

Radiologic zebra line sign in a patient with Langerhans cell histiocytosis on bisphosphonate therapy

Kenichi Sakamoto^{1,2}  | Yoko Shioda²

¹Department of Pediatrics, Shiga University of Medical Science, Otsu, Japan

²Children's Cancer Center, National Center for Child Health and Development, Tokyo, Japan

Correspondence

Kenichi Sakamoto, Department of Pediatrics, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu, Shiga 520-2192, Japan.

Email: skn1@belle.shiga-med.ac.jp

Funding information

Japan Agency for Medical Research and Development, Grant/Award Number: 20ck0106605h0001

A 3-year-old boy was diagnosed with multi-system Langerhans cell histiocytosis (LCH) with bone, skin, lung, lymph node, and bone marrow

involvement at 8 months of age. He achieved non-active disease (NAD) after chemotherapy with prednisolone, vincristine, and cytarabine.

(A) before therapy (B) 1.5 months after discontinuation of therapy (C) 7 months after discontinuation of therapy (D) 7 months after discontinuation of therapy (E) growth curve before and after therapy

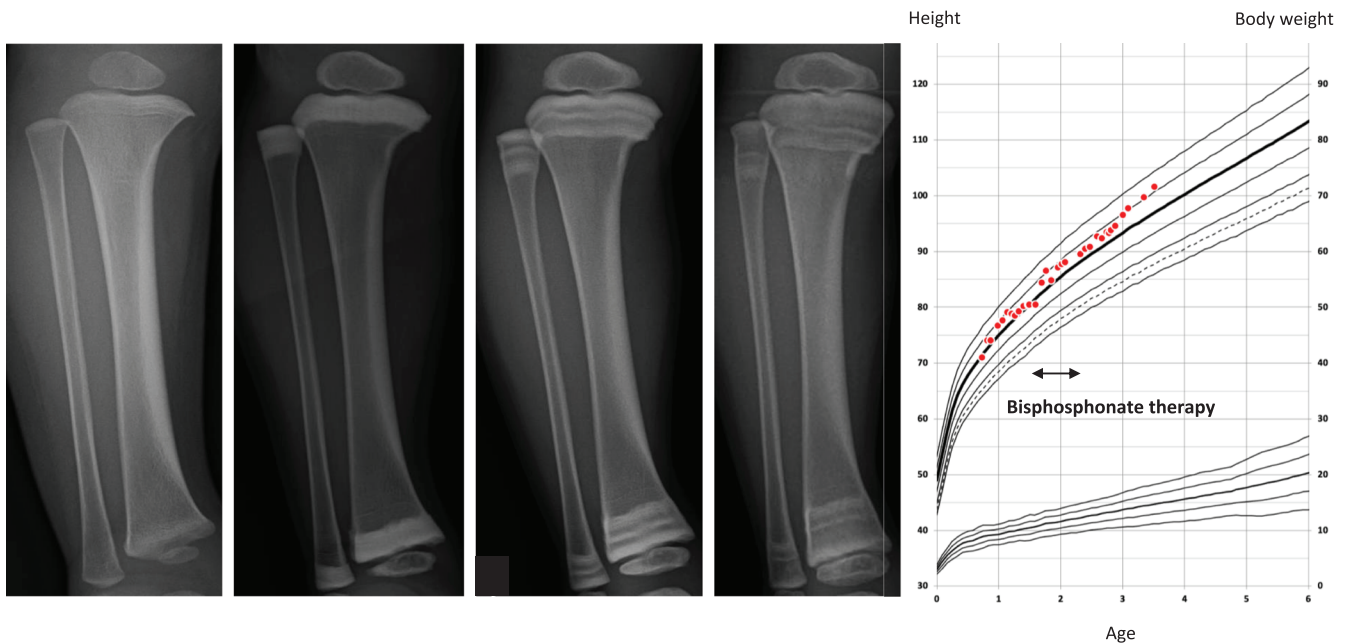


FIGURE 1 (A–D) “Dense metaphyseal band sign,” also known as “zebra line sign,” at the tibia and fibula. (E) Two years after initiation of bisphosphonate therapy, his growth remained steady

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2022 The Authors. *eJHaem* published by British Society for Haematology and John Wiley & Sons Ltd.

However, the patient presented with bone lesion relapse. Despite re-initiation of vinblastine and prednisolone, his bone lesion progressed, prompting treatment with three cycles of cladribine. While it provided some improvement, he presented with bone lesion relapse soon after cladribine therapy. Due to the recurrence of the bone lesion, we administered bisphosphonate therapy using monthly zoledronic acid for 6 months in addition to conventional chemotherapy, which resolved his bone lesion. The patient achieved NAD for 1 year. While he did not present with bone pain, radiographs obtained during bisphosphonate therapy revealed a “dense metaphyseal band sign,” also known as “zebra line sign,” at the tibia and fibula (Figure 1A–D). Nevertheless, 2 years after initiation of bisphosphonate therapy, his growth remained steady (Figure 1E).

LCH is characterized as both neoplastic and inflammatory disease. Osteoclasts are crucial in the pathogenesis of LCH, especially in lytic bone lesions. Previous reports revealed that bisphosphonate therapy, including pamidronate and zoledronate, was effective in patients with LCH. Bisphosphonates reduce the activity of osteoclasts by inhibiting their recruitment, thereby resulting in the uncoupling of bone remodeling. The zebra line sign refers to the line of cartilage calcification persisting from the metaphysis into the diaphysis [1, 2]. This radiologic finding reflects the administration of bisphosphonate [3]. Although the zebra line sign seems to be a normal reaction to bisphosphonate therapy, hematology-oncology specialists are not familiar with this finding. In addition, the long-term side effects (e.g., short stature and fracture)

remain unknown. This study highlights the importance of long-term follow-up to evaluate the safety profile of bisphosphonates in patients with LCH.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Kenichi Sakamoto  <https://orcid.org/0000-0003-1499-538X>

REFERENCES

1. Loizidou A, Andronikou S, Burren CP. Pamidronate “zebra lines”: a treatment timeline. *Radiol Case Rep.* 2017;12:850–3.
2. Al Muderis M, Azzopardi T, Cundy P. Zebra lines of pamidronate therapy in children. *J Bone Joint Surg Am.* 2007;89:1511–6.
3. Renaud A, Aucourt J, Weill J, Bigot J, Dieux A, Devisme L, et al. Radiographic features of osteogenesis imperfecta. *Insights Imaging.* 2013;4:417–29.

How to cite this article: Sakamoto K, Shioda Y. Radiologic zebra line sign in a patient with Langerhans cell histiocytosis on bisphosphonate therapy. *eJHaem.* 2022;3:1046–1047. <https://doi.org/10.1002/jha2.452>