Study of a form of pulverulent cataract in a large kindred

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SUMMARY A large kindred (64 members in four generations), affected by a form of apparently congenital pulverulent cataract, was studied for linkage of its gene locus with that of the Fy blood group. No indication of linkage was found. The involvement of the cortex distinguishes this form from the zonular pulverulent cataract (total nuclear) of Nettleship and Ogilvie,¹ the locus of which is probably linked with Fy. A correlation between morphological and genetic heterogeneity, based on the linkage with Fy, cannot be established because of the scarcity of published data.

Various forms of congenital pulverulent cataract have been described. The form, named by Nettleship and Ogilvie¹ as 'congenital pulverulent zonular cataract', had opacities limited to the nucleus and was non-progressive. Renwick and Lawler,² re-investigating the family of Nettleship and Ogilvie, found a probability of about 98% that the locus was closely linked to the locus for the Duffy (Fy) blood group. Other forms of congenital pulverulent cataract have been described with a variable distribution of opacities. Clear linkage with Fy has not been confirmed in all the affected families.^{3,4} We have studied the possible linkage with Fy in a large kindred of 64 members affected by a form of congenital pulverulent cataract.

Clinical description

The subjective perception of impairment of ocular vision begins in the second decade of life, although opacities are detectable from infancy, allowing us to presume that the disease is congenital in the family. The disease is therefore probably progressive, at least during early childhood. All the adult subjects of our family have been operated on, so that a greater opacity in adults compared with children cannot be confirmed. The beginning of the vision disturbance and the age of detection depend upon a series of factors (educational attainments, socio-economic status, standard of medical care), which

make it hard to consider a late clinical onset as a reliable criterion for progression of the disease.

Slit-lamp microscopy (fig 1) in the affected members of the family showed diffuse fine opacities in both the nucleus and the cortex of the lens with the pattern of pulverulent cataract. Anterior subcapsular opacities were present in only one patient.

Fy antigen determination

The Fy phenotype was assigned by the indirect anti-human globulin method. The antisera anti-Fy(a) and anti-Fy(b), produced by Ortho Diagnostic (Raritan, New Jersey, USA), were used.

Three genotypes were considered: Fy^aFy^a (phenotype Fy(a)), Fy^bFy^b (phenotype Fy(b)), and Fy^aFy^b (phenotype Fy(ab)). The alleles non-a, non-b (Fy^c) are confined to and are common in Negroes.⁵ On the basis of 25 blood group screening programmes in continental Italy and Sardinia,⁶ this allele (Fy^c) would not be present in the Italian population and its presence in the Sicilian population would be a sporadic event.⁷

Linkage analysis

The method of Morton⁸ was adopted to calculate the lod score (z) for the informative matings in the pedigree. The analysis of the pedigree (fig 2) shows that only the following matings can be considered: the mating of III.4, this subject being a double heterozygote with both coupling and repulsion phases being possible (the two children IV.7 and IV.8 are

FIG 1 Slit lamp microscopy shows diffuse fine opacities in both the nucleus and the cortex of the lens.

both informative); the mating of III.8, this subject being a double heterozygote with obligatory coupling phase (only the children IV.14 and IV.15 are informative); and the mating of III.13, this subject being a double heterozygote with obligatory coupling phase (all the children are informative).

TABLE The lod scores progressively increase for $\theta \rightarrow 0.5$. This trend is in favour of independent assortment ($\theta = 0.5$) against close linkage.

θ	z
0	-0.00
0.05	-2.606
0.1	-1.57
0.15	-0.940
0.2	-0.572
0.25	-0.324
0.3	-0.157
0.35	-0.051
0.4	+0.008
0.45	+0.027
0.5	0

FIG 2 Family pedigree.

The scores for the various recombination fractions (θ) in steps of 0.05, between 0 and 0.5, and the corresponding antilog of z are reported in the table.⁹

Discussion

Recombinants were present in all the informative matings, that is, four out of the nine informative subjects. Statistical analysis confirms the low probability of linkage ($<1\%$).

Morphological heterogeneity as regards the cataract pattern is present in various families reported.³ The opacity in most members of the family of Nettleship and Ogilvie¹ was limited to the nucleus (total nuclear cataract), but the involvement of the nucleus, cortical fine opacities, and incomplete riders were present in some other families. Is this phenotypical variability accompanied by a corresponding genetic heterogeneity? A clear cut correlation between the morphology of cataract and linkage with Fy has not yet emerged from the sample of families reported.

Considering genetic heterogeneity with a very similar phenotype, one must be cautious when collecting different families for the calculation of linkage. To calculate the lod scores by adding the scores of different families is perhaps justified only for a group of families with the same ancestral origin.

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