CASE REPORT

Systemic mastocytosis presenting as cardiac tamponade with CD25+ pericardial mast cells

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A 59-year-old man with a 10-year history of diffuse lymphadenopathy, presented to the Emergency Department with progressively increasing shortness of breath and pleuritic chest pain of 3 days’ duration. A diffuse hyperpigmented maculopapular rash associated with urticaria after consuming nonsteroidal anti-inflammatory drugs had been present for 30 years. Over the past decade, the patient experienced multiple syncopal episodes and chronic diarrhea triggered by consumption of animal products. The white blood cell count ranged from 11,000 to 30,300 per µL with granulocytes numbering between 5500 and 22,400 per µL. The absolute eosinophil count ranged from 720 to 1200 per µL. Computerized axial tomography scan of the abdomen in 2006 revealed diffuse lymphadenopathy, hepatosplenomegaly, and osteosclerosis. Inguinal and cervical lymph node biopsies in 2006 and 2012, respectively, only showed reactive lymphadenopathy. The stomach biopsy specimens from 2006 were restained and showed two clusters (>15 cells) of c-Kit+ and CD25+ mast cells. Finally, a repeat bone marrow biopsy showed aggregates of >15 mast cells, CD25+ and >15 mast cells, CD25+.

Key Clinical Message
In this first-in-literature case, we describe a patient with Systemic mastocytosis presenting with life-threatening cardiac tamponade associated with the presence of aberrant mast cells in the pericardium. Procedures involving surgical incisions through the pericardium in such cases can lead to uncontrolled mast cell degranulation leading to circulatory collapse.

Keywords
Cardiac tamponade, pericardial CD25+ mast cells, systemic mastocytosis.

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Among adults with SM, >90% express an activating D816V mutation of KIT that leads to the proliferation of morphologically and immunophenotypically abnormal mast cells[1]. The WHO major diagnostic criteria for SM is a bone marrow biopsy showing multifocal aggregates with >15 mast cells/hpf. Minor criteria include blood,

(Fig. 1F), CD2+ mast cells consistent with Systemic Mastocytosis (SM). Beta-blockade and ACE-Inhibitor therapy was withheld due to concern for lowering of the anaphylactic threshold, and the patient was discharged with oral colchicine, a mast cell stabilizer (Montelukast) and a selective H-1 blocker (Fexofenadine).

Figure 1. (A) Two-dimensional echocardiogram, apical four-chamber view demonstrating a large concentric pericardial effusion (B) Pulsed wave Doppler with interrogation window below mitral valve demonstrating a 32% decrease in peak transmitral flow velocity during inspiration (C) Immunohistochemical staining of pericardial biopsy showing c-kit+ mast cells. (D) H&E stain of pericardial biopsy showing mesothelium with mononuclear infiltrate, 200×. (E) Immunohistochemical staining of stomach biopsy specimen showing CD25+ mast cells. (F) Immunohistochemical staining of bone marrow biopsy showing CD25+ mast cells.
bone marrow, or extracutaneous organ biopsy showing D816V mutation; mast cells with CD25 and/or CD2 expression; multiple serum tryptase levels >20 ng/mL and >25% of mast cells having abnormal morphology on biopsy. One major and two minor or three minor criteria are sufficient to clinch the diagnosis.

Normal myocardium is populated by mast cells with granules containing fibrogenic proinflammatory cytokines such as tumor necrosis factor-α, transforming growth factor (TGF)-β, interleukin-4, platelet-derived growth factor, and fibroblast growth factor, in addition to histamine, tryptase, chymase, and renin. Many patients with mast cell activation disorders tend to develop left ventricular diastolic dysfunction. Mast cell-derived histamine also stimulates fibroblast proliferation and collagen synthesis. Administration of an H2 blocker in a prospective study improved both cardiac symptoms and ventricular remodeling in patients with heart failure [2]. In failing hearts, over 75% of fibrogenic angiotensin II is derived from the angiotensin-converting enzyme (ACE)-independent chymase pathway [3]. Chymase also mediates direct fibrogenic activity through activation of TGF-β-induced Smad-dependent pathways [4]. Chymase inhibition attenuates matrix metalloproteinases in rodent, porcine, and dog models of heart failure [5]. Systolic and diastolic dysfunction from cardiac remodeling due to both pressure and volume overload can be attenuated by mast cell stabilizers in animal models [6].

We describe the first reported case of SM presenting as cardiac tamponade with pericardial CD25+ mast cells. The episode of hypotension was likely due to distributive shock from pericardial mast cell degranulation. We propose that abnormal, hyperactive mast cells served as mediators of the inflammatory response in myocardial and pericardial tissue, contributing to production of the pericardial effusion eventually leading to tamponade. Further studies are necessary to fully understand the mechanism behind this occurrence.

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Conflict of Interest
The authors report no relationships that could be construed as a conflict of interest.

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