Transformation of Myelodysplastic Syndrome to Acute Lymphoblastic Leukemia in a Child

Vineeta Gupta · Baldev Bhatia

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Abstract Childhood myelodysplastic syndrome (MDS) is an uncommon condition. Unlike adult MDS, pediatric patients have a more progressive course and rapidly transform to acute myeloid leukemia. Evolution to acute lymphoblastic leukemia is extremely rare. We report a 5 year old female child who presented with refractory anemia with excess blasts and transformed into acute lymphoblastic leukemia 4 months after initial diagnosis.

Keywords Myelodysplastic syndrome · Refractory anemia · Acute lymphoblastic leukemia · Refractory anemia with excess blasts

The myelodysplastic syndrome (MDS) represents a spectrum of stem cell malignancies that manifests dysplastic and ineffective hematopoiesis, which is associated with a variable risk of transformation to acute leukemia. Patients have a deteriorating course with 30% evolving into acute leukemia usually of myeloid phenotype [1]. Evolution into acute lymphoblastic leukemia (ALL) is rare and seen in <1% adult cases and extremely rare in pediatric population. There is only one other case report where a child with refractory anemia (RA) transformed into ALL [2]. We report another case where a 5 year old child presenting with refractory anemia with excess blasts (RAEB) evolved into ALL.

Case Report

A five year old female child presented with one month history of fever, pallor and fatigue. There was history of petechiae over body for last seven days. She had received two units of blood transfusion before admission. On examination, the child had pallor with just palpable spleen. Liver was palpable 1 cm below costal margin. There was no lymphadenopathy. Her hemoglobin was 5 g/dL, total leucocyte count (TLC) $14 \times 10^9/L$ and platelet count was $10 \times 10^9/L$. Peripheral smear showed normocytic red blood cells with marked reduction in platelets. No abnormal cells were noted. Bone marrow aspirate was particulate hyper cellular with dyserythropoiesis and dysmegakaryopoiesis. Blasts were 12%. A diagnosis of refractory anemia with excess blasts (RAEB) was made. The child was given supportive treatment with packed cells, platelet transfusion and broad spectrum antibiotics. She showed improvement and was discharged on request.

She presented 4 months later with fever, pallor and vague pain in limbs. On examination, liver was palpable 5 cm and spleen was 3 cm below costal margin. There was sternal tenderness. The hemoglobin was 9 g/dL and TLC was $8 \times 10^9/L$. The platelet count was $40 \times 10^9/L$. A repeat bone marrow aspiration showed 90% blasts which were negative for sudan black and myeloperoxidase. Immunophenotype revealed that these blasts were positive for CD19, 20 and 22 and negative for T cell and myeloid markers. A final diagnosis of MDS-RAEB with transformation to B cell ALL was made. Cerebrospinal fluid was negative for blast cells.

Child was started on modified UK MRC X protocol with vincristine, L-asparaginase, prednisolone and intra-thecal methotrexate. She responded well to the treatment and achieved complete remission in 4 weeks. She received

V. Gupta (✉) · B. Bhatia
Department of Pediatrics, Institute of Medical Sciences,
Banaras Hindu University, Varanasi 221005, India
e-mail: vineetaguptabhu@gmail.com

Table 1 Profile of patients of MDS transforming to ALL

S. no.	Age (Years)	Gender	MDS subtype	Time to progression (months)	Phenotype	Cytogenetics	Outcome
1	68	M	RARS	31	B cell	+8	Expired
2	9	M	RA	21	B cell	NA	Lost
3	68	F	RAEB	5	B cell	−3, 5q	Expired
4	54	M	RA	30	B cell	Ph, 20q-	Expired
5	50	M	RA	4	B cell	Complex	CR
6	43	M	NA	NA	B cell	Complex	Expired
7	46	M	RAEB	2	B cell	NA	CR
8	70	M	RA	22	B cell	NA	NA
9	68	F	RA	2	B cell	NA	NA
10	65	M	RA	18	B cell	+13	PR
11	28	F	RA	11	B cell	Normal	Refractory
12	65–72	5 M 1 F	1 RA 2 RARS 3 RAEB	4–18	T cell (all 6)	Variable	2 Expired 4 CR
13	75	M	RAEB	18	T cell	Normal	NA
14	53	M	CMML	42	T cell	Normal	PR
15	53	M	RARS	50	Null cell	NA	CR
16	Elderly	M			NA	NA	NA
17	58	M	RA	20	NA	NA	Expired
18	50	F	RAEB	3	NA	Normal	Well (5 years)
19	67	M	RARS	24	NA	Aneuploidy	CR
20	20	M	RAEB	5	T cell	NA	CR (2 years)
Our case	5	M	RAEB	4	B cell	NA	CR (1.5 years)

CR complete remission, PR partial remission, NA not available, RA refractory anemia, RARS refractory anemia with ring sideroblasts, RAEB refractory anemia with excess blasts, CMML chronic myelomonocytic leukemia, MDS myelodysplastic syndrome, ALL acute lymphoblastic leukemia

early intensification with daunorubicin, cytosine arabinoside, etoposide and 6-thio guanine. Child is on maintenance therapy and has remained well for last one and a half years.

Discussion

Childhood MDS is relatively rare in comparison to MDS encountered in adults. It accounts for less than 5% of all hematopoietic neoplasms in patients less than 14 years of age [3]. A cut off value of 20% peripheral and/or medullary blasts has been used to separate MDS from acute leukemia [4, 5]. Unlike majority of cases with adult MDS who may remain asymptomatic for many years, most of the pediatric patients are symptomatic and have a more aggressive course, rapidly transforming to acute myeloid leukemia. However, evolution to acute lymphoblastic leukemia has been reported only occasionally in pediatric patients. 25 cases of MDS transforming to ALL have been reported in literature (Table 1) [6–8] of which only one patient was below 14 years of age. There was male predominance with

20 males and 5 females. The median time to transformation was 5 months (2–50 months). The different types of myelodysplasia were RA (39%), RAEB (35%), RARS (22%) and CMML (4%). Majority of the patients transformed to B-cell followed by T-cell and null cell. The cytogenetic work up where available and the treatment outcome has been presented in Table 1. There was only one patient in the pediatric age group (9 years) who presented with RA and transformed into B-cell ALL after 21 months. In our patient the initial presentation was RAEB which evolved to B-cell ALL in 4 months. The child responded well to chemotherapy and achieved complete remission. To our knowledge, this is the youngest reported case of MDS transforming into ALL. The case is being presented for its rarity.

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