



## Review Article

# Acute Myeloid Leukaemia Presenting with Cardiac Tamponade: A Case Report and Review of the Literature

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## Abstract

Acute Myeloid Leukaemia (AML) is the most common acute leukemic neoplasm, comprising approximately 80% of adult cases with a mean age of diagnosis of 68 years old. AML is characterized by the presence of a variety of malignant cells that may be classified by immunohistochemistry and genotypically. We present a case of AML in a young, African-American male who presented to the hospital reporting three days of fevers, and one episode of nighttime sweating. The patient was found to have a moderately sized pericardial effusion with features of early tamponade physiology as well as significant biventricular hypertrophy. Upon bone marrow biopsy the patient was diagnosed with AML and was promptly started on cytarabine and daunorubicin. This paper serves to raise awareness for clinicians to remain cognizant that common diseases, such as AML may present in uncommon ways and to highlight the importance of multidisciplinary care teams in the treatment of patients with neoplastic disease.

**Keywords:** Acute Myeloid Leukaemia (AML); Edema; Pericardial Effusion.

## Introduction

Acute Myeloid leukaemia (AML) is the most common acute leukaemia in adults, comprising approximately 80% of acute leukemic cases with a mean age of diagnosis of 68 years old. AML is far from a monomorphic disease with an ever-expanding genotypic landscape. At its core, like other blood cell malignancies, the disease begins in the bone marrow, most often, due to somatic mutations accumulated over time in hematopoietic precursor cells destined to terminally differentiate along the myeloid lineage of peripheral blood cells. While the bone marrow is the primary focal point of disease in most cases, extramedullary involvement of peripheral tissues, and often whole organs is a known phenomenon in leukemic malignancy, systemic manifestation as the initial presentation is an uncommonly described presentation.

Most commonly extra-medullary involvement is seen in the skin, lymph nodes, and peritoneum [16]. In a study done by fianchi et al the incidence of extramedullary involvement was reported in an examination of 364 patients diagnosed with AML, 38 were seen to have extramedullary disease such that skin was the most prevalent site, seen in 22 patients, followed by CNS in 6 patients and all other sites documented with no more than 2 patients. Interestingly, there were no patients with evidence of cardiac involvement [16]. Cardiovascular sequela such as pericardial effusion secondary to systemic leukaemia and more commonly, antineoplastic therapy is well documented, cardiac infiltrative disease as the initial manifestation of disease are considerably rarer. Thus, the specific cardiovascular complications of infiltrative AML are not well described from either a clinical, or histopathologic perspective providing a gap in the current literature on how extramedullary cardiac involvement may present in leukaemia patients.

There are several ways these malignant cells may be classified both with immunohistochemistry, and genotypically that further delineate prognosis, treatment, and phenotypic features of the disease. In short, classically the WHO system of diagnostics is based on immunohistochemical staining of bone marrow aspirate.

M0: Undifferentiated acute myeloblastic leukaemia

M1: Acute myeloblastic leukaemia with minimal maturation

M2: Acute myeloblastic leukaemia with maturation

M3: Acute promyelocytic leukaemia (APL)

M4: Acute myelomonocytic leukaemia

M4eos: Acute myelomonocytic leukaemia with eosinophilia

M5: Acute monocytic leukaemia

M6: Acute erythroid leukaemia

M7: Acute megakaryoblast leukaemia

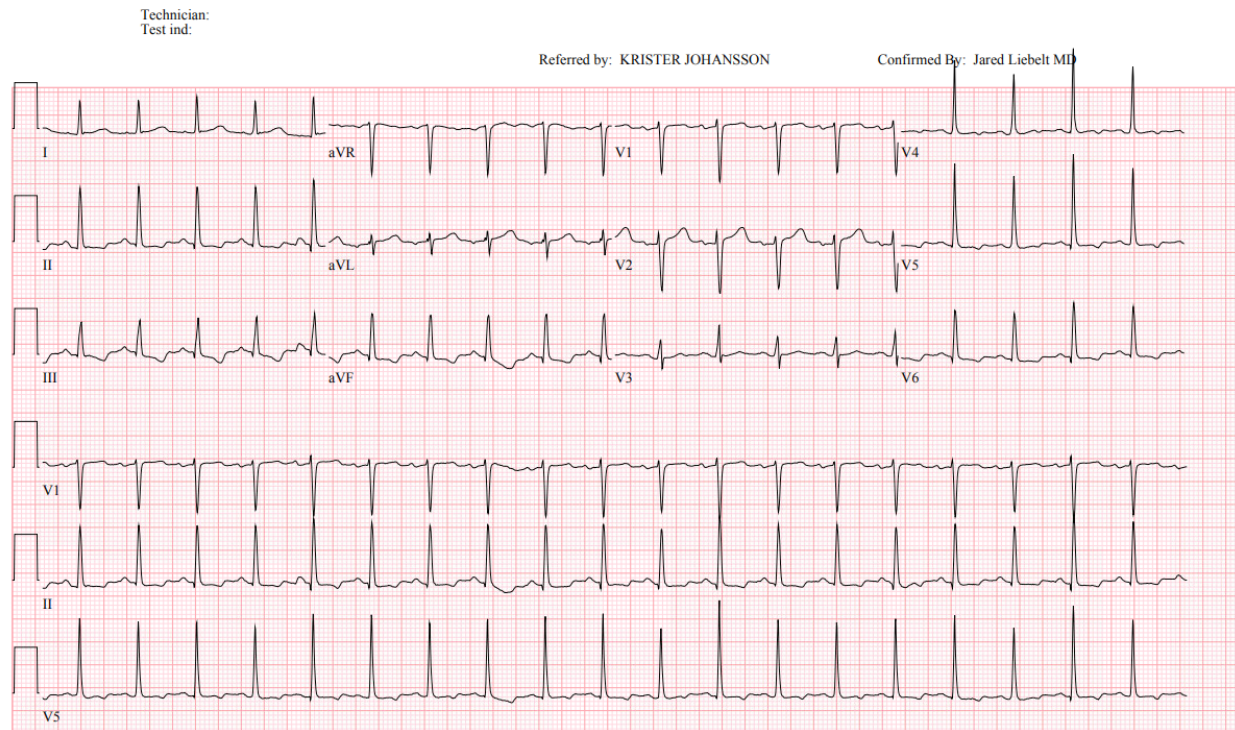
With the advancement in molecular diagnostics, immunohistochemical classification is now being used in conjunction with genome-based assays to further characterize these subtypes of AML. These genes include CEBPA, TET-2, NPM1, IDH, FLT3, DNMT3A, and c-KIT, as well as chromosomal analyses of chromosomal alterations such as t (8;21) (q22; q22), t (15;17) (q22; q12) and inv(16) (p13q22)/t(16;16) (p13; q22) are used to predict more desirable prognosis (3), (4). Chromosomal alterations such as monosomy 5 alone or in combination with monosomy 7, deletion (5q), inv (3) (q21q26), and t (3;3) (q21; q26) indicate poorer outcomes. Taken together the immunohistochemical

phenotype, the genotype, and the chromosomal landscape of bone marrow aspirate in patients with suspected AML provide sophisticated diagnostic and prognostic criteria that shape the clinical course of these patients over the course of their disease. The diverse molecular landscape of AML is mirrored in the myriad of ways that patients may present with this malignancy.

### Case Description

We present a case of a 40 -year-old male who presented to the hospital with three days of fevers (T max 100.6) and 1 episode of night sweats. At the time of his presentation, his chief complaints were weakness and shortness of breath with chest pressure. Otherwise, the review of systems on presentation to the ED was unremarkable. The patient's past medical history was remarkable for non-insulin-dependent T2DM and hypertension. During his initial evaluation in the emergency department, the patient's vital signs were as follows: BP 136/107, pulse 137, temp 97.9 (oral), respiratory rate 18, and saturation 100% on room air. While the patient's initial workup was underway, he experienced a syncopal episode as ECG leads were being applied to his chest. ECG conveyed sinus tachycardia with inferolateral T wave abnormalities see in (Figure 1) The patient subsequently regained consciousness with no resultant postictal state or residual deficits. Bedside ultrasonography was performed by the ED staff which demonstrated no signs of pulmonary embolism but noted a pericardial effusion for which a cardiology consult was initiated and formal imaging was ordered. Initial lab results were remarkable for a complete blood count showed a WBC of  $10.1 \times 10^3/\mu\text{L}$  and 19% blasts and an unremarkable basic metabolic panel.

12-SEP-1982 (40 yr)	Vent. rate	117	BPM	Sinus tachycardia
Male Black	PR interval	152	ms	T wave abnormality, consider inferolateral ischemia
	QRS duration	80	ms	Abnormal ECG
Room:4957	QT/QTc	334/465	ms	When compared with ECG of 08-JUN-2023 18:48,
Loc:1	P-R-T axes	87 55 -40		T wave inversion more evident in Inferolateral leads
				Confirmed by Liebelt MD, Jared (3500) on 6/9/2023 11:39:25 AM

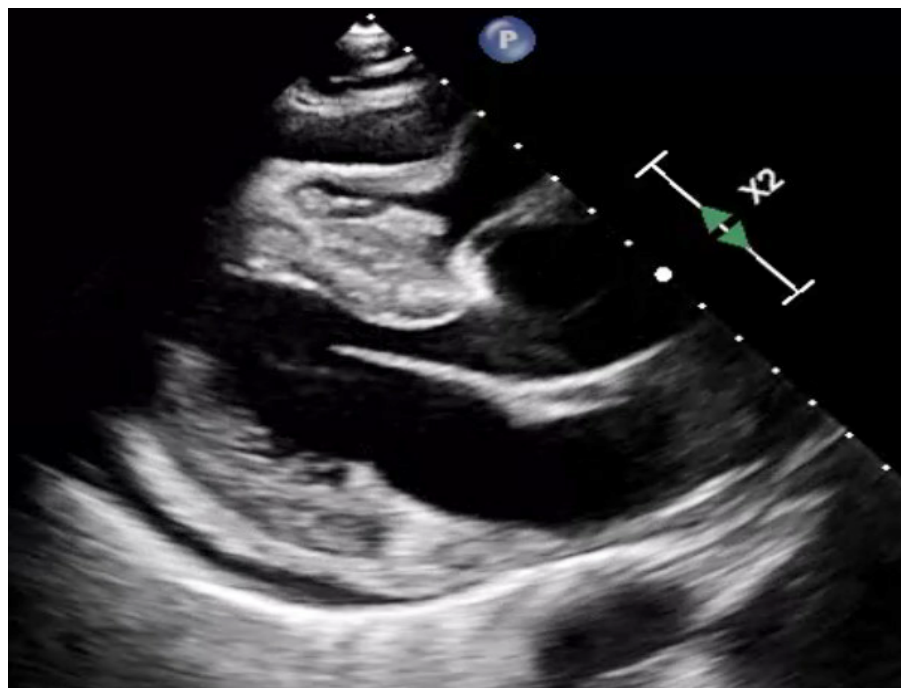


**Figure 1:** ECG conveyed sinus tachycardia with inferolateral T wave abnormalities.

Upon formal-full ultrasonographic exam, the patient was noted to have a moderately sized pericardial effusion with features of early tamponade physiology as well as significant biventricular hypertrophy see in (figure 2). The patient decompensated shortly after cardiac imaging, IVF was administered, and blood pressure initially responded, however, the patient eventually became hypotensive inevitably requiring pericardiocentesis. The pericardial drainage was serosanguinous fluid with cytologic analyses revealing 24 blasts. Pathological review of the patient pericardial fluid and admission blood smear revealed leucocytosis with anaemia and thrombocytopenia. Circulating blasts were observed and were characterized as being intermediate to large in size, exhibiting open chromatin, prominent nucleoli, and slightly irregular nuclear contours.

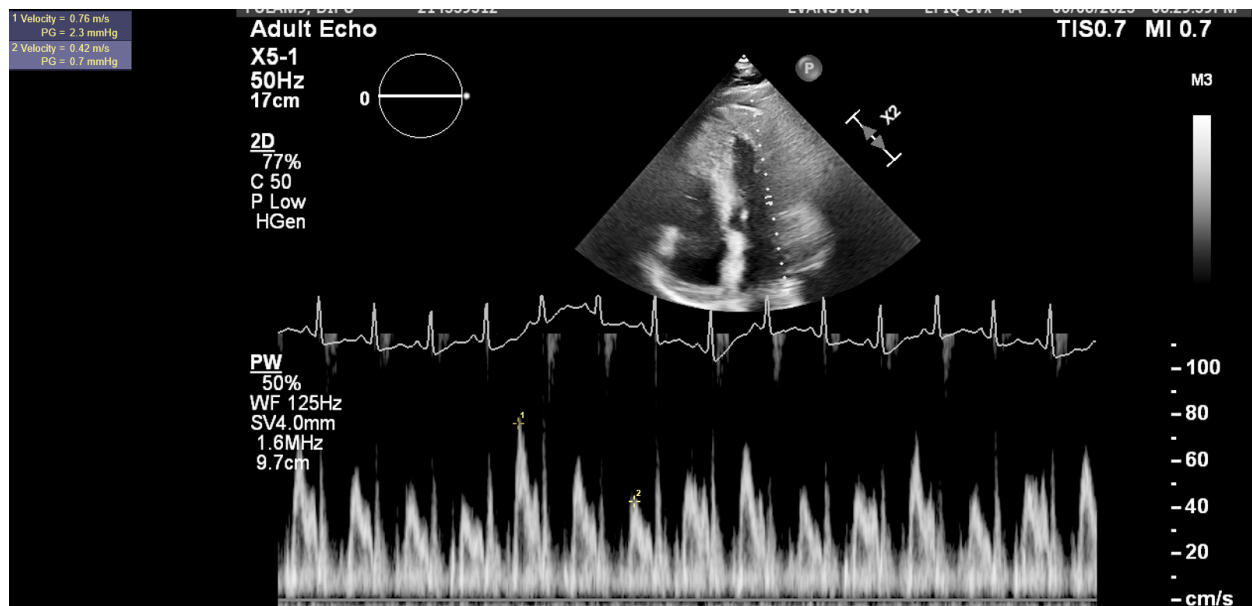


**Figure 2A:** Subcostal view of the heart showing a moderate sized pericardial effusion



**Figure 2B:** Parasternal long axis view of the heart showing diastolic invagination of the right ventricle (arrow)

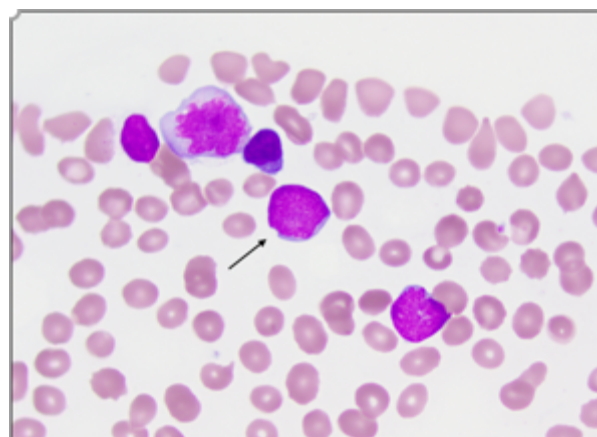




**Figure 2C:** Mitral inflow demonstrating a 45% variation in velocity consistent with tamponade physiology

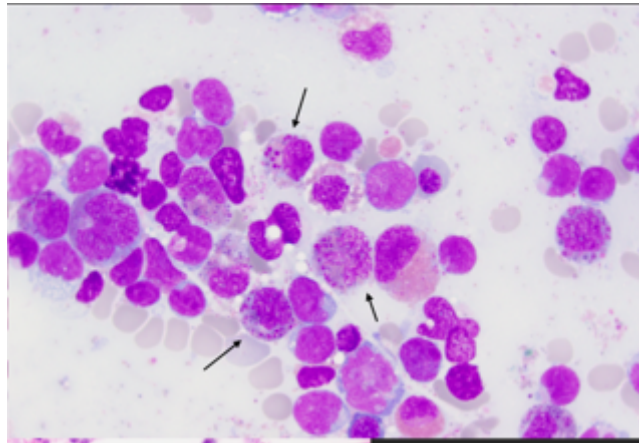
Additionally, the cytoplasm appeared scant and mostly angular. An extremely rare, thin Auer rod was also noted. Mature granulocytes occasionally displayed atypical nuclear features and hypo granular cytoplasm. The platelet count was reduced, with many of the platelets appearing to be enlarged. These findings were generally consistent with a hematopoietic neoplasm, most likely acute myeloid leukaemia, further delineated by flow cytometry to be acute myeloid leukaemia with some monocytic differentiation. The bone marrows were approximately 60% blasts at the time of diagnosis see in (Figure 3). This informed the prior finding of significant biventricular hypertrophy to be possibly leukemic cell infiltration of the myocardium. However, the cardiac MRI showed no evidence of myocarditis or edema, solely pericardial inflammation with small residual effusions. Given the diagnostic findings on both peripheral blood and bone marrow aspirate evaluation, haematology was consulted. The patient was promptly started on cytarabine 100/+mg/m<sup>2</sup> and daunorubicin 90 mg/m<sup>2</sup> in the 7+3 protocol during this admission.

A



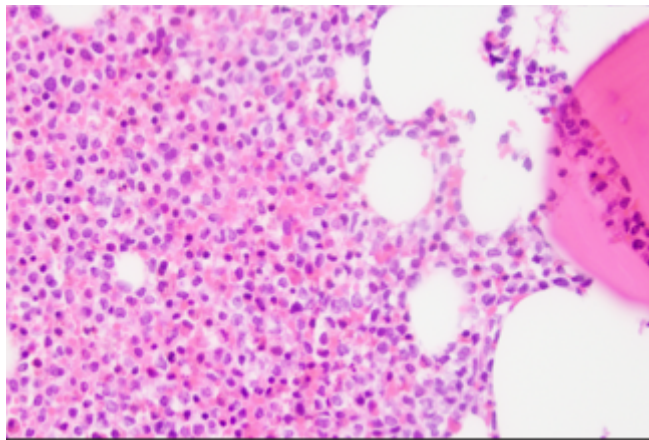
**(A)** Abnormal monocytes were also present, seen here above the indicated blast

B



**(B)** The bone marrow aspirate smear demonstrated many abnormal eosinophils and eosinophilic precursors, characterized by coarse basophilic granules (arrows, B).

C



**(C)** The core biopsy showed marked increase in bone marrow eosinophilia

**Figure 3:** The peripheral blood smear showed circulating blasts (arrow).

## Discussion

This case highlights the insidious and often unpredictable manifestation of malignancy in a young, African-American male who does not follow the classic clinical presentation of AML. It also brings to the table an opportunity to highlight the importance of allied sub-specialties in oncologic care. Extramedullary metastasis is by no means a rare phenomenon within acute leukaemia. The most frequently reported incidence of myocardial or pericardial infiltrative disease is 30-44%, however, despite this, only 1% of these patients present with acute cardiovascular complaints or clinical syndromes [5]. Of note, most of this data came from the study of post-mortem examinations of children with late-stage acute lymphoblastic leukaemia. There is minimal data available for patients with initial cardiac infiltrative disease in acute myeloid leukaemia. One study performed by Sampat et al of 1600 leukaemia patients showed that pericardial effusion was detected in 325 patients in total. 185 patients were diagnosed with AML, 68 were diagnosed with ALL, and 72 were diagnosed with MDS. In 136 of those AML patients, only 26% were present prior to initiation of therapy [7]. There was no delineation if these effusions were incidentally found or the cause of the patient's presentation. Only 10 patients of those tested required pericardiocentesis and the authors did not comment on the specific leukaemia those patients were diagnosed with.

## Conclusion

Cardiac tamponade as an acute presentation of undiagnosed acute myeloid leukaemia is a rare, and unique extramedullary manifestation of the disease rarely reported in the current literature. This paper serves to raise awareness for clinicians to remain cognizant that common diseases, such as AML may present in uncommon ways and that differential diagnosis should remain wide. It also serves to highlight the importance of multidisciplinary care teams in the treatment of neoplastic disease.

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