An Experiment with the Transplantation of Human Fetal Tissues in Children with Down's Syndrome

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Institutionalized infants with Down's syndrome were treated by transplantation of human fetal tissue. In the control group without transplantation 3 out of 7 children died of various infections during the first 6 months. Immunological tests found a more pronounced tendency toward a rise of IgG and a drop of IgA and IgM in the control group, while there was only a slight tendency toward a drop of IgG and a rise of IgA and IgM in the group treated by transplantation of human fetal tissue. A more positive dynamics in the development of psychic functions was noted in children treated by transplantation as compared with the control group when the neurologic status was assessed, and 2 out of 6 children showed a tendency toward a decrease of the muscle hypotonia. This is a preliminary report.

Key Words: *transplantation of human fetal tissues; treatment of Down's syndrome*

Down's syndrome (DS) is the most common of the various forms of mental retardation. John Langdon Down, an English pediatrician, first discribed this disease in 1866 [1].

The etiology of the disease was the subject of discussion over a number of years, giving rise to various theories of its origin (endocrine, atavistic, and racial degeneration). The hypothesis of the chromosomal nature of DS was first voiced by Waardenburg in 1932 [3]. In Russia DS has been considered a congenital nonprogressive form of mental retardation. The chromosomal defect underlying the disease for a long time cast a cloud of fatalism in the handling and treatment of these patients. Nevertheless, during the last 30 years physicians have attempted to rethink the nature of DS, and this has led to therapy based on biological methods.

The presence of metabolic disorders in all cell membranes justifies considering DS from the standpoint of biological medicine. These disorders affect primarily the quickly-growing, metabolically active tissues (the brain, endocrine glands, cartilage, liver, and immunocytes). It is common knowledge that the fuctional state of the above organs and tissues determines the clinical state and prognosis of patients with DS first and foremost [2].

In recent years marked success has been achieved in the treatment of a number of serious diseases by the method of substitution therapy, namely the transplantation of a healthy organ in place of a nonfunctioning one. However, as a result of such operations the patients are doomed to dependence on immunosuppressive drugs for life. Some organs - the brain for example - cannot be transplanted, precluding this type of treatment for those most in need of it. In this situation the grafting of individual cells and tissues (whose functions in the recipient are impaired because of a certain disease), rather than of a whole organ, seems to be promising, in particular in DS.

MATERIALS AND METHODS

Two groups of children with DS confirmed by karyotyping (trisomy 21 in all patients) were under observation.

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The children of the first group (n=6) were treated by transplantation of human fetal tissues (THFT). The control group comprised 7 children with DS.

The patients of both groups were hospitalized in the psychoneurological department of Children's Clinical Hospital No. 13. The baseline therapy, including psychostimulators, vascular enzyme preparations, and vitamins, was identical for both groups.

THFT was performed in children of the first group between December 1992 and February 1993.

Fetal tissues of the human brain (hemispheres, cerebellum, and brain stem) were used for the transplantation.

Each tissue was administered deeply s.c. by individual injections.

According to the protocol the anthropometric (height, weight, and head circumference) and laboratory indexes (the total blood count, total urine analysis, biochemical assay of the blood, blood concentrations of IgA, IgG, and IgM) were determined and skull x-rays and ultrasound examination were performed. All children were examined by an ophthalmologist and a neurologist.

RESULTS

The comparison of the above parameters in children of the two groups before and 6 months after THFT did not reveal any statistically reliable differences. Nevertheless, it should be noted that:

1. Three of the 7 children of the control group died due to intercurrent infections, whereas all children treated by THFT remained alive (Table 1).

2. A marked tendency toward a rise of IgG and a drop of IgA and IgM was noted in the control group. The children treated by THFT showed a modest tendency toward a drop of IgG and a rise of IgA and IgM (Table 2).

The assessment of the neurological state found a marked positive dynamics in the development of psychic functions in children treated with THFT as compared to the control group, namely the level of psychic activity was higher, manifesting itself in interest in the surroundings, more pronounced development of imitative activity, and the appearance of elements of differential emotional reaction to personnel and unfamiliar people.

A tendency toward a decrease of muscle hypotonia was observed in 2 of the 6 treated children. Characteristics of motor development in patients treated with THFT did not differ significantly from those in the children of the control group.

Although a statistical reliability of differences in laboratory indexes is absent, the lowering of IgA (from 166 to 85 mg%) and IgM (from 140 to 74 mg%) concentrations may be considered as evidence of a deficiency of the immune system, resulting in frequent intercurrent disorders and the death of 3 out of 7 children in the control group. The marked rise of the IgG level (from 459 to 872 mg%) in children of the control group was probably also due to the frequent intercurrent infectious diseases.

TABLE 1. Age and Death-Rate in Children with DS

Group	Number of children	Age	Death-rate
1a	6	8.79±3.0 (1–20 m)	0
1b	6	15.8±3.61 (7–25 m)	0
2a	7	6.21±2.99 (1–21 m)	0
2b	4	13.5±3.9 (6–25 m)	3

TABLE 2. Serum Immunoglobulin Concentration (in mg%) in Children with DS

Group	Number of children	IgG	IgA	IgM
1a	6	551.4±75.7	68.0±11.2	101.86±10.9
1b	6	463.25±77.2	83.75±13.7	111.5±8.96
2a	7	459.29±106.9	166.4±95.6	140.1±24.9
2b	4	872.5±46.7	85.0±9.65	74.25±11.2

The impression is gained that THFT positively affects the state of the immune system. For example, a rise of IgA (from 68 to 83 mg%) and IgM (from 101 to 111 mg%) levels was noted in children of the treated group 6 months after treatment. The IgG concentration decreased (from 551 to 463 mg%), this being most likely related to the lowered frequency of infectious diseases.This report is of a preliminary nature, however.

All children of the first group have been treated again with THFT and the results of the comparative analysis will be presented later.

Our experience lends weight to the opinion prevailing among physicians and psychologists about the negative effect of maternal deprivation on the development of psychic functions in a child. Frequent intercurrent infections, which are an inevitable aspect of life in an institutional setting, also adversely affect the developmental indexes of children with DS.

REFERENCES

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