JUVENILE MYELODYSPLASTIC SYNDROME IN A NIGERIAN CHILD-A CASE REPORT AND REVIEW OF LITERATURE

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Introduction and review of literature

Myelodysplastic (MDS) syndromes are a group of clonal disorders characterised by peripheral blood cytopaenias due to ineffective haemopoiesis and hypercellular bone marrows.[1, 2, 3] Juvenile MDS affects children under the age of 18years and may show disruption of normal marrow architecture. [1, 2] Transfusion dependence is a common feature of MDS. Although juvenile MDS is uncommon, globally, no precise prevalence data regarding MDS are available.[1] Statistics so far available show that MDS accounts for 1-1.5% of childhood malignancies in India. [1] A Turkish center reported 33 childhood MDS cases over a 12-year period.[1, 2, and 4] The precise cause of MDS is not known in the majority of patients. [2, 5] Risk factors include acquired aplastic anaemia, cytotoxic chemotherapy, radiotherapy, von Recklinghausen's disease, Bloom's syndrome, monosomy 7, trisomy 8, trisomy 9 and deletion of 5q. [4, 6, 7] At the molecular level, p53 gene mutations have complicated therapy with alkylating agents.[7, 8] Congenital myelodysplasia may be the haematological expression of a larger embryological anomaly.[1] Oncogenes like *K-ras* and *N-ras* have been activated in MDS.[10] Extramedullary features like proptosis, hepatosplenomegaly, gingival hypertrophy, thrombosis, pyoderma gangrenosum, pleural and pericardial effusion may dominate the presentation.[1, 3] Diagnosis is mainly by exclusion of other causes of cytopaenias like haematinic deficiency, chronic disease and glucose -6 dehydrogenase deficiency.[1,10] Bone marrow hypocellularity is found in 15-20% of cases of MDS. Pelger Huet neutrophils, hypogranular leucocyte progenitors, erythrocyte microcytosis and microcytosis are some morphological changes. [10] Thirty percent (30%) of patients

progress to acute myeloid leukaemia (AML).[9,10,11] Myelodysplastic (MDS) syndromes are classified into refractory anaemia (RA), refractory anaemia with ringed sideroblasts (RARS), refractory anaemia with excess of blasts (RAEB), chronic myelomonocytic leukaemia (CMML), and refractory anaemia with excess of blasts in transformation (RAEB-t), in accordance with the French American British (FAB) classification.[2, 9,10,11] Judicious blood component and anti-infective therapy are the mainstay of treatment to forestall iron overload, alloimmunization, and circulatory overload. Elimination of the abnormal clone and restoration of haemopoiesis remains the ultimate goal.[2, 5,7,10] This can be achieved by using combination of mitoxantrone, cytosine arabinoside and high dose methyl prednisolone (HDMP) with or without haemopoietic growth factors.[1, 4,5,7] Stem cell transplantation has been tried with variable outcome. Juvenile MDS runs a short and aggressive course.[1, 2, and 4]

Clinical Summary

ST is a 7year old boy well nourished whose parents are college teachers. He presented with a 3-week history of gingival haemorrhage. He was in heart failure but lymph nodes were not enlarged. Abdominal organs were not enlarged. He was previously treated for a febrile illness with chloroquine and chloramphenicol. His haematocrit was 18%, with a platelet count of 98 X 10^9 /L, a leucocyte count of 5.2X10^9 /L, and a retic count of less than 0.001%. The bone marrow aspirate was hypocellular. Erythropoiesis and Megakaryocytopoiesis were markedly reduced and dysplastic, many possessing numerous small nuclei, while myelopoiesis was within normal limits. Sideroblasts were absent. A diagnosis of a hypocellular variant of myelodysplatic syndrome in a child was made. Other tests revealed no anomaly. Cytogenetic studies were not done. Cytosine arabinoside and high dose methyl prednisolone were prescribed with repeated transfusion of red cell and platelet concentrates. Only methyl prednisolone was available, after completing the course a repeat bone marrow aspirate in the sixth week after commencement of therapy showed hypocellularity with persistence of dysplastic features. Stem cell transplantation was considered but was limited by financial constraints. He was later lost to follow up.

Discussion

The patient presented with features of hypocellularity suggestive of aplastic anaemia

but for the dysplasia which indicates MDS.[1, 7,9-10] The patient belongs to the minority that presents with marrow hypocellularity.[1, 3, 5,7] The absence of Cytogenetic studies and other logistic difficulties hindered the precise diagnosis. This is the norm in resource constrained settings as obtained in the Indian study.[1] The cytological features are in keeping with refractory anaemia (RA). [2, 9, 10-11] Bilinear cytopaenia for which Red cell and platelet transfusion were indicated is in keeping with the presentation of MDS in all ages. While Methylprednisolone alone has been successfully used with aplastic anaemia, it is inadequate in the management in the treatment of MDS, thus the need for additional agents. Socio economic factors like ignorance and poverty that determine the natural history and long-term outcome of managing such patients contributed to the default from therapy observed in the patient. The patient's age suggests a probable embryological anomaly that would have been amenable to stem cell transplantation. [1,2,6,7]

Conclusion:

Myelodysplastic syndrome can occur as a congenital lesion. We are advocating the establishment of stem cell transplantation for this and other by stem cell disorders in our centres.

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12.