Diagnostic and Interventional Imaging (2019) **100**, 529—531

LETTER /*Pediatric imaging*

Sequential radiologic findings in osteopathia striata with cranial sclerosis

Keywords Osteopathia striata; Cranial sclerosis; Lineal striation; High bone mass disorder

Dear Editor,

Osteopathia striata with cranial sclerosis (OSCS) is a rare sclerosing bone dysplasia characterized by craniofacial hyperostosis and longitudinal striations of the long bones, with the causal gene being adenomatous polyposis coli (APC) membrane recruitment protein 1 (*AMER1*), which has an X-linked dominant inheritance, and generates a range of clinical findings [1]. Affected girls show macrocephaly with dysmorphic features, and fetal or neonatal lethality has been observed in the majority of affected boys. We describe sequential radiographic findings from plain X-rays and computed tomography (CT) in a one-year-old girl with OSCS with a novel frameshift mutation in *AMER1*.

The proband was a girl at the age of 18 months, who was born after an uneventful pregnancy of 36 weeks. Her birth weight was 2810 g (+1.0 SDS), body height was 47.5 cm (+0.3 SDS), and head circumference was 33.6 cm (+0.8 SDS). At physical examination at 18 months, her height was 75.0 cm (−1.6 SDS), head circumference was 50.6 cm (+3.0 SDS), and arm span/height ratio was 0.91 (normal value, > 0.96). In addition, frontal bossing, hypertelorism, a depressed nasal bridge, a left auricular pit, and small and low-set ears were observed. Other results of the physical examination were normal. The development quotient was age-appropriate. Results of her blood tests were normal and included

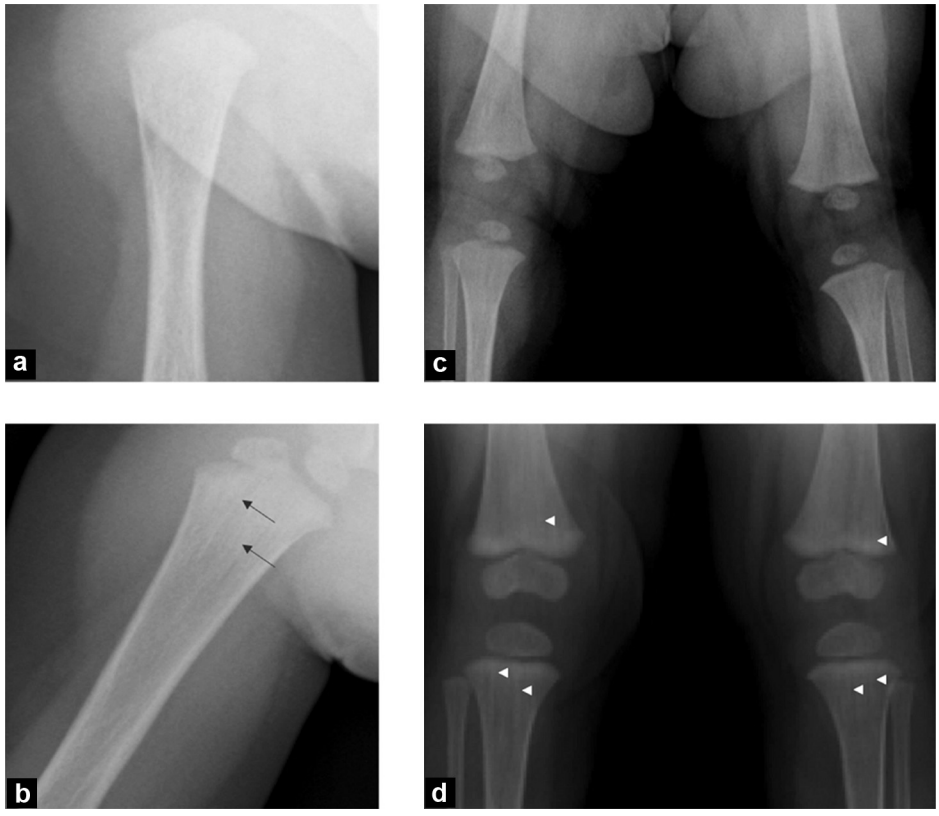

Figure 1. a: Anterior—posterior views of the proximal humerus bone at 4 months showed no visible abnormalities; b: Definite linear striations (arrows) of the humerus bone are observed at 18 months; c: X-ray image of the lower extremities at 4 months shows non-specific sclerosis; d: Linear striations (arrowheads) become evident in the metaphyseal areas of the femur and tibia bones at 18 months.

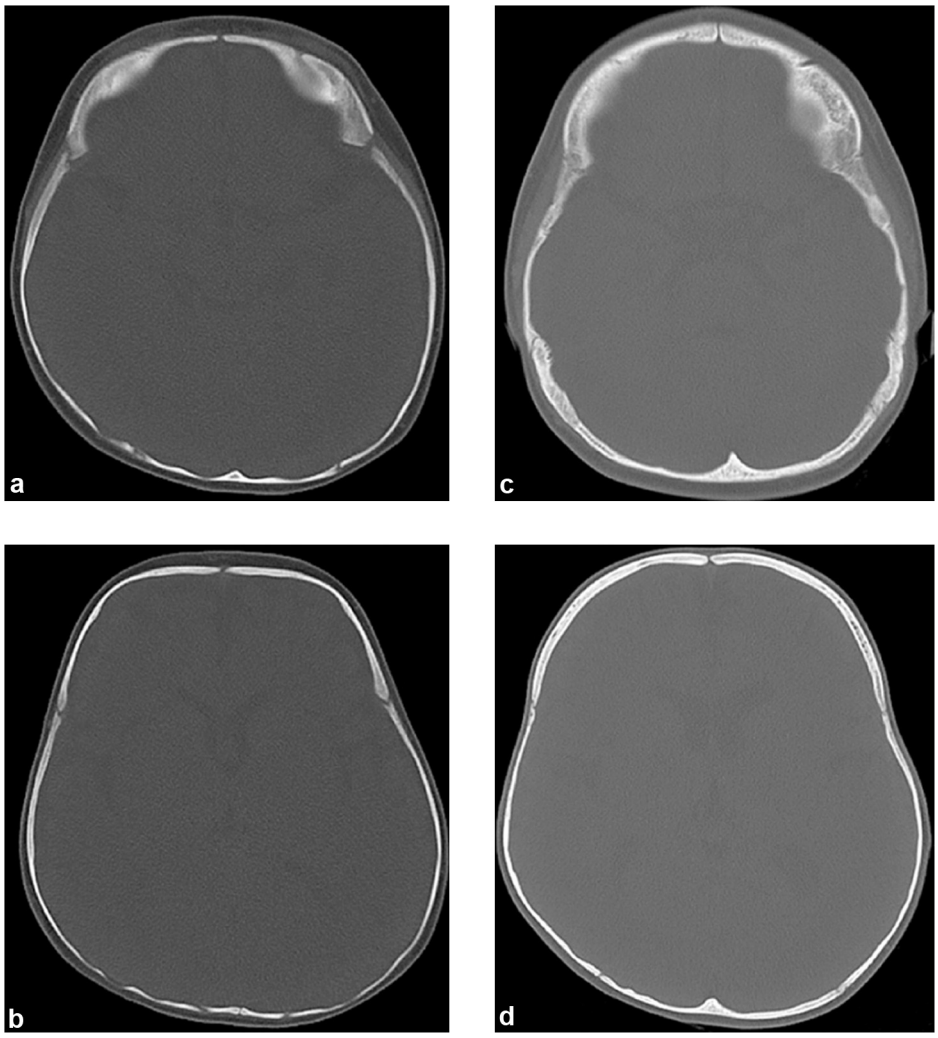

Figure 2. Cranial computed tomography (CT) image in the transverse plane using bone window at 4 months (275 mAs; 100 kV; slice thickness, 2.0 mm). a: Supraorbital slice; b: Supratentorial slice; c—d: Follow-up CT images at 18 months obtained with similar parameters than in a and b (352 mAs; 100 kV; slice thicknes,s 2.0 mm) show thickening and cranial sclerosis compared with the initial CT images at the same levels.

endocrinological and metabolic evaluations. A skeletal survey performed at 4 months showed no evident abnormalities (Fig. 1a, c). However, a follow-up survey performed at 18 months showed visible linear striations in the metaphyseal areas of the long bones (Fig. 1 b, d). Cranial CT images at 18 months obtained with similar parameters showed thickening and sclerosis of the cranial bones compared with findings of the initial investigation at 4 months, highlighting the progressive nature of the condition (Fig. 2). Radiological differential diagnosis of high bone mass disorders included OSCS, sclerosteosis, and van Buchem disease. [2]. Genetic analysis was performed using genomic DNA extracted from leukocytes of the patient and her parents after obtaining written informed consent. Targeted exome sequencing was performed using the TruSight One Sequencing Panel (Illumina, San Diego, CA). A previously unreported heterozygous *AMER1* frameshift mutation (NM_152424.3:c.394del, p.Ser132Valfs*38) was detected. Targeted sanger sequencing of the parents' genomes confirmed the mutation to be a de novo event. The mutation was predicted to be probably damaging using the PolyPhen-2 tool (score of 0.986), disease causing by mutation taster (probability value of 1), and deleterious by PROVEAN prediction (score of −4.27).

Serial radiological evaluation of our patient produced evidence of the progressive nature of bone lesions observed in OSCS. Although striations of the long bones and cranial sclerosis are hallmarks of OSCS, these radiographic findings are not seen during the early stages of the condition, which hampers early diagnosis. Follow-up radiographic findings of the thickening of cranial bones and development of lineal striations should aid in the diagnosis of suspected cases. Sequential radiographic evaluation using plain X-rays showing striations of the proximal humerus has been previously reported [3]. However, findings of sequential cranial CT have not previously been reported. *AMER1* functions as a tumor suppressor via the Wnt/β-catenin signaling pathway, binds to β-catenin, and promotes ubiquitination and degradation, thereby regulating cytoplasmic β-catenin levels. Loss of function of *AMER1* leads to the activation of Wnt signaling, which, in turn, results in excessive bone deposition and hardening, attributed to the activation of osteoblasts [1]. Characteristic dysmorphic features of cranial osteosclerosis

include macrocephaly with frontal bossing, hypertelorism, epicanthic folds, a depressed nasal bridge, and a flat face [1]. Progressive cranial sclerosis may lead to sensorineural hearing loss and facial nerve palsies. The observation of these features should prompt clinicians to consider conducting a skeletal survey. Differential diagnosis of OSCS includes osteopetrosis and other sclerosing bone dysplasias [2]. Sequential radiographic evaluation and genetic testing should be considered for a precise diagnosis of OSCS.

Author Contributions

Dr. Chong had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

Tomita: Conceptualization, data curation, investigation, original drafting of the manuscript.

Chong: Study design and conceptualization, data analysis, formal analysis, methodology, original drafting and review.

Yamamoto: Data analysis, formal analysis, supervision, validation, critical review of the manuscript.

Akamine: Data curation, data analysis, resources, review of the manuscript.

Imaizumi: Data analysis, investigation, review of the manuscript.

Kira: Study design and conceptualization, project supervision, validation, critical review of the manuscript.

All authors critically reviewed the manuscript for important intellectual contents, and approved for the submission for publication.

Disclosure of interests

The authors declare that they have no competing interest.

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https://doi.org/10.1016/j.diii.2019.04.001

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