Chapter 3

Vertebral Osteonecrosis

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Additional information is available at the end of the chapter

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Abstract

Vertebral osteonecrosis (ON) is a rare, underdiagnosed disease, also called pseudarthrosis due to ischemia following a compression fracture (CF). The main features include the air-occupied intravertebral cleft visualized as a radiolucent shade of linear or semilunar X-ray, namely an intravertebral vacuum cleft (IVC) sign. Usually, this phenomenon shows low signal intensity with all magnetic resonance imaging (MRI) sequences. Another feature of ON of the vertebral body is the intravertebral fluid analogous to edema and fibrosis in histological sections. This appears as low signal intensity on T1-weighted MRI, with high signal intensity on T2-weighted images. The risk factors for vertebral ON are multivariate, and the pathophysiological mechanisms are still unknown with certainty.

Keywords: osteonecrosis, avascular necrosis, pseudarthrosis, Kümmel's disease, ischemia

1. Introduction

Necrosis of bone tissue is a nonspecific term that is related to conditions that cause major cell stress and cell death regularly due to interruption of the vascular supply. Frequently osteonecrosis (ON) is related to local traumatic events such as fractures that induce vascular injury; however, several non-traumatic causes have also been related. The first publications of ON were referred to avascular necrosis (AVN) of the femoral head and related in most cases to trauma. Later, other etiological factors were involved in the development of ON such as alcohol consumption, fat embolism, and steroid therapy. Likewise, coagulopathies, chronic osteoarthropathies, bone infections, and tumors are also causal factors associated with it.

AVN, aseptic necrosis, ischemic necrosis, subchondral AVN, and osteochondritis dissecans are synonyms used to denote ON. Vertebral AVN has been classically related to the intravertebral

vacuum cleft (IVC) sign. This is represented by a transversal cleft of the vertebral body occupied by gas density observed in extension and not observed in flexion. Subsequently, with the advent of magnetic resonance imaging (MRI), the presence of fluid was demonstrated in association with osteoporotic vertebral collapse. In addition, ischemia was confirmed by histological analysis.

AVN of bone is otherwise characterized by massive necrosis of bone and bone marrow. This has been generally related to systemic factors such as alcohol abuse, glucocorticoid therapy, dyslipidemia, Gaucher disease or human immunodeficiency virus (HIV) infection, among others. AVN of the spine is known as Kümmel's disease (KD), usually related to osteoporotic vertebral fractures. Although the AVN associated with vertebral collapse hypothetically is a consequence of vascular damage, the pathogenesis, as well as the early diagnosis, the management protocols and prevention measures continue to be the research topics.

2. Historical background

AVN frequently associated with vertebral compression fractures (CF) in osteoporosis is called KD, first described by Herman Kümmell, a German surgeon in 1895. Also at that time, A.A. Verneuil, French, referred to some clinical cases with similar manifestations, so that occasionally this syndrome was named "Kümmell-Verneuil disease." The cases described by Kümmel had a history of minor spinal trauma, with asymptomatic periods from months to years and angular kyphotic spinal deformities of the lower thoracic or upper lumbar regions and the T12 segment with progressive painful [1, 2]. Kümmell hypothesized that there was no traumatic CF in all the patients; however, it seemed very likely that most of them had a history of minimal trauma with influence on local nutrition and progressive atrophy [3]. It should be mentioned that these observations described by Kümmell were performed before the advent of X-rays, and once these were used, the existence of the disease was questioned in "normal" radiographic studies with uncertain quality. Years later, the collapse of the delayed vertebral body was demonstrated; however, diagnostic criteria in the early stages of the disease were associated with negative radiographic findings [2, 4, 5].

Steel also classified the KD in five progressive stages [2]. Initially, it is characterized by hyperflexion of the radiographically normal vertebral column, namely, the *initial insult*. Subsequently, a second *post-traumatic stage* is categorized by minimal manifestations of the low back without functional limitation. This is followed by a *latent stage*, relative well-being, lasting weeks to months, with no significant symptoms. Then, the *stage of recrudescence*, the patient manifests pain in the back, develops gibbous and loss of progressive stature, in addition to peripheral pain. In the *terminal stage*, the patient develops a progressive back pain located in the region of the pathological fracture with angular kyphosis and compression of the spinal [2]. The cases of AVN without a history of spinal trauma should not be termed KD. **Table 1** summarizes the clinical cases of KD reported in the literature.

A frequently representative feature of vertebral ON has been named IVC sign. This was first described as a horizontal cleft with gas density in radiographic studies [6]. This entity has

Age (years)	Sex	Location	Concomitant pathologies	Management	Reference
23/28/62	Male	T10/L1/T8	None	Immobilized in hyperextension	Steel [2]
71	Male	T12	Osteopenia Occasional alcohol abuse	Unknown	Brower and Downey [14]
45	Female	L1	Type 1 Gaucher disease	Conservative	Hermann et al. [15]
75	Male	T11	Steroids	Conservative	Van Eenenaam and el-Khoury [11]
72	Male	L4	Diabetes mellitus type II	Subtotal corpectomy/autologous grafting/ posterior fusion with pedicle fixation	Young et al. [7]
79	Male	L2	Chronic steroid therapy /myasthenia gravis	Conservative	Osterhouse and Kettner [16]
71	Female	L3	None	Posterior stabilization	Kapoor et al. [17]
62	Female	L2, L3	Osteopenia, diabetes	Unknown	Maheshwari et al. [18]
55	Male	L2	Sarcoidosis	Anterior decompression/L-2 corpectomy/ anterior L1–3 spinal fusion/autologous grafting	Ito et al. [19]
60	Male	T9-T10	Diabetes mellitus type II, chronic obstructive pulmonary disease, obesity, hypothyroidism secondary to radiation treatment for Graves' disease, and depression	T9 and T10 corpectomies with T8–T11 anterior and posterior fusion/cage graft with pedicle screw fixation	Swartz and Fee [20]
87	Female	L1	None	L1 vertebroplasty	Van der Schaaf and Fransen [21]
75	Female	T12	Dementia, Diabetes mellitus type 2, hypertension, hypothyroidism	T12 vertebroplasty	Ma et al. [5]
31	Male	L1	None	L1 kyphoplasty	Matzaroglou et al. [22]
81	Female	L1	Osteoporosis, obesity, idiopathic pulmonary thromboembolic, arterial hypertension, depression	Conservative (teriparatide)	Fabbriciani et al. [23]
60	Male	L4	Osteopenia	L4 laminectomy, L3-5/transpedicular fixation	Ranjan et al. [24]

Table 1. Case reports of Kümmel's disease since 1951.

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also been called post-traumatic vertebral ON [3, 5, 7], IVC [8, 9], vertebral pseudarthrosis [10], delayed post-traumatic vertebral body collapse [11, 12] and nonunion of VCF [10, 13].

3. Clinical manifestations

KD occurs more frequently in the middle and in the elderly slightly predominant in males [7]. The incidence of KD in elderly patients ranges from 7 to 37%. One of the characteristic symptoms is an acute pain especially in the early stages of the disease usually without accompanying neurological symptomatology. In these cases, falls are generally conditioning factors of pain. The kyphotic deformity associated with recurrent pain of greater intensity in later stages usually corresponds to the collapse of the vertebral bodies and is usually located in the thoracolumbar region. Then neurological signs such as weakness of the lower extremities, paresthesias, as well as neuropathies that interfere with normal function of the digestive tract and bladder can develop.

Steel related the KD to insignificant trauma generally involving the 3rd thoracic vertebra and the 2nd or 3rd lumbar vertebra predominantly observed in males. He also described five stages namely *initial insult*, characterized by hyperflexion of the spine and association to the trauma of variable type and severity, in addition to normal roentgenograms. The second stage or *post-traumatic period* was manifested by mild back pain without functional limitation. The third stage, *latent interval or state of relative well-being*, was characterized by progressive disability in the following week or months of the traumatic event, not incapacitated. In this period, variability in time from 4 weeks to 1 year has been described [2, 5, 7, 11, 14–18, 20–23]. Fourth stage or *recrudescent stage*, in this the patient presents localized, persistent back pain, tenderness, and tendency to peripheral irradiation. In the last stage or *terminal stage*, the patient develops permanent kyphotic deformity with or without progressive pressure on roots or spinal cord [2].

Neurological symptoms are usually absent in the early stages of the disease and when pain occurs in the thoracolumbar region this usually corresponds to the collapse of the vertebral body. In the advanced stages, the patient develops paresthesias, lower extremity weakness, and bowel/bladder disturbance [7]. Besides, the kyphotic deformity associated with osteoporotic vertebral fracture limits the functionality and has repercussions on the quality of life of the patient. In addition, it increases the mortality and incidence of fractures in adjacent bone structures [25, 26].

4. Risk factors in osteonecrosis

Numerous risk factors for AVN have been described including long-term glucocorticoid treatment, diabetes, alcoholism, osteoporosis, atherosclerosis, pancreatitis, cirrhosis, hypertriglyceridemia, vasculitis, acute trauma, radiotherapy, neoplasias, air or fat embolism, barotraumas hemoglobinopathies, such as sickle cell disease and infection.

4.1. Osteonecrosis and osteoporosis

As we know, osteoporosis is one of the metabolic disorders associated with compression fractures of the vertebrae. This affects the quality of life of patients, who develop progressive spinal deformities that deteriorate gait and balance [27], increasing the risk of fracture [8] and mortality [28]. As mentioned, one of the mechanisms most involved in post-traumatic vertebral collapse is ischemic necrosis frequently associated with IVC in osteoporotic spine fractures [29]. According to what has been reported in the literature, the IVC sign is not pathognomonic of KD and is common to observe in unstable osteoporotic CF [30]. Two stages in the evolution of the KD have been considered, although the pathophysiological mechanisms are not known with certainty. First, after the initial trauma, the vertebrae present partial or incomplete healing with consequent weakening. In this stage, the consolidation of an osteoporotic vertebral compression fracture is characterized by an active remodeling process. This includes resorption of necrotic bone and cartilaginous tissue, endochondral bone neoformation, new vessel formation and restoration of bone continuity in the fracture line. Likewise, zones of hypertrophic trabecular bone or areas with lack of bone repair can be observed; in addition, fragments of bone, cartilage and intervertebral disc can be sequestered in areas of dense fibrous and collagen tissue [31].

The second stage of the evolution of KD involved in this reparative failure could be impaired vertebral blood flow, herniation of nucleus pulposus into the vertebral body (Schmorl's nodes), and stress conditions in weakened vertebrae [3]. As it is known, the blood supply of each vertebra depends on branches of the corresponding segmental arteries, which nourish the vertebral body, the spinal canal and the posterior third (equatorial, metaphyseal and peripheral branches) [32, 33]. It was also reported that the supply of the ventral part of the vertebral body derives from the anterior central branches of the segmental arteries, whereas the supply of the dorsal part comes from the posterior central branches [34]. This distribution anatomy has been the explanation of the frequency of IVC in the anterosuperior and anteroinferior portions of the vertebral body. Generally, the involvement of the anterior third of the collapsed vertebral body represents the vascular watershed zone related to alterations in the blood supply [7, 35].

Although the pathogenesis of KD remains unknown, in addition to the ischemic process, the motion between the fracture ends has been considered a preponderant factor. Since Hasegawa's description of the intravertebral cleft with the presence of serous fluid, surrounded by smooth fibrocartilaginous tissue and absence of lining, as well as the motion between the ends of the fracture, the development of pseudarthrosis has been consistent [36]. This radiographically supported motion in the progressive disappearance of a radiolucent gas-like area and the appearance of an area of fluid-like signal intensity on MRI has suggested that the IVC results from a migration of intradiscal gas between the ends of the osteoporotic spine fractures [6, 37]. Then, this nonunion would correspond to the persistence of the radiolucent line of the cleft and the hypointense line on MRI.

It is even reported when confirming the occlusion of the segmental artery on magnetic resonance angiography and identifying the presence of thrombi in microscopic analysis. Then it was postulated that an insult in the segmental artery could lead to AVN of the vertebral body

with the consequent nonunion. It was also suggested an analogy between the deficit of the blood flow and the mechanical insufficiency of the subchondral fracture in the AVN of the femoral head and the mechanisms of osteoporotic CF [38]. Occlusion of the predominantly anterior and peripheral metaphyseal arteries seems to be observed in fragments of the fracture. Necrotic cancellous bone and hyaline cartilage endplate with fracture callus, fibrosis, fibrin deposition and hemorrhage as changes in AVN have been described [38, 39]. Some observations have been made regarding these approaches. The collapse of the basivertebral foramen located between the two pedicles in osteoporotic CF could be involved in the ischemic process of the vertebral body. This foramen allows the passage of nerve branches, basivertebral veins and arteries derived from the segmental ones [33, 40–43].

4.2. Glucocorticoid treatment and osteonecrosis

Long-term glucocorticoid therapy is a predisposing factor that induces the deposition of intramedullary fat with secondary compression of intramedullary vascularity, development of fatty microemboli and microfractures associated with osteopenia [35]. Hypertrophy and hyperplasia of fat cells in the bone marrow [44], the consequent increase in intraosseous pressure, microcirculatory occlusion by emboli and/or thrombi and decreased blood flow are important elements in the pathophysiology of induced steroid-induced ON [45]. Also, these lead to a decrease in collagen synthesis and osteoblastic activity [46]. In experimental studies in animal models, it has been demonstrated in addition to the effect of lovastatin, lipid-lowering agent, on the differentiation of cells from bone marrow into adipocytes, the preventive action or reduction of steroid-induced ON [47]. Therefore, it was proposed that lovastatin suppresses steroid-induced adipogenesis, decreases the fat cell transcription factor PPARg2 expression and favors osteoblastic differentiation, as well as *in vivo* expression of *Cabf1*/*Runx2 genes* [47, 48]. Then, inhibition of hypertrophy and proliferation of bone marrow fat cells and the formation of emboli by the inhibitory action of hydroxymethylglutaryl-coenzyme A reductase decreases the possibility of microvascular occlusion [49, 50].

Several studies have reported the association of steroid use and decreased bone mineral density [51–53]. In this regard, long-term methylprednisolone treatment in immature pigs was used; it was observed that blood flow was reduced in endplates and cancellous bone in 61% of the cases and showed the correlation of ON with radiographic IVC [54]. This suggested that the reduction of blood supply could be a pathophysiological factor in glucocorticoid-induced ON and that its results did not vary depending on the projection expression (g/cm^2) or volumetric bone mineral density (g/cm^3) [54].

4.3. Vertebral osteonecrosis y pancreatitis

Few cases of vertebral intraosseous fat necrosis have been described [55, 56]. Its frequency is up to 0.8% and its main manifestations are multiple pathological fractures [56]. Pathophysiologically, the destruction of adipose tissue is a consequence of the lipolytic activity of the lipase released into the bloodstream [57]. Then, there is obstruction of the bone vascularity by drops of fat which leads to local intravascular coagulation and ON. In addition, intramedullary swelling and increased intraosseous pressure result from the release of prostaglandin E1 [58].

4.4. Type 1 Gaucher disease (GD1) and vertebral osteonecrosis

As is well known, Gaucher disease is a lysosomal storage disorder resulting from an autosomal recessive mutation in *GBA1 gene* that encodes acid β-glucosidase. Deficiency of this enzyme favors deposition of glucocerebroside in the lysosomes of mononuclear phagocytes from different organs including the skeleton [59, 60]. The main bone affections include osteopenia, fractures, and AVN [61, 62]. The clinical presentation may be silent as a spinal cord infarction due to asymptomatic obstruction of the vascularity of the bone marrow. Bone infarction is generally detected on MRI [63]. Although pathophysiological mechanisms have not been elucidated, various GBA1 genotypes associated with or without AVN have been reported [64].

Skeletal involvement in most patients with Gaucher disease is well known [59, 60, 65]. The main skeletal affections of this condition include AVN, osteopenia, and fractures [61, 62, 65]. Various authors refer to an incidence of 8–36.4% of spinal fractures in patients with GD1 [64, 66–70]. They proposed that anemia and decreased bone mineral density of the lumbar spine are strong risk factors for fractures and AVN [64].

It has been estimated that the risk of untreated AVN and GD1 is 22.8 per 1000 person-years of follow-up [71]. It has also been proposed that imiglucerase therapy reduces the presentation of AVN at 13.8 per 1000 years of follow-up [72]. The pathophysiology of AVN in GD1 is unknown, however, it is presumed to be associated with secondary spinal infarction likely to microvascular occlusion, visualized in MRI [63].

4.5. HIV and vertebral osteonecrosis

HIV infection has been reported as one of the factors associated with vertebral ON. In these patients, the use of corticosteroids, abuse of alcohol and tobacco, hypercoagulable states, treatment with antiretroviral drugs, lipodystrophy, and the use of megestrol acetate or testosterone have been reported as risk factors [73–83]. It is estimated that the incidence of ON in HIV-infected patients is 0.03–0.65 cases per 100 person-years [81, 84]. In all cases reported, the participation of one or more risk factors and multifocal involvement were considered [85, 86]. Likewise, HIV-infected patients without risk factors and ON have also been reported [87].

The prevalence of osteoporotic vertebral fractures in HIV-infected patients has been increasing [88]. Likewise, the association of ON in HIV-positive individuals has been reported [89]. In the literature, only two cases of vertebral ON in HIV-infected patients and treatment with highly active antiretroviral therapy (HAART) have been reported, which presented refractory pain and developed rapid progressive kyphotic deformity [90, 91]. Drugs such as tenofovir induce increased bone remodeling and demineralization favoring bone fragility and vertebral CF [92]. Also, therapy with protease inhibitors promotes fat infiltration of the bone marrowand increase of intraosseous pressure compromising vascular irrigation [93].

4.6. Sarcoidosis and vertebral osteonecrosis

Sarcoidosis is a systemic condition in which the involvement of the musculoskeletal system occurs in 5% of patients [94–97]. Although the spinal involvement in sarcoidosis is rare, about

30 patients in the literature have been reported. A patient with sarcoidosis discarded the possibility of osteoporotic vertebral collapse due to the shape and narrowing of the intravertebral groove, the involvement of the body and the posterior elements of the vertebra and lack of evidence of new bone formation in the collapsed body [19].

5. Radiographic characteristics

Radiographically, non-demonstrable evidence of a fracture in consecutive studies supports the diagnosis of KD [14]. However, it is important to perform the differential diagnosis between KD and nontraumatic or spontaneous vertebral ON associated with osteoporosis. Clinically, it should be emphasized that osteoporotic compression fractures are not associated with neurological symptomatology. On the other hand, chronic radiographic osteoporotic fractures are not associated with changes in signal intensity on MRI [35]. This contrasts with the variability in signal characteristics on MRI in KD [6, 98]. Usually, these appear with an increase in the signal on T1-weighted images and reduced signal on T2-weighted images. However, in both KD and spontaneous vertebral ON, a hyperintense linear area on MRI can be observed. This pattern of signal change has been referred "double line sign" and corresponds to the phenomenon of IVC. This describes the accumulation of gas in the vertebral body observed in X-ray studies (**Figure 1**). This sign has also been observed associated with malignancy and intraosseous disc herniation, so it should not be considered as pathognomonic of ON.

Another radiological sign associated with ON is the intravertebral fluid of the vertebral body. This appears as a well-circumscribed area of low signal intensity on T1-weighted MRI and high signal intensity on T2-weighted images [39, 99]. This characteristic is known as a sign of fluid. In this regard, it was reported the coexistence of air and fluid in the same vertebral body in 21.5% of the cases. It was observed a more severe vertebral collapse in those cases with only intravertebral air than in those with fluid with or without air [100].

6. Classification of Kümmel's disease

In an attempt to classify the alterations associated with KD, morphological analyses regarding the type, degree of deformity and severity of vertebral collapse with questionable clinical relevance in acute processes was proposed [101]. Later, was proposed a multidimensional scheme for the classification of VCF suggesting that it could have application in the selection of surgical treatment and follow-up of patients. This included six dimensions fracture morphometry, chronicity, repair, dynamic stability, rupture of intravertebral bone trabeculae or clefts, and involvement of the posterior cortex [102]. However, this has been considered complicated and without any correlation with a natural history of KD.

Then, another specific classification proposal for this disease is raised, dependent on the progression and sequential clinical changes of the same. For this scale, Stage I corresponded to vertebrae intact or with a loss of height of the anterior portion of the vertebral body of less than 20% and without IVC in plain X-ray films, with a small cleft and fluid sign on T2-weighted

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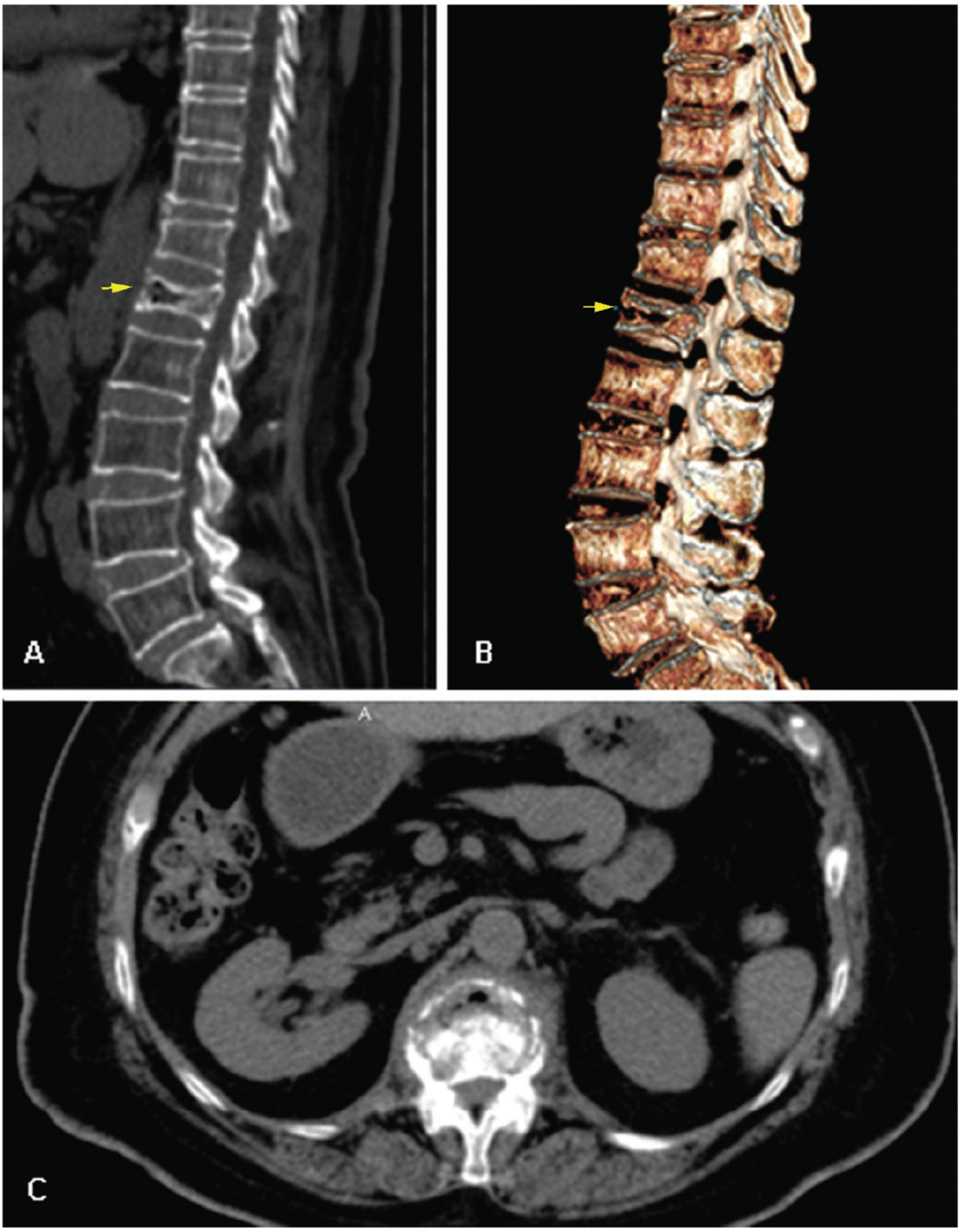

Figure 1. CT scan of the lumbar spine with compression fracture of L1 and intravertebral vacuum cleft (arrow). A Multiplanar reconstruction in sagittal, B volumetric reconstruction (3D), C axial plane.

MRI. In Stage II, loss of anterior body height would be more than 20% without an involvement of the posterior cortical, collapse of the vertebral body with dynamic mobility in the

radiographs and presence of the cleft sign on MRI. Finally, in Stage III included the severe collapse of the vertebral body with dynamic mobility and rupture of the posterior cortical, as well as IVC with retropulsion of bone fragments and compression of the spinal cord. At this stage, the patients presented back pain, deformity and neurological deficit [103].

Also were reported three stages related to the pathogenesis of progression to delayed vertebral collapse. Stage 1 showed presence of intravertebral cleft, Stage 2 showed IVC plus intravertebral instability, and Stage 3 showed complete vertebral collapse [104]. We can summarize that the main application of these classification proposals has not only been to describe the evolution of osteoporotic CF, but also to evaluate the clinical efficacy and to determine the follow-up of different surgical procedures.

7. Histopathology

There are few reports in the literature describing the histopathological features of vertebral ON. The first autopsy material related to KD was presented in 1926 [105]. It was described the destruction of spongy bone tissue and the consequent collapse of the vertebral body. Later was reported the pathological examination of the wedge-shaped collapsed L2 vertebral body, atrophic changes in bone trabeculae and multiple hemorrhagic areas [106]. These findings were termed "multiple microscopic fractures" [107].

Afterward, four concentric zones in AVN were proposed. These were a central area of cell death, followed by ischemia, congestion, and a peripheral zone of normal tissue. Early, inflammatory cells, serosanguinolent fluid, without bacterial colonies have been described. Thus, both the ischemic and the congestive zone undergo repair changes being replaced by fibrous tissue or new bone [108, 109]. Likewise, an anatomopathological study of vertebral pseudarthrosis reported a whitish, smooth, fibrocartilage-like lining with scarce chondrocytes, and flattened fibroblasts. As well, the regions after the cleft presented granulation tissue and poor bone formation. The biochemical characteristics of the fluid contained in the cleft showed a similar composition to the blood plasma, except for the lower proportion of total proteins [36].

ON reported in histopathological analysis on biopsy material demonstrated consistent data of new bone formation, bone marrow fibrosis, and bone repair [7, 17, 18, 20, 22]. However, different advances have been proposed from the original approaches, "rarefying osteitis" of inflammatory origin, multiple trauma of bone and ligamentous structures with the formation of cracks and microhemorrhages that lead to ON.

Some studies have suggested the correlation of the sign of the fluid on MRI and the histopathological data of vertebral ON demonstrated by the presence of small necrotic bone fragments between a fibrous stroma. In this regard, it was showed the presence of ON, edema, and fibrosis associated with the sign of fluid and this was significantly related to the severity of the fracture [110].

It has been considered that in the early stages vertebral ON presents edema and exudate, whereas in the late stages air could be contained in the spaces formed by the sclerotic bone [39, 111]. Hence,

possibly the changes were described from the intravertebral fluid to gas on MRI [100]. In addition to this proposal, it was reported that the sign of the fluid could be identified on MRI between 1 and 5 months, while the IVC could be noticed between 2 and 10 months after the fracture of the vertebra [112]. Subsequently, regenerative changes in more than 80% of cases occur, which are characterized by bone resorption, the formation of new bone and fibrosis. The still unstable collapse of the vertebra, the involvement of the spinal canal and neurological manifestations can be associated with these changes. However, some cases have been described with absence of unexplained regenerative histological changes [112].

Moreover, in those cases of vertebral body ON without vertebral collapse, empty lacunae, fatty necrosis with vacuolar degeneration and cell debris were described, suggesting necrosis of the bone marrow [113].

8. Differential diagnosis

The imaging characteristics described in vertebral ON such as sclerosis and calcification on computed tomography (CT) scan, hypointense images on T1 or hyperintense on T2, and nonreinforcement with Gadolinium (Gd) of the ischemic zone on MRI represent edema and necrosis. These changes could be confounded with other bone lesions such as the bone cyst, bone infarct, bone island, hemangioma, osteoblastoma, and osteoblastic metastatic tumor [113]. The literature reports cases of nontypical vertebral ON, on MRI, do not show low-intensity signal on T1 or double line sign on T2. In these cases, it has been suggested that the difference in the imaging findings could be due to the processes of ON and repair. Also, the vertebral bodies in these patients did not present collapse and the cortical intact was observed [113].

9. Treatment

As mentioned, the main symptom of delayed post-traumatic vertebral collapse is chronic back pain. This is usually localized, persistent, with a tendency to progression and irradiation to the peripheral nerve roots. Among conservative management protocols for back pain, the combination of exercise therapy and nonsteroidal anti-inflammatory drugs has been used with partially satisfactory results [114]. In addition to the medical aspects, psychosocial factors have been related to the pathophysiology of pain and response to treatment [115, 116]. Among this, anxiety, depression, notably distress and somatization have been associated, so strategies related to supportive psychotherapy, cognitive-behavioral methods and psychiatric medical treatments have been proposed in some cases [115, 117].

In some cases, teriparatide, an osteoanabolic agent frequently used in the treatment of osteoporosis, has been effective in promoting the reparative bone process and reducing pain [23, 118].

In the absence of neurological compromise and under the assumption of nonaffectation of the posterior cortical vertebral body has been suggested the conservative management of pain by analgesic drugs and bed rest [7]. It is now known that the incidence of vertebral compression

following the conservative management of osteoporotic vertebral fractures reaches 14.8% at 1 month and 21.8% at 6 months [119]. However, when conservative management fails, minimally invasive procedures such as vertebroplasty or kyphoplasty are suggested to stabilize the fracture site, align the vertebral segment and consequently alleviate pain [23]. The first reports in the literature on the treatment of KD emphasize conservative management, whereas the latest information has demonstrated that patients can be treated successfully with surgery. The choice of surgical treatment has depended to a large extent upon three factors, the severity of the back pain, the degree of kyphotic deformity, and the neurologic deficit [5, 7]. The main objective of the surgery lies in the decompression of the neural elements and sagittal alignment, consequently, earlier ambulation is promoted [120].

Techniques such as percutaneous kyphoplasty (PKP) or percutaneous vertebroplasty (PVP) with polymethyl methacrylate (PMMA) have been used in patients with osteoporotic CF with and without IVC [10, 121–127]. It was reported on both types of surgical procedures to relieve pain and restore collapsed vertebral body immediately after surgery. However, they reported aggravation of vertebral collapse and kyphotic deformity within 2 years after surgery in those patients with IVC. This also conditioned an increase in back pain, suggesting that this progression was due to intravertebral instability [121]. Therefore, both PVP and PKP have been considered as noneffective procedures in chronic spinal compression or acute vertebral compression with posterior cortical rupture, suggesting surgical stabilization via fusion [128]. The response to a foreign body that can occur with the use of PMMA with extensive fibrosis that could induce micromotion and secondary instability should also be mentioned [129, 130]. In addition, the mass of PMMA could spontaneously migrate to extra vertebral sites such as the disc space or the anterior vertebral space [8, 131–133].

Likewise, the distribution pattern and proportion of bone cement required in PVP could be predicted according to the area of ischemic necrosis on MRI [134]. Also, taking into account the proportion of necrosis on MRI recently raised that this variable could allow selecting the type of surgical procedure vertebroplasty, kyphoplasty, or surgery. Those cases with IVC, as well as those that required a surgical procedure were those that presented a higher percentage of necrosis [119].

Another reported proposal was the management of the posttraumatic osteoporotic vertebral ON with balloon kyphoplasty. It was suggested that restoration of the vertebral body and correction of kyphotic deformation could be achieved in relation to the sufficient volume of cement used. In addition, cement injection was performed in middle to later stages of solidification in patients with a defect of the anterior wall of the vertebral body or supported by X-ray fluoroscopy and balloon expansion in posterior defects to avoid leakage of the same [127].

The anterior decompression via corporectomy and fusion with intervertebral tricortical graft [135, 136] or ceramic glass spacers [137], posterior decompression with pedicle subtraction osteotomy [138–140] or the combination of both approaches [139] have been proposed in several studies. In the previous decompression, the fusion can be achieved with a spacer and a plate with a screw and in the posterior approach by means of the placement of transpedicular screws and hooks [141]. Spinal fusion, however, has been associated with procedural complications and long surgical time.

Subsequently, the technique of posterior one-segmental fixation combined with vertebroplasty and posterior-shortening osteotomy showed satisfactory results regarding correction of deformity, pain relief and functional improvement in patients with KD [142]. However, due to short segment fixation failures [143], the use of long segments to reestablish sagittal alignment was proposed. In the cases, it was reported to remove the upper end plate of the affected vertebral body and the superior intervertebral disc during the transpedicular subtraction and disc osteotomy combined with long-segment fixation, which favored bone fusion [144]. The placement of cages and long-segment fixation in pedicle subtraction osteotomy and disc resection has been useful in thoracolumbar post-traumatic kyphosis [145].

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References

[1] Kümmel H. Ueber die traumatischen Erkrankungen der. Deutsche Medizinische Wochenschrift. 1895;**21**:180-181

[2] Steel HH. Kümmell's disease. American Journal of Surgery. 1951;**81**(2):161-167

[3] Benedek TG, Nicholas JJ. Delayed traumatic vertebral body compression fracture; part II: Pathologic features. Seminars in Arthritis and Rheumatism. 1981;**10**(4):271-277. DOI: 10.1016/0049-0172(81)90004-4

[4] Rigler L. Kümmell's disease with report of a roentgenologically. American Journal of Roentgenology. 1931;**35**:749-753

[5] Ma R, Chow R, Shen FH. Kümmell's disease: Delayed post-traumatic osteonecrosis of the vertebral body. European Spine Journal. 2010;**19**(7):1065-1070. DOI: 10.1007/s00586-009-1205-4

[6] Maldague BE, Noel HM, Malghem JJ. The intravertebral vacuum cleft: A sign of ischemic vertebral collapse. Radiology. 1978;**129**(1):23-29

[7] Young WF, Brown D, Kendler A, Clements D. Delayed post-traumatic osteonecrosis of a vertebral body (Kümmell's disease). Acta Orthopaedica Belgica. 2002;**68**(1):13-19

[8] Kim DY, Lee SH, Jang JS, Chung SK, Lee HY. Intravertebral vacuum phenomenon in osteoporotic compression fracture: Report of 67 cases with quantitative evaluation of intravertebral instability. Journal of Neurosurgery. 2004;**100**(1 Suppl Spine):24-31

[9] Pappou IP, Papadopoulos EC, Swanson AN, Cammisa Jr FP, Girardi FP. Osteoporotic vertebral fractures and collapse with intravertebral vacuum sign (Kümmel's disease). Orthopedics. 2008;**31**(1):61-66

[10] Jang JS, Kim DY, Lee SH. Efficacy of percutaneous vertebroplasty in the treatment of intravertebral pseudarthrosis associated with noninfected avascular necrosis of the vertebral body. Spine (Philadelphia, PA 1976). 2003;**28**(14):1588-1592

[11] Van Eenenaam DP, el-Khoury GY. Delayed post-traumatic vertebral collapse (Kümmell's disease): Case report with serial radiographs, computed tomographic scans, and bone scans. Spine (Philadelphia, PA 1976). 1993;**18**(9):1236-1241

[12] Kim KT, Suk KS, Kim JM, Lee SH. Delayed vertebral collapse with neurological deficits secondary to osteoporosis. International Orthopaedics. 2003;**27**(2):65-69. DOI: 10.1007/s00264-002-0418-5

[13] Lee SH, Kim ES, Eoh W. Cement augmented anterior reconstruction with short posterior instrumentation: A less invasive surgical option for Kümmell's disease with cord compression. Journal of Clinical Neuroscience. 2011;**18**(4):509-514. DOI: 10.1016/j.jocn.2010.07.139

[14] Brower AC, Downey Jr EF. Kümmell disease: Report of a case with serial radiographs. Radiology. 1981;**141**(2):363-364. DOI: 10.1148/radiology.141.2.7291557

[15] Hermann G, Goldblatt J, Desnick RJ. Kümmell disease: Delayed collapse of the traumatised spine in a patient with Gaucher type 1 disease. The British Journal of Radiology. 1984;**57**(682):833-835. DOI: 10.1259/0007-1285-57-681-833

[16] Osterhouse MD, Kettner NW. Delayed posttraumatic vertebral collapse with intravertebral vacuum cleft. Journal of Manipulative & Physiological Therapeutics. 2002; **25**(4):270-275

[17] Kapoor V, Theruvil B, Foria V, Sampson M, Harley JM. Vertebral collapse in a 71-year-old woman. Clinical Orthopaedics and Related Research. 2004;**423**:291-298

[18] Maheshwari PR, Nagar AM, Prasad SS, Shah JR, Patkar DP. Avascular necrosis of spine: A rare appearance. Spine (Philadelphia, PA 1976). 2004;**29**(6):E119-E122

[19] Ito M, Motomiya M, Abumi K, Shirado O, Kotani Y, et al. Vertebral osteonecrosis associated with sarcoidosis. Case report. Journal of Neurosurgery Spine. 2005;**2**(2):222-225. DOI: 10.3171/spi.2005.2.2.0222

[20] Swartz K, Fee D. Kümmell's disease: A case report and literature review. Spine (Philadelphia, PA 1976). 2008;**33**(5):E152-E155. DOI: 10.1097/BRS.0b013e3181657f31

[21] Van der Schaaf I, Fransen H. Percutaneous vertebroplasty as treatment for Kümmell's disease. JBR-BTR. 2009;**92**(2):83-85

[22] Matzaroglou C, Georgiou CS, Assimakopoulos K, Saridis A, Khudiaev AT, et al. Kümmell' s disease: A rare spine entity in a young adult. Hellenic Journal of Nuclear Medicine. 2010; **13**(1):52-55

[23] Fabbriciani G, Pirro M, Floridi P, Callarelli L, Manfredelli MR, et al. Osteoanabolic therapy: A non-surgical option of treatment for Kümmell's disease?. Rheumatology International. 2012;**32**(5):1371-1374. DOI: 10.1007/s00296-010-1408-3

[24] Ranjan M, Mahadevan A, Prasad C, Sommana S, Susarla Krishna S. Kümmell's disease - uncommon or underreported disease: A clinicopathological account of a case and review of literature. Journal of Neurosciences in Rural Practice. 2013;**4**(4):439-442. DOI: 10.4103/0976-3147.120234

[25] Silverman SL, Minshall ME, Shen W, Harper KD, Xie S; Health-Related Quality of Life Subgroup of the Multiple Outcomes of Raloxifene Evaluation Study. The relationship of health-related quality of life to prevalent and incident vertebral fractures in postmenopausal women with osteoporosis: Results from the Multiple Outcomes of Raloxifene Evaluation Study. Arthritis and Rheumatism. 2001;**44**(11):2611-2619

[26] Hasserius R, Karlsson MK, Nilsson BE, Redlund-Johnell I, Johnell O; European Vertebral Osteoporosis Study. Prevalent vertebral deformities predict increased mortality and increased fracture rate in both men and women: A 10-year population-based study of 598 individuals from the Swedish cohort in the European Vertebral Osteoporosis Study. Osteoporos International. 2003;**14**(1):61-68. DOI: 10.1007/s00198-002-1316-9

[27] Gold DT. The clinical impact of vertebral fractures: Quality of life in women with osteoporosis. Bone. 1996;**18**(3 Suppl):185S-189S

[28] Kado DM, Huang MH, Karlamangla AS, Barrett-Connor E, Greendale GA. Hyperkyphotic posture predicts mortality in older community-dwelling men and women: A prospective study. Journal of the American Geriatrics Society. 2004;**52**(10):1662-1667. DOI: 10.1111/j.1532-5415.2004.52458.x

[29] McKiernan F, Faciszewski T. Intravertebral clefts in osteoporotic vertebral compression fractures. Arthritis and Rheumatism. 2003;**48**(5):1414-1419. DOI: 10.1002/art.10984

[30] McKiernan F, Jensen R, Faciszewski T. The dynamic mobility of vertebral compression fractures. Journal of Bone and Mineral Research. 2003;**18**(1):24-29. DOI: 10.1359/jbmr.2003.18.1.24

[31] Antonacci MD, Mody DR, Rutz K, Weilbaecher D, Heggeness MH. A histologic study of fractured human vertebral bodies. Journal of Spinal Disorders & Techniques. 2002;**15**(2) :118-126

[32] Crock HV, Yoshizawa H. The blood supply of the lumbar vertebral column. Clinical Orthopaedics and Related Research. 1976;**115**:6-21

[33] Ratcliffe JF. The arterial anatomy of the adult human lumbar vertebral body: A microarteriographic study. Journal of Anatomy. 1980;**131**(Pt 1):57-79

[34] Prakash, Prabhu LV, Saralaya VV, Pai MM, Ranade AV, et al. Vertebral body integrity: A review of various anatomical factors involved in the lumbar region. Osteoporos International. 2007;**18**(7):891-903. DOI: 10.1007/s00198-007-0373-5

[35] Chou LH, Knight RQ. Idiopathic avascular necrosis of a vertebral body. Case report and literature review. Spine (Philadelphia, PA 1976). 1997;**22**(16):1928-1932

[36] Hasegawa K, Homma T, Uchiyama S, Takahashi H. Vertebral pseudarthrosis in the osteoporotic spine. Spine (Philadelphia, PA 1976). 1988;**23**(20):2201-2206

[37] Lafforgue P, Chagnaud C, Daumen-Legré V, Daver L, Kasbarian M, et al. The intravertebral vacuum phenomenon ("vertebral osteonecrosis"). Migration of intradiscal gas in a fractured vertebral body?. Spine (Philadelphia, PA 1976). 1997;**22**(16):1885-1891

[38] Kim YC, Kim YH, Ha KY. Pathomechanism of intravertebral clefts in osteoporotic compression fractures of the spine. Spine Journal. 2014;**14**(4):659-666. DOI: 10.1016/j.spinee.2013.06.106

[39] Dupuy DE, Palmer WE, Rosenthal DI. Vertebral fluid collection associated with vertebral collapse. AJR American Journal of Roentgenology. 1996;**167**(6):1535-1538

[40] Wang C, Fan S, Liu J, Suyou L, Shan Z, et al. Basivertebral foramen could be connected with intravertebral cleft: A potential risk factor of cement leakage in percutaneous kyphoplasty. Spine Journal. 2014;**14**(8):1551-1558. DOI: 10.1016/j.spinee.2013.09.025

[41] Antonacci MD, Mody DR, Heggeness MH. Innervation of the human vertebral body: A histologic study. Journal of Spinal Disorders. 1998;**11**(6):526-531

[42] Fras C, Kravetz P, Mody DR, Heggeness MH. Substance P-containing nerves within the human vertebral body. An immunohistochemical study of the basivertebral nerve. Spine Journal. 2003;**3**(1):63-67

[43] Crock HV, Yoshizawa H, Kame SK. Observations on the venous drainage of the human vertebral body. The Journal of Bone and Joint Surgery. 1973;**55**(3):528-533

[44] Wang GJ, Cui Q, Balian G. The Nicolas Andry award. The pathogenesis and prevention of steroid-induced osteonecrosis. Clinical Orthopaedics and Related Research. 2000;**370**:295-310

[45] Koo KH, Dussault RG, Kaplan PA, Ahn IO, Kim R, et al. Fatty marrow conversion of the proximal femoral metaphysis in osteonecrotic hips. Clinical Orthopaedics and Related Research. 1999;**361**:159-167

[46] Yamamoto T, Hirano K, Tsutsui H, Sugioka Y, Sueishi K. Corticosteroid enhances the experimental induction of osteonecrosis in rabbits with Shwartzman reaction. Clinical Orthopaedics and Related Research. 1995;**316**:235-243

[47] Pengde K, Fuxing P, Bin S, Jing Y, Jingqiu C. Lovastatin inhibits adipogenesis and prevents osteonecrosis in steroid-treated rabbits. Joint Bone Spine. 2008;**75**(6):696-701. DOI: 10.1016/j.jbspin.2007.12.008

[48] Li X, Cui Q, Kao C, Wang GJ, Balian. Lovastatin inhibits adipogenic and stimulates osteogenic differentiation by suppressing PPARgamma2 and increasing Cbfa1/Runx2 expression in bone marrow mesenchymal cell cultures. Bone. 2003;**33**(4):652-659

[49] Wang GJ, Chung KC, Shen WJ. Lipid clearing agents in steroid-induced osteoporosis. Journal of the Formosan Medical Association. 1995;**94**(10):589-592

[50] Wang GJ. Pathogenesis of steroid-induced avascular necrosis and its response to lipid clearing agents. In: Hirohata K, Mizuno K, Matsubara T, editors. Trends in Research and Treatment of Joint Diseases. Tokyo: Springer-Verlag; 1992. pp. 59-71. DOI: 10.1007/978-4-431-68192-2_8

[51] Fritz PC, Ward WE, Atkinson SA, Tenenbaum HC. Tamoxifen attenuates the effects of exogenous glucocorticoid on bone formation and growth in piglets. Endocrinology. 1998; **139**(8):3399-3403

[52] Weinstein RS, Jilka RL, Parfitt AM, Manolagas SC. Inhibition of osteoblastogenesis and promotion of apoptosis of osteoblasts and osteocytes by glucocorticoids. Potential mechanisms of their deleterious effects on bone. Journal of Clinical Investigation. 1998; **102**(2):274-282

[53] Julian BA, Laskow DA, Dubovsky J, Dubovsky EV, Curtis JJ, et al. Rapid loss of vertebral mineral density after renal transplantation. The New England Journal of Medicine. 1991;**325**(8):544-550

[54] Drescher W, Li H, Qvesel D, Jensen SD, Flo C, et al. Vertebral blood flow and bone mineral density during long-term corticosteroid treatment: An experimental study in immature pigs. Spine (Philadelphia, PA 1976). 2000;**25**(23):3021-3025

[55] Allen BL, Jinkins WJ. Vertebral osteonecrosis associated with pancreatitis in child. A case report. Journal of Bone and Joint Surgery. 1978;**60**(7):985-987

[56] Sigmundsson FG, Andersen PB, Schroeder HD, Thomsen K. Vertebral osteonecrosis associated with pancreatitis in a woman with pancreas divisum. A case report. Journal of Bone and Joint Surgery. 2004;**86-A**(11):2504-2508

[57] Jones Jr JP. Fat embolism and osteonecrosis. Orthopedic Clinics of North America. 1985;**16**(4):595-633

[58] Rittenberg GM, Korn JH, Schabel SI, Stalheim R. Rapid osteolysis in pancreatic carcinoma. The Western Journal of Medicine. 1981;**135**(5):408-410

[59] Grabowski G, Kolodny E, Weinreb N, Rosenbloom B, Prakash-Cheng A, et al. Gaucher disease: Phenotypic and genetic variation. In: Scriver C, Beaudet A, Valle D, Sly W, editors. The Online Metabolic and Molecular Basis of Inherited Metabolic Disease. New York: McGraw-Hill Publishers; 2010. DOI: 10.1036/ommbid.177

[60] Charrow J, Andersson HC, Kaplan P, Kolodny EH, Mistry P, et al. The Gaucher registry: Demographics and disease characteristics of 1698 patients with Gaucher disease. Archives of Internal Medicine. 2000;**160**(18):2835-2843

[61] Stirnemann J, Belmatoug N, Vincent C, Fain O, Fantin B, et al. Bone events and evolution of biologic markers in Gaucher disease before and during treatment. Arthritis Research & Therapy. 2010;**12**(4):R156. DOI: 10.1186/ar3111

[62] Deegan PB, Pavlova E, Tindall J, Stein PE, Bearcroft P, et al. Osseous manifestations of adult Gaucher disease in the era of enzyme replacement therapy. Medicine (Baltimore). 2011;**90**(1):52-60. DOI: 10.1097/MD.0b013e3182057be4

[63] Lutsky KF, Tejwani NC. Orthopaedic manifestations of Gaucher disease. Bulletin of the Hospital for Joint Diseases. 2007;**65**(1):37-42

[64] Khan A, Hangartner T, Weinreb NJ, Taylor JS, Mistry PK. Risk factors for fractures and avascular osteonecrosis in type 1 Gaucher disease: A study from the International Collaborative Gaucher Group (ICGG) Gaucher Registry. Journal of Bone and Mineral Research. 2012;**27**(8):1839-1848. DOI: 10.1002/jbmr.1680

[65] Wenstrup RJ, Roca-Espiau M, Weinreb NJ, Bembi B. Skeletal aspects of Gaucher disease: A review. The British Journal of Radiology. 2002;**75**(Suppl 1):A2-A12. DOI: 10.1259/bjr.75.suppl_1.750002

[66] Zimran A, Kay A, Gelbart T, Garver P, Thurston D, et al. Gaucher disease. Clinical, laboratory, radiologic, and genetic features of 53 patients. Medicine (Baltimore). 1992;**71**(6):337-353

[67] Stirnemann J. Clinical study of the French cohort of Gaucher disease patients. La Revue De Medecine **Interne**. 2006;**27**(Suppl 1):S18-S21

[68] Belmatoug N, Billette de Villemeur T. Skeletal response to enzyme replacement therapy for type 1 Gaucher disease: A preliminary report of the French experience. Seminars in Hematology. 1995;**32**(Suppl 1):33-38

[69] Katz K, Sabato S, Horev G, Cohen IJ, Yosipovitch Z. Spinal involvement in children and adolescents with Gaucher disease. Spine (Philadelphia, PA 1976). 1993;**18**(3):332-335

[70] Javier RM, Moser T, Dietemann JL, Sparsa L, Natarajan-Ame S, et al. Multiple vertebral osteonecrosis. Joint Bone Spine. 2008;**75**(3):341-344. DOI: 10.1016/j.jbspin.2007.05.010

[71] Yeh M, Weinreb N, Deegan P, Vellodi A, Cole J, et al. Avascular necrosis in untreated patients with type 1 Gaucher disease. Molecular Genetics and Metabolism. 2009;**98**:62

[72] Mistry PK, Deegan P, Vellodi A, Cole JA, Yeh M, et al. Timing of initiation of enzyme replacement therapy after diagnosis of type 1 Gaucher disease: Effect on incidence of avascular necrosis. British Journal of Haematology. 2009;**147**(4):561-570. DOI: 10.1111/j.1365-2141.2009.07872.x

[73] Aguiar De Aragao P, Lemos RB, Aquino MZ, Souza Marques HH. Hyperlipidaemia a risk factor for femoral head osteonecrosis (Legg-Calv -Perthes-like disease) in children with AIDS: Case report. Brazilian Journal of Infectious Diseases. 2002;**6**:142-145

[74] Allison GT, Bostrom MP, Glesby MJ. Osteonecrosis in HIV disease: Epidemiology, etiologies, and clinical management. AIDS. 2003;**17**(1):1-9. DOI: 10.1097/01.aids.0000042940.55529.93

[75] Glesby MJ, Hoover DR, Vaamonde CM. Osteonecrosis in patients infected with human immunodeficiency virus: A case-control study. The Journal of Infectious Diseases. 2001;**184**:519-523. DOI: 10.1086/322779

[76] Hasse B, Ledergerber B, Egger M, Flepp M, Bachmann S, et al; Swiss HIV Cohort Study. Antiretroviral treatment and osteonecrosis in patients of the Swiss HIV Cohort Study: A nested case-control study. AIDS Research and Human Retroviruses. 2004;**20**(9):909-915. DOI: 10.1089/aid.2004.20.909

[77] Martin K, Lawson-Ayayi S, Miremont-Salamé G, Blaizeau MJ, Balestre E, et al; Groupe d'Epidémiologie Clinique du SIDA en Aquitaine. Symptomatic bone disorders in HIV-infected patients: Incidence in the Aquitaine cohort (1999-2002). HIV Medicine. 2004;**5**(6):421-426. DOI: 10.1111/j.1468-1293.2004.00247.x

[78] Miller KD, Masur H, Jones EC, Joe GO, Rick ME, et al. High prevalence of osteonecrosis of the femoral head in HIV-infected adults. Annals of Internal Medicine. 2002;**137**(1):17-25

[79] Molia AC, Strady C, Rouger C, Beguinot IM, Berger JL, et al. Osteonecrosis in six HIV-infected patients receiving highly active antiretroviral therapy. Annals of Pharmacotherapy. 2004;**38**(12):2050-2054. DOI: 10.1345/aph.1E154

[80] Blacksin MF, Kloser PC, Simon J. Avascular necrosis of bone in human immunodeficiency virus infected patients. Clinical Imaging. 1999;**23**(5):314-318

[81] Scribner AN, Troia-Cancio PV, Cox BA, Marcantonio D, Hamid F, et al. Osteonecrosis in HIV: A case-control study. Journal of Acquired Immune Deficiency Syndromes. 2000;**25**(1):19-25

[82] Valencia ME, Barreiro P, Soriano V, Blanco F, Moreno V, et al. Avascular necrosis in HIV-infected patients receiving antiretroviral treatment: Study of seven cases. HIV Clinical Trials. 2003;**4**(2):132-136. DOI: 10.1310/hct.2003.4.2.008

[83] Koller E, Mann M, Malozowski S, Bacsanyi J, Gibert C. Aseptic necrosis in HIV seropositive patients: A possible etiologic role for megestrol acetate. AIDS Patient Care STDS. 2000;**14**(8):405-410. DOI: 10.1089/108729100416614

[84] Gutiérrez F, Padilla S, Ortega E, García JA, Flores J, et al. Avascular necrosis of the bone in HIV-infected patients: Incidence and associated factors. AIDS. 2002;**16**(3):481-483

[85] Gutiérrez F, Padilla S, Masiá M, Flores J, Boix V, et al; HIV-related Osteonecrosis Study Group. Osteonecrosis in patients infected with HIV: Clinical epidemiology and natural history in a large case series from Spain. Journal of Acquired Immune Deficiency Syndromes. 2006;**42**(5):650. DOI: 10.1097/01.qai.0000225012.53568.20

[86] González García A, Sifuentes Giraldo WA, Blázquez Cañamero MÁ, Ahijón Lana M, Navas Elorza E, et al. Multifocal osteonecrosis associated with human immunodeficiency virus infection. Reumatologia Clinica. 2012;**8**(6):361-364. DOI: 10.1016/j.reuma.2012.01.008

[87] Monier P, McKown K, Bronze MS. Osteonecrosis complicating highly active antiretroviral therapy in patients infected with human immunodeficiency virus. Clinical Infectious Diseases. 2000;**31**(6):1488-1492. DOI: 10.1086/317503

[88] Young B, Dao CN, Buchacz K, Baker R, Brooks JT; HIV Outpatient Study (HOPS) Investigators. Increased rates of bone fracture among HIV-infected persons in the HIV

Outpatient Study (HOPS) compared with the US general population, 2000-2006. Clinical Infectious Diseases. 2011;**52**(8):1061-1068. DOI: 10.1093/cid/ciq242

[89] Fessel WJ, Chau Q, Leong D. Association of osteonecrosis and osteoporosis in HIV-1-infected patients. AIDS. 2011;**25**(15):1877-1880. DOI: 10.1097/QAD.0b013e32834af637

[90] Sifuentes Giraldo WA, Blázquez Cañamero M, Navas Elorza E, Gallego Rivera I, Vázquez Díaz M. Concomitant presentation of multiple vertebral and peripheral osteonecrosis in a HIV-infected patient. Joint Bone Spine. 2012;**79**(3):332-334. DOI: 10.1016/j.jbspin.2011.12.002

[91] Sifuentes Giraldo WA, Macía Villa CC, Rodríguez-Navarro CQ, Vázquez Díaz M. Vertebral osteonecrosis in an HIV-infected patient. Antiviral Therapy. 2012;**17**(8):1627-1630. DOI: 10.3851/IMP2262

[92] Guo FP, Yu XB, Luo L, Han Y, Qiu ZF, et al. The impact of highly active antiretroviral therapy on bone mineral density in human immunodeficiency virus infected patients. Zhonghua Nei Ke Za Zhi. 2010;**49**(8):649-652

[93] Porsch M, König DP, Popken F. Possible complication of HIV therapy. Protease inhibitor-induced femur head necrosis. MMW Fortschritte Der Medizin. 2001;**143**(Suppl 1):90-91

[94] Fallon MD, Perry 3rd HM, Teitelbaum SL. Skeletal sarcoidosis with osteopenia. Metabolic Bone Disease & Related Research. 1981;**3**(3):171-174

[95] Resnik CS, Young JW, Aisner SC, Levine A. Case report 594: Osseous sarcoidosis (osteolytic) of lumbar spine and pelvis. Skeletal Radiology. 1990;**19**(1):79-81

[96] Rúa-Figueroa I, Gantes MA, Erausquin C, Mhaidli H, Montesdeoca A. Vertebral sarcoidosis: Clinical and imaging findings. Seminars in Arthritis and Rheumatism. 2002;**31**(5):346-352

[97] Shaikh S, Soubani AO, Rumore P, Cantos E, Jelveh Z. Lytic osseous destruction in vertebral sarcoidosis. New York State Journal of Medicine. 1992;**92**(5):213-214

[98] Chevalier X, Wrona N, Avouac B, Larget-Piet B. Thigh pain and multiple vertebral osteonecroses: Value of magnetic resonance imaging. Journal of Rheumatology. 1991;**18**(10):1627-1630

[99] Malghem J, Maldague B, Labaisse MA, Dooms G, Duprez T, et al. Intravertebral vacuum cleft: Changes in content after supine positioning. Radiology. 1993;**187**(2):483-487

[100] Yu CW, Hsu CY, Shih TT, Chen BB, Fu CJ. Vertebral osteonecrosis: MR imaging findings and related changes on adjacent levels. AJNR American Journal of Neuroradiology. 2007;**28**(1):42-47

[101] Eastell R, Cedel SL, Wahner HW, Riggs BL, Melton 3rd LJ. Classification of vertebral fractures. Journal of Bone and Mineral Research. 1991;**6**(3):207-215

[102] Faciszewski T, McKiernan F. Calling all vertebral fractures classification of vertebral compression fractures: A consensus for comparison of treatment and outcome. Journal of Bone and Mineral Research. 2002;**17**(2):185-191. DOI: 10.1359/jbmr.2002.17.2.185

[103] Li KC, †Wong TU, Kung FC, Li A, Hsieh CH. Staging of Kümmell's disease. Musculoskeletal Research. 2004;**8**(1):43-55. DOI: 10.1142/S0218957704001181

[104] Ito Y, Hasegawa Y, Toda K, Nakahara S. Pathogenesis and diagnosis of delayed vertebral collapse resulting from osteoporotic spinal fracture. Spine Journal. 2002;**2**(2):101-106

[105] Schmorl G, Junghanns H. The Human Spine in Health and Disease. 2nd ed. New York: Grune & Stratton; 1971. pp. 268-296

[106] Cardis J, Walker GF, Olver RH. Kümmell's disease. British Journal of Surgery. 1928;**15** (616):25

[107] Kux E. Zur Histopathologie der posttraumatischen (Kümmellschen) Wirbelerkrankung. Archiv für orthopädische und Unfall-Chirurgie, mit besonderer Berücksichtigung der Frakturenlehre und der orthopädisch-chirurgischen Technik. 1933;**34**:18-23

[108] Sweet DE, Madewell JE, Resnick DK, Niwayama E. Pathogenesis of osteonecrosis. In: Diagnosis of Bone and Joint Disorders. Philadelphia: Saunders; 1981. pp. 2780-2831

[109] Naul LG, Peet GJ, Maupin WB. Avascular necrosis of the vertebral body: MR imaging. Radiology. 1989;**172**(1):219-222

[110] Baur A, Stäbler A, Arbogast S, Duerr HR, Bartl R, et al. Acute osteoporotic and neoplastic vertebral compression fractures: Fluid sign at MR imaging. Radiology. 2002;**225**(3):730-735. DOI: 10.1148/radiol.2253011413

[111] Sugano N, Masuhara K, Nakamura N, Ochi T, Hirooka A, et al. MRI of early osteonecrosis of the femoral head after transcervical fracture. The Journal of Bone and Joint Surgery. British Volume. 1996;**78**(2):253-257

[112] Lin CL, Lin RM, Huang KY, Yan JJ, Yan YS. MRI fluid sign is reliable in correlation with osteonecrosis after vertebral fractures: A histopathologic study. European Spine Journal. 2013;**22**(7):1617-1623. DOI: 10.1007/s00586-012-2618-z

[113] Murakami H, Kawahara N, Gabata T, Nambu K, Tomita K. Vertebral body osteonecrosis without vertebral collapse. Spine (Philadelphia, PA 1976). 2003;**28**(16):E323-E328

[114] Van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain. A systematic review of randomized controlled trials of the most common interventions. Spine (Philadelphia, PA 1976). 1997;**22**(18):2128-2156

[115] Moore JE. Chronic low back pain and psychosocial issues. Physical Medicine and Rehabilitation Clinics of North America. 2010;**21**(4):801-815. DOI: 10.1016/j.pmr.2010.06.005

[116] Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. Spine (Philadelphia, PA 1976). 2002;**27**(5):E109-E120

[117] Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. Spine (Philadelphia, PA 1976). 2003;**28**(22):2540-2545. DOI: 10.1097/01.BRS.0000092372.73527.BA

[118] Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. New England Journal of Medicine. 2001;**344**(19):1434-1441. DOI: 10.1056/NEJM200105103441904

[119] Lee JM, Lee YS, Kim YB, Park SW, Kang DH, et al. What effects does necrotic area of Contrast-Enhanced MRI in osteoporotic vertebral fracture have on further compression and clinical outcome? Journal of Korean Neurosurgical Society. 2017;**60**(2):181-188. DOI: 10.3340/jkns.2016.0707.015

[120] Li KC, Li AF, Hsieh CH, Liao TH, Chen CH. Another option to treat Kümmell's disease with cord compression. European Spine Journal. 2007;**16**(9):1479-1487. DOI: 10.1007/s00586-006-0094-z

[121] Fang X, Yu F, Fu S, Song H. Intravertebral clefts in osteoporotic compression fractures of the spine: Incidence, characteristics, and therapeutic efficacy. International Journal of Clinical and Experimental Medicine. 2015;**8**(9):16960-16968

[122] Wu MH, Huang TJ, Cheng CC, Li YY, Hsu RW. Role of the supine lateral radiograph of the spine in vertebroplasty for osteoporotic vertebral compression fracture: A prospective study. BMC Musculoskeletal Disorder. 2010;**11**:164. DOI: 10.1186/1471-2474-11-164

[123] Kim YJ, Lee JW, Kim KJ, Chung SK, Kim HJ, et al. Percutaneous vertebroplasty for intravertebral cleft: Analysis of therapeutic effects and outcome predictors. Skeletal Radiology. 2010;**39**(8):757-766. DOI: 10.1007/s00256-009-0866-8

[124] Lane JI, Maus TP, Wald JT, Thielen KR, Bobra S, et al. Intravertebral clefts opacified during vertebroplasty: Pathogenesis, technical implications, and prognostic significance. AJNR American Journal of Neuroradiology. 2002;**23**(10):1642-1646

[125] Becker S, Tuschel A, Chavanne A, Meissner J, Ogon M. Balloon kyphoplasty for vertebra plana with or without osteonecrosis. Journal of Orthopaedic Surgery (Hong Kong). 2008;**16**(1):14-19. DOI: 10.1177/230949900801600104

[126] Heo DH, Choi JH, Kim MK, Choi HC, Jeong JH, et al. Therapeutic efficacy of vertebroplasty in osteoporotic vertebral compression fractures with avascular osteonecrosis: A minimum 2-year follow-up study. Spine (Philadelphia, PA 1976). 2012;**37**(7):E423-E429. DOI: 10.1097/BRS.0b013e318238f29a

[127] Wang G, Yang H, Meng B, Zhu X, Zou J, et al. Post-traumatic osteoporotic vertebral osteonecrosis treated using balloon kyphoplasty. Journal of Clinical Neuroscience. 2011;**18**(5):664-668. DOI: 10.1016/j.jocn.2010.09.014

[128] Zhang GQ, Gao YZ, Zheng J, Luo JP, Tang C, et al. Posterior decompression and short segmental pedicle screw fixation combined with vertebroplasty for Kümmell's disease with neurological deficits. Experimental and Therapeutic Medicine. 2013;**5**(2):517-522. DOI: 10.3892/etm.2012.833

[129] Lewis G. Properties of acrylic bone cement: State of the art review. Journal of Biomedical Materials Research. 1997;**38**(2):155-182

[130] Huang KY, Yan JJ, Lin RM. Histopathologic findings of retrieved specimens of vertebroplasty with polymethylmethacrylate cement: Case control study. Spine (Philadelphia, PA 1976). 2005;**30**(19):E585-E588

[131] Cho SM, Heo DH, Cho YJ. Spontaneous migration of a polymethylmethacrylate mass after vertebroplasty in osteoporotic lumbar compression fracture with avascular osteonecrosis: A case report. Joint Bone Spine. 2011;**78**(1):98-99. DOI: 10.1016/j.jbspin.2010.08.016

[132] Wang HS, Kim HS, Ju CI, Kim SW. Delayed bone cement displacement following balloon kyphoplasty. Journal of Korean Neurosurgical Society. 2008;**43**(4):212-214. DOI: 10.3340/jkns.2008.43.4.212

[133] Ha KY, Lee JS, Kim KW, Chon JS. Percutaneous vertebroplasty for vertebral compression fractures with and without intravertebral clefts. The Journal of Bone and Joint Surgery. 2006;**88**(5):629-633. DOI: 10.1302/0301-620X.88B5.17345

[134] Oka M, Matsusako M, Kobayashi N, Uemura A, Numaguchi Y. Intravertebral cleft sign on fat-suppressed contrast-enhanced MR: Correlation with cement distribution pattern on percutaneous vertebroplasty. Academic Radiology. 2005;**12**(8):992-999. DOI: 10.1016/j.acra.2005.05.003

[135] Kanayama M, Ishida T, Hashimoto T, Shigenobu K, Togawa D, et al. Role of major spine surgery using Kaneda anterior instrumentation for osteoporotic vertebral collapse. Journal of Spinal Disorders & Techniques. 2010;**23**(1):53-56. DOI: 10.1097/BSD.0b013e318193e3a5

[136] Hasegawa K, Homma T, Uchiyama S, Takahashi HE. Osteosynthesis without instrumentation for vertebral pseudarthrosis in the osteoporotic spine. The Journal of Bone and Joint Surgery. 1997;**79**(3):452-456

[137] Kaneda K, Asano S, Hashimoto T, Satoh S, Fujiya M. The treatment of osteoporotic-posttraumatic vertebral collapse using the Kaneda device and a bioactive ceramic vertebral prosthesis. Spine (Philadelphia, PA 1976). 1992;**17**(8 Suppl)):S295-S303

[138] Mochida J, Toh E, Chiba M, Nishimura K. Treatment of osteoporotic late collapse of a vertebral body of thoracic and lumbar spine. Journal of Spinal Disorders. 2001;**14**(5):393-398

[139] Suk SI, Kim JH, Lee SM, Chung ER, Lee JH. Anterior-posterior surgery versus posterior closing wedge osteotomy in posttraumatic kyphosis with neurologic compromised osteoporotic fracture. Spine (Philadelphia, PA 1976). 2003;**28**(18):2170-2175. DOI: 10.1097/01.BRS.0000090889.45158.5A

[140] Saita K, Hoshino Y, Kikkawa I, Nakamura H. Posterior spinal shortening for paraplegia after vertebral collapse caused by osteoporosis. Spine (Philadelphia, PA 1976). 2000;**25**(21):2832-2835

[141] Kim HS, Heo DW. Percutaneous pedicle screw fixation with polymethylmethacrylate augmentation for the treatment of thoracolumbar intravertebral pseudoarthrosis

associated with kümmell's osteonecrosis. BioMed Research International. 2016;**2016:**3878063. DOI: 10.1155/2016/3878063

[142] Long HQ, Wan Y, Zhang X, Liu SY, Li FB. Two kinds of posterior approach for Kvmmell's disease after osteoporotic thoracolumbar fracture. Chinese Journal of Traumatology. 2009;**12**(3):142-147

[143] Matsuyama Y, Goto M, Yoshihara H, Tsuji T, Sakai Y, et al. Vertebral reconstruction with biodegradable calcium phosphate cement in the treatment of osteoporotic vertebral compression fracture using instrumentation. Journal of Spinal Disorders & Techniques. 2004;**17**(4):291-296

[144] Zhang X, Hu W, Yu J, Wang Z, Wang Y. An effective rreatment option for kümmell disease with neurological eficits: Modified transpedicular subtraction and disc osteotomy combined with Long-Segment fixation. Spine (Philadelphia, PA 1976). 2016;**41**(15):E923-E930. DOI: 10.1097/BRS.0000000000001467

[145] Hu W, Wang B, Run H, Zhang X, Wang Y. Pedicle subtraction osteotomy and disc resection with cage placement in post-traumatic thoracolumbar kyphosis, a retrospective study. Journal of Orthopaedic Surgery and Research. 2016;**11**(1):112. DOI: 10.1186/s13018-016-0447-1