

Case Blog

Title: The Use of Contrast Echocardiography to Identify Infiltrating Lymphoma in the Myocardium

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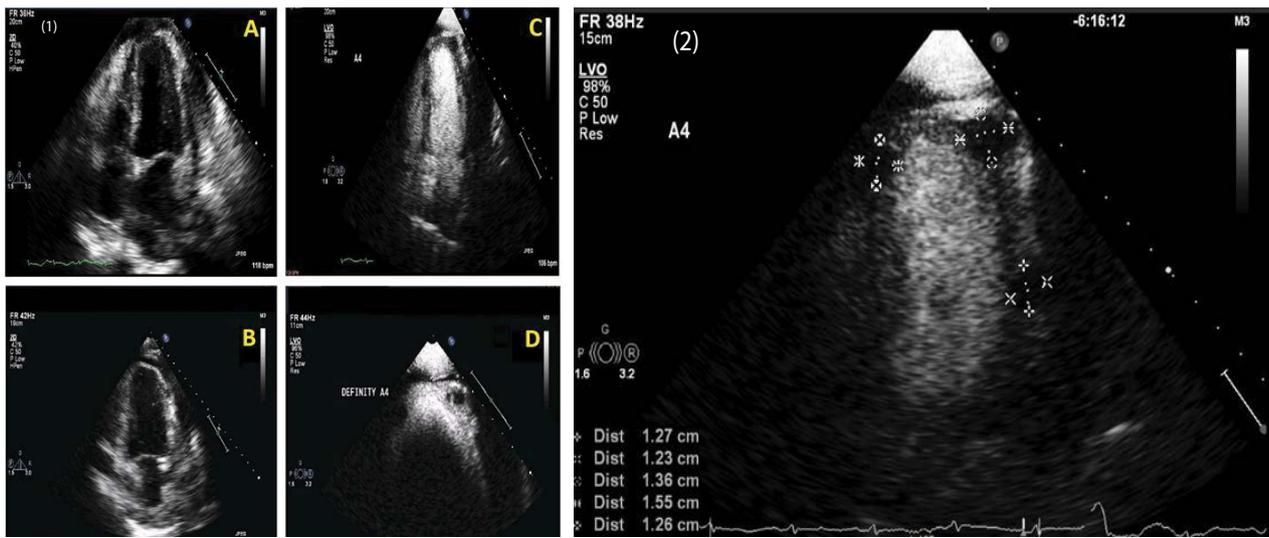


Figure 1: Transthoracic echocardiographic imaging. Images A and B gathered via echocardiography performed without contrast on day 1 following admission. Images C and D gathered via echocardiography performed with Definity intravenous contrast on day 2 following admission – highlighting intramyocardial masses.

Figure 2: Transthoracic echocardiographic image performed on using Definity intravenous contrast on day 2 following admission – highlighting intramyocardial masses.

Introduction

Echocardiographic contrast agents are approved by the US Food and Drug Administration (FDA) for delineation of the LV endocardium however its role in the assessment of myocardial disease has not been defined [1]. Contrast echocardiography has demonstrated an ability to better differentiate myocardial tissue with respect to myocardial blood flow. Ultrasound contrast agents have been demonstrated to be useful in differentiating thrombi from benign and malignant neoplasms that are confined to the endocardium [1,2]. We present a clinical example where non-contrast and contrast enhanced echocardiograms demonstrated remarkably different myocardial compositions. In our patient, contrast enhanced echocardiography identified infiltrating lymphoma in the myocardium that was not seen with standard 2D imaging.

Case Description

68 year-old African American man, with a past medical history of AITL and hepatitis C virus, presented with 2 weeks of weakness and fatigue. Symptoms were associated low grade fevers, but were non-exertional and not associated with chest pain, shortness of breath, dyspnea on exertion or cough.

Medical history included AITL with autoimmune hemolytic anemia, initially diagnosed 3 years prior to admission. Patient completed CHOP (Cyclophosphamide/Doxorubicin/Vincristine) Chemotherapy. He was in remission until 2 months prior to this admission; at which point he was found to have recurrence in his right axillary lymph node and was started on ICE (Ifosfamide/Carboplatin/Etoposide). There was no known history of cardiovascular disease.

Physical exam revealed tachycardia, positive jugular venous distention, bibasilar crackles on pulmonary exam, and +1 pitting peripheral edema. Cardiac exam displayed regular rate and rhythm, with normal S1/S2 but cardiac sounds were muffled. Labs showed a BMP within normal limits. CBC revealed a leukocytosis (Wbc=23.8 $10 \times 10^3/\text{mm}^3$) with a left shift with a new anemia (Hgb of 8.5 g/dl) and thrombocytopenia (Plt=67 $10 \times 10^3/\text{mm}^3$). Additionally, a BNP=442 pg/ml and Trop=0.12 ng/ml.

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Electrocardiography demonstrated a Sinus Tachycardia at 120bpm, PRWP, nonspecific t-wave abnormalities in the lateral leads, with no ST segment deviations, unchanged compared to prior electrocardiograms. A chest x-ray displayed bilateral PVC, with stable right pleural effusion, and increased in size of cardiac silhouette. Records showed that an echocardiogram done 3 years prior to presentation elucidated an LVEF >75%, with normal left ventricular thickness and wall motion and there was no valve abnormalities.

Hospital course

In the emergency department, the patient became febrile and increasingly tachycardic, with a sinus mechanism and rates as high as 170 beat per minute (bpm). Computed tomography (CT) of his chest confirmed a pericardial effusion with a right lower lobe pulmonary infiltrate with pleural effusion. Pulsus paradoxus was noted on physical exam. Stat bedside transthoracic echocardiogram (TTE) demonstrated a 1cm circumferential pericardial effusion without tamponade physiology. The patient was started on broad spectrum antibiotics for pneumonia coverage, and taken to the CCU.

On day 1, a TTE without contrast was performed showing a left ventricular ejection fraction of 45-50% and a large pericardial effusion - measuring 1.8 cm anteriorly by 2 cm laterally by 1.5 cm posteriorly. There was evidence of early right ventricular diastolic collapse; however the tricuspid valve and mitral valve demonstrated inflow variations of 43% and 24% respectively; which did not meet threshold for tamponade physiology. Upon further review of the 2D images, there was an echolucency noted in the myocardium of the left ventricle apex.

On day 2 of the patient's hospital course, a repeat TTE was performed using Definity® (Perflutren lipid microsphere) intravenous contrast to evaluate the echolucency. The differential for the echolucency was wide, ranging from abscess to a LV pseudoaneurysm. The contrast echocardiogram revealed multiple circumscribed intramyocardial masses (Figure 1). They did not communicate with the left ventricle and were located along the anterolateral wall and inferoseptum. The largest of which measured 1.4 cm x 1.5 cm at the apical aspect of the anterolateral wall (Figure 2). A large pericardial effusion was still present. A few beats demonstrated early right ventricular diastolic collapse.

During the first week of the patient's hospital course, his leukocytosis improved with the broad spectrum antibiotics. Cardiothoracic surgery was consulted for concerns of early tamponade, and on day 6 pericardiocentesis was performed and a chest tube was placed under general anesthesia. 800 mL of bloody pericardial effusion was drained. A pericardial biopsy demonstrated irregular, pink-tan soft tissue fragments, a pericardium with moderate chronic inflammation and fibrin deposition. There was no evidence of lymphoma, however pleural fluid cytology exhibited abnormal cells with cell markers consistent with T-cell lymphoma.

During the second week, the chest tube was removed, but the pericardial drain remained. The final two weeks of the hospital course commenced with increased pericardial drainage. Repeat computed tomography of the chest showed recurrence of pleural effusion and was equivocal for cellulitis around the drain or for fistula formation. Broad-spectrum antibiotics were restarted, though the effusions were likely secondary to his lymphoma. The patient's functional status was poor and he was too debilitated to restart chemotherapy. He rapidly decompensated, and code status was changed to DNR/DNI. Unfortunately, the patient passed away during this admission. The cardiac lesions were never biopsied and family declined autopsy.

Discussion

Angioimmunoblastic T-Cell Lymphoma (AITL) accounts for approximately 15% of all T cell lymphomas. It generally presents in an advanced stage, with symptoms such as: fevers, diffuse adenopathy, hepatosplenomegaly, skin rash, edema, pleural effusion, and ascites. AITL is diagnosed via biopsy, with lymph nodes demonstrating polymorphous infiltrate of neoplastic T cells, and is indicated by blood tests exhibiting polyclonal hypergammaglobulinemia, with a wide range of autoantibodies including cold agglutinins, rheumatoid factor, and circulating immune complexes [3]. Cardiac manifestations appearing as the primary indices of AITL are extremely rare, but have been documented [3,4].

Echocardiographic contrast agents are used to enhance suboptimal views of the left ventricle and to improve the delineation of the left ventricular endocardial border for the evaluation of global and segmental left ventricular function. The American Society of Echocardiography (ASE) Consensus Statement on the Clinical Applications of Ultrasonic Contrast Agents in Echocardiography indicate its use for differentiation of a thrombus from an intracardiac tumor [2]. One such contrast agent is Definity, or Perflutren lipid microsphere, was used in our patient for further evaluation of an echolucency seen on 2D imaging.

Contrast-enhanced echocardiography has demonstrated an ability to better differentiate myocardial tissue with respect to myocardial blood flow [2]. This is useful in the evaluation of intracardiac masses; allowing for differentiation of thrombi from benign and malignant neoplasms that are confined to the endocardium. Malignancies often have abnormal neovascularization, enabling high uptake of echocardiographic contrast, which appear as microbubbles. Conversely, fresh thrombi have little or no uptake. In benign tumors, with a paucity of blood vessels, enhancement falls somewhere in between these two extremes [2].

Some investigators have extended the use of this imaging modality. Kirkpatrick et al. tried to determine the relative perfusion of cardiac masses by a high-energy ultrasound flash to destroy the contrast microbubbles in the tumor and the surrounding cardiac tissue, then allowing repopulation of contrast bubbles in these structures [5]. This technique decreases the chance of recording a false-positive perfusion and therefore mistaking a hypovascular, benign tumor or thrombus for a malignancy [5,6].

ASE Consensus Statement on the Clinical Applications of Ultrasonic Contrast Agents in Echocardiography indicate its use for differentiation of a thrombus from an intracardiac tumor, for real-time very low MI (Mechanical Index) perfusion imaging with high-MI flash should be used if available, if thrombi are avascular and show no contrast enhancement after a high-MI flash impulse, for poorly vascularized tumors (benign stromal tumors, such as myxoma) or highly vascularized tumors (malignant tumors) that will demonstrate proportional degrees of perfusion by flash replenishment real-time very low MI imaging, and (if real-time very low MI software is not available) low-MI (<0.3) harmonic imaging can be deployed to visualize whether contrast enhancement is occurring within the mass and aid in the differentiation of cardiac masses [2].

In our patient, contrast enhanced echocardiography identified infiltrating lymphoma in the myocardium that was not seen with CT scan or standard 2D echocardiography imaging. Contrary to the norm, we found metastatic lesions in our patient with decreased pixel intensity. The use of contrast agents should be considered when evaluating patients with non-cardiac diseases that have the potential for infiltrating the myocardium, but the level of contrast enhancement may be variable with certain types of tumors.

References

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