Radiology Case Reports

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Craniosynostosis Secondary to Rickets: Manifestations on Computed Tomography

Page I. Wang, Jeffrey R. Marcus, M.D., Herbert E. Fuchs, Ph.D., M.D., and Srinivasan Mukundan Jr., Ph.D, M.D.

We present the case of a preterm 6-month-old African American infant who developed craniosynostosis secondary to rickets. This child developed rickets and macrocephaly by the age of 6 months. His head continued to enlarge, and a 3D CT obtained when the child was 2 years old revealed metopic and bilateral coronal craniosynostosis. This CT suggested increased intracranial pressure, and therefore, corrective cranial vault reconstruction was performed. Craniosynostosis secondary to rickets is rarely reported, but since neither rickets nor craniosynostosis is a reportable disease, the exact incidence of both diseases is unknown. Craniosynostosis should be suspected in any rachitic child with an abnormal head circumference or shape and craniofacial CT evaluation should be performed, so that a corrective surgery can be performed at an appropriate age.

Case Report

An African-American male was born at 31 weeks with no complications. By three months, he developed hypotonia, increased head circumference, and developmental delay. At this time, the child had been excusively breastfed. Contemporaneous magnetic resonance imaging (MRI) and computed tomography (CT) scans demonstrated no abnormality.

At six months of age, his blood chemistry lab studies revealed low serum calcium and low vitamin D levels, consistent with rickets. At the time, his head was 49 cm in circumference (4 standard deviations above the mean for his age). After supplementation therapy, his laboratory values normalized, and the hypotonia and developmental delay resolved. Nevertheless, the child's head shape progressively worsened.

By two years of age, his forehead was symmetrically flattened, with increased height, steep angulation, and an overall decrease in the total anteroposterior dimension. A three-dimensional CT scan was performed, demonstrating variable fusions of the metopic and bilateral coronal sutures, and ossification over his anterior fontanelle (Fig. 1). The sagittal and lambdoidal sutures were patent. No

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Abbreviations: 3D, three dimensional; CT, computed tomography

Page I. Wang (Email: crossette@gmail.com) is at the University of Michigan, Ann Arbor, MI, United States of America.

Jeffrey R. Marcus, M.D., is in the Department of Plastic and Reconstructive Surgery, Duke University Medical Center, Durham, NC, United States of America.

Herbert E. Fuchs, Ph.D., M.D., is in the Department of Neurosurgery, Duke University Medical Center, Durham, NC, United States of America.

Srinivasan Mukundan Jr., Ph.D., M.D., (Email: mukun001@mc.duke.edu) is in the Department of Radiology, Duke University Medical Center, Durham, NC, United States of America.

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masses, midline shift or hydrocephalus were seen at the time, however, increased intracranial pressure was suggested by the scalloping ("thumbprinting") of the endocranial surface.

Due to the clinical and radiologic presentation, including suspected increased intracranial pressure, the child underwent reconstructive surgery of the anterior two-thirds cranial vault, which is the current standard of care to reduce intracranial pressure associated with craniosynostosis. After the operation, his head returned to a normocephalic shape and size (Fig. 2).

Discussion

In children, rickets often presents with growth failure, hypotonia, muscle weakness, delayed motor development, restlessness, and poor sleep patterns. It is further characterized by craniotabes (softening of the skull), delay in fontanelle closure, costochondral beading, bowlegs, widened wrists, kyphoscoliosis, and rarely craniosynostosis. First noted by Heschl in 1873 [1], the association of craniosynostosis and rickets has sporadically appeared in the literature.

An infant receives vitamin D from breast milk, the sun, or vitamin supplementation. In turn, the mother's supply of vitamin D in her breast milk results from sun exposure and diet [2, 3]. Unfortunately, breast milk falls short of the recommended daily allowance of vitamin D [4]. One study found the incidence of premature infants developing rickets increased in breast-fed infants (40%), as opposed to bottle-fed infants (16%)[5]. The skin production of 7-dehydrocholesterol, the first-step in vitamin D synthesis, is activated by sun exposure and is inversely proportional to the amount of melanin present [6]. To generate adequate vitamin D levels, Caucasian babies anywhere from 30 minutes to 2 hours of sun exposure per day [7]. Studies have shown that African American adults require six times more sun exposure than Caucasian adults [8]. By extrapolation, African American infants would be expected to require significantly more solar exposure than Caucasian infants.

Premature infants, such as this infant, are prone to calcium and phosphorus deficiencies, because calcium and phosphorus accretion increases six-fold during the third trimester of pregnancy [9]. Since preterm infants do not complete this third trimester, they are more labile to develop rickets than term infants.

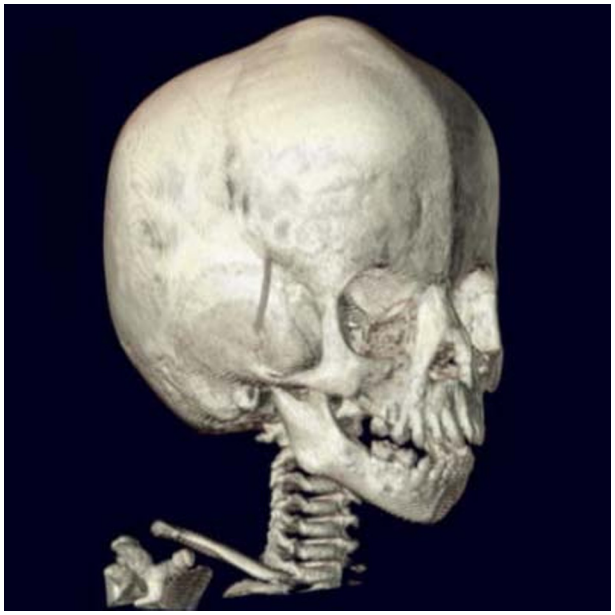

Figure 1A. Craniosynostosis in a 2-year-old boy with previous rickets. Pre-operative 3D CT shows variable fusions of the metopic and bilateral coronal sutures, and ossification over his anterior fontanelle, with resultant increase in height and decrease in anteroposterior dimension of the calvaria.

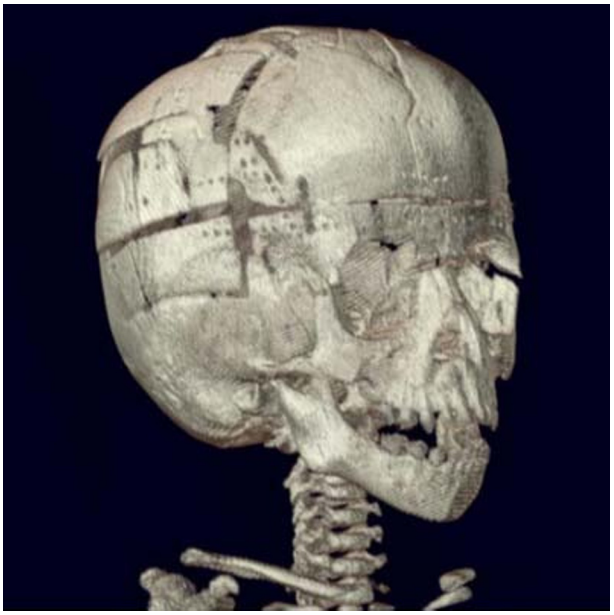

Figure 1B. Post-operative 3D CT following reconstructive surgery of the anterior two-thirds cranial vault.

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Craniosynostosis, the premature fusion of cranial sutures, is less understood, and the prevention and treatment remain elusive. Two main theories attempt to explain the pathogenesis. Firstly, the dural hypothesis, suggests that dural attachments slow down the growth of the cranial bones, which then cannot accommodate for the growing brain, resulting in premature fusion [10]. Secondly, the osteoblast hypothesis, purports that dysfunctional osteoblasts are the root cause of craniosynostosis. Fragale et al. found that in vitro osteoblast cells taken from the skull base of craniosynostotic patients are easily inhibited by osteoblast growth factor, and have a prolonged doubling time when compared to normal osteoblasts [11]. In support of this theory, Roy also found that osteoblasts taken from the skulls of hypophosphatemic mice, (which mimics vitamin-D resistant rickets) also exhibited non-linear, disunited growth and evidence of craniosynostosis by 4 weeks [12].

The mineral deficiencies induced by rickets sets the stage for craniosynostosis by delaying the vascular invasion of growth plates, resulting in hypertrophied and disorganized chrondrocytes, and accumulation of osteoid along the metaphysis [13-15]. This could explain why the skull base originally derived from endochondral bone is unable to compensate for the increase growth of the brain, and why the calvarium made of bone has excess osteoid, resulting in premature suture fusion, and thus craniosynostosis. [14, 16, 17].

Although the association between craniosynostosis and rickets is slowly becoming clear, more research should be devoted to the epidemiology of craniosynostosis, rickets in premature African American infants, and the pattern of suture fusion in craniosynostosis associated with rickets.

In conclusion, given that there is a documented association between rickets and craniosynostosis, clinicians should consider craniosynostosis in any rickettic patient with macrocephaly. Radiologists should be aware of the association between craniosynostosis and rickets and consider 3D reformats when reading head CTs of patients with known rickets.

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