

CASE REPORT

Myelodysplastic syndrome with erythroid hypoplasia

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J Clin Pathol 2005;58:320–321. doi: 10.1136/jcp.2004.020974

The incidence of myelodysplastic syndrome (MDS) with erythroid hypoplasia/aplasia is probably underestimated because in most patients it is mistaken for acquired pure red blood cell aplasia. This report describes three children who fulfilled the criteria for MDS with erythroid hypoplasia/aplasia. All these patients had transfusion dependent anaemia, reticulocytopenia, erythroid hypoplasia/aplasia, severe dysgranulopoiesis, and dysmegakaryopoiesis.

Red cell aplasia is a rare disorder characterised by a profound reduction in erythroblasts in the bone marrow. It can be a congenital disorder (Diamond-Blackfan syndrome) or can be acquired in association with an underlying disease. In the acquired group, the most common disease associations are with thymoma, viral infections, connective tissue diseases, and malignancy.¹ Occasional reports have documented the occurrence of erythroid hypoplasia/aplasia in patients with myelodysplastic syndrome (MDS).^{2,3} These patients present with severe anaemia, reticulocytopenia, and a paucity of recognisable erythroid cells (2–5%) in the bone marrow, associated with some evidence of an intrinsic cell defect.^{4–6} In addition to erythroid hypoplasia, bilineage or trilineage dysplasia in a high percentage of cells (> 20%) is a crucial determinant for the recognition of this entity.⁴ The exact prevalence of erythroid hypoplasia in MDS is not known. In a series of 360 cases of MDS diagnosed in a single institute over a 10 year period, six (prevalence of 1.6%) were found to have MDS with erythroid hypoplasia/aplasia.⁷ In a review of the literature, Garcia-Suarez *et al* came across only 16 well documented cases of MDS with erythroid hypoplasia/aplasia, including their one case.⁸ In that review, there was a male predominance (male to female ratio of 3 : 1), with a mean age of 70 years (range, 41–87). There were no paediatric cases in their series.

CASE REPORT

Recently, we encountered three children (two girls and one boy) who fulfilled the criteria of MDS with erythroid hypoplasia/aplasia. These were seen between January 2000 and June 2004. During this period, a total of 13 paediatric MDS cases were reported in our institution. The age of the children who had MDS with erythroid hypoplasia/aplasia was 13 months, 5 years (boy), and 7.5 years. There was no organomegaly or lymphadenopathy. The haemoglobin concentrations in these cases were 96, 68, and 43 gm/litre, respectively. The total leucocyte counts were 8.7, 7.9, and 7.8×10^9 /litre, respectively. The platelet count was normal to high (5.06, 4.66, and 5.7×10^9 /litre, respectively). These patients had received transfusion in the past (eight units, five units, and one unit, respectively). The bone marrow was mildly hypercellular in two cases (the first and the third cases). The myeloid to erythroid ratio ranged from 60 : 1 to 100 : 1. There was > 20% dysgranulopoiesis and dysmegakaryopoiesis. The blast counts were 9%, 7%, and 4%,

respectively. The first two cases were therefore labelled as refractory anaemia (RA) with an excess of blasts, and the third case was categorised as refractory anaemia. The second patient had mild hypocellularity but had severe erythroid hypoplasia (myeloid to erythroid ratio of 90 : 1), dysmegakaryopoiesis, dysgranulopoiesis, and 7% blast in the bone marrow. The results of cytogenetic analysis were available only for the third case, and no abnormalities were seen. Such an analysis was attempted in the other two cases but no metaphase spreads could be produced. There was no evidence of other acquired aetiological factors in these patients.

DISCUSSION

In the review by Garcia-Suarez *et al*, all 16 cases had bone marrow dysplasia in at least two of the haemopoietic cell lineages to allow the morphological diagnosis of MDS. FAB subtypes were RA in nine patients, chronic myelomonocytic leukaemia in four, RA with an excess of blasts in two, and RA with ring sideroblasts in one patient. The incidence of MDS with erythroid hypoplasia/aplasia is probably underestimated because in most patients it is misdiagnosed as acquired pure red cell aplasia.⁸ In general, the bone marrow pathology is strikingly limited to the erythroid cell lines in acquired pure red cell aplasia. The presence of bone marrow hypercellularity with a left shift of the granulocytic series, in addition to the presence of hypogranular myelocytes, mononuclear megakaryocytes, collections of monocytoid blasts, and ring sideroblasts in the iron stain should direct the diagnosis away from that of acquired pure red cell aplasia.⁵

A paucity of erythroid precursors in MDS is also seen in 5q-syndrome, which is usually characterised by refractory macrocytic anaemia, a normal to increased platelet count, and increased numbers of megakaryocytes, many of which have hypolobated nuclei. It usually occurs in elderly women although it has also rarely been described in children.⁹ In a series of 43 cases of 5q-syndrome by Mathew *et al*, the median age was 68 years and the age range was 29–86 years.¹⁰ The cytogenetic result was available in only one of our cases, but the very young age of our patients and the presence of severe dysgranulopoiesis and dysmegakaryopoiesis (in addition to nuclear hypolobation) make 5q-syndrome unlikely, although it cannot be ruled out because of a lack of cytogenetic results in two of our cases.

The mechanism of erythroid hypoplasia in MDS is unknown. It presumably has an autoimmune aetiology or is the result of an intrinsic defect of maturation and proliferation of erythroid precursors as a part of the MDS.⁷ No effective treatment has yet been reported, and most patients require repeated transfusions, with a subsequent increased risk for developing haemosiderosis.⁸ In contrast to primary acquired red cell aplasia, steroids are not helpful because of the intrinsic stem cell defect. Treatment with cytotoxic or differentiation inducing agents in the series of 16 patients was not effective.⁸ Immunosuppressive agents such as

Abbreviations: MDS, myelodysplastic syndrome; RA, refractory anaemia

Take home messages

- We report three children who fulfilled the criteria for myelodysplastic syndrome (MDS) with erythroid hypoplasia/aplasia, all of whom had transfusion dependent anaemia, reticulocytopenia, erythroid hypoplasia/aplasia, severe dysgranulopoiesis, and dysmegakaryopoiesis
- The incidence of MDS with erythroid hypoplasia/aplasia is probably underestimated because in most patients it is mistaken for acquired pure red blood cell aplasia

antithymocyte globulin can be tried. In a study by Molldrem *et al*, one third of the patients with MDS achieved sustained independence from red blood cell transfusion.¹¹ The mechanism underlying the response to antithymocyte globulin is not clear. The suppressive activity of autologous T cells that can suppress granulocyte and erythroid marrow cell progenitors is lost after antithymocyte globulin treatment.¹²

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Accepted for publication 15 September 2004

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