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DA-7911, rhenium-188 tin colloid, as a new therapeutic agent of rheumatoid arthritis

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Radiation synovectomy is one of the useful methods in treatment of patients with refractory synovitis because of its convenience, long-term effect, repeatability and avoidance of surgery. ^{188}Re is an ideal radiopharmaceutical agents because beta ray (2.1 MeV) emitted from ^{188}Re is appropriate for synovial cell ablation and gamma ray (155 KeV) is ideal for dosimetry. Ideal particle size (2-5 mm) was achieved by conjugation with tin-colloid. In this study, we investigated the toxicity, stability and biodistribution to evaluate the suitability of rhenium-188 (^{188}Re)-tin colloid as a synovectomy agent. We examined the acute toxicity of ^{188}Re-tin colloid in ICR mice (intravenous) or SD rats (intraarticular). In ICR mice, LD_{50} value of ^{188}Re-tin colloid was 60.9 mCi/kg. In SD rats, mild toxicity including skin or synovium inflammation was observed in the radioactivity of 15 mCi/kg at intraarticular injection site. However, there was no systemic toxicity. In vitro stability tests, ^{188}Re-tin colloid remained as a colloid form without critical size variation over a 2-day period. We investigated the leakage from the intraarticular injection site with gamma counting in normal rats. The mean retention percentage of ^{188}Re-tin colloid was 98.7% at 1 day. In biodistribution study, the liver produced the highest radioactivity (0.0427% ID/organ) except for the injected knees. After confirming the safety and efficacy of ^{188}Re-tin-colloid in animal models, we performed radiation synovectomy in 22 knees from 21 rheumatoid arthritis patients who were refractory to local corticosteroid injection. After the injection of 10-30 mCi of ^{188}Re-tin colloid, we evaluated the efficacy and safety of ^{188}Re-tin colloid from 3 months up to 23 months. In visual analogue scale, pain (19 cases, 86.3 %), joint tenderness (14 cases, 63.6 %), swelling (19 cases, 86.3 %) and range of motion (16 cases, 72.7 %) were improved. In blood, activity of ^{188}Re was 0.009 %/injection dose. Although transient reactive synovitis was observed in 18 cases (81.8 %), there were no abnormalities in complete blood count, liver function test and urine analysis in any patients.

In conclusion, ^{188}Re-tin-colloid is a strong candidate agent for radiation synovectomy with its superior efficacy and safety.