European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2020

Clinical Trial

OSTEOCHONDRITIS DISSECANS OF THE FEMORAL CONDYLUS TREATED WITH OZONE AND HYALURONIC ACID

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ABSTRACT

The aim of our study was to evaluate the therapeutic efficacy of treatment with oxygen-ozone therapy and hyaluronic acid in patients with osteochondritis dissecans of the knee. From September 2012 to February 2015, we treated three male patients afflicted by osteochondritis dissecans of male gender aged between 12 and 33 years (mean 21.3) with intra and peri-articular oxygen-ozone therapy and intraarticular hyaluronic acid. At the clinical check-up at the end of the treatment, we had a complete remission of the pain, with the possible return to participate in competitive sports, while the other two patients returned to amateur sports. The clinical data is supported by MRI investigations at the end of treatment. Based on the excellent therapeutic results obtained in our series, we believe that the oxygen-ozone therapy associated with the use of hyaluronic acid is to be considered a valid therapeutic alternative for the treatment of osteochondritis dissecans of the knee.

KEYWORDS: *oxygen-ozone; osteochondritis dissecans, knee, ozone, hyaluronic acid*

INTRODUCTION

Osteochondritis dissecans of the knee, or osteochondral lesion, is a pathological process characterized by the partial or total detachment of a chondral or osteochondral fragment from the articular surface of the condyles. It can be defined as a circumscribed lesion of the joint surface, characterized by aseptic epiphyseal necrosis and subsequent detachment of one or more osteocartilaginous fragments (1-3). We distinguish a juvenile form, which arises between 10 and 16 years, and a form that affects adults (4-7).

Both the conservative and surgical treatments, which depended on the subject's age, the site, and the extent of the lesion, aimed at restoring normal articular cartilage to delay as much as possible the onset of the arthritic degenerative

Received: 26 September 2019
Accepted: 05 February, 2020

ISSN: 2038-4106

process (7-16); this involves the onset of initially episodic pain (tending to become chronic), frequent presence of hydration and possible joint blockage. Suspension of sports activity and follow-up with radiography and magnetic resonance are recommended (1-16).

Evolution can lead to spontaneous healing, more frequently in children, or to the permanence and aggravation of symptoms, up to surgical indication in cases of free fragments or serious complications, such as functional impotence of the joint.

The following are the cases of a 19-year-old boy, a soccer player, a 12-year-old boy, and a 33-year-old man suffering from osteochondritis dissecans of the medial femoral condyle of the right knee, treated with oxygen-ozone therapy and acid hyaluronic.

MATERIALS AND METHODS

From September 2012 to February 2015, three male patients between 12 and 33 years (mean age 21.3), afflicted by osteochondritis dissecans, were treated with intra- and peri-articular oxygen-ozone therapy and intra-articular hyaluronic acid.

Subject to informed consent, the patients were treated with intra and peri-articular injections with oxygen-ozone. For the production of the oxygen-ozone mixture, a "Maxi Ozon Active International produced by Medica S.r.l. CE" generator device was used, equipped with a digital photometer for the regulation of ozone concentrations, with check valves for the collection of the gaseous mixture in absolute sterility. At the same time, the hyaluronic acid infiltrations were carried out at a concentration of 16mg/2ml containing 0.8 % of highly purified hyaluronic acid sodium salt with a molecular weight between 800/1200KDalton.

CASE 1

S.F., a 19-year-old boy who has been playing football since age 5, came to our observation in September 2012. The patient reported recurring episodes of mild but relapsing pain in the right knee, especially during prolonged training, starting from 2010. Due to this, in October 2010, the general practitioner decided to commission the execution of a knee X-ray, which was negative, and an MRI, which showed a hypointense area of a few mm. However, sporting activity was not suspended during this period since the pain tended to subside with rest. (Figs. 1 A-B).

Subsequently, starting from 2012, the pain recurred more frequently and, more importantly, did not resolve with rest, and the intake of NSAIDs became necessary. Finally, following the general practitioner's advice, the patient came to our observation at the beginning of September 2012, complaining of widespread pain in the right knee, especially in the medial region, which increases under load, and is now resistant to NSAIDs.

There were two episodes of hydration in the previous months, with the need for arthrocentesis (aspirates 30 cc and 35 cc respectively), and a sensation of instability, up to functional impotence, is reported. Sporting activity had been suspended for about two months. The physical examination on the first visit in September 2012 showed pain on palpation of the condyles and pain in extending the knee against resistance.

The X-ray performed in July 2012, not in possession of the patient as it was performed in the emergency room, was reported compatible with the diagnosis: the report showed the presence of edematous and hypovascularized fibro-cartilage tissue, with thickened edges and ossification evident on radiographic examination, compatible with a 1b stage.

MRI performed on 29 August 2012 confirms the diagnosis and shows

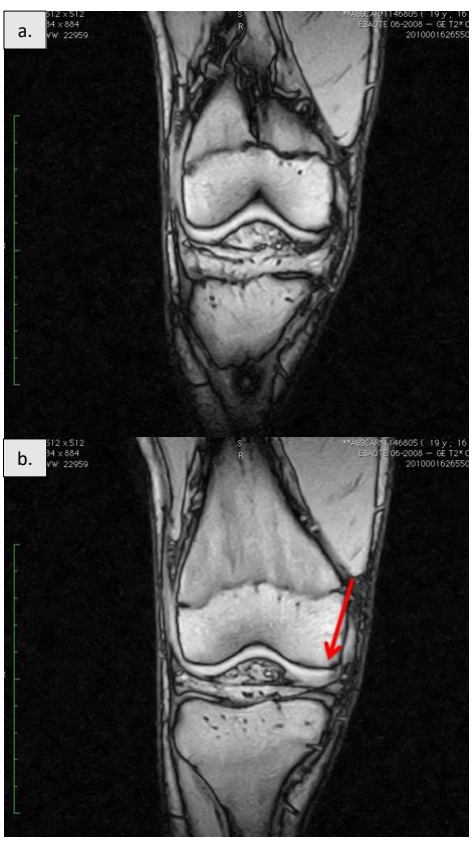

Fig 1. *(A-B): Coronal MRI October 2010: hypointense areola of a few mm.*

a lacunar shape, with a niche of the medial condyle 1.31 cm long and 1.23 cm wide (Figs. 2 A-B).

Standard treatment included, at this stage, the suspension of sports activities, instrumental follow-up, and pain control. A brace can also be associated, and if symptoms persist after 8-10 weeks, an arthroscopic evaluation of the fragment can be performed in situ. In order to alleviate the symptoms and improve the osteocartilage situation, it was decided to start a cycle of 10 sessions of local oxygen-ozone therapy, with intraarticular and peri-articular infiltrations performed every two weeks.

Intra-articular infiltration was performed with access from the external sub-quadriceps breach, while the extra-articular points treated were numerous: patella alar ligaments, goose paw, collaterals, supra-patellar region, medial compartment, patellar tendon, any supra-patellar bursa. For intraarticular injection, a 20cc syringe was used, with a 25Gx25 mm needle, at a concentration of 18µgO3/ccO2, and the dose was 5-10 cc. After each injection, the knee was flexed passively, a maneuver causing a peculiar noise due to the gas that mixes with the synovial fluid; this favors a better distribution of ozone in the joint. For extra-articular therapy, a 27Gx20 mm needle was used at a concentration of 18µgO3/ccO2 and at a 1-2 cc dose per injection.

In the third session, hyaluronic acid was used at the intraarticular level, alternating with ozone, which was instead always used in the extra-articular points. During each ozone therapy session, the patient was assessed for pain, the physical examination performed at the first visit was repeated, and he was questioned about the pain. From the third session onwards, he started reporting a gradual decrease in pain and a feeling of greater stability. Finally, having reached the tenth session of ozone therapy, the patient reported almost total disappearance of pain, recovery of joint functionality, and stability.

At the objective reassessment performed in November 2012, the patient reported an almost total well-being condition, and therefore it was decided to allow the gradual resumption of sporting activity. At the visit performed in January 2013, the permanence of well-being was highlighted, even after important training loads, and the MRI performed on 28.12.2012 shows restoration of the cartilage and bone structure of the medial condyle (Fig. 3 A-B).

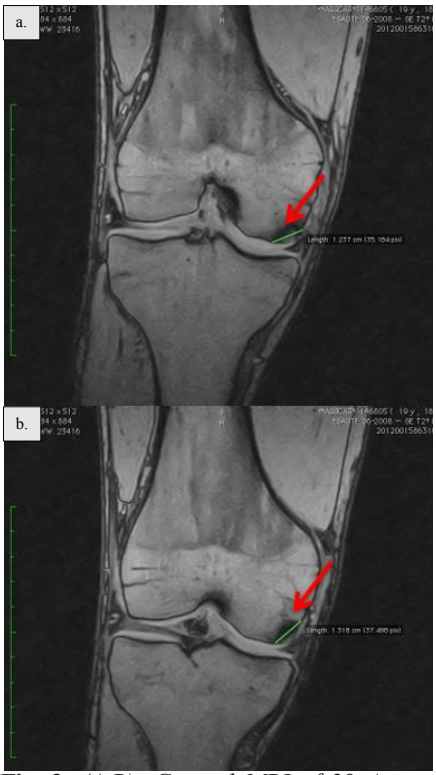

Fig. 2. *(A-B): Coronal MRI of 29 August 2012: 1.3 cm niche.*

Fig. 3. *(A-B): Coronal MRI of December 28, 2012: disappearance of the lesion.*

CASE 2

This case is of S.A., a 12-year-old boy who had been playing football since he was 7. In January 2013, he began to suffer from constant pain in his left knee, which increased under load. Despite the difficulties, he continued practicing sports until March 2013. In July 2013, following the further increase in painful symptoms, a standard radiographic examination of the knee was requested, which was reported negative.

At the next specialist check-up, it was decided to further investigate the clinical situation with an MRI of the knee that the patient performed in November 2013. MRI highlights a hypotensive area at the level of the femoral condyle with a maximum tarsal diameter of 2.1 cm that appears hypointense in the T1-weighted sequences (Fig. 4, 5). The orthopedic colleague opted for pharmacological treatment with NSAIDs, which did not result in substantial changes in painful symptoms.

The patient came to our observation in January 2014. Once the diagnosis of osteochondritis dissecans has been confirmed, we decided-with prior informed consent-to subject the young patient to a therapeutic cycle of ozone and hyaluronic acid, providing 10 therapeutic sessions with intraarticular infiltrations (hyaluronic acid 16mg/2ml and ozone at 18 µg/ml) and peri-articular only ozone, always at 18 µg/ml, performed twice a week. For intraarticular injection, a 20cc syringe was used, with a 25Gx25 mm needle, at a concentration of 18µgO3/ccO2, and the dose was 5-10 cc. After each injection, the knee was flexed passively, a maneuver causing a peculiar noise due to the gas that mixes with the synovial fluid; this favors a better distribution of ozone in the joint. For extra-articular therapy, a 27Gx20 mm needle was used at a concentration of 18µgO3/ccO2 and a 1-2 cc dose per injection.

Already from the first sessions, the patient reported a clear improvement in the clinical picture, and with the continuation of the therapeutic cycle, the complete disappearance of pain and complete recovery of functionality was achieved. Furthermore, during the MRI check-up in November, a clear improvement in the area affected by the injury was observed, with the absence of symptoms and gradual resumption of sports activity (Fig. 6).

CASE 3

S.R. man, 44 years old, practices jogging regularly but had suspended training since the summer of 2013, however, without improving symptoms. He came to our observation in October 2013, reporting pain at rest and underload in his right knee for some time. An episode of hydrarthrosis was reported in the anamnesis.

The physical examination highlighted the limitation of forced flexion. Therefore, we asked the patient to perform an MRI of the knee, which he performed in July 2013, where a hypointense area was found in the T1-dependent sequences at the level of the medial femoral condyle (Fig. 7).

Given the instrumental tests and the clinic, it was decided to subject the patient to a therapeutic cycle with ozone and hyaluronic acid, starting from January 2014. There are 10 therapeutic sessions of local oxygen-ozone therapy, with intraarticular infiltrations (hyaluronic acid 16 mg/2ml and ozone at 18 µg/ml) and peri-articular only ozone always at 18 µg/ml performed every two weeks. For intraarticular injection, a 20cc syringe was used, with a 25Gx25 mm needle, at a concentration of 18µgO3/ccO2, and the dose was 5-10 cc. At the end of the cycle, the patient reported a slight decrease in pain, not sufficient to resume sports activity.

From March to July 2014, he regularly performed muscle strengthening exercises and underwent monthly maintenance-booster sessions. As a result, the pain began to subside significantly. In addition, the control MRI performed in July 2014 documents a decrease in the width of the lesion (Fig. 8).

From September 2014 to early 2015, pain tended to occur after prolonged exertion, but the patient gradually resumed a satisfactory running activity. However, to date, pain persists after running on rough terrain or for times longer than 50-60 min. Therefore, we opted to perform maintenance sessions on a bimonthly basis.

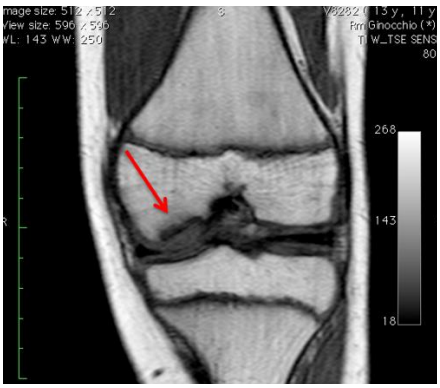

Fig 4. *Coronal MRI: osteochondritis dissecans focus of 2.1 cm. (arrow).*

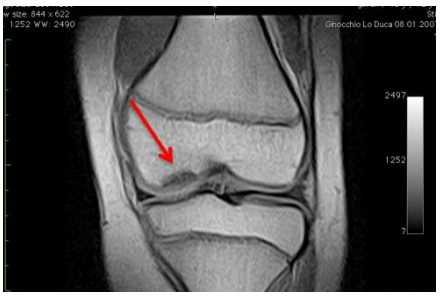

Fig 5. *Coronal MRI: osteochondritis dissecans focus of 2.1 cm. (arrow).*

Fig 6. *Coronal MRI post ozone therapy control with an almost total resolution of the osteochondritis picture.*

Fig. 7. *Coronal MRI osteochondritic focus (arrow).*

DISCUSSION

Osteochondritis dissecans of the knee (OCD) is a pathological process characterized by the partial-total detachment of a chondral or osteochondral fragment from a convex articular surface. The lesion of the articular surface is circumscribed and delimited and consists of aseptic epiphyseal necrosis, which isolates one or more osteocartilaginous fragments. These fragments initially contained in a niche are released at a later time in the joint (taking the name of "joint mouse", "Gelenk-Mause", causing joint mechanical disorders, pain, and possible episodes of hydrarthrosis (1-3). The clinical and anatomo-pathological pictures of the disease are known, while the pathogenesis is more uncertain due to numerous theories. For example, it can evolve towards complete healing with *restitutio ad integrum*, or the fragment can fall into the joint and form a free body corresponding to an empty niche on the articular surface (1-16).

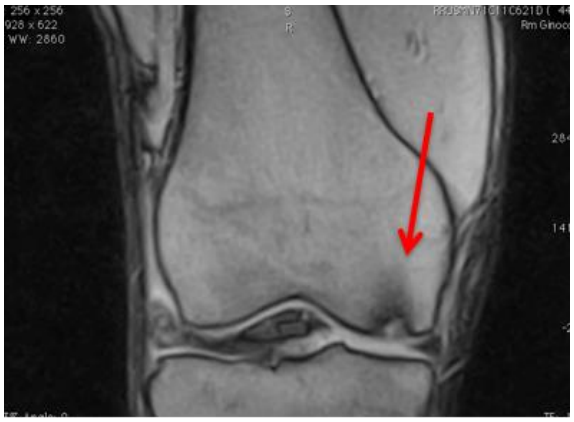

Fig. 8. *Coronal MRI noticeable reduction of the osteochondritic focus after ozone therapy (arrow).*

The process can affect many joints, such as the hip, elbow, and ankle; however, the knee is predominant. The bilateral nature of the condition is much more frequent if the external condition is involved. The male sex is more affected due to greater joint stress, and the onset of the disease occurs in puberty, but there are also cases involving adults.

Relatively frequent is the impairment of static and joint dynamics. It is usually a block in flexion, not as clear as the meniscal block (which always occurs during a specific movement), and usually transient. With chronicization of the symptoms, the ligament can be relaxed, giving the appearance of the drawer sign (anterior and posterior) (1-16). In adults, evolution is always towards the spiraling of the condition, and necrosis is accompanied by evolution into arthrosis (4-7). Diagnosis is based on a careful history, the patient's age, and habitus but is confirmed on X-ray and MRI (17-20). Often, chondral or osteochondral lesions detected on MRI or arthroscopy are asymptomatic and represent occasional findings.

The prognosis is good, especially in children; in adults, on the other hand, it is conditioned by maintaining an intact joint surface; in fact, cartilage or osteocartilage damage to the knee joint is generally considered to be a pre-arthritic degeneration. Therefore, clinical and instrumental follow-up are important (4-7). In early cases, the X-ray shows only slight prodromal structural alterations, while in full-blown cases, the necrotic fragment is surrounded by a clear halo, even more evident after detachment.

The conservative and surgical treatment, depending on the subject's age, the site, and the extent of the lesion, has changed over the years. Currently, it aims to restore normal articular cartilage to delay the onset of the degenerative osteoarthritis process as much as possible (8-16). Therefore, our protocol includes two initial sessions of intra and peri-articular ozone, followed then, in alternate sessions, by hyaluronic acid and intraarticular ozone, and peri-articular ozone at each session.

After the initial cycle, maintenance calls are performed at an increasing distance. The rationale for using ozone in numerous orthopedic pathologies lies in its anti-inflammatory, analgesic, neoangiogenic, and eutrophication properties. The anti-inflammatory action is observed in the knee since repeated trauma or microtrauma leads to cartilage damage, with an increase in PGE2 and proteolytic enzymes, which depolymerize glycosaminoglycans, resulting in edema.

Ozone acts on the mediators of inflammation and blocks the production of PGE2 (21-27). Furthermore, it increases the production of VEFG and NO, thus increasing the blood flow and the drainage of phlogogenic substances. Our experience has led us to observe better results in the case of their association, both in pathologies such as the one described and in other areas, such as neurological, osteoarticular, dermatological diseases, etc. (21-28). Therefore, it is important to observe how even the pathology affecting adults can be indicated in the associated use of ozone and ion resonance in order to improve the clinical condition and, above all, possibly postpone or avoid prosthetic replacement surgery, with important advantages for the patient from a functional point of view and an economic benefit for health.

CONCLUSION

Considering the results that can be obtained, the minimal invasiveness of ozone treatment shows how in cases of osteochondritis, without direct surgical indication, it is possible to restore a good functional and clinical situation. It is, therefore, possible to intervene in association with rest to avoid more aggressive interventions, such as arthroscopy, favoring bone and cartilage healing. Furthermore, recovery times are shortened using the described protocol compared to traditional therapy, and the results are maintained over time.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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