FIXING A BROKEN HEART: A RARE CASE OF INTRA-CARDIAC MYELOID SARCOMA IN PEDIATRIC ACUTE MYELOID LEUKEMIA

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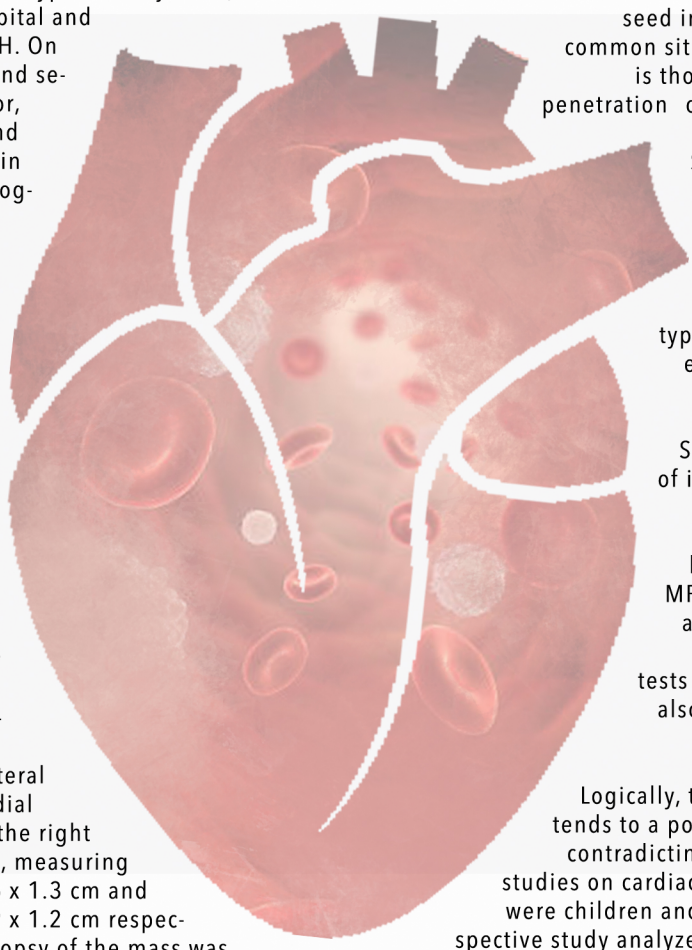
INTRODUCTION

Acute myelogenous leukemia (AML) is a hematologic malignancy characterized by malignant transformation of myeloid progenitor cells. The Philippine Pediatric Society Disease Registry reported 5,924 cases of AML during the past 10 years, only 113 (or 1.9%) of whom were also reported to have a myeloid sarcoma. International data suggests that myeloid sarcomas occur in 4-5% of AML patients, often non-cardiac.

Outside of case reports, no data exists regarding the incidence of cardiac myelosarcomas in AML patients. The lack of literature illustrates the need to document cases like this and its response to treatment.

CASE SUMMARY

A 14 year old female came in due to 1 week history of easy fatigability. CBC done at a clinic showed anemia and hyperleukocytosis (WBC 372.2). Further work-up was advised at a hospital and the patient was subsequently admitted at NCH. On admission, she was tachycardic, tachypneic, and severely wasted. On physical examination, pallor, neck vein distention, dynamic precordium, and hepatomegaly 3cm below the subcostal margin were seen. BMA and CLP revealed Acute Myelogenous Leukemia FAB M0. Chemotherapy was delayed for the first three months after diagnosis due to frequent infections and recurrent bleeding.



Baseline 2D-echocardiography showed LV dysfunction with ejection fraction 47.5% Cardiology service suggested monthly 2D-echo and on the 3rd month, a non-movable echo-dense structure was seen attached to the right ventricular wall (Fig. A). A cardiac MRI subsequently showed two small masses with irregular borders the anterior and anterolateral endocardial walls of the right ventricle, measuring 1.2 x 0.6 x 1.3 cm and 1.4 x 0.9 x 1.2 cm respectively. Biopsy of the mass was ideal but not done due to the position of the masses and a high risk of bleeding. Given the clinical history and difficulty starting treatment, these masses were considered to be Intra-Cardiac Myelosarcomas secondary to Acute Myelogenous Leukemia.

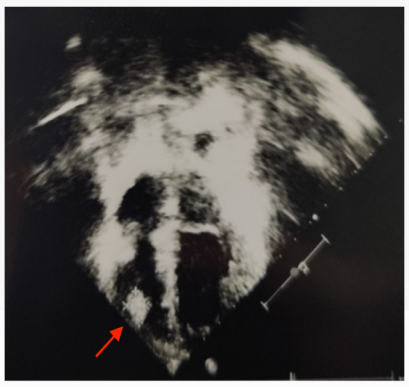


Figure A. Intra-cardiac mass seen on 2D-echocardiography (red arrow)

As soon as able, induction chemotherapy was started using the 2 + 6 Anti - AML protocol, a modification of the 3 + 7 protocol commonly used for AML. The patient's existing cardiac dysfunction limited the dose of Idarubicin to 8mg/BSA instead of 10mg/BSA. Cytarabine was given as per protocol. A repeat cardiac MRI done after 2 cycles of chemotherapy showed interval decrease of both intra-cardiac masses - from 1.2 x 0.6 x 1.3cm and 1.4 x 0.9 x 1.2cm to 0.5 x 0.6 x 0.7cm and 0.7 x 0.7 x 0.9 cm, respectively (Figure B). On the 5th cycle of maintenance chemotherapy, Idarubicin was increased to the standard dose of 10mg/BSA.

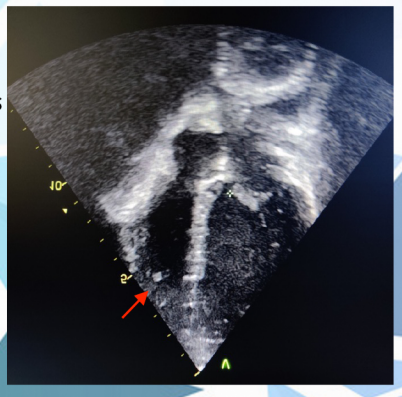


Figure B. Smaller intra-cardiac mass after 5 months of treatment (red arrow)

At present, the patient has fully completed her chemotherapy. A repeat 2D-echo done this September 2022, after a total of 15 cycles of chemotherapy, showed normal cardiac function and ejection fraction. There was no evidence of intra-cardiac masses. A repeat cardiac MRI has yet to be done due to financial constraints.

DISCUSSION

Acute Myelogenous Leukemia comprises approximately 16% of all childhood leukemias and though AML is known to present with myeloid sarcomas, only a small percentage actually do so. Most notable in FAB M4/M5 subtypes, myeloid sarcomas are malignant extramedullary tumors composed of immature myeloid cells. As such, they can occur not only in AML, but also in other malignancies involving myeloid cells. They may be present at the time of diagnosis, before diagnosis, as a manifestation of relapse, or even as a de novo tumor. Since leukemic blasts circulate through the entire body, myeloid sarcomas can seed in virtually any tissue. Despite this, the most common sites of involvement are the orbits and skin. It is thought that natural organ barriers cause poor penetration of chemotherapy leading to survival of blast cells despite adequate systemic treatment. Stefanidakis et al found that the interaction between matrix metalloproteinase-9 (MMP-9) and leukocyte surface beta integrins is required for migration and seeding of AML blasts to other organs. Another study suggests that the M4 subtype has higher MMP-9 expression - a possible explanation why it has a higher incidence of extramedullary disease.

Symptomatology largely depends on the site of involvement so they may be easily mistaken for other illnesses. A tissue biopsy is key in establishing diagnosis. Tissue samples may be sent for cytogenetic studies. A CT Scan or MRI are particularly helpful in visualizing size and tumor location, and differentiating from other masses. Morphologic and cytogenetic tests of peripheral blood or bone marrow should also be requested, most especially in the background of a hematologic malignancy.

Logically, the presence of extramedullary disease portends to a poorer prognosis but literature is surprisingly contradicting. In a large meta-analysis consisting of 30 studies on cardiac myeloid sarcomas from 1960-2016, only 3 were children and none survived. On the other hand, a retrospective study analyzed data from the Dutch Childhood Leukemia Study Group between 1972-1998 showed that among 477 children with AML, extramedullary disease at diagnosis had no significant effect on event-free survival. High initial WBC and favorable cytogenetics remained significant. There hasn't been a consensus on what treatment regimen to employ. Hematologists worldwide are relying on standard treatment regimens already proven to have an effect on AML. These protocols are adapted to patients, bearing in mind cardiac status and stability, and tolerance to drug toxicities. In low resource settings, financial capability and drug availability may dictate what regimen to use. Studies have also shown that radiotherapy doesn't have any benefit when added to the treatment regimen.

CONCLUSION

At present, there are only a handful of case reports on intra-cardiac myeloid sarcomas scattered around the globe. This might be the first case reported in the Philippines. This case exemplifies that although leukemic cells have been known to seed and hide in certain parts of the body (ie skin, orbits, etc), there is always a possibility that atypical sites might be involved. It is even more striking that a myeloid sarcoma shall be found in the heart. It is important to be reminded that though leukemia may not be as incurable as it once was, it can still be as deadly as it used to be.

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