Case Report  

Paget’s Disease Of The Spine With Low Bone Alkaline Phosphatase

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Abstract

We present a case of 35-year-old man who was referred to us with a preliminary diagnosis of multiple spinal metastasis. Laboratory studies have shown a high serum alkaline phosphatase and a low bone alkaline phosphatase levels. Spinal magnetic resonance scans demonstrated involvement of T9, T11 and L3 vertebral bodies. The involved vertebrae appeared hypointense on T1- and hyperintense on T2-weighted images and a radionuclide bone scan has shown increased uptake in involved vertebral bodies. A transpedicular open biopsy was considered necessary for accurate diagnosis. Histopathologic evaluation of the specimen revealed typical “mosaic pattern” of Paget’s disease. After surgery, urinary deoxypyridinoline and pyridinoline levels were tested and were higher than normal. The patient was given oral doses of alendronate, 40 mg per day and follow-up magnetic resonance scans at 6 months and 2 years demonstrated improvement in the signal intensity of the involved vertebral bodies. This case not only shows that Paget’s disease can occur in the setting of low bone AP but also shows that the clinical improvement can be monitored by improvement in magnetic resonance signal.

Keywords: Paget’s disease, spine, bone alkaline phosphatase

Düşük Kemik Alkalen Fosfataz Seviyesi İle Birlikte Olan Omurganın Paget Hastalığı

Özet


Anahtar Kelimeler: Paget hastalığı, omurga, kemik spesifik alkalen fosfataz
Introduction
Paget's disease (PD), also known as osteitis deformans, is a disease of the skeletal system characterized by increased bone turnover and bone remodeling macroscopically and abnormal bony structure microscopically. First described by Sir James Paget in 1877, PD most commonly affects men of sixth decade. A geographical predilection to Western Europe, North America, Australia and New Zealand has been cited. The incidence of PD progressively increases after the age of 40, but is extremely rare among younger population. We herein present a case of 35-year-old young man with multiple vertebral body involvement with PD who had demonstrated improvement both clinically and radiologically.

Case Presentation
A 35-year-old man presented with back pain. He was previously evaluated at a university hospital and the laboratory tests as well as radiologic studies were interpreted as spinal metastasis at multiple levels. Computerized tomography (CT) of the abdomen and the chest and bronchoscopy were done in search of an origin but they were found negative. On admission to our institution, the patient appeared healthy and well-nourished. He denied any loss of weight or lack of appetite. Neurological examination was normal. Laboratory has shown an elevated serum AP (Patient 137 IU/L, N:30-115). Electrophoresis for subtypes of AP has shown increased isoenzyme activity of hepatic origin. Bone AP level was below normal [Total AP 145 IU/L (N:25-100), hepatic AP 123 IU/L-85% of the total (N:26-64%) (123 U/L), bone AP 15 IU/L-10% of the total (N: 23-61%), intestinal AP 7 IU/L-5% of the total (N:%1-25%)]. Review of plain spinal x-rays revealed sclerosis at L3 vertebral body (Figure 1). The vertebral body heights and alignment were normal. Thoracic and lumbar MR scans demonstrated involvement at T9, L1 and L3 spinal levels. The involved vertebral bodies appeared slightly collapsed with decreased signal on T1- and increased signal on T2-weighted images. There was no enhancement after contrast injection (Figure 2).

Figure 1 (A) Antero-posterior and (B) lateral plain x-rays of the lumbar spine show sclerosis within the L3 vertebral body.

Figure 2 Sagittal MR scans of the thoracic and lumbar spine demonstrate involvement of T9, T11 and L3 vertebrae. The pathology appears hypointense on T1 (A,D), and hyperintense on T2-weighted images (B,E). There was no enhancement after contrast injection (C,F).
Lumbar CT better demonstrated the sclerosis at L3 vertebral body (Figure 3). Radionuclide scan showed increased uptake at T9, T11 and L3 vertebral bodies (Figure 4). A diagnostic open biopsy targeted at L3 vertebra was considered for diagnosis. The biopsy was done under general anesthesia through the left L3 pedicle using 11G Jamshidi needle. Histopathology has shown irregular and widened spicules and basophilic-cementoid material arranged in mosaic pattern in between. There was no osteoblastic activity (Figure 5).

These findings were interpreted as diagnostic for PD of the spine. Urinary pyridinoline [134 nM/Nm (N:18-40)] and deoxypyridinolin [30.2 nM/Nm crea (N:5-14)] levels were postoperatively tested and both were found to be higher than the normal range. Medical treatment for PD was then considered and alendronate 40 mg per day by mouth was started. At the end of 6 months, the patient experienced significant resolution of presenting symptoms. This improvement was verified by MR scan which also has shown improvement in the sclerotic design at the L3 level (Figure 6A-D). A late MR scan at 2 years verified the initial improvement (Figure 6E).

Discussion
The exact etiology of PD is not known. Genetic susceptibility, geographic factors and viral infections have all been suggested as causative mechanisms. Family history has been found positive in 15-30% of the cases with PD and an autosomal dominant inheritance pattern has been described. PD becomes clinically manifest either as a monostotic form (effecting only one part of one bone) or as a polystotic form (effecting multiple bony structures). The most commonly involved bony structures are the pelvis, vertebrae, femur, calvaria, tibia and humerus. The vertebral involvement occurs in approximately 35% of the cases and the lumbar spine is the most commonly affected segment although few authors have listed the thoracic vertebrae as the most common target for PD.

The most common symptom of spinal PD is pain. Neurological examination is usually normal. In addition to pain originating from the disease process itself, one-third of PD patients develop spinal stenosis and suffer from the radicular pain originating from this stenosis. Stenosis again commonly occurs at the lumbar spine but typically it is a single-level spinal stenosis. Neurological dysfunction may occur as a result of various mechanisms. These mechanisms include hypertrophy of the facet joints causing relative instability, compression of the dural sac by hyperthrophic ligaments, ischemia secondary to steal phenomenon that occurs.
when the medullary arteries supplying both vertebrae and spinal cord carry more blood to the vertebrae 3,12,22, ischemia secondary to compression of the vascular supply of the spinal cord 22, compression from spinal epidural hematoma that may occur in association with PD 18,22 and spinal cord compression due to compression fracture of the involved vertebral body (ies) 6,10,22,31.

Biochemical markers as the reflection of bone turnover are of extreme importance in the diagnosis of PD 1. Serum calcium levels are usually normal 28. Serum AP is a relatively specific indicator showing the activity of the disease 32. Yet, in cases of elevated serum AP, liver disease must be be ruled first 26,32. The diagnosis of PD is even more difficult with a normal serum AP 5. This may be the case in the monostotic form of PD or when only a small volume of bone is effected. In such instances bone AP will be more helpful 26,32. Bone AP was lower than normal in our case. Considering the fact that we have a solid histopathological diagnosis in hand despite a low bone AP value, even bone AP may not be all that specific as a screening test for PD. Urinary deoxyprydinoline and pridinoline levels are other sensitive markers and are extremely important in the diagnosis of PD 27,28,33. More recent biomarkers include Type I collagen and N-terminal telopeptides 28. Nevertheless reaching or excluding the diagnosis of spinal PD is not foolproof 9.

The histopathological picture of PD is characterized by increased number of multinucleated osteoclasts and increased bone resorption which occurs as a result of this. The reason as to why osteoclasts increase in number is still not known 29. During the initial “lytic phase” the osteoclasts dominate the bone and they cause increased bone resorption. The “intermediate phase” that follows this is characterized by increased absorption and increased new bone formation. The bone that is formed at this stage is not real bone and the resultant picture is the pathognomonic “mosaic pattern” 28,30,32. At this second stage, the bony channels are wider than normal, the bone is relatively fragile but at the same time extremely vascular 32. Then comes the third stage also known as the “sclerotic stage” during which osteoblasts predominate the picture 28,30,32.

The plain radiographic appearance of PD include increased bone density, increase in thickness of the involved bone, deformity of the involved bone, cortical thickening and increased trabecular pattern 4. PD of the spine cause expansion and thickening of the involved vertebrae and this
appearance is called ‘picture frame’. This typical image is usually seen during the second phase also known as the intermediate phase. During the sclerotic phase the plain x-rays show the ‘‘ivory vertebrae’’ image. At this stage the vertebra appears radioisodense. Using plain x-rays or even CT as the diagnostic tool, cases are usually diagnosed during the third sclerotic stage. However one must bear in mind that “ivory vertebra” is not specific for PD. Lymphoma, osteosarcoma, metastatic prostate and metastatic lung cancer may also cause vertebral involvement appearing as “ivory vertebra” On MR scans, different stages of spinal PD appear with different signal characteristics. During the lytic phase, the involved vertebra shows a lower signal intensity on T1-, and a higher intensity on T2-weighted MR images than the surrounding normal vertebra. It is the marrow of the involved vertebra that is replaced by fatty deposits, sclerosis, granulation tissue and/or edema that typically appear abnormal on the MR scans. During the early sclerotic phase, the vertebra will appear hypointense on both T1- and T2-weighted sequences. Overall, MR is sensitive for the metabolic changes within the bone yet is not specific for PD, therefore we believe that a bone biopsy may sometimes be the only other alternative for an unequivocal diagnosis of PD.

The principal treatment of PD is medical. Agents useful in the medical treatment of PD are inhibitors of bone resorption. Calcitonin, etidronate, pamidronate, alendronate, tiludronate, residronate, plicamycin (mitramycin) and gallium nitrate has all been found effective. Medical treatment with calcitonin ve bifosfonates has even been found beneficial for spinal PD associated with spinal stenosis. Some reports even suggest that medical treatment may be equal to if not superior to surgical decompression of the stenosis. One reason as to why surgery may not be a popular treatment method for spinal PD (except for biopsy) is probably the advanced age and relatively poor physical condition or relatively high mortality (11%) and reoperation (9%) rates associated with surgery. Recurrence or exacerbation of PD or even malignant degeneration may occur and that is why these patients may need years of follow-up.

Conclusion
A search for PD especially among younger patients presenting with multilevel vertebral disease does not waste time or other resources, but may save significant morbidity and/or mortality associated with progression of an undiagnosed PD. Good follow-up of spinal PD using both biochemical markers and the magnetic resonance imaging not only contributes to better control of the disease but is also extremely useful in demonstrating and/or preventing preventable complications. MR is an extremely sensitive tool to changes that take place within the bone, and it can demonstrate normalization of the bony metabolism as shown in our case.

References
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