic appearance
4. The frontal chest radiograph shows mildly enlarged central pulmonary arteries
5. The frontal chest radiograph shows no abnormal findings

Correct!

4. The frontal chest radiograph shows mildly enlarged central pulmonary arteries

The chest radiographic findings are rather subtle, but the central pulmonary arteries appear mildly enlarged (Figure 2).

Figure 2. Frontal (A) and lateral (B) chest radiography. The central pulmonary arteries (red arrow= right pulmonary artery; green arrow= left pulmonary artery; yellow arrowhead= main pulmonary artery) appear mildly enlarged. Note the filling of the retrosternal clear space, consistent with right ventricular enlargement.

The lung volumes are normal and the lung parenchyma shows no evidence of cystic change or fibrotic lung disease. Although the central pulmonary arterial enlargement is subtle and these findings could be interpreted as within the range of normal (they were not noted prospectively), the chest radiograph should not be considered normal- mild opacity with faint reticulation is present at the left apex, representing radiation change following the treated left breast malignancy. The mediastinal contours appear normal otherwise.

The patient's IgM Mycoplasma antibody test was positive, so she was treated with three doses of azithromycin empirically as well as 20 mg prednisone twice daily and intravenous immune globulin. Her upper respiratory symptoms had resolved, but her shortness of breath had become progressive. The patient underwent echocardiography, which showed right atrial and ventricular enlargement and subjectively decreased right ventricular systolic function, but with left ventricular function preserved (ejection fraction= 65%). Right ventricular systolic pressure was calculated at 55-65 mmHg, and

pulmonary hypertension was felt to be present. Moderate tricuspid regurgitation was present. A ventilation / perfusion (V/Q) scintigraphy study (Figure 3) was performed to exclude pulmonary embolism.

Figure 2: Ventilation (A) and perfusion (B) scintigraphy.

Regarding this examination, which of the following is **correct**?

1. V/Q scanning shows delayed washout of tracer on ventilation imaging suggesting obstructive pulmonary disease
2. V/Q scanning shows multiple segmental, wedge-shaped perfusion defects consistent with a high probability for pulmonary embolism
3. V/Q scanning shows multiple small, non-segmental perfusion defects
4. V/Q scanning shows normal pulmonary parenchymal perfusion consistent with a low probability for pulmonary embolism
5. V/Q scanning shows tracer accumulation in the kidneys, indicating a physiologically significant right-to-left shunt

Correct!

3. V/Q scanning shows multiple small, non-segmental perfusion defects

The V/Q scan shows normal findings on the ventilation portion of the study- no delayed tracer washout is noted to suggest obstructive pulmonary disease. The kidneys are not visible, as is normally the case; visualization of the kidneys on a V/Q scan is abnormal and indicates systemic tracer embolization, suggesting a right-to-left shunt. The perfusion portion of the study is abnormal, showing numerous small, non-segmental perfusion defects, manifesting as inhomogeneous pulmonary parenchymal perfusion, but no segmental or larger perfusion defects strongly suggesting venous thromboembolism are present. Overall the pattern is consistent with an intermediate probability for thromboembolic disease.

The patient's room air oxygen saturation was 93%, but she desaturated with ambulation to 83%. Blood gas analysis showed a PaO₂ of 63 mmHg. Further evaluation with CT pulmonary angiography (Figure 4) was performed.

Figure 4. Axial enhanced thoracic CT displayed in a relatively wide lung window.

Which of the following regarding this pulmonary CTA examination is **correct**?

1. The pulmonary CTA shows central thromboembolic disease
2. The pulmonary CTA shows findings suggesting interstitial lung disease
3. The pulmonary CTA shows normal findings
4. The pulmonary CTA shows peribronchial and mediastinal lymph node enlargement
5. The pulmonary CTA shows subtle inhomogeneous attenuation involving the lung parenchyma

Correct!

5. The pulmonary CTA shows subtle inhomogeneous attenuation involving the lung parenchyma

The CT pulmonary angiography study is *not* normal. Enlargement of the main pulmonary artery and right ventricle- consistent with pulmonary hypertension and confirming the findings at echocardiography- is present. The central pulmonary arteries show no evidence of acute or chronic thromboembolic disease. The lung parenchyma shows no infiltrative abnormalities, such as ground-glass opacity, consolidation, or features of fibrotic lung disease to explain the patient's oxygenation abnormalities. The pulmonary CTA shows normal hilar and mediastinal structures- no peribronchial or mediastinal lymph node enlargement is present. Review of the lung parenchyma shows bilateral inhomogeneous lung opacity, with areas of decreased and increased attenuation (Figure 5).

Figure 5. Axial enhanced thoracic CT displayed in a relatively wide lung window width (A-F) shows multifocal, bilateral, inhomogeneous lung opacity manifest as areas of relatively increased attenuation compared with areas of relatively decreased attenuation (lung parenchyma between arrowhead pairs).

Note that the pulmonary vessels appear rather small in the areas of decreased attenuation- this finding can reflect hypoxic vasoconstriction, although causes of pulmonary arterial obstruction, such as thromboembolic disease, and pulmonary hypertension, may rarely produce this finding.

The patient was found to have an elevated erythrocyte sedimentation rate as well as low-grade anti-nuclear antibody positivity and her anemia was thought to be hemolytic in etiology.

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

1. ^{18}F FDG-PET scan
2. ^{68}Ga -citrate scanning
3. Bronchoscopy
4. Inspiratory and expiratory chest radiography
5. Right heart catheterization

Correct!

5. Right heart catheterization

Inspiratory and expiratory chest radiography can be useful for detecting pneumothorax and for exposing air trapping in patients with large and/or small airway obstruction, but likely will not benefit this patient because the thoracic CT already obtained would have disclosed any pneumothorax overlooked at initial chest radiography, and airflow obstruction was not seen at the V/Q study already obtained. ^{68}Ga -citrate scanning can occasionally be useful for evaluation of patients with diffuse lung disease, but no such findings are evident at the recent pulmonary CTA study. There is no clear lung parenchymal target for bronchoscopy. Similarly, there is no clear abnormality to evaluate with ^{18}F FDG-PET scanning. Right heart catheterization is indicated, given the features suggesting elevated pulmonary arterial pressure at both echocardiography and pulmonary CTA, but without an explanation provided by these studies.

The patient underwent right heart catheterization which showed a mean pulmonary artery pressure of 36 mmHg, wedge pressure of 8 mmHg, central venous pressure of 7 mmHg, and pulmonary vascular resistance between 5-8 Wood units. The findings were interpreted as consistent with World Health Organization Group I pulmonary hypertension with reduced cardiac output, although a Group IV etiology was not excluded. No left-to-right shunt was noted. The pulmonary hypertension was thought to perhaps be related to an as yet undiagnosed autoimmune disease. Her platelet count had decreased over the previous 2 days since admission from $183 \times 123 \times 10^9$ cells/L and then to 69×10^9 cells/L 4 days later. The consulting rheumatologist felt a rheumatological disorder was not a likely explanation for the patient's condition. Her peripheral blood smear showed schistocytes, which prompted consideration for thrombotic thrombocytopenic purpura.

Which of the following is the **most likely** consideration for the patient's condition given the data thus far?

1. Congenital heart disease inducing pulmonary hypertension
2. Progressive interstitial pneumonitis due to pulmonary toxic medication
3. Pulmonary arterial thrombotic microangiopathy due to malignancy
4. Pulmonary arterial vasculitis
5. Venous thromboembolism

Correct!

3. Pulmonary arterial thrombotic microangiopathy due to malignancy

The pulmonary CTA largely excluded the possibility of venous thromboembolism, although there are uncommon cases of small pulmonary arterial emboli, or progressive pulmonary arterial thrombosis that occur at the small vessel level, unaccompanied by central, visible thromboembolic disease. Such patients are typically inoperable, and have a poor prognosis, and have a pulmonary CTA appearance similar to this patient- bilateral geographic areas of mosaic perfusion due to obstruction of small pulmonary vessels. While the imaging is consistent with this potential diagnosis, the patient's clinical presentation is not- chronic venous thromboembolic disease does not adequately address the bloodwork abnormalities in this patient. While congenital heart disease can produce pulmonary hypertension and could explain some of the patient's clinical presentation, congenital cardiovascular disease was not detected at the non-invasive and invasive imaging studies, nor would it account for the bloodwork abnormalities in this patient. Pulmonary vasculitis could potentially account for the elevated inflammatory markers detected in this patient, but no imaging features to suggest vasculitis were found, nor did extensive rheumatological evaluation disclose evidence supporting such a disorder and no pulmonary hemorrhage occurred. The patient's chemotherapy treatment for her breast malignancy was years prior to her presentation, and no evidence of pneumonitis was seen at imaging, making progressive interstitial pneumonitis due to pulmonary toxic medication an unlikely explanation for the patient's presentation and rapid clinical deterioration. The widespread fibrocellular intimal hyperplasia affecting small pulmonary arteries that occurs with thrombotic microangiopathy due to malignancy can present at imaging in a fashion similar to very small pulmonary emboli- bilateral geographic areas of mosaic perfusion due to obstruction of small pulmonary vessels. Clinically such patients may present with progressive shortness of breath, hypoxia, and pulmonary hypertension, as in the case of the patient presented.).

The patient was prepared for immediate plasmapheresis. During the procedure, the patient became increasingly restless, with worsening hypoxia. Her neurological status deteriorated progressively until she became unresponsive. She developed agonal respirations and cardiopulmonary resuscitation was initiated, but was unsuccessful. Autopsy was performed and showed diffuse, bilateral, microangiopathic metastatic breast carcinoma associated with thrombotic-type pulmonary hypertensive arteriopathy. No evidence of thromboembolic disease was noted.

Diagnosis: Pulmonary hypertension due to breast malignancy-induced thrombotic microangiopathy

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