Special Article

Chronic fluorosis: The disease and its anaesthetic implications

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ABSTRACT

Chronic fluorosis is a widespread disease-related to the ingestion of high levels of fluoride through water and food. Prolonged ingestion of fluoride adversely affects the teeth, bones and other organs and alters their anatomy and physiology. Fluoride excess is a risk factor in cardiovascular disease and other major diseases, including hypothyroidism, diabetes and obesity. Although anaesthesiologists may be aware of its skeletal and dental manifestations, other systemic manifestations, some of which may impact anaesthetic management are relatively unknown. Keeping this in mind, the topic of chronic fluorosis was hand searched from textbooks, scientific journals and electronically through Google, PubMed and other scientific databases. This article concentrates on the effect of chronic fluorosis on various organ systems, its clinical features, diagnosis and the anaesthetic implications of the disease.

Key words: Airway, cardiovascular system, chronic fluorosis, endocrine system, skeleton, spinal anaesthesia, teeth

INTRODUCTION

Fluorine is the 13th most abundant element in the earth's crust.[1] Prolonged ingestion of fluoride in excess of the daily requirement is associated, initially with dental fluorosis and later by skeletal fluorosis.[2]

EPIDEMIOLOGY (INCIDENCE, PREVALENCE AND DISTRIBUTION)

Endemic skeletal fluorosis is widely prevalent in India and is a major public health problem in nearly 25 countries in Asia and Africa.[3,4] Nearly 6 million people in India are disabled because of fluorosis.[3] The most seriously affected endemic skeletal fluorosis states in India are Andhra Pradesh, Punjab, Haryana, Rajasthan, Gujarat, Uttar Pradesh, Bihar, Tamil Nadu, Kerala, Karnataka and Maharashtra.[5] Skeletal fluorosis is more common among the poor in endemic areas.[6] Juvenile skeletal fluorosis has been found to be more common in males than in females.[7] Chronic Fluorosis is often found in volcanic regions rich in fluoride.[8]

PHARMACOKINETICS AND PHARMACODYNAMICS OF FLUORIDE

Fluoride is predominantly absorbed through the gastrointestinal and respiratory tracts with negligible dermal absorption. Approximately 50% of the daily fluoride intake is deposited in calcified tissue that includes teeth and bone. The highest tissue concentrations occur in the skeleton and the kidney. In adults, only about 10% of the ingested fluoride is deposited in bone, whereas in growing children >50% may be incorporated in bone. Fluoride is excreted largely by the kidneys with 40–60% of the daily fluoride excreted in the urine showing an elimination half-life of about 5 h.[9] The main mechanism of skeletal fluorosis is the fluoride incorporation into the bone hydroxy-apatite, altering the size and structure of its crystals. The fluoroapatite formed decreases the mechanical competence of the bone, resulting in abnormal structure and poor quality of bone with increased risk of fractures.[5]

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PREDISPOSING AND CAUSAL FACTORS FOR CHRONIC FLUOROSIS

Prolonged ingestion of fluoride through drinking water, in excess of the daily requirement of 1.5 mg/L as the upper limit (as set by the WHO) is associated with dental and skeletal fluorosis.[2] Signs of skeletal fluorosis become evident on consumption of 8–10 ppm of fluoride in drinking water for approximately 10 years or more.[9] Groundwater at many places is rich in fluoride and large numbers of Indians rely on groundwater for drinking purposes. Hence, fluorosis is an important public health problem in India.[2] Intake through beverages is also significant.[5] Severe juvenile skeletal fluorosisis is associated with inadequate calcium in the diet.[7] Intake of large quantities of tea made from indigenously grown tea (with high fluoride content) appears to have an association with increased risk of juvenile skeletal fluorosis.[7,10] Prolonged use and ingestion of fluoride containing products such as fluoridated toothpastes, topical gels, and mouth washes can lead to chronic fluorosis.[9] Prolonged inhalation of fluoride dusts from atmosphere that arise from volcanic gases, industry waste and burning of coal fires can also lead to chronic fluorosis.[9]

EFFECT OF CHRONIC FLUOROSIS ON VARIOUS ORGAN SYSTEMS AND ANAESTHETIC IMPLICATIONS

Dental fluorosis

Fluorosis of the dental enamel occurs when excess fluoride is ingested during the first seven years of life. It is characterised by mottling of dental enamel that is one of the first and earliest signs of chronic fluorine intoxication.[2,6] On prolonged exposure to fluoride, the teeth become hard and brittle. Discrete or confluent pitting occurs in the teeth in the severe stages.[2] The tooth surface index of fluorosis has been used to assess the severity and prevalence of dental fluorosis.[9]

Skeletal system

Exposure to very high fluoride over a prolonged period results in acute to chronic skeletal fluorosis.[2] Vague, diffuse aches, muscle weakness, chronic fatigue and stiffness of joints with decreased range of motion are common initial symptoms.[2,11] These symptoms may be dismissed as functional but may, in fact, be early signs of fluoride damage to tendinous insertions and ligaments as well as joint capsules.[12] During later stages, calcification of the bones takes place, osteoporosis in long bones and symptoms of osteosclerosis where the bones become denser and develop abnormal crystalline structure develop.[2] In advanced stages, bones and joints become weak rendering movement difficult and painful. Fusion of vertebrae is observed in many areas of the spine.[2] The greatest changes are observed in the spine, particularly in the cervical region.[6] Calcification of the neural arch, narrowing of the spinal canal and intervertebral foramina occurs[5] in severe cases. Kyphosis with limited spinal mobility, flexion contracture of lower extremities and restricted chest wall expansion occur.[11] "Poker back" spine (kyphosis) is a late manifestation of skeletal fluorosis wherein the entire spine becomes one continuous column of bone.[4,13] In the final stage, the patient is left crippled.[14]

Neurological manifestations of fluorosis

There is no evidence of direct neurotoxicity of fluorine. However, in severe skeletal fluorosis, *de-novo* neurological complications can occur.[5] These are primarily from mechanical compression of the spinal cord and nerve roots resulting from the osteophytosis, gross reduction of the antero-posterior diameter of the spinal canal and intervertebral foramina, sclerosed vertebral column and ossified ligaments. The cervical cord is affected earlier than the dorsal cord. Though the lumbar spine is the first to exhibit skeletal changes, compression of cauda equina can rarely occur.[2] The progressive cervical radiculomyelopathy of fluorosis is characterized by marked wasting and atrophy of the small muscles of the hands, spastic paraparesis or quadriparesis often in flexion.[15] Widespread fasciculations can occur and smaller muscle atrophies can occur in the lower limbs.[15] Incontinence of urine, flexor spasms and signs of long tract involvement are seen. The patient will be in a bedridden state.[15]

The endocrine system

The thyroid gland has a strong capacity for absorbing and accumulating fluoride. Fluoride can induce structural changes and dysfunctions in the thyroid gland.[16] Hypothyroidism and anaemia have occurred with fluorosis in dairy cattle.[17] In humans, effects on thyroid function are seen with fluoride exposures of 0.05–0.13 mg/kg/day when iodine intake is adequate, and at lower (0.01–0.03 mg/kg/day) levels when iodine intake is inadequate.[18] When calcium supply is inadequate, the absorbed fluoride exacerbates this by binding with calcium in the body thus causing ionic calcium to decrease.[7] Thus, fluoride directly or indirectly stimulates the parathyroid glands causing secondary hyperparathyroidism leading to bone loss.[19]

Secondary hyperparathyroidism can contribute to a number of diseases like osteoporosis, hypertension, arteriosclerosis, degenerative neurological disease, diabetes mellitus, some forms of muscular dystrophy and colorectal carcinoma.[20] Fluoride is a risk factor in the development of obesity and diabetes.[21] The Russian Academy of Sciences has published a review on how fluoride induces endoplasmic reticulum (ER) stress. ER stress plays a role in the pathogenesis of type II diabetes mellitus, insulin resistance and obesity.[22,23] Impaired glucose tolerance occurs with fluoride concentrations in drinking water of 4 mg/L or less.[18]

The pineal gland is a major target for fluoride accumulation in humans. Studies have found that calcified deposits in the pineal gland are associated with decreased numbers of functioning pinealocytes and reduced melatonin production. This can lead to accelerated sexual maturation and early puberty in females.[24,25] The reduced melatonin production and consequent reduction in chronobiosis can lead to impairments in the sleep-wake cycle.[26]

Cardiovascular system

Fluoride exposure causes oxidative stress that promotes inflammatory mechanisms, atherosclerosis, vascular stiffness and myocardial cell damage. Oxidative stress and inflammation are important mechanisms involved during ischemic stroke.[27,28] Fluoride accumulates in aortic vascular walls and a significant correlation exists between fluoride uptake and coronary calcification.[29] Bradycardia has been reported among phosphate workers suffering from fluorosis.[30] A study of electrocardiograms of dental fluorosis sufferers indicated that 29.5% had abnormal heart rhythms, and 12.8% had reduced myocardial function.[31] Another study showed that 50–73% of patients with skeletal fluorosis had abnormal electrocardiograms with a clear demonstration of the increase in abnormal heart rhythms and signs of myocardial damage.[30] Hypothyroidism, diabetes mellitus and obesity may also contribute to the development of ischemic heart disease.[32]

Brain

Fluoride has adverse effects on the brain, especially in combination with aluminium.[18] Rats chronically exposed to fluoride showed a number of histopathological changes in the brain including demyelination and a decrease in the number of Purkinje cells.[33] A study showed damage to hippocampus and histopathological changes similar to those traditionally associated with Alzheimer's disease when chronically exposed to fluoride.[18] Exposure of children to high levels of fluoride may carry the risk of impaired development of intelligence.[34]

Gastrointestinal system

Several functional and structural dose and time related changes occur in the gastric mucosa with fluoride ingestion. The fluxes of water, sodium, potassium, protons and other ions increase sharply. The mucus secretion increases followed by patchy or widespread loss of the mucus layer, hypaeremia, oedema, and haemorrhage.[9] Rupture of the stomach lining may also be seen.[35]

Renal, and hepatic effects

The liver is one of the target organs attacked by high amounts of fluoride in drinking water.[36] Abnormal function, metabolism and histopathological changes have been found in the liver of sheep, calves, rats and mice by several research groups.[37] Fluoride toxicity to nephrons causes pathological changes in the glomeruli and the proximal and distal collecting tubules of experimental animals[38] with less severe effects on the glomerular function than the proximal tubules.[39]

The respiratory system

Animal studies have demonstrated emphysematous changes and lung parenchymal inflammation associated with loss of alveolar architecture in the second generation of animals exposed to fluoride in drinking water.[40]

DIAGNOSIS OF CHRONIC FLUOROSIS

Skeletal Fluorosis should be strongly suspected in any person with features of stiffness, rigidity, restricted movements at the spine and joints, bone and joint pains and who has been residing continuously for >6 months in a fluorosis-endemic area.[5] The clinical investigations for the confirmation of the diagnosis include the following:[4]

- Haemoglobin%: Anaemia due to reduced erythropoietin activity secondary to fluorosis induced osteosclerosis of medullary cavities
- Cerebrospinal fluid analysis: There may be a moderate rise of protein due to fluorotic spinal compression
- Renal function tests: These may show impaired urea clearance, decreased glomerular filtration rate, increased blood urea nitrogen
- Electrophysiological studies:

Nerve conduction studies may show late responses. Nerve conduction velocities may be decreased in case of peripheral nerve entrapment. Electromyographic studies may show neurogenic atrophy.

- Fluoride level estimation: Urine fluorides: They are the best indicator of fluoride intake.[4] There is a linear relation between urinary fluoride levels and fluoride intake. Since fluoride excretion is not constant throughout the day, 24 h samples of urine are more reliable than random or morning samples.[3] In normal individuals, urinary fluorides fluctuate widely between 0.1 and 2.0 ppm with an average of 0.4 ppm when the fluoride content of drinking water is 0.3 ppm.[3] In cases of skeletal fluorosis, values will be >0.4 ppm.[4]
- Serum fluoride levels: Normal values in non-endemic regions range from 0.002 to 0.008 mg/dl. Patients with skeletal fluorosis show high levels up to 0.02–0.19 mg/dl.[3,4] Bone fluoride estimation, bone biopsy and scintigraphic studies may help to support the diagnosis of skeletal fluorosis.[3,4]
- Pulmonary function tests: Due to involvement of the rib cage, fluorosis causes restrictive lung disease with reduction in vital capacity and forced expiratory volume in 1 s/forced vital capacity ratios >85%.[4]
- Radiology: Osteosclerosis, hypercementosis, and periapical root absorption may be seen in the teeth. The incidence of root resorption is highest in the lower first permanent molars.[6] The most pronounced changes are seen in the vertebral column with marked osteosclerosis and irregular osteophyte formation resulting in beak-like lipping and a chalky-white ground-glass appearance.[6] Calcification of the interosseous membrane of the forearm is a radiographic sign of fluorosis.[3]
- Computed tomography: This can help to visualise alterations in spinal canal, indentations of epidural space and calcified ligaments.[3,4]
- Magnetic resonance imaging: This can show presence of pseudomeningocele and spinal cord changes due to prolonged compression and secondary vascular compromise.[3,4]

DIFFERENTIAL DIAGNOSIS OF CHRONIC FLUOROSIS

Some of the clinical symptoms of chronic skeletal fluorosis mimic arthritis and hence the first two clinical phases of skeletal fluorosis could be easily misdiagnosed.[41] The only characteristic feature in skeletal fluorosis is multiple joint involvement.[42] Skeletal fluorosis can easily be mistaken for rheumatoid arthritis, osteoarthritis or seronegative spondyloarthropathy.[43] There is a lot of clinical similarity between neurofluorosis and cervical spondylosis.[15]

PERI-OPERATIVE AND ANAESTHETIC CONCERNS IN CHRONIC FLUOROSIS

- Patients with fluorosis may manifest difficulty in intubation during anaesthesia because of rigid cervical spine with limited motion at the intervertebral joints.[3,44,45]
- There could be difficulty in positioning of the patient during surgery because of limitation of movement at the intervertebral joints[3,44]
- There is a high risk of postoperative respiratory complications because of restricted chest movement and reduced vital capacity.[3,44,45]
- There could be problems associated with anaesthesia and surgery in the sitting/prone position for cervical laminectomy.[45]; limited motion at the lumbo-thoracic intervertebral joints in the patient of skeletal fluorosis might render subarachnoid, epidural, intercostal or paravertebral blocks[44] very difficult
- Endocrine problems like decreased thyroid function, impaired glucose tolerance, type II diabetes mellitus and obesity produced by chronic fluorosis have to be borne in mind.[18,21] There is high risk of cervical cord injury during positioning for airway instrumentation, placing neck catheters and surgery.[46] Decreased cervical cord perfusion because of either neck positions that distort the cervical canal or peri-operative hypotension can lead to post-operative neurological deterioration following cervical or non-cervical surgeries.[46] Reduced myocardial function and the possibility of abnormal heart rhythms and coronary arteriosclerosis exists.[30]

Hence, the following points need to be kept in mind while encountering cases of suspected chronic fluorosis:

- Entertain a high suspicion of chronic fluorosis in a patient who complains of neck ache, and generalised skeletal discomfort with associated gastric complaints and hails from areas endemic for fluorosis. A serum fluoride estimation and an X-ray of the spine may help in the diagnosis.

- Preanaesthetic evaluation mandates careful airway evaluation along with the C-spine. Subsequently, appropriate preparations can be made in the operating room for difficult airway management. Screening for endocrine abnormalities like hypothyroidism and diabetes mellitus in the preoperative evaluation is important. Hypothyroidism can lead to adverse peri-operative responses like increased sensitivity to depressant drugs, hypodynamic cardiovascular system, slowed drug metabolism, delayed gastric emptying, hypothermia and hypoglycaemia.[32]
- Cardiological evaluation with an electrocardiogram and an echocardiogram is essential preoperatively to screen for ischaemic heart disease and to determine the cardiovascular risk
- A chest X-ray and pulmonary function tests should be requested to look for restrictive lung disease
- Previous history of difficult lumbar puncture (two to three pricks in the back) may be elicited, as reported by Saxena *et al*.[44] Preoperative X-ray of lumbar spine may be useful to evaluate the possibility of difficult lumbar puncture. Potentially difficult neuraxial block should be anticipated. Use of techniques like C-arm, ultrasonic guidance, paramedian approach and Taylor's approach can be adopted in such cases.[13,47] Successful use of transforaminal sacral approach for spinal anaesthesia has been reported for cases of chronic fluorosis.[13]
- Elective post-operative mechanical ventilation and Intensive Care Unit care may be needed in patients with severe reduction in pulmonary function, especially after major/prolonged surgery
- Care should be taken to avoid excessive neck movements during airway instrumentation/ placing neck catheters/surgery.

SUMMARY

Chronic fluorosis apart from affecting the skeleton and teeth has significant effects on the cardiovascular, respiratory, gastrointestinal, and endocrine function which can have important anaesthetic and peri-operative implications. Anaesthesiologists need to be aware of the multi-system involvement in chronic fluorosis which will favourably impact the peri-operative management of these difficult patients and their outcome.

REFERENCES

1. Paasivarta J. Long term effects of bioaccumulation in ecosystems. In: Beek B, editor. The Handbook of Environmental Chemistry. Berlin: Springer Publications; 2000. p. 201-33.
2. Arlappa N, Aatif IQ, Srinivas R. Fluorosis in India: An overview. Int J Res Dev Health 2013;1:97-102.
3. Reddy DR. Neurology of endemic skeletal fluorosis. Neurol India 2009;57:7-12.
4. Ramakrishna K, Sasikiran NO. Fluorosis-an update. Int J Res Pharm Biomed Sci 2013;4:1084-8.
5. Teotia SP, Teotia M, Singh KP. Highlights of Forty Years of Research on Endemic Skeletal Fluorosis in India. 4th International Workshop on Fluorosis Prevention and Defluoridation of Water. Colombo, Sri Lanka; March 2-6, 2004.
6. Singh A, Vazirani SJ, Jolly SS, Bansal BC. Endemic fluorosis. Postgrad Med J 1962;38:150-6.
7. Jarvis HG, Heslop P, Kisima J, Gray WK, Ndossi G, Maguire A, *et al.* Prevalence and aetiology of juvenile skeletal fluorosis in the south-west of the Hai district, Tanzania – A community-based prevalence and case-control study. Trop Med Int Health 2013;18:222-9.
8. Cinar A, Selcuk M. Effects of Chronic fluorosis on thyroxine, triiodothyronine and protein-bound iodine in cows, Van, Turkey. Fluoride 2005;38:65-8.
9. Pratusha NG, Banji OJ, David B, Ragini M, Pavani B. Fluoride toxicity – A harsh reality. Int Res J Pharm 2011;2:79-85.
10. Izuora K, Twombly JG, Whitford GM, Demertzis J, Pacifici R, Whyte MP. Skeletal fluorosis from brewed tea. J Clin Endocrinol Metab 2011;96:2318-24.
11. Fisher RL, Medcalf TW, Henderson MC. Endemic fluorosis with spinal cord compression. A case report and review. Arch Intern Med 1989;149:697-700.
12. Anand JK, Roberts JT. Chronic fluorine poisoning in man: A review of literature in English (1946-1989) and indications for research. Biomed Pharmacother 1990;44:417-20.
13. Sujay M, Madhavi S, Arvind G, Hasan A, Venugopalan VM. Transforaminal sacral approach for spinal anaesthesia in orthopaedic surgery: A novel approach. Anaesth Essays Res 2014;8:253-5.
14. Brindha K, Elango L. Fluoride in groundwater: Causes, implications and mitigation measures. In: Monroy SD editor. Fluoride Properties, Applications and Environmental Management. New York: Nova Publishers; 2011. p. 111-36.
15. Haimanot RT. Neurological complications of endemic skeletal fluorosis, with special emphasis on radiculo-myelopathy. Paraplegia 1990;28:244-51.
16. Liu GY, Chai CH, Kang SH. Effects of fluoride on the ultrastructure of thyroid in chicks. China J Vet Sci 2002;22:512-4.
17. Hillman D, Bolenbaugh DL, Convey EM. Hypothyroidism and anemia related to fluoride in dairy cattle. J Dairy Sci 1979;62:416-23.
18. Carton RJ, Park A. Review of the 2006 United States National Research Council Report: Fluoride in drinking water. Fluoride 2006;39:163-72.
19. Krishnamachari KA. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. Prog Food Nutr Sci 1986;10:279-314.
20. Fujita T, Palmieri GM. Calcium paradox disease: Calcium deficiency prompting secondary hyperparathyroidism and cellular calcium overload. J Bone Miner Metab 2000;18:109-25.
21. Balasubramanyam M, Lenin R, Monickaraj F. Endoplasmic reticulum stress in diabetes: New insights of clinical relevance. Indian J Clin Biochem 2010;25:111-8.
22. Agalakova NI, Gusev GP. Sechenov Institute of Evolutionary Physiology and Biochemistry Russian Academy of Sciences. Molecular mechanisms of cytotoxicity and apoptosis induced by inorganic fluoride. Int Sch Res Netw ISRN Cell Biol

2012:16. [Article ID 403835].
23. Balasubramanyam M, Singh LP, Rangasamy S. Molecular intricacies and the role of ER stress in diabetes. Exp Diabetes Res 2012;2012:958169.
24. Kunz D, Schmitz S, Mahlberg R, Mohr A, Stöter C, Wolf KJ, *et al.* A new concept for melatonin deficit: On pineal calcification and melatonin excretion. Neuropsychopharmacology 1999;21:765-72.
25. Mahlberg R, Kienast T, Hädel S, Heidenreich JO, Schmitz S, Kunz D. Degree of pineal calcification (DOC) is associated with polysomnographic sleep measures in primary insomnia patients. Sleep Med 2009;10:439-45.
26. Kurdi MS, Patel T. The role of melatonin in anaesthesia and critical care. Indian J Anaesth 2013;57:137-44.
27. Lakhan SE, Kirchgessner A, Hofer M. Inflammatory mechanisms in ischemic stroke: Therapeutic approaches. J Transl Med 2009 17;7:97.
28. Profumo E, Buttari B, Riganò R. Oxidative stress in cardiovascular inflammation: Its involvement in autoimmune responses. Int J Inflam 2011;2011:295705.
29. Li Y, Berenji GR, Shaba WF, Tafti B, Yevdayev E, Dadparvar S. Association of vascular fluoride uptake with vascular calcification and coronary artery disease. Nucl Med Commun 2012;33:14-20.
30. Xu RY, Xu RQ. Electrocardiogram analysis of patients with skeletal fluorosis. Fluoride 1997;30:16-8.
31. Zhou QH, Zhang DC. Electrocardiogram analysis of 271 dental Fluorosis cases. Chin J Epidemiol 1988;5:296-7.
32. Stoelting RK, Dierdorf SF editors. Endocrine disease. In: Anaesthesia and Coexisting Disease. 3rd ed. NewYork: Churchill Livingstone; 1983. p. 339-74.
33. Guan ZZ, Wang YN, Xiao KQ, Dai DY, Chen YH, Liu JL, *et al.* Influence of chronic fluorosis on membrane lipids in rat brain. Neurotoxicol Teratol 1998;20:537-42.
34. Seraj B, Shahrabi M, Falahzade M, Falahzade F, Akhondi N, Roohi N. Effect of high fluoride concentration in drinking water on children's intelligence. J Dent Jehran Univ Med Sci 2006;19:80-6.
35. Teotia SP, Teotia M. Secondary hyperparathyroidism in patients with endemic skeletal fluorosis. Br Med J 1973;1:637-40.
36. Wang YN, Xiao KQ, Liu JL, Dallner G, Guan ZZ. Effect of long term fluoride exposure on lipid composition in rat liver. Toxicology 2000;146:161-9.
37. Bouaziz H, Ketata S, Jammoussi K, Boudawara T, Ayedi F, Ellouze F. Effects of sodium fluoride on hepatic toxicity in adult mice and their pups. Pest Biochem Physiol 2006;86:124-30.
38. Takagi M, Shiraki S. Acute sodium fluoride toxicity in the rat kidney. Bull Tokyo Med Dent Univ 1982;29:123-30.
39. Bouaziz H, Ghorbel H, Ketata S, Guermazi F, Zeghal N. Toxic effects of fluoride by maternal ingestion on kidney function of adult mice and their suckling pups. Fluoride 2005;38:23-31.
40. EU Director General for Health and Consumers. Strategy for Europe on Nutrition, Overweight and Obesity Related Health Issues. Implementation Progress Report; Dec, 2010.
41. Hileman B. Fluoridation of water. Questions about health risks and benefits remain after more than 40 years. Chem Eng News 1988;66 :26-42.
42. Czerwinski E, Nowak J, Dabrowska D, Skolarczyk A, Kita B, Ksiezyk M. Bone and joint pathology in fluoride-exposed workers. Arch Environ Health 1988;43:340-3.
43. Kumar S, Kakar A, Gogia A, Byotra SP. Skeletal fluorosis mimicking seronegative spondyloarthropathy: A deceptive presentation. Trop Doct 2011;41:247-8.
44. Saxena HN, Mehta Y, Trehan N. Anaesthesia and fluorosis. Anaesthesia 1999;54:96-7.
45. Rao M, Menon K. Anaesthetic management for cervical laminectomy in patients of skeletal fluorosis. J Anaesthesiol Clin Pharmacol 1987;3:207-10.
46. Kar P, Durga P, Gopinath R. Cervical fluorosis: A lurking peril. J Cardiothorac Vasc Anesth 2013;27:e72-3.
47. Jindal P, Chopra G, Chaudhary A, Rizvi AA, Sharma JP. Taylor's approach in an ankylosing spondylitis patient posted for percutaneous nephrolithotomy: A challenge for anesthesiologists. Saudi J Anaesth 2009;3:87-90.

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