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Summary: We report the results over 15 years (1977–1991) for biochemical diagnoses of patients referred from throughout Italy and suspected of having a mucopolysaccharidosis. Of these, 147 patients were diagnosed as being homozygous or hemizygous for a specific lysosomal enzyme deficiency; 74 pregnancies at risk were monitored in their families; 76 heterozygote diagnoses were performed on their relatives, with a total of 48 positive diagnoses.

We also report the analysis of genomic DNA from 11 unrelated Italian Hunter patients, using pc2S15 probe. DNA from two patients, digested with Pst-I, showed a variant pattern of hybridization caused by deletion or rearrangement of the gene.

The mucopolysaccharidoses (MPS) are a group of ten lysosomal storage diseases caused by a deficiency in one of the enzymes involved in the catabolism of mucopolysaccharides (the sulphated glycosaminoglycans dermatan sulphate, heparan sulphate, keratan sulphate and chondroitin sulphate) (for reviews see Neufeld and Muenzer 1989; Hopwood and Morris 1990).

Patients excrete elevated amounts of mucopolysaccharides in their urine and accumulate these polysaccharides in cells and tissues. Multiple clinical symptoms include facial dysmorphism, skeletal abnormalities, corneal opacities and organomegaly. Clinical variability is one of the characteristics of these diseases, each presenting mild, intermediate and severe forms. Clinical variability has also been reported within the same sibship (Andria et al 1979; Di Natale 1991).

With the exception of Scheie (MPS IS), Morquio (MPS IV) and Maroteaux–Lamy (MPS VI) syndromes, where normal intelligence is retained, the other mucopolysaccharidoses, i.e. Hurler syndrome (MPS IH), the severe form of Hunter syndrome (MPS II), and the four subtypes of Sanfilippo syndrome (MPS III), are all characterized by profound mental retardation.

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Clinical features common to mucopolysaccharidoses are shared by related disorders such as mucolipidoses and multiple sulphatase deficiency, also known as mucosulphatidosis or Austin disease (for reviews see Nolan and Sly 1989; Kolodny 1989).

Because of overlapping phenotypes, clinical diagnosis alone is often impossible. Therefore, an accurate enzymatic diagnosis should be established for all suspected cases of mucopolysaccharidoses (for reviews see Di Natale and Neufeld, 1979; Di Natale 1982).

Simple enzyme assays are available for the diagnosis of these diseases using fibroblasts, leukocytes or serum. Prenatal diagnosis following amniocentesis or chorionic villus biopsy is possible for all MPS (Pannone et al 1986c; Poenaru 1987). By contrast, identification of heterozygotes remains difficult because of overlap of normal and heterozygous levels of activity. Identification of carriers is of particular importance in Hunter syndrome, the only X-linked mucopolysaccharidosis. Several procedures have been proposed (Migeon et al 1977; Nwokoro and Neufeld 1979; Tonnesen et al 1983; Morabito et al 1989) but they remain cumbersome and sometimes the results are uninformative.

Accurate enzymatic diagnosis can be accompanied by molecular studies such as the cloning of complementary DNAs (cDNAs) (Hopwood and Morris 1990). Characterization of mutations showed deletions for MPS I, II and III D (Hopwood and Morris 1990) and point mutation for MPS VI (Wicker et al 1991). RFLPs were reported at Xq27-q28 (Suthers et al 1991), the region where the Hunter locus maps, thus allowing the potential for discrimination of carriers in families with informative polymorphisms.

The purpose of this article is to report our experience of biochemical diagnoses of mucopolysaccharidoses in a 15-year period (1977–1991) for cases referred from throughout Italy.

MATERIALS AND METHODS

Patients: Samples (usually fibroblasts, lymphocytes or sera) from patients suspected of having a mucopolysaccharidosis were referred to us from hospitals throughout Italy and occasionally from further afield (Belgium, Spain). A brief clinical summary accompanied each sample. Usually mucopolysacchariduria has been found but, if not, 10–20 ml urine is sent frozen without added preservative. A 10 ml sample of sterile, heparinized whole blood may also be sent for preparation of a lymphoblast line (Morabito et al 1989). Urine, sera, tissue, lymphocytes and chorionic villi were sent frozen in solid CO₂. Sterile heparinized blood or skin biopsies, skin fibroblasts, cultured villi and amniotic cells, were sent in tissue culture medium, in insulated containers. All samples reached our laboratory within 24 hours.

In the period 1977–1991 a total of 297 samples were sent to us. Of these, 133 diagnoses were requested from Gaslini Institute, Genova, the others being requested from several Italian Universities: 25 diagnoses from Catholic University, Rome; 28 cases from University of Ancona; 11 diagnoses from University of Catania; 8 diagnoses from Institute of Neurology 'Besta', Milan; 42 cases from University of Naples; 16 cases from University of Bologna; 22 cases from Policlinico Umberto I Rome; the other cases were from Universities of Pavia, Padova, Firenze, Siena, Bari, Messina.