A Haptoglobin Johnson Family with Non-hypohaptoglobinaemic Hp^J/Hp^2

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Haptoglobin 2-1 (Johnson), a rare phenotype of the haptoglobin serum groups, was described by Giblett (1959) in its heterozygous form. On starch gel electrophoresis it differed from the common Hp 2-1 phenotype, in two ways: its two fastest bands were doubled, and there was retardation of all the bands representing polymeric haptoglobin molecules in the starch gel electrophoresis. The cause of these differences is likely to be seen in the modification of Hp^2 allele, representing a triplication formed by unequal homologous crossing over in a homozygote Hp^2/Hp^2 during displaced synapsis. This was suggested by Smithies, Connell, and Dixon (1962) because of the presence of normal hp 1S α and slower migrating hp 2J α polypeptide chains. Parker and Bearn (1963) regard the Hp 2-1 (Johnson) phenotype as a product of three independent alleles producing Hp units with different charges. Ramot, Kende, and Arnon (1962) described a Kurdish pedigree, in which Hp 2-1 (Johnson) and Hp 2-1 mating produced children: Hp 1-1, Hp 2-1, Hp 2-1 (Johnson), and three children with severe hypohaptoglobinaemia, the latter being presumably products of genotypes

Hp^J/Hp^2 , according to the genotypes Hp^1/Hp^2 and Hp^2/Hp^2 of the two children of one of them.

As the phenotypical pattern of this genotype has not yet been observed with a sufficiently high level of haptoglobin, the starch gel electrophoretic patterns seen in two such affected members of a Moravian family may be of interest.

Present Investigation

In the course of routine forensic starch gel electrophoretic examinations, a Hp 2-1 (Johnson) child was found (IV.1 in Fig. 1) with an apparently ahaptoglobinaemic father, whose paternity could not be excluded by further examination of blood groups, including the ABO and MNS systems, and the Rh genotype in the Cc,Dd,Ee groups, and of the serum groups Gm(1), Gm(2), and Inv(1).

Horizontal starch gel electrophoresis of sera in the father's family revealed other rare phenotypes (Fig. 2). Their supposed genotypes are summed up in Fig. 1. The quantitative analysis of the apparently ahaptoglobinaemic sera I.1, II.4, III.6 according to a modified electrophoretic method of Javid and Horowitz (Wiedermann and Pintera, 1967) showed the haemoglobin binding capacity to be 40,43,43 mg./100 ml., respectively. After two- to threefold concentration by means of Sephadex G 50 a starch gel electrophoresis pattern was

FIG. 1. The pedigree of the haptoglobin Johnson family phenotypes. EX = expired, NT = not tested, 2-2 = Hp 2-2, 2-1 = Hp 2-1, J-1 = Hp 2-1 (Johnson), J-2 = Hp 2-2 (Johnson), O = apparently ahaptoglobinaemic.

FIG. 2. Haptoglobin patterns. Horizontal starch gel electrophoresis of the sera after an addition of haemoglobin. Poulik's (1957) discontinuous system of buffers was used, and the gel stained with benzidine. The numbers refer to the pedigree in Fig. 1.

noticed which was more definite, even without concentration, in the sera of II.7 and III.7. This pattern is described in Fig. 3 and designated Hp 2-2 (Johnson). The haemoglobin binding capacity in the sera of II.7 and III.7 was found to be 72 and 62 mg./100 ml., respectively.

In serum of III.8, designated Hp 2-2 in Fig. 1, the 4th and further polymeric bands were absent (Fig. 2), the pattern resembling thus the modification seen in the rare phenotype Hp 2-1 (mod.) described by Connell and Smithies (1959). A similar, but not such pronounced shortage of the pattern was observed in the Hp 2-1 sera of III.17 and III.19.

Discussion

The Hp 2-2 (Johnson) phenotype is similar to the patterns observed by Ramot *et al.* (1962) after concentration of the hypohaptoglobinaemic sera, and their conclusion that the respective genotype is Hp^J/Hp^2 fully agrees with the pedigree described in Fig. 1. It is clear, however, on the basis of our observations that this phenotype may be found even in routine starch gel electrophoresis of unconcentrated sera. The designation Hp 2-2 (Johnson) was used in analogy with the term Hp 2-1 (Johnson),

even though the existence of an independent allele Hp^J would be better expressed by terms Hp J-2 and Hp J-1, respectively.

In the haptoglobin molecules of the Hp 2-2 (Johnson) phenotype a different activity of haptoglobin was observed, described in another communication (Pintera, 1969), which may explain the slight difference between the haemoglobin binding capacity regarded as hypohaptoglobinaemia in this communication and the haptoglobin level determined by means of a different method, and regarded as hypohaptoglobinaemia by other authors (Murray, Robinson, and Visnich, 1966).

The single reproducible observation of the phenotype III.8, the pattern of which could be tentatively described as Hp 2-2 (mod.), remains unexplained.

Summary

The phenotypical starch gel electrophoretic pattern, representing the haptoglobin genotype Hp^J/Hp^2 , is described. Its characteristic feature is a slow migration rate of the complex of the main haptoglobin component with haemoglobin, which is localized nearer the start than the slowest component of Hp 2-2 phenotype. Recognition during

FIG. 3. Diagram of some haptoglobin phenotypes. The patterns of the Hp 2-1, Hp 2-2, and Hp 2-1 (Johnson) phenotypes are designed according to Parker and Bearn (1963).

routine starch gel electrophoretic analysis was due to a rare coincidence of this phenotype with a sufficiently high serum haptoglobin concentration. As sera with this genotype usually are hypohaptoglobinaemic, they may well be mistaken for ahaptoglobinaemic phenotypes.

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