CORRESPONDENCE

Congenital Haptoglobin Deficiency

To the Editor:

Haptoglobin is a dimeric glycoprotein comprising two β chains that bind to hemoglobin α dimers and two α chains.1,2 In patients with active hemolysis, the hemoglobin escaping into the plasma is bound to the free haptoglobin and the haptoglobin-hemoglobin complex is cleared from the plasma with a T1/2 of 10 to 30 minutes.3 Free haptoglobin, in contrast to the haptoglobin-hemoglobin complex, has a T1/2 of 5 days; hence, the depleted plasma levels in patients with active hemolysis and the clinical practice of measurement of plasma haptoglobin as a marker for hemolysis.4

This report describes two families with congenital deficiency of haptoglobin—an entity that has received little recognition in the hematology literature.

Report of Cases. A 47-year-old woman (Anglo-Saxon) presented in December 1990 with severe anemia and was found to have autoimmune hemolysis due to anti-e antibodies. Despite successful treatment with corticosteroids (normalization of hemoglobin and reticulocyte count and a negative antiglobulin test), her haptoglobin (measured by rate nephelometry [Beckman Instruments Inc]) remained very low, at less than 0.4 g/L (normal range, 1 to 3.8), for more than four years. The isolated nature of this abnormality prompted me to proceed with family studies. The family studies showed similar low haptoglobin levels in one of her brothers 51 years of age and her daughter 31 years of age; both were clinically well. Three other family members (a brother 55 years of age and 2 sons 28 and 20 years of age, respectively) had normal levels.

A 15-year-old (Greek) girl with Gilbert’s syndrome (mild, hereditary glucuronyl transferase deficiency) was found to have very low serum haptoglobin level at less than 0.4 g/L (normal range, 1 to 3.8) without any other clinical or laboratory evidence of hemolysis. Family studies showed a similar low haptoglobin level in her brother 6 years of age, but the levels were normal in both parents and in her 17-year-old sister.

Reports of congenital deficiency of haptoglobin are rare.5,6 Two of these reports5,6 have highlighted the association with familial epilepsy, with the latter being attributed to encephalic inflammation secondary to oxidation of brain lipids by the free interstitial hemoglobin. One report7 has documented a high incidence of haptoglobin deficiency amongst patients with respiratory allergies; this association was attributed to an increased prostaglandin synthesis resulting from the haptoglobin deficiency, with haptoglobin being a prostaglandin synthesis inhibitor. The haptoglobin-deficient subjects described in the present report did not manifest either of these associations.

Haptoglobin is genetically determined by two autosomal codominant allelic genes, Hp 1 and Hp 2, with three possible phenotypes Hp 1-1, Hp 2-1, and Hp 2-2.5,6 The low levels of haptoglobin in three members from two generations in the first family suggests an autosomal dominant type of inheritance, but the negative/normal results in the parents of the second family do not support this. It is interesting to note the coexistence of Gilbert’s disease—a congenital deficiency state of uncertain inheritance pattern—in the second family. Further studies are required to clarify the mode of inheritance and the incidence of congenital haptoglobin deficiency state.

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REFERENCES

Evidence That the RHDkn Deletion Genotype Does Not Exist

To the Editor:

The Rhesus (RH) blood group system, one of the most complex polymorphic systems in humans, encompasses at least 45 antigens. These antigens are carried by at least two red blood cell membrane proteins that are encoded by two homologous genes, RHD and RHCE.7 The RHD antigen is a mosaic structure of at least 37 epitopes. Rearrangements of the RHD gene with the RHCE gene or point mutations in the RHD gene result in the loss of one or more D epitopes. Individuals with partial D phenotypes can produce antibodies to the missing epitopes in response to transfusion with D-positive blood or by pregnancy with a D-positive fetus. Until now, the following partial D phenotypes have been described: Dα, Dβ, Dγ, Dαβ, Dασ, Dγσ, Dαγ, Dαβσ, Dαβγ, Dαβγσ, Dαβσγ, Dαβσγσ, Dαβσγαβ, Dαβσγαβσ, Dαβσγαβσγ, and Rha.2

Of the partial D phenotype, the partial D category that is most frequently leading to alloimmunization, two genotypes have been described: the conversion type and the deletion type. In the conversion type, exons 4, 5, and 6 of the RHD gene are replaced by RHCE equivalents occurring in individuals of the Dααee phenotype. Individuals of the Dααee phenotype were originally described as belonging to the deletion type in which exons 4, 5, and 6 of the RHD gene are lost. Recent evidence indicates that these two types can also be distinguished at the serologic level using anti-BARC serum8 or several monoclonal antibodies (IgG MoAbs NO1, SAL17-
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