

## Case Report



# Radiosynovectomy with $^{188}\text{Re}$ -Colloid in Behcet's Patient with Drug-Resistant Arthritis: A Rare Case Report

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### Abstract

Behçet's disease is a rare vasculitis that can cause arthritis refractory to standard treatments. This case report describes the use of radiosynovectomy with  $^{188}\text{Re}$ -colloid in a patient with drug-resistant Behçet's arthritis. A 33-year-old man with Behçet's disease and knee arthritis refractory to conventional therapies underwent radiosynovectomy with  $^{188}\text{Re}$ -colloid. The patient experienced symptom relief for 4–8 weeks; however, the symptoms subsequently recurred, leading to surgical synovectomy, which produced unsatisfactory outcomes. This case highlights the complexity of treating arthritis in Behçet's disease, especially when conventional treatments fail. Although radiosynovectomy with  $^{188}\text{Re}$ -colloid may benefit selected patients, this case suggests that it may not be universally effective and highlights the need for further clinical studies to define the full potential of this therapy. In conclusion, this case emphasizes the importance of differential diagnosis in distinguishing the various forms of arthritis associated with Behçet's disease, since accurate differentiation is essential for avoiding misdiagnosis and ensuring appropriate treatment.

### Introduction

Behçet's disease is a rare, systemic vasculitis characterized by recurrent oral and genital ulcers, skin lesions, and ocular inflammation. While the disease can affect multiple organ systems, musculoskeletal involvement, particularly arthritis, is a common manifestation<sup>1, 2</sup>. Arthritis in Behçet's disease typically presents as a non-erosive, oligoarticular inflammation, often affecting the knees, ankles, and wrists. Symptoms are usually mild and self-limiting and characterized by pain, swelling, and stiffness in the affected joints. However, due to the subtle nature of these symptoms and the predominance of systemic manifestations (such as oral and genital ulcers, skin lesions, and ocular inflammation), arthritis in Behçet's disease is frequently overlooked or misdiagnosed. This is particularly true when systemic symptoms are more pronounced, leading clinicians to focus on other aspects of the disease rather than musculoskeletal involvement<sup>3</sup>.

In cases of Behçet's disease with drug-resistant arthritis, conventional therapies such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying antirheumatic drugs (DMARDs) often fail to provide adequate symptom relief. Although biologics, such as TNF-alpha inhibitors and Interferon-alpha, have shown efficacy in some patients, they are not universally effective and may be associated with significant side effects or high costs<sup>4, 5</sup>. Additionally, newer

agents such as apremilast and IL-1 inhibitors, although promising, are not always accessible or suitable for all patients. Radiosynovectomy (RSV) with  $^{188}\text{Re}$ -colloid offers a localized, minimally invasive alternative for managing resistant synovitis. This approach targets the inflamed synovial tissue directly, minimizing systemic exposure and potentially reducing the risk of adverse effects associated with systemic therapies. Given the refractory nature of arthritis in this case and the need for a targeted intervention, RSV with  $^{188}\text{Re}$ -colloid was considered a viable option to achieve symptom control and improve joint function<sup>6, 7</sup>.

Targeted radionuclide therapies, particularly radiosynovectomy (RSV), have gained increasing attention for the treatment of refractory inflammatory joint diseases while minimizing systemic exposure<sup>8</sup>. RSV involves intra-articular injection of radiolabeled colloids such as  $^{188}\text{Re}$ -sulfur colloid, to ablate inflamed synovium and symptom relief in 60-80% of cases when conventional therapies fail.  $^{188}\text{Re}$  is considered suitable for medium-to-large joints because of its beta emission energy of 2.12 MeV, tissue penetration of up to 11 mm, and short half-life of 16.9 hours, allowing effective synovial irradiation while minimizing systemic exposure<sup>9</sup>. Its accompanying gamma emission enables post-procedural imaging and assessment of radiopharmaceutical distribution. These characteristics make  $^{188}\text{Re}$ -colloid particularly valuable

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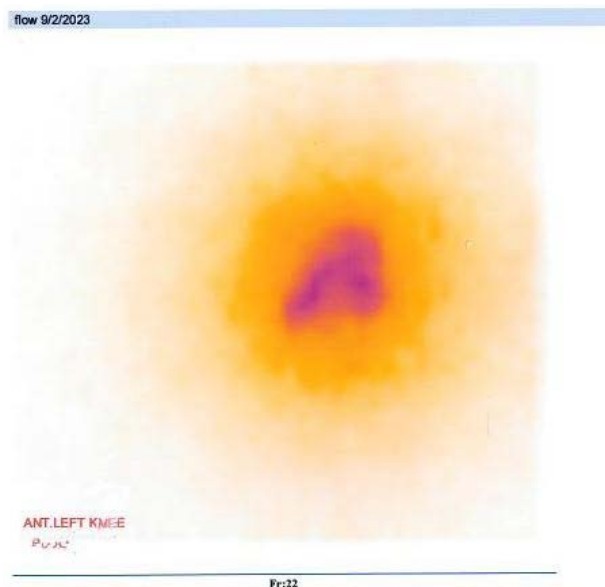
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for persistent synovial effusions in conditions such as rheumatoid arthritis and Behçet's disease, as investigated in the present case<sup>10</sup>.

This case report presents a 33-year-old man with Behçet's disease and drug-resistant knee arthritis who underwent radiosynovectomy with <sup>188</sup>Re-colloid. The case underscores the complexity of managing arthritis in Behçet's disease and highlights the need for further clinical studies to evaluate the efficacy of radiosynovectomy in such patients. Additionally, it emphasizes the importance of accurate diagnosis and differentiation of arthritis in Behçet's disease to prevent mismanagement and ensure appropriate therapeutic interventions. These considerations led us to use RSV with <sup>188</sup>Re-colloid in our 33-year-old male patient with Behçet's disease and refractory knee arthritis, as detailed below.

### Case Presentation

The patient is a 33-year-old man with a history of Behçet's disease diagnosed in 2018 and ocular involvement that had been treated surgically. Since 2021, he had experienced pain and swelling in both knees, predominantly on the left side. He had no significant response to oral methotrexate, 15 mg weekly for three months, or oral prednisolone, 15 mg daily, for arthritis management. Despite treatment, he continued to experience recurrent arthritis symptoms. At the time of presentation, the patient was taking only prednisolone, 15 mg daily. Radiosynovectomy, involving intra-articular injection of <sup>188</sup>Re-colloid, a radiopharmaceutical that emits both beta and gamma radiation, was selected because of the poor response to conventional treatments. The radiopharmaceutical was injected after the rheumatologist assessed the patient's left knee pain using the Numerical Rating Scale (NRS). On this scale, patients rate their pain from 0 to 10, with 0 representing no pain and 10 indicating the worst possible pain. In this case, the patient reported a pain intensity score of 9. Additionally, the rheumatologist measured the circumference of the knee, which was 42 cm. The treatment was performed following the guidelines of the European Society of Nuclear Medicine and the rules and regulations of radiation protection<sup>11</sup>. A dose of 15 mCi of <sup>188</sup>Re-colloid, provided by Pars Isotope Company, affiliated with the Atomic Energy Organization of Iran, was injected intra-articularly into the left knee after sterilization of the injection site, with the patient in the supine position and the knee semiflexed. Before radiopharmaceutical injection, 30 ml of joint fluid was aspirated. Dynamic and static gamma-camera images were acquired immediately after injection into the left knee injection. These images were acquired to assess radiopharmaceutical distribution and confirm the absence of leakage at the injection site. A nuclear medicine specialist reviewed the imaging and found no radiopharmaceutical leakage. Colloidal radiopharmaceutical accumulation was observed in the patient's left knee joint, as shown in Figure 1. The joint was immobilized with a suitable splint for at least 48 hours. After splint removal, the patient was advised to



**Figure 1.** Homogeneous <sup>188</sup>Re-colloid distribution in left knee joint space without extra-articular leakage

avoid strenuous activity for one week. Additionally, light joint and muscle exercises were recommended.

Accordingly, his attending physician examined him at three distinct points after the injection: 4 weeks, 8 weeks, and 12 weeks. The pain intensity after 4 weeks decreased to 7, while the knee circumference was 40 cm. The patient noted some subjective functional gains during daily activities at 4 weeks, consistent with the pain reduction, though these were not formally quantified. In contrast, at 8 weeks after injection, the pain intensity was 8 while the knee circumference was 41 cm. Eventually, the pain intensity reached 9 and the knee circumference reached 42 cm 12 weeks after the injection. The rheumatologist referred the patient to an orthopedic surgeon due to increasing pain and swelling in his left knee. As a result, the patient underwent knee synovectomy surgery. The surgical synovectomy was performed using a standard arthroscopic approach. No signs of infection or other complications were found during the surgery. Three months after the surgery, the results of the synovectomy were not satisfactory.

### Discussion

Multidrug-resistant rheumatoid arthritis (MDR-RA) affects 10-20% of patients who are unresponsive to multiple therapies. This resistance is linked to intrinsic factors, such as specific immune cell signatures and genetic variations, alongside extrinsic factors like comorbidities and non-compliance<sup>12, 13</sup>. Recent studies have identified an innate immune signature in MDR-RA patients, with increased neutrophils and other immune cells contributing to chronic inflammation and treatment failure<sup>12</sup>. Genetic analyses have revealed rare HLA phenotypes and damaging variants in candidate genes associated with drug resistance<sup>14</sup>. Clinically, MDR-RA is associated with higher disease activity, multimorbidity, and lower quality of life, necessitating innovative

therapeutic strategies such as bispecific T-cell engagers targeting B-cell-mediated pathology<sup>13, 15</sup>.

Effective treatment strategies for managing Behçet's disease (BD) symptoms require a personalized, multidisciplinary approach tailored to individual clinical manifestations and severity. Initial management typically involves local and systemic corticosteroids to control inflammation, often combined with immunosuppressive agents such as azathioprine, colchicine, and cyclosporine<sup>16</sup>. In this case, conventional therapies failed to provide adequate symptom relief due to the refractory nature of the patient's arthritis and the severity of his condition, which was progressive. In cases where these conventional therapies are ineffective, biologic therapies, particularly TNF-alpha inhibitors and Interferon-alpha, have shown significant efficacy in reducing disease activity and preventing organ damage<sup>17</sup>. Newer agents such as apremilast and IL-1 inhibitors are emerging as promising options<sup>18</sup>. As a result of concerns about potential side effects, high costs, and the patient's preference for minimally invasive treatment options, biologic therapies were not considered as a first-line alternative for this patient. Considering his localized joint inflammation and the necessity of a targeted intervention, radiosynovectomy (RSV) with <sup>188</sup>Re-colloid was deemed a viable option to improve joint function and relieve symptoms. Although biologic therapies, such as TNF inhibitors and JAK inhibitors, are standard treatments for refractory Behçet's arthritis, they were not considered in this case due to the patient's preference for a minimally invasive approach, the localized nature of the synovitis, and concerns regarding potential side effects and high costs. However, in refractory cases with systemic involvement or inadequate response to RSV, a combination approach with biologics could be beneficial.

Radiosynovectomy (RSV) with <sup>188</sup>Re-colloid presents a promising treatment option for arthritis related to Behçet's disease, particularly when compared to traditional therapies. This minimally invasive procedure has shown efficacy in alleviating pain and improving joint function, with studies indicating a favorable response rate similar to that of other radionuclides like lutetium-177, which showed 21 out of 27 patients responding positively<sup>19</sup>. Additionally, <sup>188</sup>Re-tin colloid has demonstrated safety and feasibility in patients with refractory knee pain, with significant reductions in symptoms and minimal side effects<sup>20</sup>. Overall, RS is a viable alternative for managing Behçet's disease-related arthritis, especially in cases where conventional treatments have failed<sup>21</sup>.

Although RSV with <sup>188</sup>Re-colloid has shown promise in treating refractory synovitis in patients with Behçet's disease, similar studies have reported treatment failure in specific subgroups. For example, Jahangier et al.<sup>22</sup> found that RSV was less effective in patients with severe or progressive arthritis, suggesting that the severity of the disease plays a crucial role in determining treatment outcomes. Furthermore, Karavida & Notopoulos<sup>23</sup> emphasized that patients with thickened synovial membranes may experience reduced efficacy with RSV.

Our case may fall into this category, where the disease's severity and the refractory nature of arthritis led to less favorable results with <sup>188</sup>Re-colloid. These findings highlight the need for careful patient selection and suggest that RSV may not be universally effective.

RSV is most beneficial for patients with localized, refractory synovitis who have failed conventional treatments. It is particularly effective for those with minimal systemic involvement and for patients who prefer minimally invasive treatment options. However, RSV should be avoided in patients with active systemic disease, severe joint damage, or extensive synovial effusions, as the treatment targets localized synovial inflammation and may not address underlying systemic issues or severe joint pathology.

In certain cases, overlapping clinical characteristics may lead to a misdiagnosis of pseudoseptic arthritis or destructive arthropathy as rheumatoid arthritis in Behçet's disease<sup>24, 25</sup>. BD-related arthritis is characterized by non-erosive, non-deforming arthritis that shows a favorable response to colchicine; however, instances of destructive or refractory arthritis may arise occasionally. These phenomena may hold significance in our case, as it raises the possibility of a misdiagnosis. Accurate differentiation is essential to prevent inappropriate treatment and to ensure effective management.

RSV may not be effective for every patient. Research indicates that radiosynovectomy achieves a success rate of 60-80% after six months<sup>22</sup>. Consequently, around 40% of patients do not derive substantial benefits from this treatment. Our case may fall into this category, as <sup>188</sup>Re-colloid might not produce the anticipated therapeutic response. Alternatively, research shows that some radiopharmaceuticals, such as erbium-169<sup>23</sup>, lutetium-177<sup>19</sup>, and yttrium-90<sup>26</sup>, have shown promise in managing refractory synovitis in Behçet's disease. For instance, Erbium-169 emits low-energy beta particles, making it suitable for smaller joints with minimal radiation risk<sup>23</sup>. Lutetium-177 has a longer half-life and emits both beta and gamma radiation, enabling therapeutic effects and simultaneous imaging. Due to these properties, it is suitable for larger joints where deeper tissue penetration is required<sup>19</sup>. High-energy beta emission of Yttrium-90 allows deeper penetration of tissues, making it the ideal treatment for joints with thick synovial membranes<sup>26</sup>. Based on these properties, these agents might be more effective than <sup>188</sup>Re-colloid in certain cases. However, additional research is needed to evaluate their effectiveness and safety profiles in patients with Behçet's disease-related arthritis.

The lack of long-term success of RSV in this case may be attributed to multiple factors. First, the severity of Behçet's disease in this patient, characterized by persistent and refractory synovitis, could have contributed to the limited therapeutic effect. In cases of severe or chronic inflammation, the synovial membrane may become hypertrophic, reducing the efficacy of radionuclide penetration<sup>8</sup>. Additionally, underlying synovial pathology,

such as fibrosis or thickening of the synovial tissue, may have hindered the effectiveness of RSV. Studies have shown that patients with chronic synovitis or significant joint damage are less likely to achieve sustained symptom relief with RSV alone <sup>10</sup>. This highlights the need for a multimodal treatment approach in refractory Behçet's arthritis, including potential surgical intervention or combination therapies <sup>21</sup>.

## Conclusion

This case emphasizes the complexity of treating arthritis in Behçet's disease, particularly when conventional treatments fail. Although RSV with <sup>188</sup>Re-colloid is a useful tool for treating resistant synovitis in Behçet's disease, the results in this patient show that more research and clinical testing are needed to fully understand this complex condition and its optimal management. While RSV may offer short-term relief, it may not be effective for all patients, especially those with chronic or refractory arthritis. Furthermore, accurate diagnosis and differentiation among the various types of arthritis in Behçet's disease is essential to prevent misdiagnosis and ensure appropriate treatment. There is a necessity for innovative treatment strategies and additional research into targeted therapies and advanced treatments to effectively manage these complex diseases. It is crucial to continue exploring the potential limitations of RSV and other alternative treatments, considering their role in the broader context of Behçet's disease management.

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## Authors' Contribution

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## Availability of Data and Material

Requested data will be available based on reasonable request.

## Competing Interests

The authors declare no conflict of interest.

## Consent to Participate (Include Appropriate Statements)

Written informed consent was obtained from the patient for both the treatment procedure and the publication of the case report, including the use of anonymized clinical data and images.

## Ethical Approval

The local ethics committee at Tabriz University of Medical Sciences approved this study.

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