Short communication

Bisphosphonate-related enamel hypoplasia in a child with idiopathic arterial calcification of infancy

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Abstract

We report bisphosphonate-related enamel hypoplasia as a rare side effect in a child with idiopathic arterial calcification of infancy. © 2012 The British Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Keywords: Bisphosphonate; Enamel hypoplasia; Side effect; Idiopathic arterial calcification of infancy

Introduction

Idiopathic arterial calcification of infancy (IACI) is a rare disorder characterised by extensive calcification and stenosis of large and medium-sized arteries. It has a poor prognosis, with a mortality of 85% before the age of 6 months, usually from cardiac failure. Although treatment is challenging, etidronate can reduce the amount of vascular calcification. The aim of the drug is to prevent and reverse abnormal deposition of calcium rather than radically and rapidly altering calcium metabolism by inhibition of osteoclasts, which is the main mechanism of action of bisphosphonates. However, the safety of bisphosphonates in infants and children has yet to be established. As a rare side effect of such treatment, we report bisphosphonate-related enamel hypoplasia in a child with IACI.

Case report

A 12-year-old girl with IACI was referred to our department for examination of abnormal teeth. She had been taking etidronate since she was 2.5 years old. There was no history of maxillofacial trauma or abnormal teeth. Oral examination showed hypoplasia of the enamel of the permanent teeth (Fig. 1). Only the second deciduous molar of the right mandible remained. Panoramic radiograph showed that only the right mandibular second premolar was impacted, and there were no congenital missing or supernumerary teeth (Fig. 2). According to the family there was no enamel hypoplasia of the deciduous teeth. The age at which she started taking etidronate matched the pattern of the enamel hypoplasia of the teeth, and she was therefore diagnosed as having bisphosphonate-related enamel hypoplasia.

Discussion

Bisphosphonates are potent inhibitors of bony resorption and are commonly used in the treatment of osteoporosis and other diseases of bone. They have beneficial effects on some bony diseases in childhood such as osteogenesis imperfecta,
as well as in adults. Bisphosphonate-related osteonecrosis of the jaw was recently reported as a complication, but to our knowledge there have been few if any clinical reports of enamel hypoplasia as a complication, because bisphosphonates are not usually given to infants or young children during the development of teeth. Enamel hypoplasia usually has a genetic cause, but can be associated with systemic diseases and dentomaxillofacial trauma during tooth development. In the present case the enamel hypoplasia was probably the result of etidronate being given to improve arterial calcification before the formation of permanent crowns.

Several animal studies have shown the effects of bisphosphonates on teeth. If etidronate, alendronate, or zoledronate are given during tooth development they have the potential to inhibit eruption and development of teeth and cause several dental abnormalities including defective mineralisation of enamel or enamel hypoplasia. While their mechanism of action has been exhaustively studied in bone, their effects on the formation of enamel are still poorly understood.

Although animal studies have suggested that etidronate has an inhibitory effect on mineralisation of enamel, there is little evidence for an inhibitory effect of etidronate on the formation of enamel protein. Yamada et al. suggested that the pathogenesis of enamel hypoplasia in rats injected with etidronate might not be related to a disturbance in amelogenin synthesis but to a disturbance in a later process, presumably the secretion of enamel protein. An animal study reported by do Espírito Santo et al. showed that etidronate, but not alendronate, induces severe alterations in the morphology of mature enamel. Bisphosphonates such as etidronate that do not contain nitrogen have inhibitory effects on the mineralisation of enamel, whereas nitrogen-containing bisphosphonates such as alendronate or zoledronate do not. Because nitrogen-containing bisphosphonates with high inhibitory effects on the resorption of osteoclastic bone are typically prescribed for adult patients, and etidronate is not usually given to infants and young children during tooth development, the present clinical finding of bisphosphonate-related enamel hypoplasia is important. Further extensive clinical study is needed to examine the effects and safety of bisphosphonates on the development of teeth in children.

References