Case Report

Skeletal fluorosis with progressive quadriparesis U.M.N. type, non compressive myelopathy, chronic kidney disease and secondary hyperparathyroidism and hypothyroidism - A case report

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Abstract

Endemic fluorosis leads to dental fluorosis, skeletal fluorosis and visceral fluorosis. This case described about the crippling skeletal fluorosis with neurological manifestations in the form of myelopathy, due to exposure to high fluoride level in water for many years. The complications of fluoride deposition in bones resulted in generalised sclerosis, osteophytosis, with narrowing of inter vertebral disc spaces in vertebral column. In this case the skeletal fluorosis leads to severe spastic quadriparesis. This case had features of visceral fluorosis; the affected organs include thyroid gland with hypothyroidism, parathyroid gland with secondary hyperparathyroidism, pancreas with intra pancreatic calcification and the kidneys with chronic kidney disease.

Key words

Skeletal fluorosis, Non-compressive myelopathy, Quadriparesis UMN type, Chronic kidney disease (CKD), Secondary hyper parathyroidism, Hypothyroidism, Pancreatic calcification.

Introduction

Fluorine, a gaseous element is a halogen which being the most electronegative and reactive of all the elements does not occur in free form in the nature. Excessive ingestion of fluoride through water, food and dust cause acute intoxication and chronic debilitating disease called Fluorosis. The word fluorosis was first coined and used by Cristiani and Gautier in 1925.

Fluorosis is of three type i.e. dental, skeletal and visceral fluorosis. Neurological manifestations occur late in skeletal fluorosis [1]. Clinical features due to mechanical compression of spinal cord and nerve roots by osteophytosis and vertebral column compression. These result in radiculo- myelopathy, CVAs, peripheral neuropathies and cranial nerve lesions.

Iodine Deficiency Disorders (IDD) and fluorosis are the two most prevalent endemic diseases which coexist in certain regions in India [2]. As early as 1928, Stocks observed that children consuming well water in the village of Somerset, England exhibited both goiter and mottled enamel (dental fluorosis). Besides dental fluorosis and cretinism, children in endemic fluorosis areas of India often have low IQ, deaf mutism, knock-knee and bow-legs [3]. Fluorine and Iodine – both belong to the Halogen group. Fluorine is more reactive than Chlorine > Bromine > Iodine. Both occur as soluble salts in water and are ingested. Fluorine is competitive to Iodine in chemical reactions. Decreased iodine causes Goitre, Fluoride excess competitively inhibits I_2 availability to thyroid and causes hypofunction. In our country both deficiency of I_2 and excess of F_2 are endemic (endemic goitre and endemic fluorosis).

High fluoride ingestion has a definite relation with increased calcitonin concentration, which may be the major cause of hypocalcemia in fluorotic patients, which may further leads to the increased parathyroid function i.e. raised PTH levels in the serum to maintain serum calcium levels and may have a role in toxic manifestations of clinical and skeletal fluorosis [4].

Fluoride has been suggested to exert an effect on the calcium homeostatic system leading to secondary hyperparathyroidism and changes in parathyroid glandular structure and hormone secretion. Glandular hyperplasia has likewise been observed in humans living in areas of endemic fluorosis in India [5].

Kidney damage to tubular function and structure, and reduction in glomerular filtration rate occurred in residents of endemic fluoride areas [6] and anecdotal cases of fluoride intoxication [7] suggested a causal relationship between fluoride intake and renal failure.

Case report

A 45 year male patient was admitted to the hospital with complaints of low back ache, weakness of all four limbs, and difficulty in walking for the past 2 years. Low backache was insidious in onset gradually progressed over 2 years. Weakness of Proximal group of muscles in lower limbs and distal group in upper limbs was present. There was stiffness of all the limbs and spine leading to difficulty in walking and sleeping in supine position. Sensory system and autonomic system were not involved.

On examination, patient was thin built with kyphosis and exostosis. Neurological examination revealed normal higher mental functions, Cranial examination was normal, Sensory system was normal, Motor system examination - bulk of muscles normal in both

upper limbs and lower limb, with increased tone and Power was 4/5 in both upper limbs, 3/5 in both lower limbs. Deep tendon reflexes- Biceps 3+, Triceps 2+, Supinator 2+ in both UL. Knee jerk 3+, Ankle jerk 1+ in both lower limbs. Superficial reflexes were normal but bilateral plantars were up going. Pt had spastic gait with no abnormal body movements. Hoffman reflex was positive, Wartenberg's sign was positive. Spine showed kyphosis. Examination of cardio vascular system, respiratory system, abdomen were normal.

Laboratory investigations

Complete Blood Picture; Hb-9.8g/dl, Total WBC count 6000 cells/mm3, Differential Count – Neutrophils 64%, Eosinophils 02%, Basophils 00%, Lymphocytes 32%, Monocytes 02%, Platelet count 2.2 lakhs/mm^3. Peripheral smear showed normocytic normochromic picture, CUE; ALB-NIL, Sugar-NIL, Serum creatine - 2.2 mg/dl , Serum Calcium - 7.0 mg/dl , Serum phosphorus - 2.8 mg/dl, Serum alkaline phosphatase - 912 IU/ml, Thyroid profile - TSH - 150 mIU/ml, PTH - 321 ng/lt , RA factor - negative, HLA B - 27 was negative. Chest x-ray showed increased bone density, widening of ribs (**Figure - 1**). X-ray cervical spine showed - degenerative changes, osteophytes, increased bone density narrowed disc space –C 3 and C 4 (**Figure - 2**). X-ray Dorso lumbar spine AP/LAT View showed P.L. Ligamentum calcification, pancreatic calcification (**Figure - 3**). X-ray forearm showed inter osseous membrane calcification (**Figure - 4**). X-ray pelvis showed – ligamentum calcification, calcification of left lesser trochanter (**Figure - 5**). Ultrasonography – both kidneys are small, left kidney 7.1x3.8 cm, right kidney 7.1x3.2 cm. CT Scan Abdomen revealed generalised sclerosis of bones and increased density, calcific and atrophic pancreas (**Figure - 6**). Pancreatic calcification was present in PA view of MRI (**Figure - 7**), and Pancreatic calcification was also evident in lateral view (**Figure - 8**).

Figure – 1: Chest X-Ray shows increased bone density, widening of ribs.

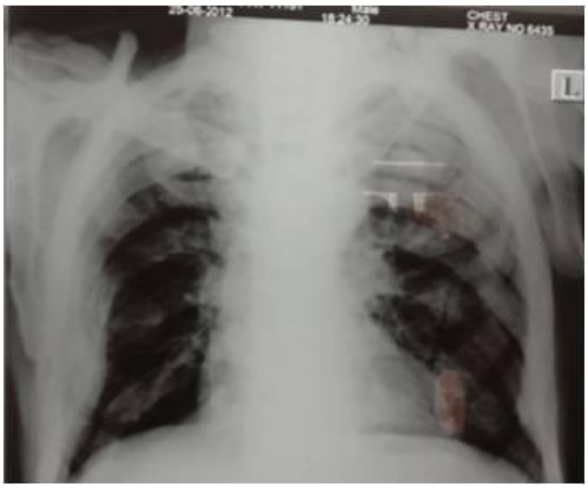


Figure – 2: X-Ray cervical spine shows degenerative changes, osteophytes, increased bone density, narrowed disc space – C3 and C4.

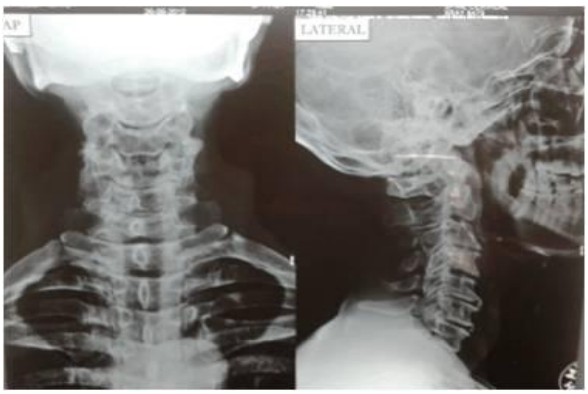


Figure – 3: X-ray Dorso lumbar spine AP/LAT View shows P.L. ligamentum calcification, pancreatic calcification.

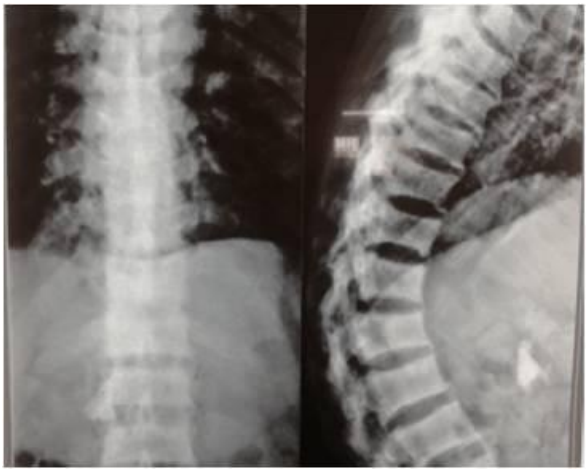


Figure – 4: X-ray forearm shows interosseous membrane calcification.

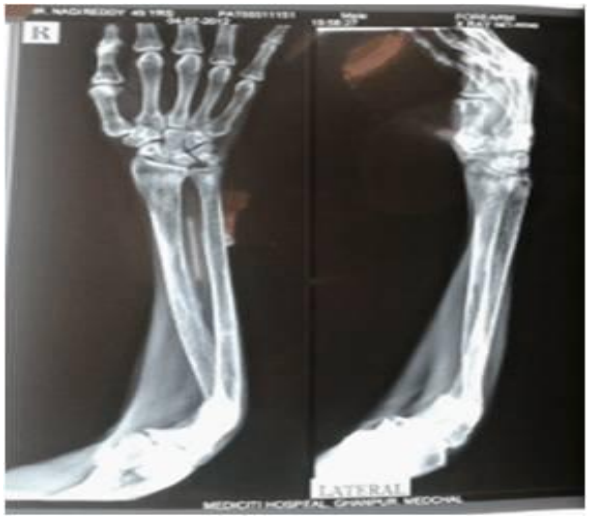


Figure – 5: X-Ray Pelvis Shows – Ligamentum calcification, calcification of left lesser trochanter, looser zones present.

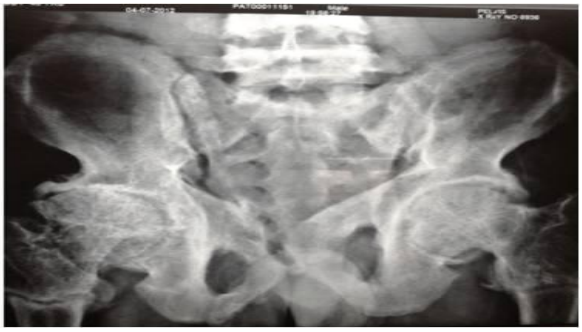


Figure – 6: CT Scan Abdomen shows generalised sclerosis of bones and increased density, calcific and atrophic pancreas.

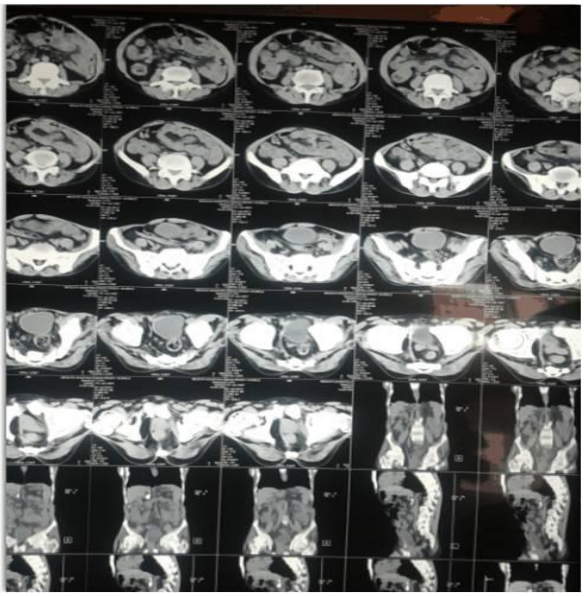


Figure – 7: CT scan - Pancreatic calcification.

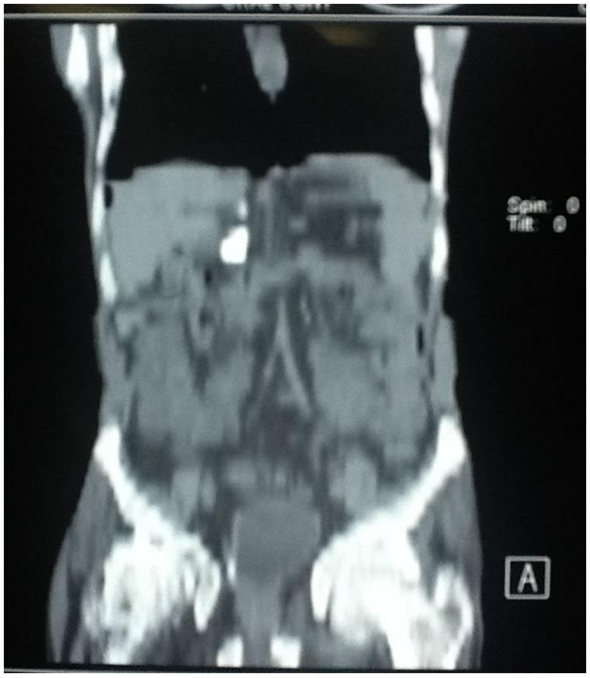
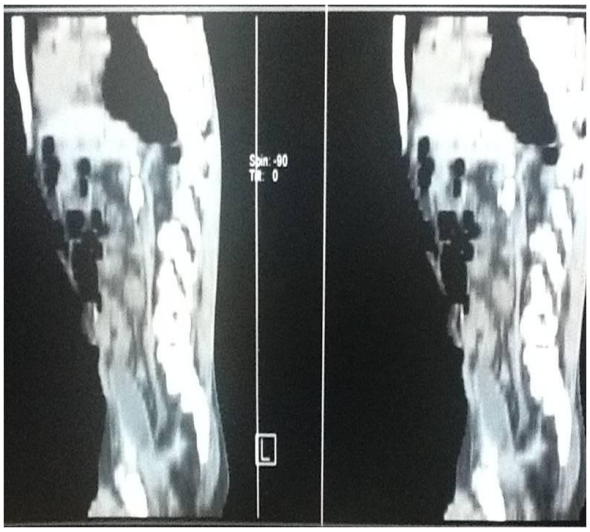


Figure – 8: CT scan shows pancreatic calcification lateral view.



Discussion

Chronic fluorine intoxication in people who live in endemic areas while their permanent teeth are erupting produces the well known sign of mottling of the enamel, the most distinctive features of chronic endemic fluorosis are the skeletal changes, which are responsible for most of the symptoms [8]. The incidence of skeletal changes, however, is very rare as compared to mottling (Murray and Wilson 1942). The various

skeletal changes in fluorosis are best described under various headings. Macroscopical changes - The irregularity of the bony contours stems from the irregular deposition of fluorides and is worst at the attachments of ligaments, muscles, tendons and fascia. Bony excrescences are usually found on the medial surface of the tibia, on the olecranon process and at the lower ends of radius and ulna. The greatest changes occur in the vertebral column [9].

Radiological features are diagnostic. The earliest changes are seen in the spine and pelvis; later the ribs, skull and bones of the extremities may be involved in that order. In the radiographs the bones show diffuse sclerosis-with many osteophytes and a characteristic whiteness like marble. Roholm (1937) divided the radiological changes into three phases:

Firstly the spinal column and pelvis become roughened, with blurring of the trabeculae;
Secondly the trabeculae merge together and the bone structure is blurred, and
T**hirdly** the bones have the appearance of white marble, which is most marked in the central bones, while those of the extremities show the irregular periosteal thickening and calcification of the ligamentous and muscular attachments.

Deformities - Fluorine intoxication at the rate of about 20 milligrams daily for over ten years leads to crippling deformities, including kyphosis, flexion deformity of the trunk, hips and knees. Chemical composition - Roholm (1937) believed that the fluorides were probably deposited in the form of calcium fluoride in the calcium phosphate of the bones; however, the work of Weidmann, Weatherell and Whitehead (1959) has shown a decrease of carbonate and an increase of magnesium in the exostotic bone [10]. This suggests a replacement of the carbonate or bicarbonate groups in the bone salts and a precipitation of magnesium fluoride upon- or within-the bone matrix. These changes are mediated by altered enzymic reactions, but the exact mechanism by which fluorine exerts its deleterious effects is not known.

Fluorosis and hypothyroidism

Fluoride and iodine are both halogens. The fluoride, the negative ion of the element fluorine easily displaces iodine in the body because it is much lighter and therefore more reactive. In fact the activity of any one of the halogens is inversely proportion to its atomic weight. In other words, one halogen can displace another one of a higher atomic weight but cannot displace one of lower weight thereby, results fluoride- thyroid-iodine antagonism which in turn lead to interference with iodine uptake. The fluoride is a universal G-protein activator/inhibitor. The stimulation of certain G-proteins occurs due to the toxic effects of fluoride, which has the effects of switching off the uptake into the cell of the active thyroid hormone. The thyroid control mechanism is compromised. The TSH output from pituitary gland is inhibited by fluoride, thus reducing thyroid output from thyroid glands. Fluoride competes for the receptor sites on the thyroid gland which respond to TSH; so that this hormone reaches the thyroid gland and so fewer hormone is manufactured [11]. There is significant relationship between serum fluoride and TSH, serum fluoride and FT_3/FT_4, TSH and FT_3/FT_4 [11]. High fluoride exposure can cause functional abnormalities of thyroid and different degrees of dental fluorosis could be observed with significant deviation in the serum thyroid hormone levels [12].

Fluorosis - Secondary hyperparathyroidism

Earlier studies [13] reported that fluoride and PTH have a definite role in bone metabolism. Studies have documented that ingestion of fluoride causes decrease in the ionic calcium [14]. Schwartz P, et al. observed significantly elevated PTH concentration in the presence of normal, total and ionized calcium concentrations. The hypocalcemia caused by high fluoride ingestion leads to changes in internal milieu of the body to maintain the calcium levels and

causes secondary hyperparathyroidism. Lowering of blood ionized calcium by an amount as low as 0.02 mmol/l within 30 min elicited an immediate large, transient peak release of PTH amounting to 6-16 times the baseline concentration [15].

This secondary hyperparathyroidism results in two effects,

(a) Maintenance of serum calcium: An increase in serum calcium concentration is always the consequence of at least one of the following events: 1. an increase in the net calcium input in extracellular fluid, 2. a decrease in glomerular filtration rate, and 3. an increase in the tubular re-absorption of the filtered calcium. The parathyroid helps in maintaining the calcium balance mainly by inducing tubular calcium reabsorption and mobilization from bone [16].

(b) An increased bone resorption, defective bone formation and defective collagen (ground substance) formation.

In conclusion, high fluoride ingestion causes secondary hyperparathyroidism, which may be responsible for maintaining serum calcium levels and may play a role in causing toxic manifestations of fluorosis.

Fluorosis-Chronic kidney disease

There are no known adverse effects associated with the ingestion of relatively low levels of fluoride (1–2 ppm in drinking water) on a chronic basis. However, the actual levels of intake have to include fluoride not only in water, but also in the diet and in other fluoride containing products. Patients with chronic renal insufficiency are at an increased risk of chronic fluoride toxicity. Patients with reduced glomerular filtration rates have a decreased ability to excrete fluoride in the urine. These patients may develop skeletal fluorosis even at 1 ppm fluoride in the drinking water [17]. Whether or not the body burden of fluoride may further damage the diseased kidneys is unknown. The National Kidney Foundation in its 'Position Paper on Fluoride - 1980' as well as the Kidney Health Australia express concern about fluoride retention in kidney patients. They caution physicians to monitor the fluoride intake of patients with advanced stages of kidney disease.

Children drinking water with more than 2 ppm fluoride were found to have increased levels of NAG and yGT in their urine—both markers of renal tubular damage [18]. The safety margin for exposure to fluoride by renal patients is unknown, measurements of fluoride levels are not routine, the onset of skeletal fluorosis is slow and insidious, clinical symptoms of this skeletal disorder are vague, progression of renal functional decline is multi-factorial and physicians are unaware of side effects of fluoride on kidneys or bone.

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