GH THERAPY IN TWO PATIENTS WITH OSTEOCHONDRODYSPLASIA

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Pharmacological therapy for short stunted children is feasible only for a very limited number of cases: when the short stature is due to a well-defined cause and when this cause is specifically correctable. Hypopituitarism and coeliac disease are typical examples of this situation; in fact, growth hormone and a gluten-free diet, respectively, may achieve spectacular results. Therefore, no specific therapy is available nowadays for the great majority of patients with growth retardation, including achondroplastic subjects. However, many attempts with aspecific drugs have been performed and some of these are criticizable both theoretically and also ethically. The basis of this therapeutical concept is the hope of finding a substance with no side effects, capable of improving the final adult height (1). In particular, androgens were very commonly employed in treatment (2,3). Today it is known that androgens can certainly increase growth rate, but that they cause at the same time an increase in bone maturation, so that the advantage is rendered null (4). As was mentioned in the beginning, GH therapy should only be used for those subjects who previously showed a specific deficiency; this diagnosis is supported by the association of short stature and a deficient GH response to the provocative tests. Nevertheless, today this is open to discussion, both for the difficulty in defining the normal GH secretion using the response of stimulation tests and for the good therapeutical results obtained in short stature normal variant children (5,6). Patients with osteochondrodysplasia have a normal GH secretion and normal levels of SmC (7,8,9). Following the previous criteria they should not undergo GH therapy. In fact, the achondroplastic children treated with growth hormone showed poor or even negative results (10,11).

In our paediatric department, among the subjects affected by different types of osteochondrodysplasia, only two fulfilled the suitable criteria for GH therapy. The first patient is a McKusick metaphyseal chondrodysplasia (12), while the second is an Ellis Van Creveld syndrome (12); both are male. The first was 5 years old and 90 cm. tall when he was referred to our clinic in 1974. In order to examine his growth hormone response, arginine and L-dopa tests were performed. We usually
consider those subjects whose GH response is less than 8 ng./ml. partially GH deficient. In this child the maximum GH level reached after two tests was 7.9 ng./ml. It is obvious that this response is very close to what we consider a normal threshold. However, given the severity of the statural handicap, we started GH therapy. Growth hormone was administered i.m. 3 times a week at a dose of 10 IU/m² per week; three therapeutical cycles lasting 3 months each were carried out, with intervals of three months without therapy in between. Two GH stimulation tests, performed two months after the end of the treatment, showed elevated GH levels throughout the test. We considered anti-GH antibodies to be the cause of these results; for this reason we withheld GH treatment. After two years two tests had normal GH response. Figure 1 shows the growth rate of this patient before, during and after therapy. During treatment there was an increase in growth rate, not sustained in the following months without therapy; in these months there was a near stand-still in his growth rate, but he caught up in the following years. It is hard to say whether this happened as a consequence of the endogenous anti-GH antibodies. Both the evaluation (Table I) of the GV SDS (13) for BA and CA (14) and the relationship between CA and BA increment indicate a true improvement in the growth rate. In retrospect, being now able to exactly evaluate the anti-GH antibodies titre, we probably would not interrupt treatment.

The second patient was 6 years old and 104.3 cm. tall when he was recently admitted to our department. The following GH stimulation tests were performed: Arginine, L-dopa, sleep test and GRF test. The first 2 pharmacological tests presented a GH response below 4 ng./ml. The sleep test (15), which may be considered as the most powerful physiological stimulus for growth hormone, showed a maximal response of only 6.8 ng./ml.