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CASE REPORT

Growth velocity increase in children with Turner syndrome treated with growth hormone following a brief therapy interruption

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ABSTRACT

Growth failure is a substantial feature of Turner syndrome (TS) and typically progresses from infancy to adulthood. Proper growth hormone (GH) treatment in TS is essential to increase growth velocity and improve the final height. The aim of the study was to perform a preliminary assessment of the influence of short interruptions in GH therapy on the growth process in children with TS. Growth velocities were analyzed in 5 patients with TS, treated long term with GH, who experienced short breaks in drug administration, followed by the re-introduction of treatment. The average growth velocity after the treatment interruption increased 2-fold compared to the continuous therapy and 1.3/1.5-fold compared to the period of initial GH therapy. The results suggest that the catch-up growth typical for the beginning of the GH therapy is not a single phenomenon and may recur in TS children in the case of re-introduction treatment after a short interruption.

KEY WORDS:

growth hormone, Turner syndrome, children, catch-up growth.

INTRODUCTION

Growth failure is a substantial feature of Turner syndrome (TS) and typically progresses from infancy to adulthood. The average height of untreated adult females varies between 143 and 146 cm depending on the population and is approximately 20 cm lower than in unaffected women [1, 2]. It is well known that early and proper treatment with growth hormone (GH) in children with TS is essential to increase growth velocity and improve their final height [1–5]. However, the response to this therapy is not as effective as it is observed in children with growth hormone deficiency (GHD) [4], due to the different pathophysiology of the two diseases. It has been found that short stature in TS is a consequence of haploinsufficiency of the SHOX gene [1, 2, 6]. As GH secretion seems to be normal, growth delay appears to be related to diminished tissue sensitivity to growth factors. Therefore, supraphysiological GH doses are used in the treatment of TS and have proven to accelerate growth [4, 7, 8]. The use of such high doses is believed to overcome the tissue resistance.

During the GH treatment in GHD children, usually at the beginning of the therapy, a catch-up growth phenomenon occurs, with growth velocity greater than appropriate for age and gender [9, 10]. It lasts for several months to a year. Similar observations were also made in patients with TS [11, 12].

In a previous study [13], it was found that in GHD children, re-introducing the treatment after the interruption during the GH therapy resulted in a significant increase in height velocity, even greater than during the primary catch-up growth at the very beginning of the therapy.

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TABLE I. Growth velocities of patients with Turner syndrome assessed during the initial growth hormone therapy implementation (GV0, after first 3 and 6 months), during continuous treatment (GV1), and after an interruption followed by the re-introduction of therapy (GV2)

Parameters	GV0 [cm/year]		GV1 [cm/year]	GV2 [cm/year]	Therapy break duration (days)
	After 3 months	After 6 months			
Mean value	7.58	8.8	5.68	11.55	48.4
Value range	3.4–11.4	3.4–12.0	3.2–10.9	8.2–13.1	12–90

In this paper, we analyze growth velocity in 5 patients with TS, treated long term with GH, who had short interruptions in drug administration, followed by the re-introduction of treatment. The aim was to perform a preliminary assessment of the influence of such interruptions on the growth process.

MATERIAL AND METHODS

The retrospective analysis of clinical data revealed five patients of developmental age (6–14 years) with TS who were treated with recombinant human GH (rhGH) (Omnitrope, Sandoz) and experienced short therapy interruptions (12–90 days) due to non-medical reasons, related to temporary unavailability of the medication. All subjects were previously treated with GH at a dose range of 0.32–0.35 mg/kg/week for more than one year (3–11 years). Their growth velocities were compared to the group of 10 TS patients of similar age, who had no interruptions in the treatment and were continuously treated with GH. Also, the patients' growth velocities during the treatment beginning (after the first 3 and 6 months) were collected. Included patients presented no additional medical conditions affecting growth. This analysis was performed in accordance with the World Medical Association Declaration of Helsinki regarding the ethical conduct of research. It was based on the research protocol approved by the Bioethical Committee of Poznan University of Medical Sciences (No. 318/16).

RESULTS

The average growth velocity after the treatment interruption increased 2-fold compared to the value during continuous therapy prior to the interruption. Also, the average growth velocity after the interruption was 1.3–1.5 times greater compared to values observed in the period after the primary rhGH therapy introduction (catch-up growth after 3 and 6 months). Detailed data regarding growth velocities of patients with TS during the primary catch-up growth, continuous therapy, and after restarting the treatment are presented in Table I and Figure I.

DISCUSSION

According to the authors' knowledge, there are no studies on the re-occurrence of the catch-up growth phenomenon in GH-treated girls with TS after interruptions during long-term therapy. Such cases occur sporadically and cannot be planned due to the fact that the treatment is, by definition, continuous. Nevertheless, in the past, some studies were conducted regarding the influence of planned intermittent therapies on growth in certain groups of GH-treated children. Research involving patients born small for gestational age suggests no negative effect of interruptions in GH administration on the achieved height [14]. Another study with GHD children showed no negative growth results of less frequent GH administration: three times vs. six times a week gave similar effects [15].

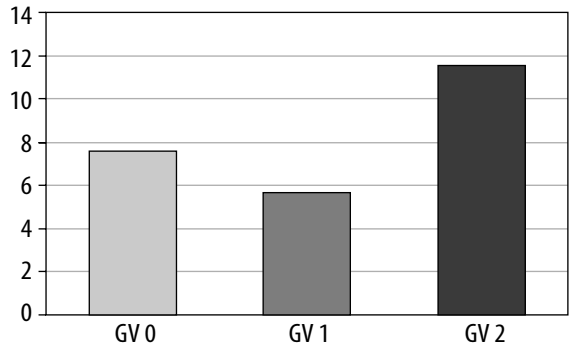

FIGURE 1. Mean growth velocities of patients with Turner syndrome during the primary catch-up growth (GV0), continuous therapy (GV1) and after restarting the treatment (GV2)

Earlier observations proved the re-occurrence of catch-up growth in patients with GHD who restarted GH therapy after a break [13]. Due to various mechanisms of growth failure, there were doubts about whether the catch-up effect would recur after a therapy interruption also in TS children and how significant it would be. Our present observations show similar results as in the GHD children. When the treatment was restarted, the TS patients' growth velocity increased to greater values than during the previous continuous treatment. Furthermore, this was also even more pronounced than during the period of initial treatment introduction. Thus, it strongly suggests that the catch-up effect is not a single phenomenon during GH therapy also in TS children.

Numerous studies show that the main factors influencing the intensity of catch-up growth in GH-treated children are bone age delay, the degree of growth deficit, and the severity of GH deficiency [9, 16]. In presented cases of TS patients with therapy interruptions, due to former long-term GH treatment, the height deficiency must have been less pronounced than at the therapy's very beginning, and the bone age delay could not be greater.

Also, in TS the secretion of GH and IGF1 is preserved, so we should not consider the degree of their deficiency. In the picture presented above, this rapid growth response, stimulated by the GH administration, must be regulated by some other factors and mechanisms that still need to be clarified.

CONCLUSIONS

The analyzed data suggest that a single brief GH treatment interruption should not cause a major concern regarding the growth delay in children with TS. It seems that it could even temporarily accelerate the growth velocity, due to the re-occurrence of the "catch-up growth" phenomenon. However, increasing the size of the study group and further, prolonged observation of patients' height after a break in the therapy would make it possible to conduct a broader analysis of long-term effects of such interruptions.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Quigley CA, Fechner PY, Geffner ME, et al. Prevention of growth failure in turner syndrome: long-term results of early growth hormone treatment in the "Toddler Turner" cohort. Horm Res Paediatr 2021; 94: 18-35.
2. Blunden C, Nasomyont N, Backeljauw P. Growth hormone therapy for Turner syndrome. Pediatr Endocrinol Rev 2018; 16: 80-90.
3. Wasniewska M, De Luca F, Bergamaschi R, et al. Early treatment with GH alone in Turner syndrome: prepubertal catch-up growth and waning effect. Eur J Endocrinol 2004; 151: 567-572.
4. Al Shaikh A, Daftardar H, Alghamdi AA, et al. Effect of growth hormone treatment on children with idiopathic short stature (ISS), idiopathic growth hormone deficiency (IGHD), small for gestational age (SGA) and Turner syndrome (TS) in a tertiary care center. Acta Biomed 2020; 91: 29-40.
5. Danowitz M, Grimberg A. Clinical indications for growth hormone therapy. Adv Pediatr 2022; 69: 203-217.
6. Iughetti L, Madeo S, Predieri B. Growth hormone therapy in patients with short stature homeobox-gene (SHOX) deficiency. J Endocrinol Invest 2010; 33: 34-38.
7. Van Pareren YK, de Muinck Keizer-Schrama SM, Stijnen T, et al. Final height in girls with Turner syndrome after long-term growth hormone treatment in three dosages and low dose estrogens. J Clin Endocrinol Metab 2003; 88: 1119-1125.
8. Davenport ML, Crowe BJ, Travers SH, et al. Growth hormone treatment of early growth failure in toddlers with Turner syndrome: a randomized, controlled, multicenter trial. J Clin Endocrinol Metab 2007; 92: 3406-3416.
9. Van Dommelen P, Koledova E, Wit JM. Effect of adherence to growth hormone treatment on 0-2 year catch-up growth in children with growth hormone deficiency. PLoS One 2018; 13: e0206009.
10. Gafni RI, Baron J. Catch-up growth: possible mechanisms. Pediatr Nephrol 2000; 14: 616-619.
11. Dacou-Voutetakis C, Karavanaki-Karanassiou K, Petrou V, et al. The growth pattern and final height of girls with Turner syndrome with and without human growth hormone treatment. Pediatrics 1998; 101: 663-668.
12. Ramos AV, Silva IN, Goulart EM. Turner syndrome: searching for better outcomes. Clinics (Sao Paulo) 2008; 63: 173-178.
13. Kędzia A, Majewska KA, Korcz M. Do the intervals in growth hormone therapy positively affect the growth velocity? Pediatr Endocrinol Diabetes Metab 2020; 26: 113-117.
14. Phillip M, Lebenthal Y, Lebl J, et al. European Norditropin SGA Study Group. European multicentre study in children born small for gestational age with persistent short stature: comparison of continuous and discontinuous growth hormone treatment regimens. Horm Res 2009; 71: 52-59.
15. Cavallo L, De Luca F, Bernasconi S, et al. The effect of different growth hormone administration frequencies on growth in growth hormone-deficient patients. Horm Res 1998; 49: 73-77.
16. Wit JM, Ranke MB, Albertsson-Wikland K, et al. Personalized approach to growth hormone treatment: clinical use of growth prediction models. Horm Res Paediatr 2013; 79: 257-270.