SUCCESSFUL OUTCOME OF A CHILD WITH CARDIAC MYELOID SARCOMA – A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Myeloid sarcoma refers to the extramedullary deposition of myeloblasts characteristically seen in AML-FAB types M2, M4 and M5. Commonest sites include skin, orbit and lymph nodes. Myeloid sarcoma in heart is an extremely rare occurrence and usually leads to delayed diagnosis owing to consideration of other differentials and technical difficulties in obtaining tissue for biopsy. Overall survival rate as per available literature is 20-30%. Non-invasive mode of diagnosis, timely initiation of chemotherapy and meticulous supportive care are the keys to successful outcome.

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ABSTRACT:

Myeloid sarcoma refers to the extramedullary deposition of myeloblasts characteristically seen in AML-FAB types M2, M4 and M5. Commonest sites include skin, orbit and lymph nodes. Myeloid sarcoma in heart is an extremely rare occurrence and usually leads to delayed diagnosis owing to consideration of other differentials and technical difficulties in obtaining tissue for biopsy. Overall survival rate as per available literature is 20-30%. Non-invasive mode of diagnosis, timely initiation of chemotherapy and meticulous supportive care are the keys to successful outcome.

INTRODUCTION:

Extra-medullary presentation of acute myeloid leukemia(AML), labelled as myeloid sarcoma(MS) involving heart is exceedingly rare in children (1). We report successful outcome with chemotherapy in a boy with AML and cardiac-MS at diagnosis.

CASE REPORT :

A 5year old boy of Indian origin was retrieved from Dubai by air ambulance to our centre in a sick condition with an underlying cardiac mass. In Dubai, child presented with a 2-week history of fever, breathing difficulty and puffiness of face. Child had anasarca, respiratory distress and hepatomegaly. Chest X-ray showed pleural effusion. Investigations revealed mild thrombocytopenia, transaminitis, disseminated intravascular coagulation (DIC) with elevated PT, APTT and hypofibrinogenemia, elevated serum ferritin, Lactate Dehydrogenase(LDH)and hyperuricemia. Computed tomography (CT) of chest showed an ill-defined solid mass in right atrium(RA) of size 5x6x3cm, engulfing right coronary artery and obstructing tricuspid outflow with

multiple mediastinal lymphnodes and bilateral pleural effusion. Parents were informed about need for cardiac mass biopsy and as they wished to bring child back to native place, child was air-lifted from Dubai and retrieved by our emergency team.

At our centre, child had pallor, anasarca, tachypnea requiring oxygen, elevated JVP (jugular venous pressure) and hepatomegaly. Hemogram showed mild anaemia and thrombocytopenia with elevated WBC count. Peripheral smear showed leucocytosis with blasts andpromyelocytes. Investigations are summarised in Table-1. Chest X-ray showed bilateral pleural effusion without cardiomegaly. Pleural fluid cytology was negative for malignant cells.

Echocardiography showed a mass arising from RA immediately superior to anterolateraltricuspid leaflet, subtotally obstructing tricuspid valve (TV) causing significant dilatation ofRA, inferior venacava and hepatic veins without involvement of other chambers of heart. Mass measured 20x32 mm and superiorly, there was a thick walled cystic lesion measuring20x21 mm across. Thin layer of pericardial effusion was present with no infiltration of parietal pericardium (Fig-1).

Bone marrow aspirate and biopsy revealed hypercellular marrow infiltrated by blasts withmoderate amount of eosinophilic cytoplasm with large nucleus and prominent nucleoli suggestive of myeloid blasts(Fig-2). Flow cytometry showed blast population with moderate expression of CD38, CD64, CD56, CD11b, HLADR, CD36, CD4, CD11c, CD33, dim expression of CD45, CD13, CD34, CD117 and MPO, suggestive of AML with monocyticdifferentiation. Karyotyping showed normal pattern (46-XY). Fluorescent in-situ hybridization (FISH) analysis on interphase nuclei showed inv(16) and molecular studies showed FLT3D853 mutation.

With a final diagnosis of AML-M4 with cardiac-MS, child was started on chemotherapy as per UKMRC AML-17 protocol with Cytarabine and Etoposide. Daunorubicin was deferred for avoiding cardiac toxicity. After cycle-1induction, echocardiography showed a reduction in mass (10x10mm), with no obstruction of TV (Fig-3). Bone marrow examination revealed morphological remission with minimal residual disease(MRD) of 0.9%. After cycle-2 induction including daunorubicin, MRD was not detected and ECHO revealed significant reduction in size of mass and disappearance of cystic lesion. Shrunken mass was hyperdense on ECHO and non-FDG avid on PET-CT suggesting fibrotic change (Fig-4). He was consolidated with 2cycles of high dose arabinoside (HiDAC). His bone marrow at the end of treatment was found to be in remission and is doing well on follow-up for past 2.5years.

DISCUSSION :

AML accounts for 15-20% of pediatric acute leukemia. Myeloid sarcoma(MS), seen in 2-8% of AML, is also referred to as chloroma or granulocyticsarcoma (GS) and is characterized bydeposition of myeloblasts in an extramedullary site (2). The age of patients at MS presentation is highly variable, however, is common in children and young adults with a male pre-ponderance (1). Expression of CD56 helps to invade/infiltrate extramedullary tissues and is common with AML-FAB types M2, M4 and M5(3).

MS can occur with (leukemic-AML/CML) or without concurrent marrow disease(isolated/nonleukemic/denovo) at diagnosis, or relapse after chemotherapy or hematopoietic stem cell transplant(HSCT). MS may also occur in association with myeloproliferativeneoplasm(MPN) or myelodysplastic disorder(MDS) (4).

In a study on 33 MS patients, most common site of involvement included skin followed by orbit, lymphnodes and rare sites included central nervous system (CNS), genitourinary tract,chestwall, lungs, lacrimal gland and breast (1). In another series of 9 patients, 2 were childrenwith MS in right middle meatus and orbit(5).

In a known patient with MDS/AML, diagnosis is straight-forward, however, significant challenges and delays are evident in isolated-MS, as the masses can mimic other differentials including soft tissue sarcoma, neuroblastoma or primitive neuroectodermal tumours(6).Technical difficulties like biopsy from inaccessible/deep tissues pose a significant challenge.

Histology plays a major role with pleomorphic infiltrate of mononucleate andgranulocytic-cells. Eosinophilic metamyelocytes may be a significant clue. In an isolated-MS, diagnosis is favored by expression of CD61, CD56, MPO, CD34, CD117 on immunohistochemistry(IHC) (7).

Coagulation abnormalities like DIC, hyperfibrinolysis commonly seen in AML-M3 happens in 7-9% of non-M3-AML; possible Factor-X-activating enzymes in monoblasts and liver dysfunction have been proposed as underlying mechanisms. In our case, thrombocytopenia and DIC led to suspicion of AML and diagnosis was obtained from less invasive bone marrow examination rather than a risky cardiac mass biopsy(8).

Cytogenetic studies reveal chromosomal aberrations including monosomy7, trisomy8, MLL-rearrangement, inv(16), t(8:21), monosomy16 and trisomy11 in around 55% MS and-NPM1(nucleophosmin) mutation has been significantly noted in patients with MS(6).

Cardiac-MS is exceedingly rare with incidence of <1% cases of MS, predominantly diagnosed on autopsy. To the current knowledge, number of children with cardiac-MS is very few. In a largest meta-analysis including 30 studies over 10years, only 3 were children among 32 patients with cardiac-MS (9).

In most cases, symptoms of cardiac illnesses predominate than those of leukemia. Striking predisposition for involvement of right atrium(RA) and right ventricle(RV) is well documented, with other sites including pericardium and septum. Mass in RA is much commoner and presents with features of cardiac failure (10). Echocardiography, CT and magnetic resonance imaging are standard techniques to diagnose extent of involvement.

The gold standard for diagnosis is histopathology of biopsy specimen. Yield of biopsy can be increased by image-guided techniques. However, the procedure could be fatal due to location and proximity to vital structures. Least invasive technique is the best strategy to avoid morbidities and may include bone marrow aspiration/trephine biopsy and pericardial/pleural diagnostic tap, as appropriate. Subtle abnormalities in hemogram usually happen with marrow involvement and such clues are to be sought prior to venturing out an invasive cardiac mass biopsy.

There are no standard treatment protocols for MS. Chemotherapy remains the mainstay and includes cytarabine and anthracyclines used for AML. With a fear of cardiotoxicity, other regimens like EMA (etoposide/mitoxantrone/cytarabine) have been used(3,11). Fractionated radiotherapy upto 24Gy, used for acute symptom relief and also as consolidation, has been found to be effective(12). Role of HSCT is well documented as in relapsed/refractory AML or those with high risk cytogenetics after achieving morphological remission with chemotherapy.

Extramedullary disease was considered to have a poor prognosis due to aggressive nature of the disease, however, it is controversial(13); prognosis is mainly driven by the underlyingcytogenetics and in presence of favourable cytogenetics, there was no significant differences in survival between those with or without MS(1). Reported poor prognosis in case of cardiac-MS has been associated partly with advanced disease in view of difficult/delayeddiagnosis or treatment related complications. The long term survival rate reported as per available literature is only 20-25%(14).

CONCLUSION:

Meticulous examination and careful scrutinising of baseline laboratory investigations help us to avoid life-threatening invasive diagnostic procedures like a cardiac mass/mediastinal mass biopsy. Multidisciplinary team effort and accurate histopathological diagnosis with cytogenetics are crucial for the successful outcome of rare diseases like MS.

CONFLICT OF INTEREST: None

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Figure legends:

Fig 1: Echocardiography at diagnosis showed a mass arising from right atrial wall, subtotally obstructing tricuspid valve orifice causing significant dilatation of right atrium, inferior vena cava and hepatic veins. Mass measuring 20 x 32 mm

Fig 2: Bone Marrow aspirate with monocytic blasts MGG stain 100X view and biopsy

Showing hypercellular marrow replaced by blasts Hematoxylin and Eosin stain 20X view

Fig 3: Post cycle 1 induction ECHO showing significant reduction in the size of mass to 10 x 10 mm

Fig 4: End of treatment ECHO showing shrunk hyperdense lesion suggesting a residual scar tissue

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