



Metastatic Breast Cancer with Pulmonary Tumor Emboli Causing Dyspnea, Hypoxemia, and Pulmonary Hypertension

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Introduction

In patients with a known or suspected malignancy, especially breast cancer, who present with dyspnea and evidence of pulmonary hypertension, one possible etiology to consider should be tumor microembolism. We report an unusual case of microscopic pulmonary tumor embolism from an undiagnosed breast cancer leading to severe pulmonary hypertension and death. We also detail the rare phenomena of widespread dissemination of tumor related to paradoxical microembolization via a patent foramen ovale, and a subdural hematoma from dural metastasis of breast cancer.

Case Summary

•A 43 year old African American female, diagnosed two weeks earlier with a subdural hematoma at an outside hospital, presented to our emergency department with worsening headaches and slurred speech.

•Aside from the neurologic findings, the physical examination was normal. A computed tomography (CT) scan of her head showed an acute on chronic subdural hematoma. The patient was also noted to be extremely hypoxic (Pulse Oximeter 98-99% on 15 liters of oxygen via a non-rebreather mask) and tachypneic (RR = 26) upon presentation.

•The Neurosurgical team rapidly evacuated the hematoma. Post-operatively, however, they were unable to wean the patient off the ventilator due to marked hypoxia on high FIO₂ levels. The ABG showed a pH of 7.44, pCO₂ of 35, pO₂ of 59 on 60% FIO₂; the chest radiograph was unremarkable.

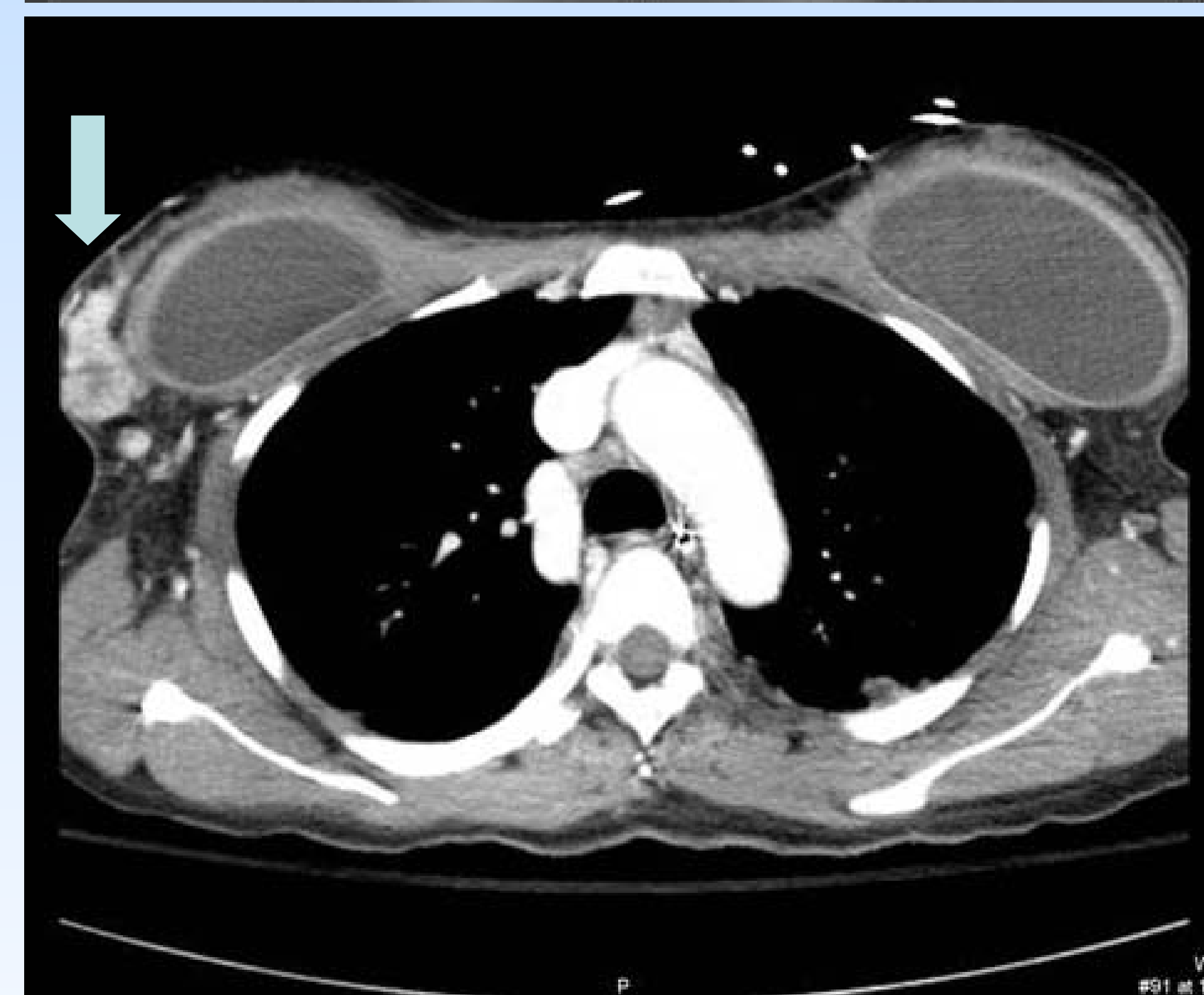
•Due to concern for a pulmonary embolism, a spiral CT examination was performed, showing no evidence of pulmonary embolism but demonstrated bilateral ground glass opacities, intralobular septal thickening, and a right lateral breast mass with axillary lymphadenopathy.

•Due to the profound hypoxemia out of proportion to the parenchymal lung disease, a transthoracic echocardiogram was performed showing a severely dilated right ventricle and severe pulmonary hypertension with a right ventricular systolic pressure of 88 mmHg. A bubble study was markedly positive for a right to left intracardiac shunt.

•A right heart catheter was placed and verified the markedly elevated pulmonary artery pressures. There was no response to infused epoprostenol, the patient's hypoxemia worsened despite aggressive ventilatory support, and the patient expired.

•An autopsy was performed, which revealed metastatic breast carcinoma with severe hypoxia and pulmonary hypertension with right to left shunt via a patent foramen ovale resulting in arterial embolization of tumor cells to multiple organ systems. Metastatic disease was found in the thoracic cavity, lymph nodes, liver, bone, kidneys, pituitary, dura, and brain.

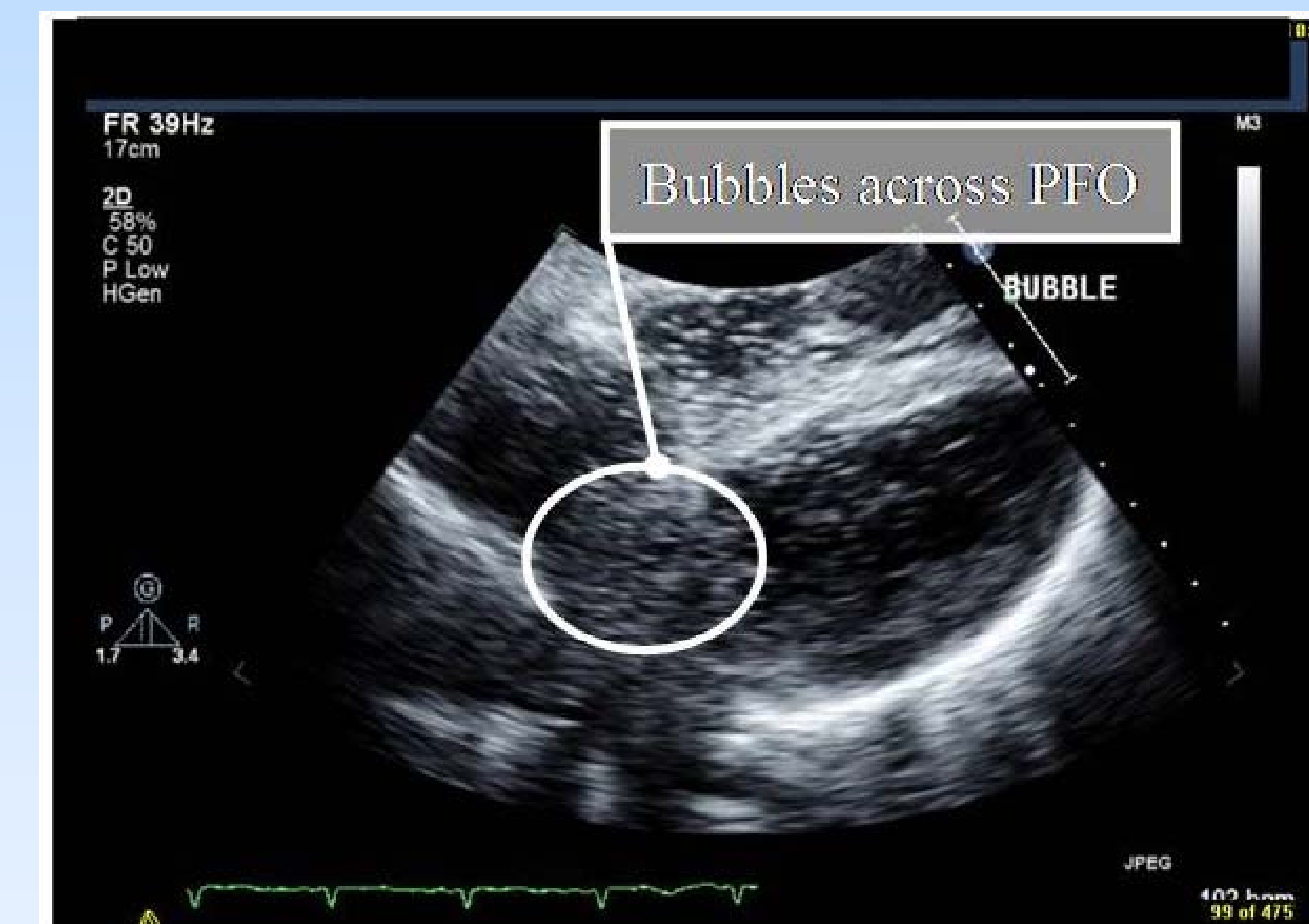
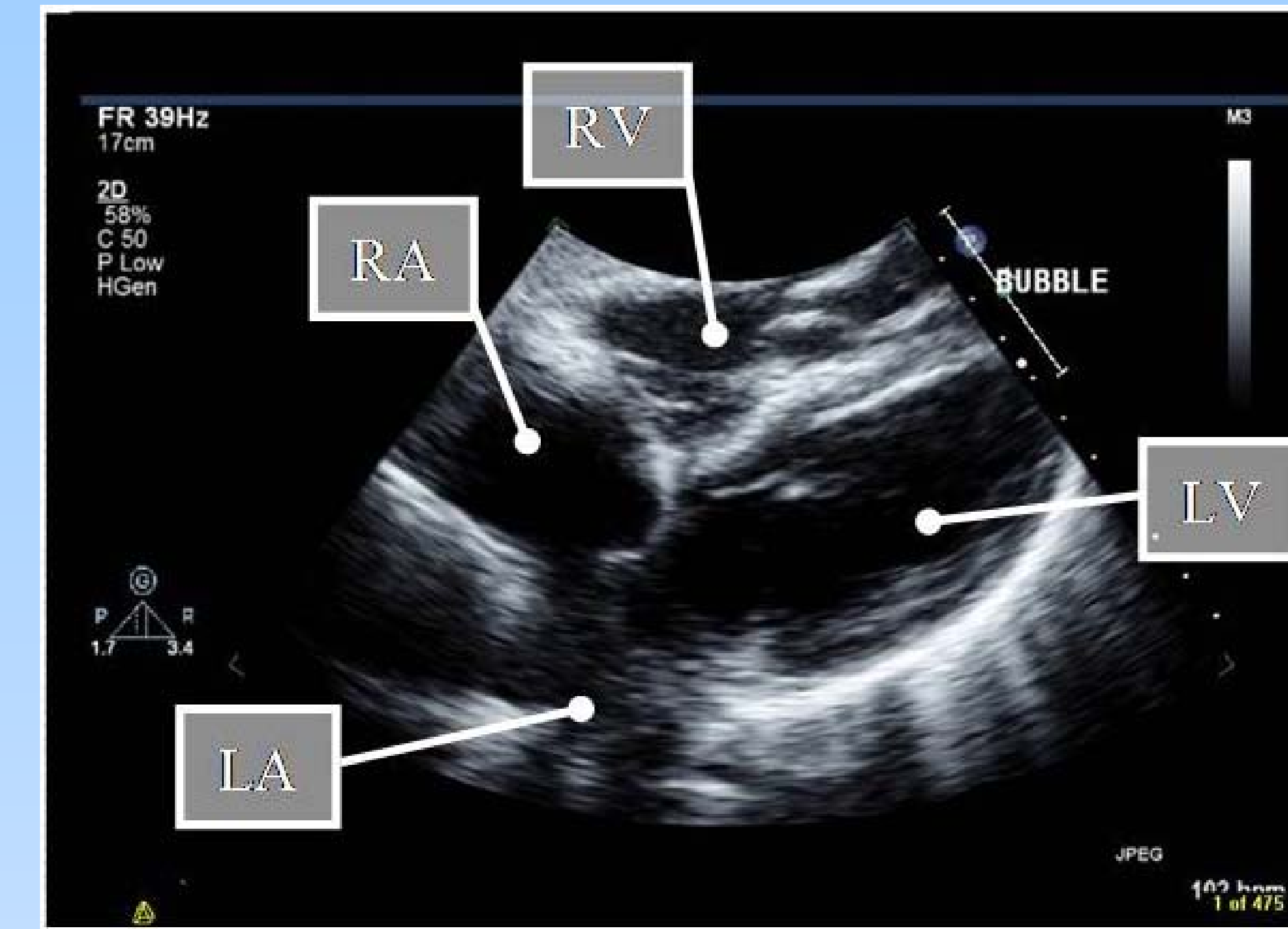
Results



Above are two cross sections of the CT scan of the chest with intravenous contrast, which showed no evidence of pulmonary embolism, but did show bilateral patchy areas of ground glass opacification, interlobar septal thickening in the lung fields, a right lateral breast mass (arrow) with axillary lymphadenopathy, and bilateral breast implants.

On the right are pathological images taken from autopsy. **Figure A:** breast mass with high grade adenocarcinoma, **Figure B:** lung with tumor cells/clot in small pulmonary artery, which resulted in the severe pulmonary hypertension, **Figure C:** kidney with arterial embolization of tumor cells, **Figure D:** dural metastasis, **Figure E:** gross heart specimen with a probe through the patent foramen ovale

Results



Above are images from the transthoracic echocardiogram performed, which showed a severely dilated right ventricle with markedly reduced systolic function, a large right atrium, 4+ tricuspid regurgitation, and severe pulmonary hypertension with a right ventricular systolic pressure of 88 mmHg. A bubble study was markedly positive for a right to left intracardiac shunt.

Discussion

- Tumor embolization to the lungs has been grouped into four categories: 1) microscopic pulmonary tumor emboli occluding small arteries and arterioles; 2) emboli which occlude large, proximal pulmonary arteries; 3) microvascular invasion through lymphatic spread; and 4) a combination of these findings.
- Patients with microscopic pulmonary tumor embolism can be very difficult to diagnose as they may present with subacute cor pulmonale, with onset of symptoms over the course of a few weeks to months. The initial laboratory evaluation of a patient typically shows hypoxemia with a clear chest xray, right ventricular systolic pressures exceeding 50 mmHg, and an abnormal ventilation-perfusion scan.
- The diagnostic utility of studies can be limited:
 - Chest radiographs are frequently normal.
 - CT scans can show multiple subsegmental peripheral perfusion defects, and this has been called a "segmental contour". Dilated and "beaded" peripheral pulmonary arteries have been described with intravascular tumor emboli.
 - Pulmonary angiograms in several previous case reports were negative for evidence of large vessel emboli.
 - Ventilation perfusion scans may reveal a segmental contour or "mottled" appearance with a normal ventilation scan.
 - Transthoracic echocardiograms typically show elevation of right ventricular systolic pressures exceeding 50-60 mm Hg. Multiple malignancies have been linked to this phenomenon including breast, liver, pancreatic, gastric, and bladder cancers, however breast represents the majority of these cases.
- Although tumor microembolism to the lung is not uncommon in metastatic breast cancer, it is rarely recognized as a presenting feature of breast cancer. The diagnosis, which requires an open-lung or transbronchial lung biopsy for confirmation, is difficult even if the suspicion for metastatic breast cancer is high.
- More recent papers have reported an innovative and less invasive procedure, namely microvascular cytology obtained from a pulmonary artery catheter. In this technique, the catheter is placed in a wedge position, and blood is aspirated from the pulmonary arterial port. It is useful to consider in a patient presenting with severe pulmonary hypertension where tumor emboli is being considered and other more invasive procedures are not practical.
- Pulmonary tumor embolism causing pulmonary hypertension is frequently only discovered postmortem. The reason for this is related to its infrequent occurrence relative to the other more common causes of hypoxemia.
- One case report describes a complete clinical response to chemotherapy in a patient with pulmonary artery tumor embolization secondary to breast adenocarcinoma. The patient received letrozole, an aromatase inhibitor. It appears that symptomatic tumor microembolism is more responsive to treatment than lymphangitic carcinomatosis in the lung.
- A recent review identified approximately 51 cases of spontaneous subdural hematomas from dural metastasis. The most common tumors involved with dural metastasis are stomach, prostate, and breast, with adenocarcinoma being the most common histological type. The prognosis in these patients overall was poor.

References

•Bhuvaneshwaran JS, Venkatchalam CG, Sandhyamani S. Pulmonary wedge aspiration cytology in the diagnosis of recurrent tumor embolism causing pulmonary arterial hypertension. *International Journal of Cardiology* 1993; 39:209.

•Feller JA, Janis JF. Pulmonary hypertension, resulting from tumor emboli to pulmonary arteries. *Chest* 1968; 54(1):68-70.

•Gajdos C, Niernan DM, Moqtaderi FF et al. Microscopic pulmonary tumor emboli: An unusual presentation of breast cancer. *Breast Journal* 2000; 6(4):273-275.

•Kane RD, Hawkins HK, Miller JA et al. Microscopic pulmonary tumor emboli associated with dyspnea. *Cancer* 1975; 36:1473-1482.

•Konduri S, Khan Q, Stites S. Pulmonary hypertension caused by metastatic breast cancer and its response to antihormone therapy and chemotherapy. *Breast Journal* 2007; 13(5):506-508.

•Konjuri S, Khan Q, Stites S. Pulmonary hypertension caused by metastatic breast 170 cancer and its response to antihormone therapy and chemotherapy. *Breast Journal* 2007; 13(5):506-508.

•Kunii N, Morita A, Yoshikawa G et al. Subdural hematoma associated with dural metastasis. A case report. *Neurol Med Chir (Tokyo)* 2005; 45:519-522.

•Massey RJ, Ruggieri J. Pulmonary microvascular cytology: A new diagnostic application of the pulmonary artery catheter. *ch* 1985; 88(6):908-914.

•Masson RG, Krikorian J, Luki P et al. Pulmonary microvascular cytology in the diagnosis of lymphangitic carcinomatosis. *NEJM* 1989; 321:71-76.

•Schriner RW, RYU JH, Edwards WD. Microscopic pulmonary tumor embolism causing subacute cor pulmonale: A difficult antemortem diagnosis. *Mayo Clin Proc* 1991; 66:143-148.

