Congenital Non-Spherocytic Hemolytic Anemia (CNSHA) Due to Pyrimidine 5'Nucleotidase Deficiency

Congenital non-spherocytic hemolytic anemia (CNSHA) is a rare spectrum of autosomal recessive disorders due to deficiency of enzymes of glycolysis and RBC nucleotide metabolism. We report a family of three male members with CNSHA due to deficiency of pyrimidine 5'nucleotidase (P-5'-N).

Two boys, 12- and 9-year-old siblings, born out of non-consanguineous marriage presented with mild non-progressive jaundice and mild pallor. There were no bleeding manifestations or cholestasis. There was no history of blood transfusion or medications. KF ring was absent. On examination, growth and development were in the normal range with splenohepatomegaly.

Their investigation results were similar on repeated testing. Hb was 10 g/dL, WBCs and platelets were normal. Reticulocyte count was between 5 and 10 percent. Peripheral smear showed hemolytic picture with moderate anisocytosis, hypochromia, microcytosis and basophilic stippling with a few polychromatophilic cells and normoblasts. Spherocytes and Heinz body were absent.

Serum bilirubin was in the range 2 to 5 mg/dL. Osmotic fragility showed mild increase in fragility (Test 0.5-0.28: Control 0.44-0.34). Hb electrophoresis was normal. HbF was <2%, G6PD enzyme level was normal. Direct Coomb's test and sickling test were negative. HBSAg and HCV and ANA were negative. USG abdomen showed splenohepatomegaly.

The pedigree showed that the mother's uncle also had similar illness and laboratory findings. He was investigated 15 years ago at 28 years of age and is doing well. Both the parents were clinically and hematologically normal. No one was affected on the paternal side.

A diagnosis of CNSHA was made. Polychromatophilia and basophilic stippling occur in lead intoxication and P-5'-N deficiency. Serum and urine lead levels were not increased. An autohemolysis test showed increased hemolysis corrected by glucose confirming defect inherent to RBCs. This clinched the diagnosis of P-5'-N deficiency in the absence of lead poisoning. Enzyme estimation was not done due to the nonavailability of the test.

CNSHA due to altered erythrocyte metabolism are characterized by the absence of spherocytes and inclusion bodies, positive autohemolysis test and autosomal recessive inheritanc(1). Hemoglobin structure, heat stability and synthesis will be normal. Acid hemolysis and immune hemolytic studies will be normal. Among deficiency of pyruvate kinase and enzymes of glycolysis and erythrocyte nucleotide metabolism, basophilic stippling is seen in P-5'-N deficiency.

P-5'-N deficiency is an autosomal recessive hemolytic anemia of moderate severity(2). Heterozygotes have no clinical manifestation, but exhibit 50% reduction in enzyme activity. Since this enzyme is present in brain, severe deficiency can lead to mental retardation. Reticulocyte maturation requires disposition of intra erythrocytic RNA, which is no longer, needed for protein synthesis. Pyrimidine nucleotides formed by the action of ribonucleases on the ribosomal RNA is hydrolyzed by P-5'-N enzyme. In its deficiency, substrates accumulate inside the cell leading to

hemolysis(3-5). Magnetic resonance imaging or UV spectroscopy for cellular extracts and enzyme assay are confirmatory. No specific treatment is available.

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Polio Declining but AFP on the Rise

The number of polio cases in the country has shown a decline but there has been a sharp rise in AFP (Acute Flaccid Paralysis) cases as is evident from non polio AFP rates (*Table 1*) (1). A sensitive surveillance system detects a rate of 1 per 1 lakh children less than 15 years old. Non polio AFP rate in India has exceeded 5 while that in Bihar and UP have touched figures of 10.9 and 11.2 respectively(1). Values exceeding one need introspection and careful evaluation.

Prodromal infections or vaccines in several reports have been found to be temporally followed by a new onset of autoimmune diseases. This has been accepted for diphtheria and tetanus toxoid, polio and measles vaccines and GBS (Guillain Barre Syndrome)(2).

Several studies have been conducted on GBS or its relation with nation wide oral polio vaccination. Results have demonstrated a temporal association between polio virus infection caused by either wild virus or live attenuated vaccine, and an episode of increased occurrence of GBS. However,

TABLE I–*Trend of Non-polio AFP Rate in India.*

Year	Non-polio AFP rate (per 1 lakh children < 15 years)
2001	1.88
2002	1.87
2003	1.97
2004	3.11
2005	5.06