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Umbilical Cord Mesenchymal Stem Cells Secretome in Osteoarthritis Patients: A Case Reports

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Osteoarthritis (OA) remains a leading cause of pain and disability, and current therapies offer limited regenerative benefit. Secretome derived from umbilical cord mesenchymal stem cells (UC-MSCs) has emerged as a promising cell-free biologic capable of modulating inflammatory signalling and supporting cartilage repair. A 56-year-old woman with severe knee OA (Kellgren–Lawrence grade 3) received intra-articular UC-MSC secretome injections weekly for five weeks. This treatment significantly reduced pain compared to the control, using a Visual Analog Scale (VAS), with pain scores reducing from 7/10 to 3/10. Moreover, the patient showed marked functional capacity improvement, as indicated by a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score from 65 to 30. Her Kellgren-Lawrence grade also improved radiographically from 4 to 2 indicating either an initiation of cartilage regeneration or a reduction in degenerative change, no adverse event recorded during intervention and 6 month follow up. The favourable clinical and radiographic responses in this case support the therapeutic potential of UC-MSC secretome in OA management, particularly as a safe and practical alternative to cell-based therapies. Larger controlled trials are required to confirm efficacy, define optimal dosing strategies, and characterise bioactive components responsible for therapeutic effects.

Keywords: Secretome, Stem Cells, Mesenchymal Stem Cells, Osteoartritis

INTRODUCTION

Osteoarthritis (OA) is a progressive degenerative joint disease and one of the leading causes of disability worldwide, characterised by articular cartilage loss, subchondral bone remodelling, osteophyte formation, and varying degrees of synovial inflammation (Aitken et al., 2020; Yubo et al., 2017). Chronic illness causes pain, stiffness, and reduced physical function and makes a major contribution to the burden of disease for millions of people globally. Worldwide, OA is expected, with estimates of 9.6% of men and 18% of women aged >60 experiencing it (Aitken et al., 2020). Despite its high prevalence, particularly among older adults, current therapeutic strategies remain largely symptomatic, aiming to relieve pain and improve function rather than modify the underlying disease process. Conventional treatments including NSAIDs, intra-articular corticosteroids, hyaluronic acid, and structured exercise programmes often provide only transient benefit and do not restore damaged cartilage (Imani & Patel, 2019; Rehman et al., 2017), in very severe cases, arthroplasty that not yet suitable for all individuals. However, those strategies do not address cartilage degeneration and only offer transient relief (Partan et al., 2023). These limitations highlight the demand for innovative therapeutic approaches to target the disease process and enhance cartilage healing.

Recent clinical and preclinical studies have reported beneficial effects of MSC-derived secretome in OA, including pain reduction, improved joint function, and favourable modulation of inflammatory biomarkers (Guicheux, 2025; Partan et al., 2023). Repeated dosing of umbilical cord-derived MSCs (UC-MSCs) has also demonstrated superior clinical and structural outcomes compared to single-dose regimens and hyaluronic acid injections, highlighting the relevance of sustained paracrine signalling (Tapia-Limonchi et al., 2019). In addition, exosome-rich components of the secretome have been shown to inhibit catabolic mediators such as MMP-13 and ADAMTS-5, reduce IL-1β and TNF-α activation, and protect cartilage from apoptosis-mediated degeneration (Cosenza et al., 2017; Miller et al., 2014; Wang et al., 2025; Yang et al., 2024; Zhu et al., 2018).

Despite these encouraging findings, clinical evidence for UC-MSC secretome remains limited, especially relating to standardised treatment protocols, optimal dosage and frequency, and long-term radiographic or structural outcomes. Few reports have documented radiographic improvement following secretome therapy, and the extent to which cell-free biologics may modify structural progression in OA remains uncertain. Thus, well-documented clinical cases are valuable in expanding early evidence and guiding the design of future trials.

This case report describes the clinical and radiographic response of a patient with symptomatic knee OA treated with repeated intra-articular UC-MSC secretome injections. By presenting detailed pain, functional, and imaging outcomes, this report contributes to the growing evidence supporting secretome-based therapy as a potentially safe and practical cell-free approach in OA management, while highlighting the need for controlled studies to validate these initial observations.

CASE PRESENTATION

Patient Information

A 56-year-old woman presented with progressive right knee pain that had gradually limited her ability to walk, stand from a seated position, and perform routine daily activities. She had previously worked in a physically demanding occupation involving repetitive lifting, which likely contributed to chronic mechanical stress on the joint. No significant systemic comorbidities were reported.

Clinical Findings

Physical examination revealed tenderness over the medial joint line, reduced range of motion secondary to pain, and stiffness after periods of rest. At baseline, the patient described her pain as severe, corresponding to a Visual Analogue Scale (VAS) score of 7/10.

Diagnostic Assesmen

Initial radiographs demonstrated medial compartment osteoarthritis with marked joint space narrowing, marginal osteophytes, subchondral sclerosis, and subchondral cysts. These findings were consistent with Kellgren–Lawrence grade 3 disease. Functional impairment was quantified using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), with a baseline score of 65, indicating substantial limitations in pain, stiffness, and physical function.

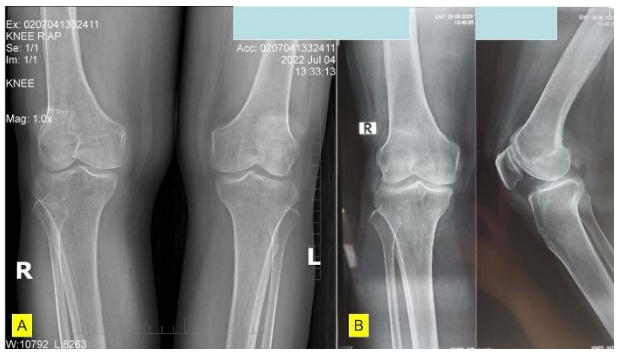
Therapeutic Intervention

Following detailed counselling on risks, benefits, and alternatives, the patient consented to receive intra-articular umbilical cord–derived mesenchymal stem cell (UC-MSC) secretome. The treatment consisted of weekly injections over a five-week period, each administering 3 mL of secretome into the affected knee. No adjunctive procedures or systemic medications were introduced during the treatment course. UC-MSC secretome originated from PT. Bifarma Adiluhung, Jakarta, Indonesia, an accredited good manufacturing practices (GMP) facility certified by the Indonesian Food and Drug Authority (Certification Number: PWS.01.04.1.3.333.09.21-0082). The manufacturing process was authorized by the Ministry of Health, Indonesia (License No: 11/1/10/KES/PMDN/2018) for stem cell-based products.

Follow-Up and Outcomes

Clinical reassessment after the injection series showed a meaningful reduction in symptoms. Pain improved from VAS 7/10 to 3/10, reflecting a clinically relevant change. Function improved with a WOMAC reduction from 65 to 30, indicating improved mobility and decreased stiffness. Radiographic evaluation demonstrated widening of the medial joint space, with overall severity improving from Kellgren–Lawrence grade 3 to grade 2 (see Picture 1). The patient reported enhanced comfort during daily activities and greater walking tolerance. No adverse events or treatment-related complications were observed during follow-up.

Figure 1. (A) AP Knee C-ray before injection (B) AP and



lateral view knee Xray after injection

Outcome Measures: At baseline, radiography revealed medial compartment osteoarthritis (Picture 1A) with moderate to severe joint space constriction, osteophyte development, subchondral sclerosis, and subchondral cysts consistent with Kellgren-Lawrence Grade 3 (osteoarthritis. After therapy (Picture! B), joint space improved significantly; however, osteophytes, subchondral sclerosis and cysts improved minimally. OA severity decreased between baseline and final followup (Kellgren-Lawrence grade; 3 at baseline, 2 final followup). Besides, pain levels in the patient were reduced, as reflected in the Visual Analogue Scale (VAS) score falling from 7/10 to 3/10. I did better on the WOMAC which went from 65 to 30, showing improvements in mobility, stiffness and ease of daily living).

RESULT AND DISCUSSIONS

This case highlights the potential value of UC-MSC secretome as a regenerative and anti-inflammatory therapy for knee osteoarthritis. The improvements in pain, function, and radiographic severity observed in this patient align with evidence suggesting that the MSC secretome

exerts its benefits predominantly through paracrine mechanisms (Mancuso et al., 2019; Tapia-Limonchi et al., 2019). The significant reductions in Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores observed in various studies highlight the clinical relevance of these outcomes in osteoarthritis (OA) treatment. Notably, many patients experienced improvements that surpassed the minimal clinically important differences (MCID), indicating meaningful benefits from interventions (Kuebler et al., 2022; Prodromos et al., 2020; Saraf et al., 2023)

The biological plausibility of secretome therapy is supported by accumulating evidence that MSCs act not primarily through differentiation, but through secretion of bioactive molecules. These components—growth factors, cytokines, chemokines, and extracellular vesicles—create a microenvironment conducive to tissue repair, immunomodulation, and anti-apoptotic signalling (Harrell et al., 2019; Teixeira & Salgado, 2019). Secretome products have been shown to suppress key pro-inflammatory pathways, including IL-1β, TNF-α and NF-κB activation, thereby reducing catabolic enzyme expression such as MMP-13 and ADAMTS-5 (Miller et al., 2014). These processes collectively slow cartilage matrix degradation and improve nociceptive signalling, matching the clinical improvements seen in this case.

The patient's radiographic improvement from KL grade 3 to 2—while unusual—has been described in early-phase trials using MSC-derived biologics. Tapia-Limonchi et al. (2019) reported structural improvements on MRI and X-ray following repeated UC-MSC injections, with repeated dosing outperforming single-dose regimens. Partan et al. (2023) demonstrated that UC-MSC secretome improved both clinical outcomes and inflammatory biomarkers in OA patients, consistent with our findings. Additionally, recent exosome-focused research has shown consistent benefits in cartilage protection and symptom reduction, supporting the broader concept of cell-free regenerative therapy (Cosenza et al., 2017; Guicheux, 2025).

Secretome therapy offers several advantages compared to conventional MSC transplantation. Cell-free biologics avoid concerns related to cell viability, batch variability, immune rejection, and theoretical tumorigenicity (Umar, 2023). Secretome formulations also permit easier storage, transport, and standardisation—key attributes for clinical deployment (Arifka et al., 2022). These features position secretome-based therapies as a practical next step in regenerative medicine, bridging the gap between laboratory MSC research and scalable clinical applications.

This case finding indicates that UC-MSC secretome is safe, well tolerated, and provides significant therapeutic benefits in patients with knee OA, consistent with emerging data in regenerative medicine applications. Functional improvement and pain reduction, as evidenced by diminished VAS and WOMAC scores, suggest that MSC secretome may have a therapeutic role in relieving the chronic pain and mobility disabilities caused by OA. Indeed, this is in accordance with reports showing the anti-inflammatory and pro-regenerative potential of secretome from MSCs in the treatment of joint degeneration (Mancuso et al., 2019). Modulation of inflammatory pathways in osteoarthritic joints is one of the key mechanisms through which the MSC secretome is thought to exert its beneficial effects. The secretome contains bioactive compounds (e.g., growth factors, cytokines, extracellular vesicles) that act within the microenvironment, first controlling inflammation, then enhancing repair and regeneration (Tran & Damaser, 2015). This is especially crucial in OA, in which inflammatory processes accelerate cartilage breakdown and pain (Miller et al., 2014). The MSC secretome has anti-inflammatory properties that may lead to local inflammation resolution, pain relief, and maybe slow OA progression.

As a single case, causality cannot be established, and spontaneous fluctuation of OA symptoms cannot be excluded. Radiographic improvements should also be interpreted cautiously, given the modest sensitivity of plain imaging. Biomarker evaluation (e.g., COMP, CTX-II, hs-CRP) or MRI-based cartilage assessment was not performed, representing additional limitations. Further research is needed to determine optimal dose, frequency, preparation protocols, and long-term durability.

This case-study design has limitations, as conclusions from a single patient cannot be generalized, although the findings may be encouraging. More extensive, carefully controlled studies are required to confirm these findings and clarify how MSC secretome improves OA tissue restoration and symptom reduction (Tapia-Limonchi et al., 2019). Future studies must address the optimal dosage, frequency, and specific bioactive components of the secretome that correlate most with favourable effects in OA. Other potential therapeutic enhancers may be combined with MSC secretome therapy (for example, physical therapy) to maximise MSC secretome's therapeutic potential and provide a maximal holistic mean of OA management.

MSC secretome therapy has the potential to be a game changer in the conventional management of OA. The non-invasive procedure targets underlying causes of cartilage degeneration and is a new treatment to free long-term clinical effects on symptoms and joints. With the evolution of regenerative medicine, MSC secretome might become a pillar treatment in OA because it could offer a sustainable, effective and safer alternative to current therapies.

This case report should be further investigated with larger sample sizes to strengthen generalizability and statistical power. Clinical validation is needed to not only confirm the therapeutic efficacy of MSC secretome but also provide a clear understanding of the mechanism of action of this approach on cartilage homeostasis over the disease process in the context of appropriate auto-grafted standard for care or placebo controls and appropriate randomisation and control trials of the two arm comparisons of MSC secretome. This requires long-term

follow-up studies to highlight the durability of the benefits on joints and the maintenance of structural remission.

Further studies could also seek to optimise dosage, frequency of administration, and specificity of bioactive components in the secretome most associated with positive results. Given the promising utility and potency of secretome therapy, studies might evaluate combining secretome therapy with other interventions, such as physical therapy, further to enhance pain relief and functional improvements in osteoarthritis patients. Ongoing efforts should prioritise controlled trials, detailed molecular characterization of secretome components, and head-to-head comparisons with established OA treatments such as hyaluronic acid, PRP, and MSC transplantation. Integrating imaging biomarkers and objective functional assessments may further strengthen evidence for its disease-modifying potential.

CONCLUSION

In this case of advanced knee osteoarthritis, intra-articular administration of umbilical cord–derived mesenchymal stem cell secretome was associated with clinically meaningful reductions in pain, improved functional status, and radiographic downgrading of disease severity, without observed adverse events. The pattern of response is consistent with a paracrine, immunomodulatory and pro-regenerative mode of action described in preclinical and early clinical work on MSC-derived products.

Taken together, these findings support UC-MSC secretome as a promising cell-free biologic that may complement or extend current osteoarthritis management, particularly for patients in whom conventional therapies provide inadequate relief or who are poor candidates for surgery. The minimally invasive method presents a potential replacement for both pain alleviation as well as surgical methods by focusing on the causes of degenerative joints —without the dangers of cell-based therapies. Using bioactive molecules in secretome therapy has improved the administration route, risk of immune rejection, and dosage constancy. It thus becomes a novel, safe, effective, and potentially alternative treatment for OA treatment. However, as this report reflects a single patient, the results should be interpreted as hypothesis-generating rather than definitive. Robust, adequately powered randomised controlled trials—with standardised secretome preparation, dose optimisation, long-term follow-up, and incorporation of imaging and biomarker endpoints—are required to confirm efficacy, clarify mechanisms, and determine its precise role within future osteoarthritis treatment algorithms.

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