Vertebral osteonecrosis, also known as Kümmell’s disease, is a disorder resulting in non-consolidation of a vertebral fracture caused by ischaemia. The main differential diagnosis of vertebral osteonecrosis is osteoporotic vertebral fracture; however, the former is associated more frequently with severe pain and neurological complications. Although HIV-infected patients have an increased risk of developing osteonecrosis in peripheral locations and osteoporotic vertebral fractures, the occurrence of vertebral osteonecrosis has not been previously reported in any of the large series of HIV-associated osteonecrosis. Here, we report an HIV-infected patient who developed vertebral osteonecrosis with refractory pain and displayed rapid kyphotic deformity development during HAART. HIV-infected patients have a 100-fold greater risk than the general population of developing osteonecrosis of the hips and other peripheral locations. An increased prevalence of previously recognized risk factors for osteonecrosis, such as corticosteroid use, hypercoagulable states, alcohol abuse and tobacco use has been described in HIV-infected patients [1,2]. Osteonecrosis affecting the vertebral body is less frequently diagnosed and considered as the result of a non-consolidation of a vertebral fracture caused by ischaemia [3]. HIV-infected patients have an increased prevalence of osteoporosis and vertebral fractures [4] and, recently, it has been reported that osteoporosis and osteonecrosis occur concurrently in HIV-infected patients more often than expected [5]; therefore, vertebral osteonecrosis (VON) occurrence could be expected in these patients. However, VON is not reported in any of the large studies of HIV-associated osteonecrosis [1,2] and there is only one published case to-date [6].

Here, we report the second case of VON in an HIV-infected patient receiving HAART.

Case report

A 45-year-old Spanish homosexual man was diagnosed with HIV infection with intestinal cryptosporidiosis in November 2009 (CD4+ T-cell count 190 cells/mm³ and HIV RNA plasma viral load 3,162 copies/ml). Shortly after cryptosporidiosis treatment with paramomicine, HAART was initiated, including tenofovir plus emtricitabine and ritonavir-boosted atazanavir. Undetectable viral load and CD4+ T-cell count normalization were achieved within a few months. The patient had no previous history of osteoporosis risk factors or fragility fractures.

In September 2011, he presented with back pain that appeared after a mild exertion 1 month before seeking medical help. Pain was moderate and was not controlled with opiates associated with non-steroidal anti-inflammatory drugs. He quickly developed dorsal hyperkyphosis without associated neurological signs. Blood chemistry including levels of creatinine, calcium, phosphorus, alkaline phosphatase, cholesterol and triglycerides were in normal ranges; however, mild 25-hydroxyvitamin D3 deficiency was detected. Calciuria, tubular phosphate reabsorption, parathormone and testosterone levels were also normal. Dual energy X-ray absorptiometry scans showed osteoporosis in the lumbar spine (L1-L4: T -2.9, Z -2.1) and osteopaenia in the femoral neck (T -1.4, Z -0.3). Lateral spine X-rays showed angular kyphosis in lower thoracic spine secondary to anterior wedge fractures involving T12, T11 and T10, and upper endplate fractures in T9, L2 and L3. Computed tomography (CT) scans of the spine revealed presence of an intravertebral air collection in T12 (vacuum cleft sign) with slight displacement of the posterior wall (Figure 1). VON involving T12 was diagnosed and the patient was treated with...
vitamin D3 supplementation and fitted with a back brace. HAART was modified: tenofovir plus emtricitabine were replaced by abacavir plus lamivudine, and ritonavir-boosted atazanavir by etravirine. Pain was controlled gradually over a few weeks and he did not develop neurological complications or osteonecrosis in other locations during follow-up.

Discussion

In 1891, the German surgeon, Henry Kümmell, described a series of five patients with a rare disorder characterized by development of progressive, painful kyphosis at the lower thoracic or upper lumbar regions after a trivial spinal trauma followed by an asymptomatic period of months to years [7]. The advent of X-rays revealed that the cause of kyphosis development was a delayed vertebral body collapse. This collapse represents a failure of the fracture healing process caused by the development of an avascular necrosis zone below the superior endplate, eliminating healing potential and resulting in an atrophic or avascular non-union; hence, this process is known as VON or Kümmell’s disease [8].

The most characteristic radiological sign of VON is the formation of an intravertebral air collection, recognizable on plain X-rays as linear or semi-lunar radiolucent shadow – a so-called ‘vacuum cleft sign’ [9]. The presence of this sign is highly suggestive of VON, having been demonstrated as a strong correlation with biopsy-proven osteonecrosis, with a sensitivity of 85%, specificity of 99% and a positive predictive value 91%. However, this sign is often difficult to identify and might appear only on hyperextension radiographs; therefore, its absence does not exclude VON diagnosis [3,10]. Vacuum cleft sign is more easily seen on axial CT, showing a heterogeneous distribution and an irregular shape compared with on X-rays [11]. Vacuum cleft can be also
identified on magnetic resonance (MR) as a zone with low-signal intensity in all sequences, or can secondarily be filled with fluid and appear as a well-circumscribed area of low-signal intensity on T1-weighted and high-signal intensity on T2-weighted images. This finding is called the ‘fluid sign’ [11].

VON usually occurs in adults older than 50 years of age, mostly women, with previous osteoporosis history, and involves more frequently only one vertebral body at the T8 through to the L4 level, with the anterior third of the vertebral body being the most affected [9,12]. VON is thought to result from the disruption of vertebral body nutritional supply caused by medullary arterioles occlusion secondary to fracture; however, fatty infiltration of vertebral body and microemboli have also been implicated [3].

VON has been associated with other traditional risk factors for peripheral osteonecrosis [3]; however, its association with HIV infection has not been previously reported in any of the large series of osteonecrosis in HIV-infected patients [1,2]. Our group reported the first case of VON in a long-term HIV-infected patient receiving HAART who presented several concurrent risk factors for both osteonecrosis and osteoporosis, and who developed concomitantly multiple osteonecrosis in several vertebral bodies and peripheral locations [6]. The present case had no traditional risk factors for osteonecrosis, but he presented other factors related with HIV infection, such as severe immunosuppression and low nadir CD4+ T-cell count [1,2]. A reduced regenerative capacity by osteoblasts has been suggested as a common mechanism to explain surplus of both osteonecrosis and osteoporosis in HIV infection [5]. HAART could also have contributed to VON development in this patient. Tenofovir treatment is associated with increased bone remodelling and demineralization that could lead to increased fragility and subsequent vertebral compression fracture [13,14]. Protease inhibitors could also induce bone marrow fatty infiltration causing increased intraosseous pressure and vascular collapse, both contributing to VON development [15].

The main differential diagnose of VON is the osteoporotic vertebral fracture. It is important to differentiate both conditions because VON is more frequently associated with development of gross kyphotic deformity and neurological complications as a result of posterior wall displacement [11]. However, this differentiation is not always easy because of difficulty in detecting the vacuum cleft sign and both conditions may even coincide in the same patient. Antonacci et al. [16] performed a post-mortem study of 27 fractured human vertebral bodies and 24 unfractured vertebrae from adjacent levels using histological and high-resolution radiographic techniques, and they found that osteonecrosis was a common histopathological finding in osteoporotic fractured vertebrae and it was also present up to 16% of the neighbouring yet unfractured vertebrae. Subsequent studies have confirmed this observation. Libicher et al. [10] found osteonecrosis in 7% of vertebral biopsies from 266 patients who underwent balloon kyphoplasty for osteoporotic vertebral fractures, and Wiggins et al. [17] reported vacuum cleft sign in 48% of 65 patients who were also treated with vertebroplasty for osteoporotic fractures. Therefore, although VON is traditionally considered a rare disorder, its true incidence is probably underestimated.

There are no specific guidelines for VON treatment and current management follows an approach similar to osteoporotic vertebral fracture, which is to be initially conservative. However, recent reports favour surgical intervention for prevention of neurological complications, having traditionally used decompression with instrumentation and fusion. Minimally invasive procedures, such as vertebroplasty, have also been used for pain relief in refractory cases, with similar results to osteoporotic vertebral fractures [7].

Conclusions

To summarize, VON deserves to better known and should be considered in the differential diagnosis of osteoporotic vertebral fractures in HIV-infected patients. These patients have an increased prevalence of osteoporosis and risk factors for osteonecrosis; therefore, VON occurrence in HIV infection may be underestimated as it occurs in the general population. Although VON diagnosis is not easy, some clinical features such as severe pain, rapid development of kyphosis and neurological symptoms, and imaging features such as vacuum cleft sign or other findings on CT or MR may guide to its diagnosis. HIV clinicians must be aware of VON diagnosis before quickly attributing vertebral collapse to osteoporosis in HIV-infected patients because early VON recognition may lead to better pain management and rapid intervention for prevention of neurological complications.

Disclosure statement

The authors declare no competing interests.

References


