

Radiosynovectomy of ankle joint synovitis in juvenile rheumatoid arthritis treated with rhenium-188 tin colloid and imaging with SPECT/CT

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Rheumatoid arthritis is a chronic disease that is mainly characterized by asymmetric erosive synovitis, particularly affecting peripheral joints. Radiation synovectomy, or radiosynovectomy, was first described in 1950s as an adjuvant treatment for rheumatoid arthritis. Radiosynovectomy is based on the irradiation of the synovial joint by means of intra-articular administration of various β -emitting radiopharmaceuticals. As a generator-produced beta-emitting radionuclide, the importance of rhenium-188 (Re-188) in radionuclide therapy is increasing rapidly. There are previous studies that used Re-188 tin colloid in knee joint synovitis, but its use in ankle joint has not yet been reported. We describe the use of Re-188 tin colloid in a 19-year-old male patient who presented with ankle joint synovitis.

Keywords:

ankle joint, radiosynovectomy, rhenium-188 tin colloid, SPECT/CT

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Introduction

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory joint disorder, the primary treatment for which consists of medical regimens aimed at controlling synovial inflammation of the joint [1]. Radiation synovectomy (RS) involves the injection of a radiopharmaceutical into the joint with the intention of destroying the inflamed synovium, in the expectation that the regenerated synovium will be disease-free and symptoms will thereby be alleviated [2]. Rhenium-188 (Re-188) is considered to be a promising radionuclide for use in RS of joints owing to its favorable decay characteristics. Re-188 is readily available on routine bases from the tungsten-188/Re-188 generator system [3], which has a shelf-life of several months. Re-188 tin colloid RS is a useful treatment modality for patients with chronic inflammatory knee joint conditions refractory to conventional treatment [4]. We describe the first case of application of Re-188 tin colloid in the treatment of ankle joint synovitis in RA.

Case report

A 19-year-old male patient presented with right ankle joint pain and swelling for a duration of 6 months. His blood investigations revealed elevated C-reactive protein (60 mg/ml) and was diagnosed to have juvenile RA. He was treated with antirheumatoid drugs and had no symptom relief. He was referred for three-

phase bone scintigraphy and RS. Blood pool images (Fig. 1) shows increased blood pooling consistent with synovitis. Whole-body images (Fig. 2) showed increased uptake in the right ankle joint. RS injection was performed according to EANM guidelines [5]. RS was performed with precise intra-articular injection of a typical dose of 555 MBq Re-188 tin colloid under sterile conditions and fluoroscopic guidance. Before joint puncture, local anesthesia was administered with 2% lidocaine-hydrochloride. Before the injection of Re-188 tin colloid, Depo Medrol (40 mg in 1 ml) was injected into the joint to reduce the risk of acute radiation-induced synovitis and to avoid skin radiation necrosis. Subsequently, 555 MBq dispersed in 1 ml of sterile, apyrogenic normal saline was administered intra-articularly into the ankle, subtalar, and calcaneocuboid joint and then the needle was flushed with 2–4 ml of normal saline. Arthrography was performed to check the correct location. An orthopedic bandage was applied as a semirigid splint. Images were acquired with a dual-head gamma camera (Siemens Symbia True point, Siemens Medical Solutions, Illinois, USA) in a high-energy general-purpose collimator with 155 ± 20 keV. Re-188 tin colloid static of the ankle

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joint (Fig. 3), and SPECT/CT images (Fig. 4) showed good distribution of tracer in the ankle, subtalar, and calcaneocuboid joint. His ankle was immobilized for 48 h. On follow-up after 3 months, pain and swelling of the ankle joint decreased significantly.

Discussion

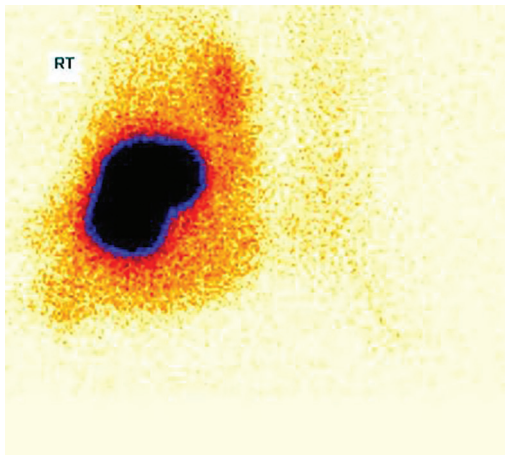
RS is a local intra-articular injection of radionuclides in colloidal form. RS may relieve synovitis, joint pain, knee flexibility, and joint effusion in about 60–80% of the cases [6]. First used by Fellingner *et al.* [7] in 1952, the technique has been applied for over 50 years in the treatment of resistant synovitis in individual joints after the failure of long-term systemic pharmacotherapy and intra-articular steroid injections. Three radionuclides are currently in use: yttrium-90 (Y-90 silicate/citrate), rhenium-186 (Re-186 sulfide), and erbium-169 (Er-169 citrate), which have been indicated for large, medium, and small joints, respectively [8].

Figure 1



Anterior and posterior blood pool images demonstrate increased blood pool concentration in the right ankle joint consistent with synovitis.

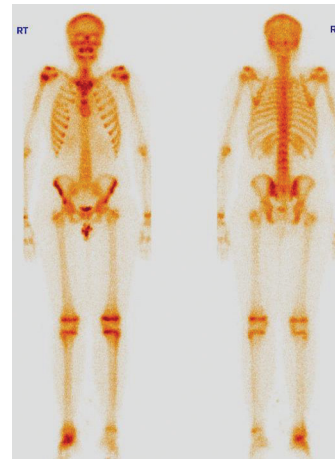
Figure 3



Re-188 tin colloid images of ankle joint showing good tracer distribution in the right ankle joint.

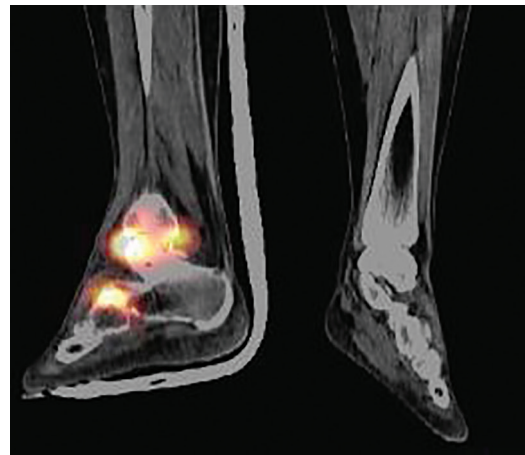
Re-188 is an attractive radionuclide for RS because of its suitable chemistry, $t_{1/2}=16.9$ h and average beta energy of 776 keV ($E_{max}=2.11$ MeV, 79%). These properties enable ankle treatment due to its maximal tissue penetration of 11 mm and its mean range of 3.8 mm [9]. Re-188 decays to the stable Os-188, with a gamma ray emission of 155 keV (15%) that is suitable for image acquisition. Leakage has been particularly difficult to quantify when the isotope used has been Y-90 or P-32, both of which are pure beta emitters with no accompanying gamma emissions that might be used to quantify biodistribution and dosimetry. This fact allows target uptake evaluation, as well as the estimation of the absorbed radiation dose. Besides this, Re-188 is readily available on routine bases from the tungsten-188/Re-188 generator system, which has a shelf-life of several months [3,9].

Figure 2



Whole-body images showing increased tracer uptake in the right ankle joint.

Figure 4



Coronal SPECT/CT of ankle joint showing good tracer distribution in the ankle, subtalar, and calcaneocuboid joint.

Re-188 tin colloid can be potentially used as an ideal agent for RS of the joints. As per the limited number of stability and animal studies performed by scientists, it has been observed that Re-188 tin colloid is highly stable and that leakage from the synovial site is negligible compared with that from Re-188 sulfur colloid [10]. Studies by Savio *et al.* [11] and Jeong *et al.* [12] concluded that Re-188 tin colloid could be selected as the best formulation for RS, taking into account the ease in labeling procedure, kit formulation, requirement of minimum facilities, suitable physical and biological characteristics, and the lowest absorbed dose for the patient. Because of this the highest benefit/risk relation was found for Re-188 tin in comparison with Re-188 ferric hydroxide macroaggregates coated with tin colloid and Re-188 hydroxyapatite particles. In a study by Shin *et al.* [13] on ovalbumin-induced arthritic rabbits, the Re-188 tin colloid improved the macroscopic and histological score and reduced the knee joint diameter when compared with the arthritic control. In conclusion, a Re-188 tin colloid is considered a strong candidate for RS with a superior efficacy and safety.

Lee *et al.* [14] performed the first human study of RS using Re-188 tin colloid in 22 knees from 21 RA patients refractory to intra-articular corticosteroid injection. No clinical side-effects or abnormalities in leukocyte count, platelet count, liver function tests, or urine analysis were observed in any patient. In conclusion, in that first study of RS using Re-188 tin colloid for patients with RA, the treatment resulted in the improvement of arthritis and was well tolerated. Shin *et al.* [15] showed that RS using Re-188 tin colloid in refractory RA patients improved MRI findings as well as clinical parameters. Shamim *et al.* [4] studied 61 knee joints in 48 patients with chronic synovitis and concluded that Re-188 tin colloid RS is a useful treatment modality in patients with chronic inflammatory knee joint conditions refractory to conventional treatment. Patients with shorter duration of disease, normal or minor X-ray findings, little or no swelling, mild tenderness, and better mobility are better candidates for RS. Our case describes the use of Re-188 tin colloid in ankle joint synovitis and has shown good response to therapy.

Conclusion

Radiation synovectomy is a useful treatment modality in patients with rheumatoid synovitis. We have used Re-188 tin colloid as a new radiopharmaceutical agent

and evaluated its efficacy and safety in patient with RA in ankle joint. No clinical side-effects were observed in the patient. Radiation synovectomy using Re-188 tin colloid for patients with RA in ankle joint resulted in the improvement of arthritis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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