HEREDITARY METHAEMOGLOBINAEMIA DUE TO CYTOCHROME b-5 REDUCTASE DEFICIENCY - A CASE REPORT

U.K. SAHA*, I. CHAKRABORTY**, S. GHOSH*, P. BANERJEE* and A.K. CHAKRABARTI***

Departments of *Paediatric Medicine and **Biochemistry, P.G. Kar Medical College, 1 Belgachia Road, Calcutta 700 004 and ***Dept. of Pathology (Haematology Section) Calcutta National Medical College, Calcutta 700 017.

Hereditary methaemoglobinaemia is a very rare condition. It is either due to Haemoglobin-M disease or Cytochrome-b-5-reductase deficiency (1).

A 10 year old boy presented with bluish discolouration of lips, oral mucous membrane, palms, soles and nails noticed since first month after birth. There was no symptom. He is the 2nd of 3 siblings, with no consanguinity among parents. None in the family had similar disease. He was born at full term at home with an uneventful neonatal period and a normal growth and development. Examination revealed a central cyanosis without any clubbing and a mild pallor. Pulse respiration and blood pressure were normal. Clinically heart and lungs were normal. Other system examination showed no abnormality.

The venous blood of the child showed a chocolate brown colour which did not change to red on shaking in air for 15 minutes. Haemoglobin was 10.7 gm%, reticulocyte count 13% with a normal total and differential count of leucocytes. Chest X-ray, E.C.G. and echocardiography (including colour doppler) failed to detect any abnormality.

Estimated methaemoglobin on admission was 24% (i.e. 2.57 gm%), Haemoglobin electrophoresis on cellulose acetate membrane at alkaline pH did not show any abnormal band. For detection of HbM a haemolysate of patient's blood (b in figure 1) had been subjected to cellulose acetate membrane electrophoresis at alkaline pH and compared with haemolysate of control blood (HbA-a in figure 1) and prepared methaemoglobin solution (HiA-c in figure 1). No difference in the electrophoretic mobility was observed between the control and the patient, but HiA moved more cathodally. This con-

cludes no HbM was present in patient's blood (2). Absorption spectra of haemoglobin solution (figure 2) showed two large peaks at 400 nm and 540 nm like other haemoglobin but another small peak around 630nm at neutral pH (7.1) suggested methaemoglobin possibly due to enzyme deficiency and this characteristically differs from Hb-M (2).

Fig. 1 : Cellulose acetate electrophoresis at alkaline pH for the detection of HbM in hemolysate

Fig. 2 : Absorption spectrum of hemolysate

Address for correspondence:

Dr. I. Chakraborty, at above address.

Methaemoglobin is formed continuously within the RBCs and simultaneously reduced to haemoglobin - about 95% by cytochrome-b5-reductase and 5% by flavin reductase (3). When methaemoglobin level is 15% of total Hb there is central cyanosis. When it approaches 30%, symptoms relating to tissue hypoxia usually start. The tissue hypoxia is due to inability of methaemoglobin to carry oxygen and also lowered ability to release oxygen to tissue (3,4). The present case with methaemoglobin level of 24% was asymptomatic. The mild anaemia (Hb-10.7 gm%) might be nutritional and can not be explained by methaemoglobinaemia.

The child was treated with ascorbic acid with which the cyanosis gradually subsided and ultimately

disappeared within one month. The condition can also be treated with methylene blue or riboflavin which stimulate NADPH flavin reductase system where-as ascorbic acid directly reduces methaemoglobin (3). I.V. methylene blue acts more promptly (5), but was not available. The elimination of clinical cyanosis by ascorbic acid confirms the diagnosis of hereditary methaemoglobinaemia due to cytochrome-b5-reductase deficiency, as it remains unchanged in HbM disease.

However we decided not to put the child on prolonged therapy with ascorbic acid and to keep on close follow up because no treatment of methaemoglobinaemia is necessary when there is only cyanosis and no other symptom (1).

REFERENCES

1. Bum, H.F. (1994) Methaemoglobinemia In: Harrison's Principles of Internal Medicine. Eds. Isselbacher, K.J., Braunwald, E., Eilson, J.D., Martin, J.B., Fauci, A.S. and Kasper, D.L., McGraw Hill Inc. New York p. 1740-1741.
2. Dacie, V.J. and Lewis, S.M. (1993) Detection of Haemoglobin M In: Practical Haematology, Churchill Livingstone, Edinburgh, p. 253-254.
3. Miller, D.R. (1995) Congenital and acquired methemoglobinemia, In: Blood diseases of Infancy and childhood. Eds. Miller, D.R. and Bachner R.L., Mosby, St. Louis, p. 365-370.
4. Tomoda, A., Imoto, M., Hirano, M. and Yoneyama, Y. (1979) Analysis of metform haemoglobins in normal erythrocytes of normal adults and of patients with hereditary methaemoglobinaemia due to deficiency of NADH-Cytochrome-b5-reductuase. *Biochem. J.* 181, p. 505-507.
5. Honig, G.R. (1996) Hemoglobin disorders. In: Nelson Text book of Pediatrics, Eds. Nelson, W.E. Behrman R.E., Kliegman, R.M. and Arvin, A.M., W.B. Saunder's Company, Philadelphia, p. 1401.