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Treatise

The Imaging Value of Bone Turnover of Skeletal Fluorosis

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Objective To probe into X-ray, CT and MRI manifestations of bone turnover in skeletal fluorosis and diagnostic values of different examination technologies. **Methods** Comparisons and analyses were made on the imaging manifestations of bone turnover in 28 reported cases with skeletal fluorosis. **Results** All 28 cases had dental fluorosis of different degrees. The chief symptoms included arthralgia and aching muscle pains in four limbs; 13 cases had joint motion limitation and dysfunction, 28 cases had spinal pain and 26 cases (92.85%) had pain in the lumbar region and legs. As to the imaging manifestations, 17 cases mainly had hyperostosis and 11 cases mainly had osteopenia; 5 had fuzzy bone trabecula, 9 loosening of cortical bone and 19 sclerosis of cancellous bone; 7 cases were complicated by biconcave deformity of vertebral body and 6 cases by pelvic deformity; 4 cases manifested the formation of false fracture line, and 7 cases manifested disorder of bone growth and development. **Conclusions:** MRI may distinctly display early changes of bone turnover in patients with skeletal fluorosis with high diagnostic sensitivity.

Key words: Skeletal fluorosis; bone turnover; imageology

As a widespread endemic and occupational disease that threatens people's health, skeletal fluorosis is widely distributed around the world. Related investigations demonstrated that 300 million persons live in fluorine-polluted regions in China, of which 3 million persons have skeletal fluorosis and dental fluorosis; the occurrence of fluorosis is related to drinking water in 26 provinces, related to coal in 14 provinces, and related to high-fluorine tea in regions of Southwest China such as Sichuan Province, which demonstrates that fluorides have become a serious public health problem [1].

Skeletal fluorosis mainly causes injury to the human skeleton and its peripheral soft tissues, often leads to changes of different nature such as hyperostosis or osteopenia, and the osseous changes are varied and complex. In this article, we will report 28 cases with skeletal fluorosis whose bone turnover was examined with X-ray, CT and MRI; analyses were made on the imaging diagnostic value of these three different examination technologies in connection with this disease, and preliminary explorations were conducted on the mechanism responsible for formation of imaging manifestations of these three different examination technologies. Now we present our results as follows.

1 Information and Methods

1.1 Information

Twenty-eight cases with skeletal fluorosis whose bone turnover was examined with X-ray, CT and MRI, 16 male cases and 12 female cases, at the ages of 13–76, the mean age being 54.5. All cases underwent epidemiological and clinical examinations, and all of them came from high-fluorine regions. All cases had X-ray characteristics specific to skeletal fluorosis, as examined by radiography.

1.2 Methods

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Brief Introduction to Author: LIU Jun (1957-), male, born in Shandong, professor, master's student mentor, mainly engaged in the medical imaging research of diseases of bone joints and soft tissues.

1.2.1 Examination by radiography: All cases in this research underwent routine X-rays of bone joints, including anteroposterior and lateral films of cervical, thoracic and lumbar vertebrae, and anteroposterior films of pelvis. 15 cases underwent radiography of anteroposterior and lateral films of ulna, radius and elbow joints, 8 cases had anteroposterior and lateral films of tibia, fibula and knee joints, 3 cases had anteroposterior films of wrist joints and 4 cases had anteroposterior films of shoulder joints.

1.2.2 CT examination: CT Vision spiral CT scanner made by PHILIPS Co. was employed. Sixteen cases underwent CT scan of transverse sections of thoracic and lumbar vertebrae in routine bone windows of spine and intervertebral disc and windows of soft tissues. Matrix: 512 × 512, thickness of spinal layer: 10 mm, spacing: 10 mm; layer thickness of intervertebral disc: 5 mm, spacing: 5 mm.

1.2.3 Magnetic resonance imaging (MRI) examination: Gyroscan Intera 1.5T superconducting magnetic resonance imaging device made by PHILIPS Co. was employed. Six cases underwent plain MRI scan of thoracic and lumbar vertebrae; surface coil and routine TSE protocol were used to perform sagittal and transverse scans. T1W1 sagittal scan: TR/TE = 400–500 ms/13–15ms; T2W1 sagittal and transverse scan: TR/TE = 3,000–3,500 ms/110–130ms; slice thickness: 4 mm; spacing: 0.4 mm; matrix: 256–323 × 512; FOV: 150–350 mm; RFOV: 80–100%. Analyses were made on data from the above X-ray, CT and MRI examinations.

2 Results

2.1 Clinical Results

All 28 cases came from high-fluorine epidemic regions and had dental fluorosis of different degrees. Their clinical manifestations varied due to the different degrees of joint injuries and individual sensitivity to the injuries. The clinical symptoms mainly included arthralgia and muscle ache (myodynia) of four limbs of different degrees. Thirteen cases had joint motion limitation and dysfunction, 28 cases had pain in the spine (rachialga) and 26 cases (92.85%) had pain in the lumbar region (lumbago) and legs (skelagia). Twelve cases developed spinal curve deformity, 8 cases numbness or paresthesia of four limbs, 9 cases achillodynia, 2 cases genu valgum and 5 cases genu varum.

2.2 Radiographic Results

Seventeen cases showed X-ray manifestation mainly characterized by hyperostosis, and 11 cases showed X-ray manifestation mainly characterized by osteopenia. Seven cases had general elevation of density of spinal cancellous bone, 12 cases had focal elevation of bone density, 9 cases had reticular elevation of bone density complicated by loosening and thinning of cortical bone, 7 cases had spinal biconcave deformation and 6 cases had pelvic deformity including one case with flat pelvis. Eleven cases manifested loosening of cortical bone of four limbs, of which 9 cases developed general reduction of bone density of different degrees of four limbs, fuzzy bone trabecula and laminating and thinning of cortical bone, 4 cases had false fracture line, 2 cases had genu valgum and 5 had cases genu varum. Six cases developed bending of fibula and tibia complicated by thickening of cortical bone in the bent side and laminating, fuzzing and thinning of cortical bone in the contralateral side. Two cases developed widening of diaphyseal epiphysis of long bones so that the epiphysis end assumed the appearance of a cup rim; 3 cases manifested fuzzy temporal calcification belt including one case whose temporal calcification belt had a brush-like appearance; 2 cases manifested widening of epiphyseal plate which assumed the appearance of a cup rim; 7 patients had lines of growing disorder of different degrees. Twenty-eight cases were complicated by calcification of ligaments, attaching sites of muscles, interosseous membranes, muscular tendons or joint capsules of different degrees.

2.3 CT Results

Of 16 cases undergoing CT examination of the spine, 7 cases underwent CT scan of thoracic vertebrae and 9 cases lumbar vertebrae. The CT manifestations included elevation of vertebral cancellous bone density and CT values higher than normal plus loosening of cortical bone, complicated by thickening and calcification of different degrees of anterior vertical ligament, posterior vertical ligament, and yellow ligament between multiple vertebrae. Five cases had hyperostosis and sclerosis of small intervertebral joints complicated by protrusion of intervertebral disc, leading to stenosis of spinal canal, disappearance of extradural fat clearance, and compression of dural sac. Three cases developed serious spinal stenosis which assumed an appearance of three-leaf clover, and transverse diameter, anteroposterior diameter and area of spinal canal were all significantly smaller than normal values.

2.4 MRI Results

All 6 cases had noticeable skeletal fluorosis and spinal stenosis of different degrees; their spines and nerves were compressed, manifesting as centripetal changes; one case had spinal compression in the thoracic segment, 2 cases had it in thoracic and lumbar segments, and 3 cases had compression of dural sac in the lumbar segment. One case manifested focal degeneration of compressed spine that gave rise to lamellar long T1 and long T2 signal intensities. Five cases had general reduction of intensity of spinal vertebral signals, giving rise to relatively uniform long T1 and short T2 signal intensities. One case had nonuniform reduction of spinal vertebral signal intensities; three cases developed thickening of posterior vertical ligament, and 5 cases developed thickening of stepwise multiple thickening of yellow ligaments. Four cases developed thickening of anterior vertical ligament. Three cases developed multiple dilations and hypertrophies of intervertebral joints, leading to shrinkage of intervertebral holes, compression of nervous roots, and transverse stenosis of spinal canals. Two cases had multiple protrusions of intervertebral discs, and 2 cases had bulging intervertebral discs. Multiple thickening of yellow ligaments, multiple protrusions of intervertebral discs and bulging of intervertebral discs leading to the compression of spine and dural sac and consequential spinal bead-like stenosis and anteroposterior stenosis of spinal canals. All cases in this research were complicated by hyperostosis of spinal edge and formation of bone bridges of different degrees, giving rise to noticeable long T1 and short T2 signal intensities.

3 Discussion

After the completion of bone development, bone metabolism will continue for life. The metabolic process of the skeleton is the process during which osteoblasts form new bones and the process during which osteoclasts absorb old bones, and this metabolism of osseous tissue is called bone turnover that comprises two opposite and integrated processes: bone absorption and bone formation. During the period of bone growth, skeletal bone turnover manifests itself as bone modeling; during the period of bone development and maturation, skeletal bone turnover manifests itself as bone reconstruction. Bone reconstruction occurs in the basic multicellular unit; in each basic multicellular unit, the activity of osteoblasts and osteoclasts is in a persistent and dynamic equilibrium. The bone turnover continues in the skeleton for life; this process is relatively slow under physiological conditions, and the acceleration of this process is considered to be a common phenomenon of chronic fluorosis and one important characteristic of skeletal fluorosis [2].

The radiological manifestations of skeletal fluorosis mainly include changes associated with hyperostosis and with osteopenia that manifest themselves as follows: general elevation of spinal cancellous bone density, focal elevation of bone density, reticular elevation of bone density complicated by loosening and thinning of cortical bone, biconcave deformity of spine, pelvic deformity, and loosening of

cortical bone. In case of appendicular skeleton, there may be: general reduction of bone density of different degrees; fuzzy bone trabecula and laminated and thinned cortical bone; formed false fracture line, genu valgum and genu varum; thickened cortical bone in the bent side, and laminated, fuzzy and thinned cortical bone in the contralateral side. The diaphyseal epiphysis of long bones widens to assume the appearance of a cup rim; temporal calcification belt becomes fuzzy and assumes a brush-like appearance; the epiphyseal plate widens and assume the appearance of a cup rim; lines of growing disorder form, and calcification of ligaments, attaching sites of muscles, interosseous membranes, muscular tendons or joint capsules occur to different degrees. CT manifestations include elevation of vertebral cancellous bone density and CT value higher than normal and loosening of cortical bone, complicated by thickening and calcification of different degrees of anterior vertical ligament, posterior vertical ligament, and yellow ligament between multiple vertebrae. Certain cases may have hyperostosis and sclerosis of small intervertebral joints complicated by protrusion of intervertebral discs, leading to stenosis of spinal canal, disappearance of extradural fat clearance, and compression of dural sac. In severe cases, the spinal canal assumes an appearance of three-leaf clover, and transverse diameter, anteroposterior diameter and area of spinal canal are all smaller than normal values. MRI may reveal spinal stenosis of different degrees leading to compression of spine and nerves manifesting as centripetal changes, and most cases show compression in the thoracic segment and thoracic and lumbar segments, as well as compression of the dural sac in the lumbar segment. The compressed spine may show focal degeneration and show lamellar long T1 and long T2 signal intensities.

Comprehensive comparisons and analyses made on the above three imaging methods are as follows: X-ray films show 2D images to display the radiological manifestations of skeletal fluorosis of different types with strong specificity, and the diagnosis of skeletal fluorosis based on this method may be made definite; however, its sensitivity is relatively low, and the radiological manifestations revealed by this method would occur generally at the middle or advanced stage of skeletal fluorosis. CT scan produces 3D images, thus it may offer more information as compared with X-ray films; not only may CT scan display the skeletal changes, but it may also display protrusion of intervertebral discs, stenosis of spinal canal, disappearance of extradural fat clearance, and compression of dural sac, and may also measure transverse diameter, anteroposterior diameter and area of spinal canal. MRI produces multi-dimensional images, therefore it may offer images in transverse, sagittal and coronal sections and in oblique planes at different angles. Furthermore, MRI may show the early changes of bone turnover related to skeletal fluorosis. In skeletal fluorosis, the intensity of spinal vertebral signals shows an overall reduction on MRI manifestation as well as uniform long T1 signal and short T2 signal intensities. MRI may reveal thickening of posterior vertical ligament, stepwise multiple thickening of yellow ligament, thickening of anterior vertical ligament, multiple dilations and hypertrophies of intervertebral joints, which leads to the shrinkage of intervertebral holes, the compression of nervous roots and transverse reduction of spinal canal. MRI may also reveal multiple protrusions of intervertebral discs or bulging of intervertebral discs, and multiple thickening of yellow ligament leading to the compression of spine and dural sac and consequential spinal bead-like [stenosis] and anteroposterior stenosis of spinal canals. All cases in this research were complicated by hyperostosis of spinal edge and formation of bone bridges of different degrees, giving rise to noticeable long T1 and short T2 signal intensities.

The skeletal changes in patients with skeletal fluorosis include osteosclerosis, osteoporosis, osteomalacia, and calcification of soft tissues in periphery of bone joints. The early change of bone turnover revealed by MRI in cases with skeletal fluorosis is general reduction of intensity of spinal vertebral signals, which may be attributed to the following factors. First, excessive fluorine in vertebrae may induce

increased bone density, demonstrating that the basic action of fluorine on bone turnover is to promote osteogenesis; for the spine that is mainly consisted of cancellous bone and that has more area for bone turnover as compared with appendicular skeleton, thus the bone mass would be increased more easily. Fluorides may promote karyomitosis of osteoblasts to promote the settlement of osteoblasts in tissues, leading to a stepwise acceleration of growth to increase the number of osteoblasts. Fluorine in bones may interchange with hydroxyl groups and bicarbonate ions on the surface of bone mineral crystals to settle down rapidly. During osteoblastic and osteoclastic activities, ions on the crystal surface would gradually enter crystals during recrystallization, and various bone components such as calcium, magnesium and phosphorus would be stabilized in the skeleton, but only fluorine may still enter tissues, which is the primary reason why accelerated bone turnover is considered a common phenomenon of chronic fluorosis and one important characteristic of skeletal fluorosis. Fluorides have a relatively high affinity with hydroxyapatite composed of calcium and phosphates; fluorine combines with calcium through its affinity to form calcium fluoride, or combines with phosphorus through its affinity to form fluorapatite, and calcium fluoride and fluorapatite as bone salts would settle down in the osseous matrix, causing increase of bone density to promote osteogenesis [3-4]. Second, excessive fluorine in bones may lead to the concurrent existence of osteoporosis and osteomalacia, reflecting that fluorine may locally decrease the bone mass in bone turnover. REN Li-qun made observations on the change of tibial diaphysis in rats as a model of skeletal fluorosis and found that perivascular gaps in the cortical bone of tibial diaphysis were enlarged, osteoclasts increased in number, and the whole cortical bone was involved in osteoporosis such that the cortical bone appeared to be worm-eaten, demonstrating the concurrent existence of osteoporosis and osteomalacia [5]. While hyperactive osteogenesis combined with insufficient calcium supply causes osteomalacia, secondary hyperparathyroidism may occur. Often skeletal fluorosis is accompanied by increased secretion of parathyroid hormone (PTH) that may mobilize calcium in the local skeleton and transfer the additional calcium in bodily fluids to soft tissues, causing the increased inflow of free calcium in cells and leading to intensified osteoclastic bone absorption and osteoporosis [6-8].

In summary, both hyperostosis and osteopenia may be manifested in an MRI as general reduction of intensity of spinal vertebral signals such that MRI would reveal relatively uniform long T1 signal and short T2 signal intensities. Both hyperostosis and osteopenia may reduce the bone marrow tissue to remarkably lower the density of hydrogen protons in cancellous bones, causing general reduction of intensity of spinal vertebral signals. Therefore, MRI may distinctly display early changes of bone turnover in patients with skeletal fluorosis with high diagnostic sensitivity.

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