Gaucher Disease—Norrbottnian Type

I. General Clinical Description*

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Abstract. We report follow-up studies of 22 cases of the Norrbottian type of Gaucher disease ("type III"). The series was divided into 2 main groups of families depending on their birth province (Norrbotten, Västerbotten). The distribution and types of organ manifestations and complications were the same in both groups, each of which was considered to be genotypically homogeneous. The severity of the clinical symptoms and signs and the course of the disease differed markedly not only between families but also between siblings. Splenectomy accelerated deterioration, particularly with regard to skeletal and central nervous system manifestations. On a clinical basis it is concluded that the Norrbottian type of Gaucher disease, which has now been diagnosed in about 40 cases, is probably due to a unique mutation which may have happened several hundreds of years ago in northern Sweden.

Key words: Gaucher disease – Glucosylceramide – Cerebrosidosis.

Introduction

Gaucher disease was first described by Gaucher in 1882 as a type of cancer in adults. In 1934 Aghion established the fact that this disease is a storage disorder with accumulation of glucosylceramide. This substance is stored in the lysosomes of the reticuloendothelial cells, leading to secondary organ manifestations. The disease is inherited as an autosomal recessive. The primary genetic defect has been shown to be a decrease of the enzyme β-glucosidase (Brady et al., 1965; Patrick, 1965).

Patients with these metabolic abnormalities have been found to present different clinical manifestations. For this reason Knudsen and Kaplan (1962) and later Fredrickson and Sloan (1972) proposed a classification into three main types: Type I, the adult or non-neuropathic type; Type II, the infantile or acute neuropathic type; and Type III, the juvenile or subacute neuropathic type. The presence of a special Type III has been doubted, however, by several authors, including Fredrickson and Sloan (1972). The largest number of patients assigned to this type in the literature (Fredrickson and Sloan, 1972) are known to derive from the province of Norrbotten in northern Sweden (Hillborg, 1959; Hillborg and Svennerholm, 1960; Herrlin and Hillborg, 1962; Hillborg and Estborn, 1964, and Hillborg, 1978).

The aim of this paper is to give a clinical description of the Norrbottian type of Gaucher disease based on experience with 22 patients. Detailed information will follow in a series of papers in which investigations of specific organ manifestations will be reported separately.

Clinical Material

The group consists of 22 patients, 10 girls and 12 boys. There are 4 pairs of sibs, nos. 3 and 4, 5 and 6, 12 and 21, and 13 and 22 (Table 1). Patients 1–7 and 9 had been examined in the early 1960’s by Hillborg. Reports on patients 1–6 were published by Hillborg and co-workers (1959, 1960, 1962, 1964). Since 1969 all patients except no. 3 have been repeatedly studied by 2 of

the authors (S.D. and A.E.). The main clinical data of the 22 patients are summarized in Tables 1 and 2 and in Fig. 1.

The 22 patients can be divided into 2 main geographic groups: A. 10 patients from the province of Norrbotten; and B. 12 patients from the province of Västerbotten.

A. Norrbotten Cases. Hillborg (1978) showed that 10 of the present patients, and 6 older patients who are not included in this series, all have the same ancestor, born in 1951 in Överkalix, and his wife, and are thus probably genetically homogeneous. Överkalix is a rural district in the province of Norrbotten, the most northerly county of Sweden (Fig. 2).

B. Västerbotten Cases. The remaining 12 patients derive from the surroundings of the town of Skellefteå in the province of Västerbotten, only 60–80 km from the Norrbotten border; 9 of these were born within Norrbotten. There is genealogical evidence that the parents of all these patients on both sides derive from a very limited area. Three of the families are mutually related through 3 to 5 different lines in complex inbreeding patterns. In some families more than one common ancestor further complicates the picture. Ongoing genealogical studies (Hillborg, unpublished data) are expected to show with high probability that the Västerbotten patients are all related.

Genealogical connections between the Västerbotten patients and the patients from Överkalix are

Fig. 2. Map of Sweden showing the two places from which all patients in this study are derived, Överkalix and Skellefteå, in relation to Boden and Stockholm