A Case of Growth Failure Caused by 13-CIS-Retinoic Acid Administration after Bone Marrow Transplantation for Neuroblastoma

YASUJI INAMO*, TAKASHI SUZUKI AND HIDEO MUGISHIMA

**Department of General Pediatrics, Nihon University Nerima-Hikarigaoka Hospital, Tokyo 179-0072, and
Department of Pediatrics, Nihon University School of Medicine, Tokyo 173-0032, Japan*

Abstract. We report an 11-year-old girl with growth failure caused by long-term administration of 13-cis-retinoic acid after bone marrow transplantation for neuroblastoma. Her growth velocity was 1–2 cm/year after 13-cis-retinoic acid administration. Her endocrinological findings were normal except for peak growth hormone levels of 6.4 ng/ml (clonidine) and 9.7 ng/ml (arginine). IGF-1 and IGFBP-3 were normal. It is not possible to conclude that her severe growth failure was caused by partial growth hormone deficiency, but premature epiphyseal closure was seen on radiographic examination. We concluded that the growth failure was caused by pediatric cancer therapy for the musculoskeletal system but not by endocrinological disturbance.

Key words: Growth failure, 13-cis-retinoic acid, Premature epiphyseal closure, Cancer therapy
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VITAMIN A synthetic analogue (e.g., 13-cis-retinoic acid) would produce such effects on the musculoskeletal system as axial osteophyte formation, osteopenia, enthesopathy, premature fusion of the epiphyses, modeling abnormalities. We present the case of a young girl being treated with 13-cis-retinoic acid after bone marrow transplantation for neuroblastoma. She had severe growth failure caused by long-term administration of 13-cis-retinoic acid.

Case Report

A 5-year-old Japanese girl presented with a posterior mediastinal mass. She was diagnosed

with neuroblastoma stage IV and was treated with chemotherapy.

At age 6 she underwent autologous bone marrow transplantation.

She was treated with 13-cis-retinoic acid (40 mg/day) because of bone metastases in the neuroblastoma at age 8. Her growth velocity was 1–2 cm/year after 13-cis-retinoic acid administration. Her endocrinological findings are normal except for peak growth hormone levels of 6.4 ng/ml (clonidine) and 9.7 ng/ml (arginine). IGF-1 (110 ng/ml) and IGFBP-3 (4.62 mg/ml) are now normal. Although her bone age is 8 years, chronological age is 10-year and 9-month old, her premature epiphyseal closure was shown in a radiographic examination.

Correspondence to: Dr. Yasuji INAMO, Division of Pediatric Rheumatology and Endocrinology, Department of General Pediatrics, Nihon University Nerima-Hikarigaoka Hospital, Nihon University School of Medicine, 2-11-1 Hikarigaoka, Nerima-ku, Tokyo 179-0072, Japan

Discussion

Growth failure after pediatric cancer therapy is well known. Growth failure is caused not only by GH deficiency, but also by damage to the

Fig. 1. She showed severely growth failure after 13-cis-retinoic acid administration.

musculoskeletal system caused by cancer therapy [1].

Vitamin A and its derivatives (retinoids) have been known to cause premature epiphyseal closure. Retinoid-induced epiphyseal plate closure induced the loss of epiphyseal plate chondrocytes and invasion of the epiphyseal plate by osteoclasts in

guinea pigs [2].

It is important for all physicians who care for pediatric oncology patients to be aware of the potential for metabolic bone disease after pediatric cancer therapy.

Fig. 2. An AP view of both knees reveal epiphyseal plate closure and cone-shaped epiphyses of both distal femoral and both proximal tibial epiphyses.

Conclusion

We concluded that the growth failure was caused by the effect of pediatric cancer therapy on the musculoskeletal system and not by endocrinological disturbance.

References

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