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CASE REPORT

CLINICAL CASE

High-Output Heart Failure in Multiple Myeloma

Novel Application of Tc-99m MAA to Identify Intramedullary Shunting

Enklajd Marsela, MD,[a] Eric Hirsch, MD,[a] Leandro Slipczuk, MD, PhD,[a] Mark I. Travin, MD,[b] Renée M. Moadel, MD, MS,[b] Ulrich P. Jorde, MD,[a] Sasa Vukelic, MD, PhD[a]

ABSTRACT

We introduce the innovative use of technetium-99m–labeled macroaggregated albumin to diagnose high-output heart failure in a patient with multiple myeloma with persistent congestion symptoms. Symptom resolution occurred with lenalidomide and steroids. This marks the first clinical use of technetium-99m–labeled macroaggregated albumin for clarifying high-output heart failure etiology. (J Am Coll Cardiol Case Rep 2024;29:102387) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 51-year-old man with multiple myeloma (MM) was directly admitted to the hospital from the oncology clinic after reporting several weeks of worsening dyspnea. He also experienced palpitations, nausea, early satiety, and bilateral leg swelling. On admission, the patient was afebrile with a heart rate of 122 beats/min, blood pressure of 106/49 mm Hg, and oxygen saturation of 97%. His physical examination was notable for signs of volume overload, with jugular venous distension to the level of the mandible, bibasilar rales, and 3+ pitting edema in the lower extremities.

LEARNING OBJECTIVES

- To understand the role of scintigraphy with Tc-99m MAA in the diagnosis of HOHF.
- To identify and evaluate differential diagnoses for new-onset congestive heart failure in patients with MM.

MEDICAL HISTORY

A recent 18F-FDG (Fludeoxyglucose F18) positron emission tomography/computed tomography scan had shown worsening myelomatous osseous disease despite a regimen of venetoclax and decitabine. The patient was planned for allogeneic stem cell transplantation, but in the weeks leading up to his clinic appointment, he experienced progressive exertional dyspnea, which limited his exercise tolerance to short distances around his home.

From the [a]Montefiore-Einstein Center for Heart and Vascular Care, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA; and the [b]Division of Nuclear Medicine, Department of Radiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.

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ABBREVIATIONS AND ACRONYMS

AV = arteriovenous

HOHF = high-output heart failure

MM = multiple myeloma

Tc-99m MAA = technetium-99m-labeled macroaggregated albumin

DIFFERENTIAL DIAGNOSIS

Identifying the underlying cause of ongoing congestion in individuals with myeloproliferative disorders can pose a considerable challenge. Typically, potential causes encompass a range of cardiovascular and noncardiovascular conditions, such as low-protein levels, kidney dysfunction, amyloid-related nephrotic syndrome, or heart failure. In our specific case, congestive heart failure was suspected, prompting a differential diagnosis that involved considering amyloidosis, severe anemia, ischemia, and high-output heart failure (HOHF).

INVESTIGATIONS

The laboratory work-up was significant for pancytopenia, with a white blood cell count of 3.8 k/μL, a hemoglobin level of 7.4 g/dL, and a platelet count of 12 k/μL. A complete metabolic panel was normal. B-type natriuretic peptide was elevated to 1,444 pg/mL with normal troponin I at 0.01 ng/mL. An echocardiogram revealed normal left ventricular function with a new finding of moderate right ventricular dilatation and hypokinesis. After the patient did not respond to escalating doses of intravenous diuretics, a right heart catheterization was performed. Catheterization revealed elevated biventricular filling pressures (right atrium: 18 mm Hg; right ventricle: 38/18 mm Hg; pulmonary artery: 38/22/27 mm Hg; pulmonary capillary wedge pressure: 17 mm Hg) with evidence of high cardiac output (Fick cardiac output: 17.1 L/min; Fick cardiac index: 7.9 L/min/m^2). In the context of congestive symptoms, elevated cardiac filling pressures, high cardiac output, and underlying MM with extensive osseous metastases, we had a strong clinical concern about HOHF. To differentiate whether the patient's high-output state was a consequence of long-standing anemia or the result of intramedullary arteriovenous (AV) shunting in MM bone lesions, a multidisciplinary team decided to perform scintigraphy with technetium-99m-labeled macroaggregated albumin (Tc-99m MAA) . During the left heart catheterization, which revealed normal coronary arteries, 5.1 mCi of Tc-99m MAA was injected into the abdominal aorta. After approximately 105 min, whole-body planar images were obtained in anterior and posterior projections (**Figure 1**). Regions of interest over the bilateral lungs and lower extremities were drawn. Then, the geometric means of the anterior and posterior counts were obtained, and AV shunting was estimated. The scan revealed evidence of lower extremity AV shunting with a proportion of 6%. The patient was diagnosed with HOHF secondary to intraosseous AV shunting.

MANAGEMENT

The patient was started on lenalidomide and pulse-dose dexamethasone with the goal of reducing shunting via chemical ligation of his AV fistulas in metastases.[1] This resulted in improved response to diuretics and resolution of heart failure symptoms.

DISCUSSION

We report on the novel application of Tc-99m MAA to identify intramedullary shunting in a patient with MM who presented with persistent congestion in the setting of high cardiac output and to guide further therapy.

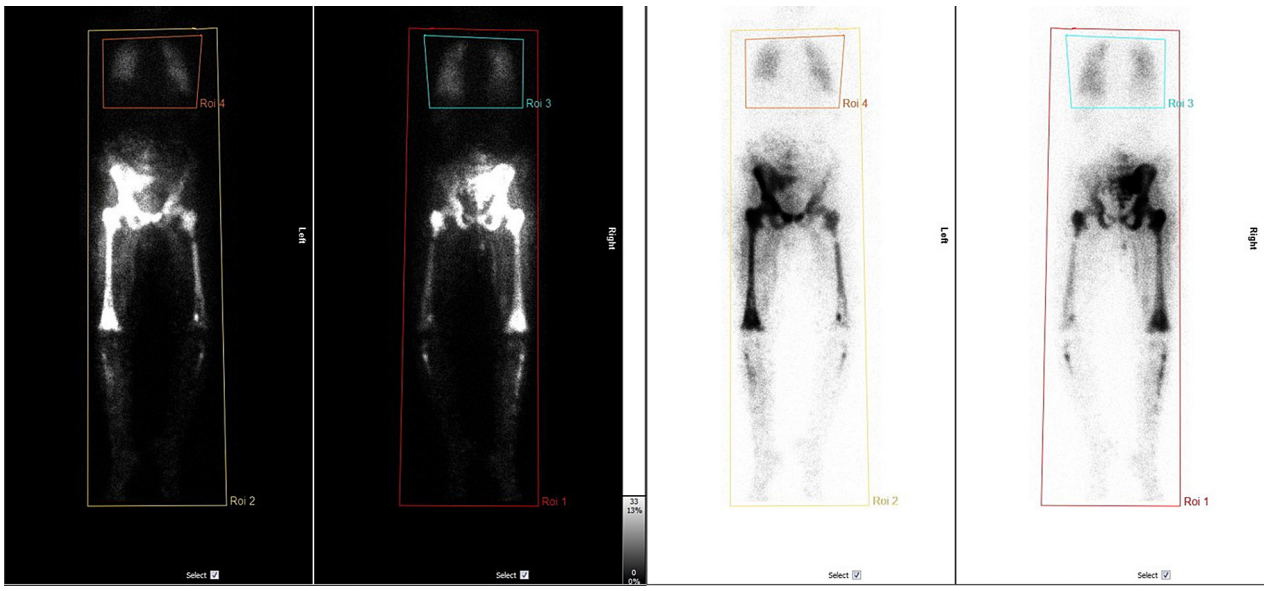
HOHF is a syndrome in which signs and symptoms of congestion occur in the setting of a high cardiac output, described as being >8 L/min or a cardiac index >3.9 L/min/m^2. Reduced vascular resistance due to AV shunts or peripheral vasodilatation is considered the main underlying pathogenetic mechanism.[2] HOHF can occur in multiple hematologic malignancies, particularly in MM, where it is thought to be related to AV shunting within osseous lesions.[3]

In a prospective study of 34 patients with MM, McBride et al[4] demonstrated that severe bone involvement was the only clinical characteristic significantly more frequent in those patients with high cardiac output states when compared with patients with MM with normal cardiac output ($P = 0.001$).

Scintigraphy with Tc-99m MAA is routinely used to identify shunting in hepatopulmonary syndrome. In a previous experimental study, Tc-99m MAA was similarly used to describe the exact mechanism by which bone involvement contributes to a high-output state in 11 patients with MM who had a cardiac index ≥4 L/min/m^2. Comparing cardiac indices with AV shunting ratios revealed a high correlation ($r = 0.79$; $P = 0.004$), suggesting that increased AV shunting within the affected skeleton plays a significant role in the development of high-output cardiac failure in MM.[5]

Timely diagnosis is crucial because HOHF related to shunting carries a 5-year mortality rate in excess of 50%.[6] These patients fail to respond to conventional

FIGURE 1 **Whole-Body Scintigraphy**



After injection of Tc-99m MAA in the abdominal aorta, increased activity at the osseous structures of the pelvis and bilateral lower extremities as well as radiotracer activity within bilateral lungs consistent with AV shunting are demonstrated. AV = arteriovenous; Tc-99m MAA = technetium-99m-labeled macroaggregated albumin.

heart failure therapies but may experience resolution of symptoms on treatment of their underlying malignancy with the antiangiogenic agents lenalidomide or thalidomide.[1]

FOLLOW-UP

Two days after starting combination therapy with lenalidomide/dexamethasone, the patient showed an improved response to diuretics. After 5 days, the patient's signs and symptoms resolved due to efficient diuresis with a net weight loss of 12 lbs. The diuretic dose was subsequently reduced. A follow-up echocardiogram, performed after 1 week, showed normalization of the right ventricular size and function, accompanied by a reduction in B-type natriuretic peptide levels from 1,444 to 134 pg/mL. The patient eventually underwent a successful allogeneic stem cell transplantation during the hospital admission.

CONCLUSIONS

HOHF is a rare, but underdetected cause of persistent congestion in patients with MM. This case is, to our knowledge, the first time Tc-99m MAA has been used to clarify the etiology of HOHF in the clinical setting. Given the mortality rate and the importance of a timely diagnosis, this technique may be of use in a wider population of patients with HOHF suspected to have occult shunting.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Sasa Vukelic, Montefiore Medical Center, 111 East 210th Street, Bronx, New York 10467, USA. E-mail: svukelic@montefiore.org. @EnklajdM, @UlrichJordeMD, @CardioMDPhD, @MdMoadel.

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KEY WORDS **arteriovenous shunting, high-output heart failure, multiple myeloma, technetium-99m-labeled macroaggregated albumin**