Case Report

Bulging anterior fontanelle: an unusual presenting sign of nutritional rickets

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Aim: To report the first case series of infants with nutritional rickets who presented with bulging anterior fontanelle

Methods: infants who were admitted to Alrass General Hospital, Qassim, Saudi Arabia, between October 2004 and October 2007, with bulging anterior fontanelle and later found to have nutritional rickets were reviewed. Diagnosis of rickets was based on typical biochemical and radiological findings with or without clinical signs of rickets and with a good response to treatment with vitamin D with or without calcium.

Results: Nine cases of nutritional rickets who presented with bulging anterior fontanelle are reported. All were below 12 months of age and the majorities are boys. All patients are exclusively breast-fed. Five cases had hypocalcaemia and three of them presented with hypocalcaemic seizures. Five cases showed no clinical signs of rickets. Clinical, biochemical and radiological signs of rickets as well as the status of the anterior fontanelle reverted to normal within six weeks after treatment with vitamin D in all except one patient who took four months to respond.

Conclusion: Nutritional rickets remains a problem in Saudi Arabia. A bulging anterior fontanelle is an important, but under- recognized presenting feature of nutritional rickets. Recognition of this association will alley anxiety when confronted with a case of rickets with a bulging anterior fontanelle.

Keywords: hypocalcaemic seizures, vitamin D, hypophosphataesia.

Nutritional rickets classically presents with symptoms of bony deformity such as bowed legs, knock – knees, swelling of the wrists, rachitic – rosary, frontal bossing of the skull, and pathological fractures in severe cases[1], as well as poor growth, delayed dention and muscle weakness with developmental delay[2]. Another group may present with symptoms of hypocalcaemia which may cause convulsions, strider and neuromuscular irritability[3,4]. Some cases of nutritional rickets may present with bulging anterior fontanelle, which is well known in non- nutritional rickets like infantile hypophosphataesia[5]. However, only two cases of this presentation were reported from Saudi Arabia[6,7].

This study reports nine cases of nutritional rickets, who presented with bulging anterior fontanelle,

Methods

Nine infants with bulging of the anterior fontanelle (AF) and who were later proved to have nutritional rickets were admitted to Alrass General Hospital, Alrass. Qassim, Saudi Arabia, between October 2004 and October 2007. In each case the diagnosis of nutritional rickets was based on the finding of typical biochemical and radiological changes, with or without clinical feature, and who responded well to treatment with vitamin D3 with or without calcium, with a complete recovery. Infants who had other explanations for the bulging AF, such as CNS infection, hydrocephalus, etc, were excluded. However, those with associated iron deficiency anemia (IDA) were included, as the association between NR rickets and IDA is very common. Factors such as age at presentation, gender, nationality, dietary history, the presence or absence of clinical signs of rickets, biochemical and radiological findings, associated anaemia and C T scan of the brain and cerebrospinal fluid (CSF) examination- when done- were noted and analyzed. Each patient was treated with vitamin D3 drops, 3000 IU per day with or without calcium and

iron drops when IDA was diagnosed. The biochemical, radiological and clinical changes of rickets with the status of the AF was reviewed at the outpatient clinic six weeks later.

Verbal informed parental consent was obtained for each patient, and the study was approved by the local ethical committee.

Results

The details of the clinical cases in the study are shown in table (1)

The average age of the infants was 6.3 months (range 5 – 12 months). Seven (77.8%) were boys. Five were Saudis, three were Sudanese, and one was an Egyptian. Four infants were of dark skin. All infants were exclusively breast – fed at presentation, without any vitamin D supplementation.

All infants were admitted to our paediatric ward with bulging of the AF, with a duration ranging from 1 day to 7 days. It was either noticed by the mother at home (cases 1, 2 and 7), or by the referring doctor (cases 3 and 4), or was found during examination at the emergency room (cases 5, 6, 8 and 9). Three infants (cases 5, 8 and 9) presented with generalized short seizures. Two infants had associated coryazal symptoms and mild fever. No infant was known to have been previously diagnosed with nutritional rickets.

On clinical examination, four cases showed clinical signs of rickets, in the form of widening of the wrists and ankles, rachitic rosary and frontal bossing with wide AF. The other five cases did not show any clinical feature of rickets, diagnosis was made by the typical biochemical and radiological changes. The AF was wide and persistently bulging in all cases, it was tense in seven cases and soft in two cases. All the infants were active and alert without any focal neurological sign

The biochemical and radiological findings are shown in table (2)

Serums 25-OHD, which is used as a measure of vitamin D status, was not routinely performed among the cases. However the biochemical profiles in all the cases were consistent with vitamin D deficiency rickets. Five cases (55.5%) had hypocalcaemia, three of them presented with hypocalaemic seizures. One patient had hypophosphataemia, two had hyperphosphataemia and the other six patients had normal phosphate (P) levels (P level range 0.7 to 1.8 mmol/l). All patients had elevated alkaline phosphatase (ALP) levels (range 637 – 4226 in/l)

X- Ray of the wrist joints showed signs of rickets in all cases; five showed early rickets (ER), three showed active rickets (AR) and only one showed florid rickets (FR).

Lumber puncture (LP) was done in four patients and the CSF analysis and cultures were normal in the four. CT scan of the brain was done in three patients and all scans were normal. Blood and urine cultures were sterile in all patients. Anaemia (haemoglobin (Hb) less than 11.0 g/dl) was found in six patients (66.7%), with Hb range of 7.5 – 11.8 g/dl. The serum iron levels were low in 7 patients with the iron range of 0.8 – 9.7 ummol/l.

Six weeks after treatment with vitamin D3 with or without calcium and iron; the clinical, biochemical, radiological and the status of the AF reverted to normal in all except one patient. In case 4, because of non- compliance with the treatment, it took four months for the rickets changes to revert to normal. These improvements are shown in table (3).

Discussion

This case series documents the existence of nutritional rickets as a cause of infant morbidity in Saudi Arabia. There is a preponderance of males over females in our study. The reason for this is not clear. Similar results have occurred in other studies [4]. A genetic factor was postulated in one study, which showed boys and children with blood group A are more affected with nutritional rickets [8].

In this study, all the infants affected were exclusively breast-fed beyond six months of age without any vitamin D supplementation. This has also been found as a causative factor in other studies [9,10]. As there is relatively little vitamin D in breast milk, it has been recommended that lactating women should supplement their diet with vitamin D (10 ug daily) [11].

Other risk factors include no or minimal exposure to sunlight, indoor life style and dark skin[12]. In our study four out of the nine cases had dark skin. However, it has been argued, in studies from Saudi Arabia, that, there were no difference between dark pigmentation and general Arab complexion regarding vitamin D levels, which were found to be lower than those in Western countries[13]. In countries like sunny Saudi Arabia, minimal exposure to sunlight will induce the synthesis of vitamin D3. Continued exposure, however, will result in photodegredation of vitamin D3, which is very sensitive to photodegredation by the sun. So, in such countries where the sun shines almost every day of the year, 25-hydroxyvitamin D levels should not be different in light and dark – skin people [14].

Five out of nine cases in this study had hypocalcaemia and three of them presented with hypocalaemic seizures. This was a manifestation of the early stage of the disease; as two cases showed evidence of early rickets (ER) on radiological investigations and both did not show any clinical sign of rickets. This is not an uncommon presentation of nutritional rickets, as shown by many studies[3,4,15]. It would be understandable that, such presentation of seizure combined with bulging AF will cause a lot of worries among the parents as well as the paediatric staff. This also may lead to more expensive investigations like CT or MRI of the brain and invasive like CSF examination to exclude CNS infection or a space occupying lesion, while the cause is relatively benign. Recognition of this association will alert clinicians to look for rickets in infants with bulging AF and may alley their anxiety.

Bulging AF in infancy is a sign of intracranial hypertension (ICH), and it has several causes including CNS infections, hydrocephalus, space- occupying lesions and benign intracranial hypertension (BIH). In this study LP was done in four cases and the CSF analysis and cultures were normal. Likewise, CT scan of the brain was done in three cases and it was normal, excluding infections and space- occupying lesions.

BIH or otherwise called pseudotoumor cerebri, presents commonly as a headache syndrome characterized by raised CSF pressure in the absence of intracranial mass lesion or ventricular dilatation. It is usually associated with a normal level of consciousness, papilloedema and occasional 6th nerve palsy with an otherwise normal neurological examination[16]. It is not strictly benign, as it can be a cause of permanent visual impairment[17]. In a reappraisal of the condition by Digre and Carbell[18], the merits of a clinical approach to diagnose primary or idiopathic form where no cause is found and a secondary, non-space –occupying form was discussed.

BIH in infancy can be caused by a heterogeneous group of conditions, some of which are benign and transient. These include IDA, vitamin A and tetracycline toxicity, endocrine disturbances such as hypoparathyroidism and Addison's disease and withdrawal of corticosteroids after long term use[19]. BIH also occurs following vaccination against diphtheria – pertussis – tetanus [20].

The pathogenesis of ICH in nutritional rickets is not certain. Bulging AF is not a well known feature of nutritional rickets, although it is known in rickets with hypophosphatasia[5]. This might be due to delayed bone growth in the presence of normal brain growth. Vitamin D deficiency rickets may well have the same effect, as vitamin D deficiency has been shown to affect postnatal head and linear growth [21].

Vitamin D has wide ranging steroid hormonal effects which can produce clinical symptoms and signs unrelated to calcium homoestasis. The explanation appears to be that, the receptors of 1,25 vitamin D are present in most cells of the body [22], and there is wide spread exterarenal expression of 1-alpha – hydroxylase which catalyses synthesis of this hormone [23]. Therefore, it is likely that, this hormone may have a link to the pathogenesis of the ICH in nutritional rickets through a yet unknown mechanism.

Hypocalcaemia may also be important in

the pathogenesis, since calcium plays a central role in regulating arterial vascular resistance and BIH has been reported with hypoparathyroidism [19]. Zafer, in his study of hypocalcemic convulsions due to nutritional rickets, found seven cases out of 93 infants (7.5%) to present with AF bulging[24]. In this study only five cases had hypocalcaemia, while in the other four cases, hypocalcaemia had no role in the pathogenesis of the ICH. Likewise, most of our patients have associated IDA which is a well known cause of BIH[19]. In anaemia the hyperdynamic circulation may play a role. However, the mechanism of the development of BIH in the face of anemia is unclear, but several theories have been posited [26]. It has been suggested that, anemia itself increases the production of CSF[27]. It is also possible that anemia and tissue hypoxia cause altered cerebral haemodynamics and increased brain capillary permeability, which could lead to papilledema and increased intracranial pressure[28].

It is presumably the combination of rickets and anaemia that is crucial in the development of ICH with nutritional rickets[25]. However, two of the patients in this study had no associated IDA, which suggests vitamin D3 deficiency as the primary cause of the BIH.

In conclusion, bulging AF is an important but under recognized sign of nutritional rickets. However, it is a transient problem if promptly recognized and treated. We recommend that, nutritional rickets should be included as one of the causes of the BIH

REFERENCES

1. Jacobsen ST, Hull CK, Crawford AH. Nutritional rickets. J Pediatr Orthop 1986; 6: 713–6
2. Thomas MK, Demay MB. Vitamin D deficiency and disorders of vitamin D metabolism. Endocrinol Metab Clin N Am 2000; 29: 611 – 27
3. Ladhani S, Srinivasan L, Buchanan C, et al. Presentation of vitamin D deficiency. Arch Dis Child 2004;89: 781 – 4
4. Biswas AC, Molla MAM, Ijemba JC. Febrile convulsions in infancy: beware of nutritional rickets. Middle East Paediatrics 2004; 9: 12 – 14
5. Biswas AC, Al Khalaif RA, Molla MAM. Infantile hypophosphatasia. Annal Saudi Med 1999; 19: 345 – 6
6. Biswas AC, Molla MAM; Al – Moslem K. A baby with bulging anterior fontanelle. Lancet 2000; 356: 132
7. Al- Najjar FY. Bulging anterior fontanelle and transient intracranial hypertension. Middle East Paediatrics 2005; 10: 88 - 9
8. El – Kholy MS, Abdel Maged FY, Farid FA. A genetic study of vitamin D deficiency rickets. 2 – sex differences and ABO typing. J Egypt Public Health Association 1992; 62: 213 – 22
9. Adekunle D, Mukesh A, Kochiyel HM et al. Hypovitaminosis D and vitamin D deficiency in exclusively breast-feeding infants and their mothers in summer: A justification for vitamin D supplementation of breast-feedinf infants. J Pediatr 2003:142:169-173
10. Hag A, Rajah J, Abdel-Wareth LO. Vitamin D: measurement, deficiency, and health consequences. Middle East Laboratory. 2009;12:6-10
11. Zipitis CS, Markider GA, Swann IL. Vitamin D deficiency: prevention or treatment?. Arch Dis Child 2006;91: 1011-14.
12. Clemens JL, Adams JL, Henderson SL, et al. Increased skin pigmentation reduces the capacity of the skin to synthesizes vitamin D3. Lancet 1982;i: 74 -6
13. Sedrani S Elidrissy ATH, El Arabi KM. Sunlight and vitamin D status in normal Saudi subjects. Am J Clin Nutr 1983; 36: 129 – 32
14. Holick MF. Photosynthesis, metabolism and biologic action of vitamin D. In Nestle Nutrition Workshop Series Vol 21, Nestic Ltd, Vevey/ raven press, ltd. New York 1991; 1 – 22.
15. Ahmed I, Atiq M, Igbal M, et al. Vitamin D deficiency rickets in breast – fed infants presenting with hypocalcaemic seizure. Acta Paeditr 1995; 84: 941 – 2
16. Kesler A, Fattal-Valevski A. Idiopathic intracranial hypertension in the pediatric population. J Child Neurol.2002;17 : 745-748
17. Lim M, Kurian M, Penn A, et al. Visual failure without headache in idiopathic intracranial hypertension. Ach Dis Child 2005; 90: 206 – 10
18. Digre KB, Cabett JJ. Idiopathic intracranial hypertension (pseudotumor cerebri) : a reappraisal. Neurologist 2001; 7: 2 – 67
19. Haslam RHA. Pseudotumor cerebri. In; Behrman RE, Nelson Textbook of Pediatrics, 18th ed 2007, Sauners, Elsevier Sciences; 2525 – 26
20. Cross TP, Milstien JB, Kuritskey TN. Bulging fontanelle after immunization with diphtheria – tetanus – pertussis and diphtheria – tetanus vaccine. J Pediatr 1989; 114: 423 – 425.
21. Brunvond L, Quigsted E, Urdal P et al. vitamin D deficiency and fetal growth. Early Hum Dev 1996; 45: 27 – 33
22. Sandgreen ME, Bronnegard M, Deluca HF. Tissue distribution of the 1,25 dihydroxyvitamin D3 receptor in the male rat. Biochem Biophys Res Commun 1999; 81: 611 – 16

23. Zehnder D, Bland R, Williams MC, et al. Extrarenal expression of 25 – hydroxyvitamind (3) – 1 – alpha – hydroxylase. J Clin Endocrin Metab 2001; 86: 888 – 94
24. Zafer B. The relationship of hypocalcemic convulsions related to nutritional rickets with age, gender, season and serum phosphorus levels. Neurosciences 2007. 12: 302-305
25. Yager TY, Hartfield DS. Neurologic manifestations of iron deficiency in childhood. Pediatr Neurol 2002;27:85-92
26. Henry M, Driscoll MC, Miller M et al. Pseudotumor cerebri in children with sickle cell disease: A case report series. Pediatrics 2004;113: e265-e269
27. Jeng MR, Rieman M, Bhakta M et al Psudotumor cerebri in two adolescents with acquired aplastic anemia. J Pediatr Hematol Oncol 2002; 24: 765-768
28. Tugal O, Jacobson R, Berezin S et al. Recurrent benign intracranial hypertension due to iron deficiency anemia. Case report and review of the literature. Am J Pediatr Hematol Oncol 1994;16:266-270.