RESPONSE OF A CASE OF MYELODYSPLATIC SYNDROME WITH PARTIAL MYELOPEROXIDASE DEFICIENCY TO CONTINUOUS INFUSION OF LOW-DOSE CYTOSINE ARABINOSIDE

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SYNOPSIS

A 33 year old Malay man suffered from myelodysplastic syndrome with partial myeloperoxidase deficiency was treated with continuous infusion of low-dose cytosine arabinoside. He responded to the treatment and remained well without further blood transfusion and admission to the hospital for 14 months. The mechanisms underlying the response and the associated myeloperoxidase deficiency were discussed.

INTRODUCTION

Myelodysplastic syndrome denotes a group of acquired disorders characterised by abnormal and ineffective haemopoiesis. The FAB cooperative group (1) has recently proposed to classify them into various subtypes. It is a group of preleukemic disorders but many patients die of complications before acute myeloid leukemia develops. Treatment has been largely unsuccessful and no standard regime exists. Wisch et al (2) has reported usefulness of low-dose continuous infusion of cytosine arabinoside in the treatment of this condition. We report our experience with a case associated with myeloperoxidase deficiency.

CASE REPORT

A 33 year old Malay man was admitted to the Kuala Lumpur General Hospital because of pallor. Ten days prior to admission, while he was drinking cold sugar cane water by a roadside hawker stall, he suddenly had loss of consciousness. It lasted for a short while. No abnormal movements or frothing of the mouth was noted. He recovered with no sequelae. Later, his colleagues told him that he looked very pale. He then went to see a medical specialist who did a blood count for him. His haemoglobin was 6.4 g/dl. He was advised admission to the hospital.

On admission, it was revealed that he had bronchial asthma, so had his father. He was allergic to Brufen, Lomotil, Atropin, Baralgin and Aspirin. Physical examination showed marked pallor and mild jaundice. Others were within normal limits. Full blood picture revealed leucoerythroblastic anemia with macrocytosis, hypogranular neutrophils and thrombocytopenia. Bone marrow was hyperplastic with megaloblastic erythroblasts, atypical megakaryocytes, 15% myeloblasts and increased iron store. Cytochemical study showed that the neutrophilic series were partially deficient in myeloperoxidase. Unconjugated serum bilirubin, SGOT, serum uric acid, serum folate and serum B12 were mildly raised. Other investigations which included urinary examination, stool for occult blood, blood malarial parasites, liver, bone and renal profiles, Coomb's test, LE cells, antinuclear factor, HbsAg, TORCHES screen, serum immunoglobulins and protein electrophoresis, and chest X-ray were within normal limits. He was diagnosed to have myelodysplastic syndrome and consented to receive a trial of low dose cytosine arabinoside infusion, 10 mg/m2/day for 21 days. He responded to the treatment as shown in the progress chart and was discharged from the hospital completely well. However, a repeat bone marrow aspirate before discharge revealed no change in the bone marrow morphology and hypogranular neutrophils were still seen in the peripheral blood even though the cell counts had reached normal levels. He was followed-up monthly for the last 14 months without further blood transfusion and admission to the hospital.

DISCUSSION

The mechanism by which low-dose cytosine arabinoside induces partial or complete remissions in patients with myelodysplastic syndrome remains unclear. This drug may act as a myelosuppressive agent which suppresses leukemic clones and allows suppressed normal haematopoietic clones with greater potential for maturation to emerge. On the other hand, the drug may have induced differentiation of the leukemic clones. Cytosine arabinoside has been shown to induce differentiation in mouse leukemic myeloblast (3). Besides, human HL-60 promyelocytic leukemic cells have also be induced by the drug to differentiate into monocyte-like cells (4). Improvement in the peripheral cell counts without normalisation of cell morphology and bone morrow blasts count tend to support the induction theory. Although we used the intravenous route for administration of low-dose cytosine arabinoside, Inbal et al (5) had reported success with low-dose subcutaneous injection of cytosine arabinoside. This has obvious advantages because patients can be treated on an outpatient basis.

It is well recognised that myeloperoxidase deficiency of a variable degree are found in neutrophilic leucocytes of patients with preleukemic or leukemic states. Electron microscopy study did not suggest any deficiency in the number of granule. Cytochemical electron microscopy study showed azurophilic granules devoid of myeloperoxidase activity (6). The nature of this enzyme deficiency is unclear. Excess iron store is associated with myelodysplastic syndrome. The toxic effect of iron on myeloperoxidase was described by Schultz (7) in 1959. This may be the mechanism underlying the enzyme deficiency in the neutrophilic leucocytes.

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ACKNOWLEDGEMENT

The Singapore Medical Journal Editorial Board would like to thank the following who have assisted in reviewing and writing editorials for the articles published in 1987:

Dr Jimmy Sng

Dr Woo Keng Thye

Dr Mavis Yeo