CLINICAL AND NEUROPHYSIOLOGICAL CHANGES IN CARRIERS FROM A FAMILY WITH TYPE 0 CHRONIC GM2-GANGLIOSIDOSIS WITH ALS PHENOTYPE

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INTRODUCTION

The problem of minor clinical findings in carriers of dysmetabolic conditions has long been discussed and a correlation between low enzyme activity and nerve functions hypothesized\(^1,2\).

In 1986, two cases of chronic GM2-Gangliosidosis type 0, with motor neuron disease phenotype in which the main symptoms were slowly progressive ataxia, fasciculations, peripheral neuropathy, autonomic nervous system involvement, anxiety and depression, have been reported\(^3\). We extended the biochemical study to all possible family members, the majority of which were identified as carriers. Here we report the results of the clinical and neurophysiological investigations in the biochemically defined carriers.

METHODOLOGY and RESULTS

The family

Fig. 1 shows the pedigree of the family San... Al., from Piancastagnaio, Siena. Subjects IV,3 and IV,10 were affected by chronic GM2-Gangliosidosis type 0 with motor neuron disease like phenotype as previously reported\(^3\). III,1, the father of the two affected subjects, died at the age of 58. After the third decade, he had progressive difficulty in walking, ataxia and autonomic nervous system involvement suggesting that he could be either carrier with clinical signs (see IV,5; IV,15; IV,19; IV,21) or affected by the same disorder. The high frequency, between his sons, of subjects with Hex activity in carrier range, lead us to privilege the hypothesis that he was affected. III,9, his wife, is carrier of Hex A and B deficiency. All the offspring of a supposed affected subject and a carrier will either be or affected or carrier, suggesting a "pseudodominant" type of inheritance.

Abbreviations: Hex, hexosaminidase; ENG, electronystagmogram; EMG, electromyography; MNCV, motor nerve conduction velocity; SNCV, sensory nerve conduction velocity; MPA, motor potential amplitude; SPA, sensory potential amplitude; MUP, motor unit potential; PP, Polyphasic potentials.
Fig. 1. Pedigree of the family San...Al. □ walking abnormalities, dead at 58 years old age; ▼ patients; △ carriers; □ down syndrome; □ walking abnormalities; X examined

Biochemical study

Leucocyte lysosomal enzymes were determined fluorometrically with 4-methylumbellipheryl derivatives as substrate. Enzyme activity and thermolability of Hex were determined according to Galjaard with modifications. Cellogel electrophoresis of Hex isoenzymes was performed according to Brett. Protein measurement was according to Lowry.

Fig. 2 shows leucocyte Hex activity. IV,3 and IV,10, the two affected subjects, had 10% of the minimum control activity, while IV,19 and IV,2 showed a 30% of residual activity and all the carriers a 40-50% of control values.

Fig. 3 shows cellogel electrophoresis of Hex enzyme: Hex A and Hex were not detectable in the affected cases, whereas in carriers Hex A was low and only a faint spot was evident for Hex B.

Fig. 2. Leukocyte Hex activity (nmol/h/mg prot.). Numbers on the abscissa correspond to patients (for patients 1-14 see legend of Fig. 4; 15 = IV,19; 16 = III,9).