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CASE REPORT

Hyperbaric oxygen therapy in stage III C Kienböck disease: Time is bone

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Abstract

Kienböck disease, also known as lunatomalacia, is a rare condition which can lead to progressive wrist pain and abnormal carpal motion. We present the case of a 30-year-old patient with Down syndrome who came to our observation for treatment of stage III C Kienböck disease. In September 2019, the patient reported wrist pain with limitation in movements and initially underwent conservative treatment without benefit. In October 2020, pain symptoms and difficult movements with reduced strength worsened and surgical treatment was proposed, but the patient and his family declined. Thereby the patient underwent conservative treatment with hyperbaric oxygen therapy (HBOT) 60 sessions, 100% oxygen at 2.5 absolute atmospheres (ATA), oxygen total time 60 min, once daily, five times per week. After 6 months, a positive clinical and radiological evolution were observed, with an improvement in the patterns of pain, motion, and strength and an almost complete involution of the process of aseptic necrosis of the semilunar. To the best of our knowledge, this is the first report of stage III C Kienböck's disease in Down's syndrome patient treated with HBOT.

KEYWORDS

aseptic necrosis, hyperbaric oxygen therapy, Kienbock disease, Lunatomalacia, osteonecrosis

1 | BACKGROUND

In 1910, Robert Kienböck published his article on traumatic malacia of the lunate[1]; in his work he presented radiographic evidence of changes in the proximal portion of the lunate and the radiolunate articulation. Its natural history, etiopathogenesis, and triggering factors have not yet been clarified, but it presumably develops as a reaction of losing blood supply.[2]

2 | CASE REPORT

Our patient is a 30-year-old man affected by trisomy 21 (also known as Down Syndrome), a condition in which he was born with an extra copy of their 21st chromosome.

In his past medical record, he underwent to cardiac surgery to correct the Fallot Canal and systemic-pulmonary shunt completed in two stages (surgery performed in 1992 and 1996, respectively). Actually, the patient is followed

FIGURE 1 No acute osteoarticular lesions or degenerative changes.

by the pediatric cardiology clinic of our hospital and the checks periodically performed (maximal stress test, holter ECG, and echocardium color doppler) shows levocardia with left ventricle of normal size and thickness, preserved kinetics, and ejection fraction 60%. The ECG shows sinus rhythm with heart rate 69 bpm, right branch block with anterior left hemiblock. Hemodynamic compensation is called good.

The patient reported in September 2019 pain in his right wrist which apparently was linked to previous traumatic event (fall to the ground while playing sport). A wrist radiograph revealed no acute osteoarticular lesions or degenerative changes (Figure 1). He was treated with drugs (analgesics and nonsteroidal anti-inflammatory drugs) and the wrist was immobilized with plaster cast forearm for 70 days. After this conservative treatment, the pain and limitation in movements showed an improvement. In October 2020, wrist pain recurred accompanied by swelling, reduced strength, and considerable limitation in the movements of the wrist flexion backs (Figures 2 and 3).

FIGURE 2 Wrist pain recurred accompanied by swelling and reduced strength.

The pain was continuous, spontaneous, and was accentuated by movements. The measurement of pain performed with the visual analog scale VAS showed a value of 6 at rest, while during physical activity the level of the VAS rose up to 10. The patient was of sound mind and well understood the meaning and mode of administration of VAS. The pain was located at the level of the scaphoid-lunate space, with no irradiation and worsened by the dorsiflexion of the wrist.

A new radiographic study revealed a subcondral sclerosis of the lunate and the cuboid. Then, a nuclear magnetic resonance (MRI) showed a reduction in the size of the semilunar with a large area of bone necrosis occupying about half of the bone, to be reported to osteonecrosis (Figure 4). The MRI also described an edema involving lunate and capitate and the presence of deep and irregular incisures of the bone cortical to be attributed to fractures (Figure 5). The picture described depose for Kienböck disease at stage III C according to the Lichtman classification.[3] Surgical treatment based on lunate excision with silicon replacement arthroplasty[4] was proposed, but the patient and his family declined. The patient came to our observation in February 2021, 5 months after diagnosis and more than a year after the onset of symptoms, sent by the orthopedic specialist to run a conservative treatment

FIGURE 3 Considerable limitation in the movements of the wrist flexion backs.

FIGURE 4 Coronal SE T1-weighted image. Fractures (arrowed) and partial osteonecrosis (arrow) of the lunate bone with low saignal intensity.

of HBOT in order to reduce edema and stimulate the revascularization of areas of bone necrosis. The patient initially underwent 30 sessions of HBOT, 100% oxygen at 2.5 ATA, oxygen total time 60 min, once daily, five times per week. The treatments were performed in the multiplace hyperbaric chamber of our hospital, in compliance with the anti-COVID-19 rules (COVID-19 molecular swab every 48 h, distance of at least 1 meter among patients, continuous use of the facial mask with dedicated patient circuit) dictated by the Italian Society of Underwater and Hyperbaric Medicine (SIMSI).[5]

Blood chemistry tests performed before the start of HBOT showed a slight increase in CPR (2.85 mg/dl) while PCT, Hb, RBC, WBC, and myoglobin showed values within the limits of normal. The values of the indices of renal and hepatic function, thyroid (TSH, FT3, FT4), and parathyroid hormones (PTH, Calcitonin) were also within the limits of normal. The compliance with HBOT was excellent. After 30 treatment, a new MRI of the wrist showed disappearance of edema to the carpal bones, except for a slight share of edema that remain in the capitate. The finding relating to the areas of osteonecrosis that still appeared to be present remained unchanged. Therefore, it was decided, in agreement with the orthopedic colleagues, to extend the

FIGURE 5 Coronal Se T1-weighted MR image. Diffuse edema of the lunate (arrow) and cuboid (arrowed) bones with low signal intensity on t1 image.

FIGURE 6 Coronal FSE Sat PD image shows no edema in the cuboid bone and just mild residual edema in the remaining lunate bone. There are eventually two small cystis in both bones.

treatment up to 60 sitting of HBOT. Thus, after 4 weeks of discontinuation from treatment, the patient underwent 30 additional sessions of HBOT at the end of which a new MRI showed a total disappearance of the edema (Figure 6). Unfortunately, the areas of osteonecrosis with the cortical fracture zones persisted. From a clinical point of view, the functional recovery was complete with the disappearance of the painful symptoms. The reassessment of the VAS scale performed at the end of the treatment showed a clear improvement by noting the absence of pain both at rest and during movement (VAS = 0) with full recovery of the mobility of the wrist in flexo-back extension, a condition that allowed the patient to resume his sporting activity with great satisfaction of himself and his family. One year after the end of the treatment, the patient remains in good health and has not shown a recurrence of painful or dysfunctional symptoms of the wrist.

3 | DISCUSSION

Kienböck disease is an idiopathic avascular necrosis of the lunate. It is most common in men and more frequent in young adult between 25 to 45 years old but cases are reported in younger and older patients.

There are eight carpal bones arranged into two rows of four. The lunate is one of four carpal bones in the proximal row, resting between the scaphoid and triquetrum. The lunate has four surfaces which are covered with articular cartilage and have no sites for ligament attachment. Proximally, the lunate articulates with the triangular fibrocartilage and the distal radius, which transmits 80% of the axial loading through the wrist. Distally, the lunate will generally only articulate with the capitate but in 45% of cases, there will be a second joint surface present.[6] Medially, the lunate articulates with the triquetrum and laterally with the scaphoid.

It seems that the shape of the lunate and ulnar variance are predisposing factors. Zapico Antuña[7] described three shapes of the lunate and noted that the type 1, trapezoid-shaped lunate, was more likely to develop Kienböck's disease. Other authors have shown that patients with Kienböck's disease have slender wrists.

With regard to the arterial organization of the semilunar, there are three different patterns, but we still do not know if there is a link between a pattern and disease. In deeper way the dorsal and palmar lunate vascularity consist of the dorsal radiocarpal and intercarpal arches. Through various ligaments (radioscapholoulnate, radiolunate triquetral, and ulnar triquetal ligaments), the vessels can enter the palmar pole. These vessels enter the lunate through the bone foramina.[8]

Despite the different hypothesis proposed as the cause of origin of the disease, to date it remains uncertain. Several authors have hypothesized that a combination of factors related to local vascularization together with bone anatomical variations may play a role in the genesis of avascular necrosis of the lunate.

At this moment, there are two primary assumptions on the cause of lunate bone ischemia: traumatic or atraumatic.[9]

The initial clinical manifestation may be mild and underestimated. In fact, it often mimics a sprained wrist or any inflammatory condition that affects the limb. Joint mobility may be affected by the associated pain.

Dorsal and palmar edema and crackling on palpation are associated sign. Pain plays a key role in the reduction of mobility to which is associated, with varying degrees, the decrease of grip strength. The pain is aggravated by the movements of maximum extension and maximum flexion of the wrist. So, pain for itself is a factor that can further aggravate the dysfunctions. Clinical suspicion together with MRI are essential elements to achieve a rapid diagnosis, allowing us to start treatment early.

It is also essential to exclude the presence of pathological conditions that can contribute to the appearance of the disease such as coagulopathies, haemoglobinopathies, obesity, arterial diseases, autoimmune diseases, use of steroid drugs, and smoking.[10]

As mentioned above in our patient, aseptic necrosis of the lunate, as evidenced by MRI and in accordance with Lichtman's classification, was reported at a stage III C. The proposed treatment options for this stage are lunate excision and arthrodesis, or row carpectomy.[4] The patient and relatives decided to decline the surgical treatment because, as the orthopedist explained, despite the surgical technique applied, the outcome regarding bone regeneration has not yet been established,[11] thus, he could not exclude the need to have to perform new corrective interventions in the future. At this point, HBOT has been proposed as a conservative nonconventional treatment.

The usefulness of HBOT in the treatment of osteonecrosis was clearly stated during the consensus conference held in Lille in 2016.[12] In fact, clear indications to the use of HBOT have been placed for osteoradionecrosis of the jaw, osteonecrosis of the femoral head, and prevention of osteoradionecrosis after dental extraction. Based on the beneficial effects that HBOT is able to produce on the mobilization of mesenchymal cells,[13] wound healing,[14] and neo angiogenesis,[15] many published works have proposed the use of HBOT as an experimental therapeutic option also for osteonecrosis in other bone districts such as the wrist.[16]

Hyperbaric oxygen therapy is a treatment in which patients breathe 100% oxygen while inside a hyperbaric chamber pressurized to greater than sea level. For clinical efficacy, the Undersea and Hyperbaric Medical Society (UHMS) stated that the pressure must be greater than or equal to 1.4 ATA; in clinical practice, pressures applied usually range from 2 to 3 ATA.[17] Under hyperbaric condition, in patients white healthy lungs and normal arterial flow, the alveolar partial pressure of oxygen (PaO2) is acutely elevated proportionally to the atmospheric pressure and at 2 ATA PaO2 and tissue oxygen pressure rise up to 1500 mmHg and 200 mmHg, respectively.[18]

The partial pressure of oxygen in healthy bone is similar to that measured in other tissues (6%–9%) but in diseased or necrotic bone partial pressures of 0.5%–4% have been recorded and hypoxia is a hallmark of many skeletal disorders associated with excessive osteoclast formation and bone resorption.

Hypoxia regulates the expression of many genes via the αβ heterodimeric transcription factor HIF.

The HIF transcriptional cascade includes pathways encompassing angiogenesis, apoptosis, glycolysis, and pH regulation, processes central to cell survival and expansion in an oxygen-deficient environment.[19] Several works have highlighted how hypoxia is able to induce different effects on the growth, mineralization, and differentiation of osteoblasts. Osteoblastic cell and stem cells induce the expression of HIF and vascular endothelial growth factor (VEGF) in response to hypoxia.[20] Hypoxia is known to activate cells of the monocyte/macrophage line from which osteoclasts derive. Moreover, osteocytes become hypoxic in response to mechanical unloading. It has been proposed that hypoxia might represent a newly pathway, regulated by induction of proteins including HIF and osteopontin, mediating osteocyte directed disuse-induced osteoclastic bone resorption.[21,22]

Actually, the precise role of HBOT is not yet established. In summary, bone remodeling is a process that basically involves two types of cells: osteoblasts, responsible for bone formation, and osteoclasts, responsible for bone resorption, and the balance between the activities of these two cytotypes plays a key role in the process of bone remodeling. HBOT may increase the molecular signaling that promotes bone remodeling. It induces the osteogenic differentiation of mesenchymal stem cells via Wnt-dependent pathway.[13] The effect of HBOT on osteogenetic differentiation of osteoblasts was assessed by bone nodule formation, calcium deposition, and alkaline phosphatase activity. Bone nodules were observed after 7 days of HBOT treatment, whereas in the nontreated cultures, no clear bone nodule could be detected until Day 12. Overall, increased numbers of nodules as well as increased nodule size were found present within the HBOT treated cultures compared with the untreated controls.[23] Another study showed that HBOT has a suppressive effect on osteoclast differentiation and activity. This effect would appear to be linked with a reduced response to RANKL secondary to change in HIF, RANK, and NFATc1 expression. Therefore, the beneficial effect of adjunctive HBOT on necrotic bone tissue may in part related to a reduction in aberrant osteoclast activity.[24]

At the cellular and molecular levels, the beneficial effects of HBOT appear to be mediated by serum osteoprogeterin levels through the RANK/RANKL system. Serum osteoprotegerin accelerating osteoblast differentiation and suppressing osteoclasts genesis activation, shifting the balance between bone formation and bone resorption in a direction that promotes bone regeneration.[25] Hyperoxia acts on bone metabolism by stimulating osteoclastic activity on necrotic bone.[26]

4 | CONCLUSIONS

The pathogenesis of Kienbock syndrome seems to be related to a combination of factors of mechanical and vascular origin in subjects with genetic predisposition. The natural evolution of the disease provides, if not early diagnosed and treated, a progressive evolution from stage I to stage IV.

In the patient treated at our center, the diagnosis was made and the HBOT began at a stage III C, which

is an advanced evolutionary phase, characterized by an important bone necrosis and cortical fractures well highlighted at MRI. According to our knowledge, our case report is the first that deals with the use of HBOT at such an advanced stage of the disease. Therefore, we cannot exclude that an earlier onset of HBOT could produce positive effects also in terms of revascularization of osteonecrosis areas. HBOT has certainly produced beneficial effects in terms of functional recovery with complete disappearance of edema, resolution of painful symptoms and complete functional recovery, problems that had been resolved only transiently by the therapies used before HBOT. The hyperbaric treatment was discontinued after 60 sessions because the patient refused to perform an additional cycle of 30 sessions proposed by us. The few experiences reported in the literature related to the treatment with HBOT of aseptic necrosis of the semilunate have extended the duration of treatment up to 120 sessions.[16] Consequently, we cannot exclude that a further extension of the HBOT treatment could improve the radiological-anatomical picture.

Our work has some limitations: we did not measure the mean grip strength values and the mean degree of flex extension, being off label treatment, we did not follow a precise HBOT treatment protocol, but we based our approach on the basis of data extrapolated from other experiences reported in the literature that used HBOT in the treatment of ostronecrosis in other bone districts. We have planned and implemented a "therapeutic" suspension of HBOT lasting 4 weeks interspersed between the two blocks of 30 sessions and this in order to reduce the risk of complication onset related to prolonged exposure to hyperoxia. We cannot exclude that this discontinuation could have had an effect on the effectiveness of the therapy. An indisputable fact is that our patient has happily resumed practicing competitive sports (Figure 7) and that 7 months after the end of the HBOT is in good health and does not report functional alterations or pain in the wrist.

FIGURE 7 Our patient has happily resumed practicing competitive sports.

AUTHOR CONTRIBUTIONS

D.M.Palma, A.N. Cracchiolo, M. Palmeri, and M. Finazzo have made substantial contributions to conception and design, or acquisition of data, or analysis, and interpretation of data. B. Bonanno, R. Lo Bue, D. Tantillo, G. Re, and F. Genco have been involved in drafting manuscript.

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None.

CONFLICT OF INTEREST

None of the authors have any conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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