Case Reports

Hyperphosphatasemia in an adult

Clinical, conventional roentgenographic, and CT findings

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ABSTRACT

تصف هذه الدراسة سيدة سعودية قصيرة القامة، وصماء، وتبلغ من العمر 47 عاماً. لقد كانت تشكو من عدم القدرة على المشي، كما أنها تشكو من وجود تشوهات منتشرة في الجهاز الهيكلي العظمي، وتضخم متزايد في الجمجمة. أظهرت الفحوص المخبرية ارتفاعاً ملحوظاً في مستويات أنزيم الفوسفاتيز القلوي. وكانت الصور الشعاعية للهيكل العظمي متماشية مع تلك المشاهدة عند مرضى فرط الفوسفاتيز القلوي. إلا أن التصوير الطبقي المحوري للجمجمة قد أظهر تغيرات كبيرة في عظام الجمجمة وذلك بشكل لم تتم دراسته مسبقاً. نستعرض في هذا المقال الآفات المختلفة المتعلقة بارتفاع الفوسفاتيز القلوي والتي يرافقها أو لا يرافقها تغيرات عظمية.

A 47-year-old Saudi deaf lady with short stature presented being unable to walk. She had long standing diffuse skeletal deformities, and progressive head enlargement. She had markedly elevated serum alkaline phosphatase. The radiographic changes were those of hyperphosphatasemia, and the CT scanning of the skull, which was not studied before, further elicited the extensive calvarial and basilar changes. The various entities of hyperphosphatasemia with and without bony changes are reviewed.

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Hyperphosphatasemia is a rare disease of infancy and childhood, which could present as isolated and transient, or inherited and persistent, with or without a disease. Characteristic bone dysplasia usually occurs in this latter form. Cases of hyperphosphatasemia in adults have been reported previously[1,2] with systemic, generalized, and symmetrical distribution of the bone lesions distinguishing it from Paget's disease, which is the characteristic form of hyperphosphatasemia with bone dysplasia, classically occurring as a solitary lesion or occasionally as multifocal lesions in adults. A new case of inherited hyperphosphatasemia in an adult with generalized and symmetrical severe bony changes is presented, in which the skull and the basilar changes in particular are more extensively studied than previously reported. Our objective in presenting this case is to highlight the role of different imaging modalities in the diagnosis of this rare disease entity, and disclose the cause of an associated deafness, blindness, or even hydrocephalus.

Case Report. A 47-year-old Saudi lady presented to the hospital unable to walk, with back pain and progressive head enlargement. She is of short stature, with diffuse bone deformities since childhood, and deafness developed 20 years ago. She was treated several times as a case of osteomalacia. She denied a family history of similar problems. The physical examination revealed a short stature, obese lady with macrocephaly and a mixed type of hearing loss. Dorsal kyphosis, and severe bowing of the long bones with some restriction of movement of almost all major lower limbs joints were also noted. There was no evidence of endocrine or renal disease. The relevant biochemical results were as follows: serum calcium 8.7mg/dl (8.5-10.5mg/dl); serum phosphorous 2.9mg/dl (2.5-4.5mg/dl); serum alkaline phosphatase was markedly elevated on several occasions ranging between 1648-1976IU/L (30-85IU/L). A skeletal x-ray survey revealed severe modeling deformities with generalized osteopenic

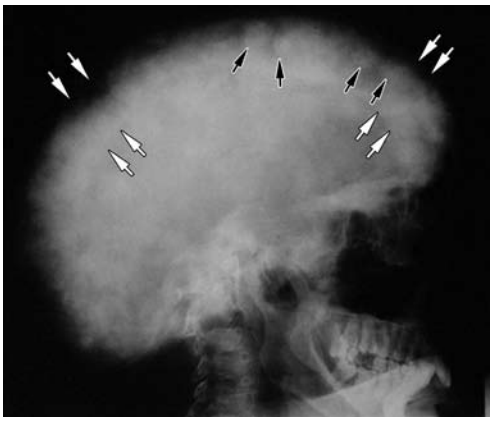

Figure 1 - Lateral view of skull demonstrates marked calvarial thickening (white arrows) and scattered patches of increased density giving the "cotton wool" appearance (black arrows). There is also basilar invagination. Note the spared mandible and upper cervical vertebrae.

bone changes. The skull x-ray showed marked calvarial and basal thickening with patches of increased density scattered throughout the skull giving a "cotton wool" appearance. Basilar invagination was present as well. The facial bones were relatively spared and the mandible appeared normal (**Figure 1**). The brain CT results showed the presence of mild ventricular dilatation, and the bone window clearly demonstrated the extensive calvarial thickening of the diploe with dense bony islands seen scattered within it giving the "woven bone" appearances (**Figures 2a & b**). The caudal images demonstrate involvement of petrous bone with subsequent encroachment of the auditory canal as well as the presence of basilar invagination (**Figures 3a & b**). The pelvic view showed generalized osteopenia with severe deformity and bilateral protrusio acetabuli. This also showed bowing of the proximal shaft of the right

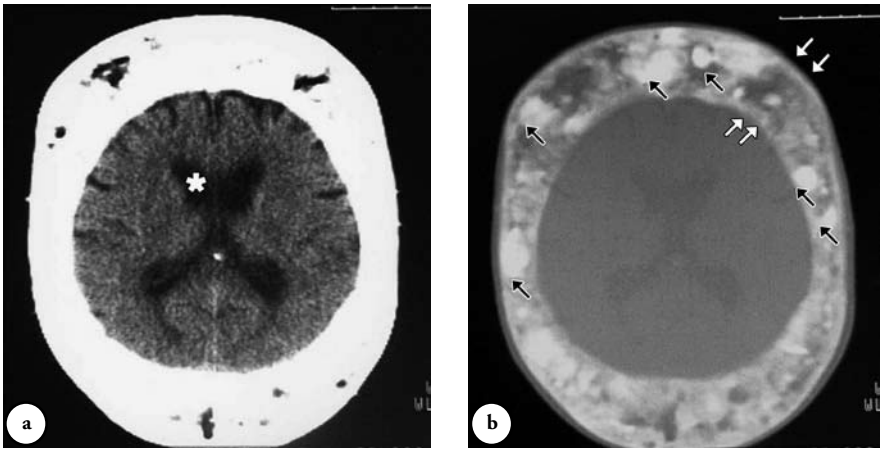

Figure 2 - Computed tomography scan of brain showing: **a**) mild degree of ventricular dilatation (*) with normal brain parenchyma bone window **b**) clarify the calvarial thickening (white arrows), and scattered bone islands (black arrows).

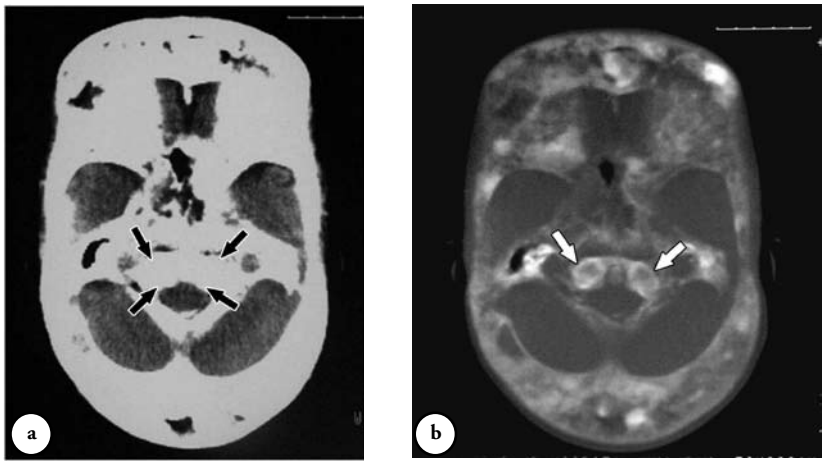

Figure 3 - Computed tomography scan of the brain at a more caudal level: **a** & **b**) demonstrating the basilar invagination (black arrows in **a** and white arrows in **b**), and the marked thickening of the bone with intervening dense bone islands and areas of decreased density (osteoid tissue) giving the woven bone appearance.

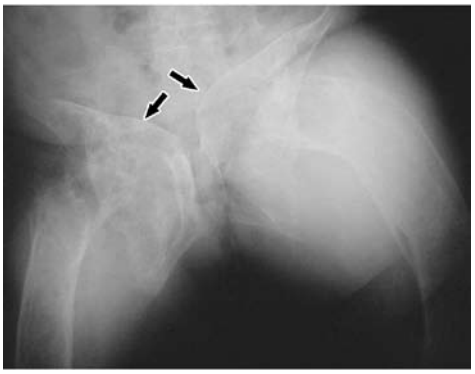

Figure 4 - Antero-posterior view of the pelvis. There is marked osteopenia and deformity of the pelvis with bilateral protrusio acetabuli (black arrows). Note bowing of proximal portion of right femur, and reduction of the heights of the lower lumbar vertebral bodies.

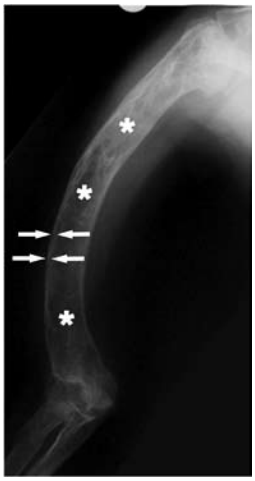

Figure 5 - Antero-posterior view of the long tubular bones of the left humerus. Note the thickened, widened medullary cavity (*) with thick trabeculae and cyst-like intramedullary changes as well as loose lamellar cortex (white arrows).

femur (**Figure 4**). The long tubular bones demonstrated the cylindrical modeling deformities, thickened and coarsened trabeculae, a widened medullary cavity with cyst-like lucencies within it, and a loose lamellar cortex (**Figure 5**).

Discussion. Hyperphosphatasemia indicates increased activity of serum alkaline phosphatase. This could present as an isolated and transient phenomenon in infants,[3,4] or as inherited and persistent with or without a disease.[5,6] Cases of inherited and persistent disorder, characterized by non-endocrine, non-renal dysplastic bone changes with a high serum alkaline phosphatase but normocalcemia and normophosphatemia, have been reported under a plethora of names due to their varied clinical and radiological presentations such as hyperostosis corticalis deformans juvenilis, fragile bones with macrocranium, familial osteoectasia with macrocranium, osteoectasia with hyperphosphatasia, and osteochalasia desmalis familiars. However, the recently reported cases have been described as chronic and/or familial hyperphosphatasemia, hereditary or congenital hyperphosphatasia, chronic idiopathic hyperphosphatasia, and juvenile Paget's disease. It is also important to differentiate this disorder from the syndrome of hyperostosis and hyperphosphatemia,[7,8] in which there is a constant elevation of serum phosphate in the absence of renal or endocrine disorders. The head enlargement with the radiographic calvarial thickening has been reported to be the most common initial finding of hyperphosphatasemia. However, 2 cases have been reported in which the radiographic changes in the long bones have preceded that seen in the skull.[9] Moreover, Lancu et al[10] reviewed the radiographic findings in 20 cases of this condition and found characteristic calvarial thickening in 19 cases, but no changes in the base of skull were seen except for one of the 2 siblings he reported.[10]

In the reported adult case by Einhorn et al,[2] the skull radiographs showed calvarial thickening with sclerosis including the sinuses, but sparing the mandible. These extensive calvarial changes with the relative sparing or less involvement of the skull base are consistent with the basic disorder of this disease, a disorder of growing membranous bone in which primitive fibrous bone fails to mature into compact Haversian bone with concurrent over-production and over-destruction of bone and collagen, which usually presents in the first 2 years of life. In the case we present, the skull changes involve both membranous (calvarial) and endochondral (base of skull) bones, and the CT of the head elicited these changes more clearly in the basilar changes, which included the basilar invagination and bone thickening that extends to the petrous and facial bones. We do believe that the basilar changes with involvement of the petrous bone are responsible for the deafness in this patient by the encroachment they caused upon the middle ear cavity and internal auditory meatus, which has been reported also by Muntaner et al.[7] The basilar changes could be also contemplated for the deficient visual and auditory acuity, which have been noted in previous reports. Also, the brain CT scan results in these cases may disclose the presence of an occult, gradually developing obstructive hydrocephalus due to the basilar invagination, an added factor of macrocrania.

In conclusion, brain CT or MRI, or both are essential in investigating patients with hyperphosphatasemia. Skeletal changes may disclose the cause of an associated deafness, blindness, or even hydrocephalus.

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Case Reports

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