Brief Reports

Unstable Hemoglobin as a Cause of Congenital Hemolytic Anemia

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Unstable hemoglobinopathy though not common, is an important condition often overlooked when dealing with childhood hemolytic anemias. This is either due to its rarely or lack of awareness of the condition.

Since it was first documented by Cathie in 1952, over 90 such hemoglobin variants have been reported worldwide(l). The first case from India in an adult was documented in 1990 from Chandigarh(2). We now report 5 pediatric cases of unstable hemoglobin diagnosed between 1984 and 1992. The parents of 1 child also had the disease.

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Case Reports

In 1992 we encountered 2 cases of unstable hemoglobin. Retrospective analysis revealed 7 other cases since 1984. The clinical and laboratory data on these 5 cases and the parents of 1 of the children are given in *Table I.*

The first case diagnosed in 1984 was a female still born preterm (33 weeks gestation) with hydrops fetalis who died 15 minutes after birth. She was born of a consanguineous marriage after two abortions and one live child. There were 4 females and 3 males in the study. Four out of the 7 subjects were children less than 30 months of age at presentation and were acutely ill with fever and a history of being treated with several drugs prior to admission. Anemia, jaundice and hepatosplenomegaly were the common presenting symptoms. Dark colored urine was also common to all children. Hemoglobin was below 6g/dl in all the 5 patients. Blood picture in all showed an anisocytosis, microcytosis, spherocytosis and presence of nucleated red blood cells. G6PD level done in 3 of the patients was within normal limits. Coomb's test was negative in the 4 patients tested. Bone marrow examination done in 3 patients showed erythroid hyperplasia with normal white blood cells and megakaryocytes.

TABLE I–*Clinical and Hematological Profile of Unstable Hemoglobinopathy.*

Case No.	Age at onset years	M/F	Precipitating Factor	Jaundice	Hepato-spleno-megaly	Hb (g/dl)	Retic (%)	Heinz body (%)
1.	0*	F	–	–	+	ND	ND	ND
2.	16/12	F	Measles	+	+	4.1	16.5	80
3.	30/12	F	Infection Gentamicin Griseofulvin	+	+	5	18	65
4.	9	M	Infection	+	+	4	1	78
5.	1/12	M	Pneumonia	+	+	6.2	3.3	98
6.**	28	M	Nil			ND	ND	15
7.**	24	F	Nil			ND	ND	54

M-Male, F-Female, ND-Not done.
Heinz body controls <40% is normal.
* Died 15 minutes after birth with hydrops fetalis.
** Adults, parents of case No. 5.
Heat instability test was positive while electrophoresis was normal.

Heat instability test for unstable hemoglobin was positive in all the 7 patients. Hemoglobin electrophoresis was normal in all the 7 patients tested. Urine tested in the first patient had shown numerous red blood cells while in 3 others urine hemoglobin was positive.

Discussion

Unstable hemoglobins are due to a substitution or deletion of the normal aminoacids in the globin chains, 75% being in the beta globin chain. This leads to instability in the hemoglobin molecule and membrane lipids. Increased oxidant stress as in fever, infections or certain drugs may lead to increased hemolysis and pigmenturia(3). Inheritance is autosomal dominant but in many, the parents are normal suggesting spontaneous mutation. In our cases, 2 of the 5 children were born of consanguineous marriage.

The clinical presentation can vary from asymptomatic to mild anemia to severe hemolysis resulting in anemia, jaundice, splenomegaly and pigmenturia(3). In our study, the parents of 1 child (case nos. 6 & 7) were asymptomatic. All the children showed a varying degree of severity of illness ranging from hydrops fetalis in a preterm to a 9 year old who was asymptomatic till presentation. Three children presented before the age of 3 years. Two of the 5 children were from Tamil Nadu while the remaining 3 hailed from the States of Orissa, Assam and Karnataka. An acute febrile illness precipitated hemolysis and hemoglobinuria severe enough to merit transfusion in 4 children.

Although unstable hemoglobins have been reported due to substitutions in the hemoglobin F gamma chains, these are usually of short duration as the hemoglobin changes from fetal to adult by 3 to 6 months of age(4). Our case of hydrops

fetalis had no evidence of immune hemolysis or alpha thalassaemia or congenital infections at autopsy. The heat instability test was positive. Hence we assume this child had unstable hemoglobinopathy.

Diagnosis of this condition requires a positive result in one of the tests to demonstrate unstable hemoglobin(5). We find the heat instability test to be simple and reliable. Hemoglobin electrophoresis is not a useful diagnostic test as it rarely gives an abnormal band. None of our cases showed an abnormal band.

This condition should be suspected in any child who presents with acute onset of severe anemia and brown colored urine following fever and drug ingestion. This clinical presentation could be due to malaria, G6PD deficiency, or unstable hemoglobinopathy. The heat instability. test is simple and diagnostic of the last condition

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