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CASE REPORT

Radiosynoviorthesis in pigmented villonodular synovitis using Re-188 labelled tin colloid: a case report

Aakif U Khan[1], Hameedullah[*,2], Abdul Saeed Shah[2], Muhammad Rauf Khattak[2]

[1]Swat Institute of Nuclear Medicine, Oncology and Radiotherapy (SINOR), Saidu Sharif, Swat, Pakistan

[2]Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan

Abstract

Radiosynoviorthesis (RSO) is an attractive alternative to surgical synovectomy for controlling symptoms of rheumatoid arthritis and many other chronic proliferative joint diseases. The procedure is not widely used in our country because of the non-availability of suitable radionuclides and radiopharmaceuticals. The production of rhenium-188 (^{188}Re) from ^{188}W/^{188}Re generator and by labelling it with particles of appropriate size, has a promise to offer. We labelled ^{188}Re with tin colloid and analyzed its biodistribution and clinical efficacy after injecting it to a patient with recurrent pigmented villonodular synovitis. Gamma camera imaging performed after 1, 24 and 48 hrs showed no leakage of the radiopharmaceutical from the injected joint. The clinical outcome of this study was also excellent, which suggests that ^{188}Re labelled tin colloid is a potentially effective radiopharmaceutical for recurrent PVNS and can be used for other chronic inflammatory joint diseases.

Key words*: PVNS, Particle size, Radiosynoviorthesis, ^{188}Re tin colloid*

***Correspondence**

Mr. Hameedullah
Institute of Radiotherapy &
Nuclear Medicine (IRNUM),
Peshawar, Pakistan
Tel: +92-091-9216114-7
Email: hameedullahirnum@gmail.com

Introduction

Radiosynoviorthesis (RSO) is an effective alternative tool for restoration of synovium in chronic inflammatory joint diseases (CIJD) in carefully selected patients. The procedure is based on an intra articular injection of ß-emitting radiopharmaceuticals directly into the affected joint space in an effort to ablate the synovium [1-3]. The radiopharmaceutical deposits almost all of its ß energy on the internal lining of the inflamed and proliferative synovium. This destroys the proliferating synovial cells of the involved joint and will enable it to restore a near normal lining. RSO can be helpful in a number

Table 1 *Radiopharmaceuticals clinically used in radiosynovectomy*

Radiopharmaceticals	β E_{max} (MeV)	γE_{max} (KeV)	$T_{1/2}$	Penetration (mm)	Particle size (µm)
^{32}P chromic phosphate colloid	1.71	--	14.3d	7.9	500-2000
^{90}Y citrate or silicate	2.27	--	2.7d	11	100
^{165}Dy FHMA	1.29	95	2.33h	5.7	3000-8000
^{165}Dy FHMA	1.29	95	2.33h	5.7	3000-8000
^{188}Re microspheres	2.12	155	17h	10	10-20
^{169}Er citrate	0.34	--	9.4d	1.0	10

of conditions including rheumatoid arthritis (RA), osteoarthritis, haemophiliac synovitis, synovial chondromatosis, PVNS and some other rare inflammatory arthritic diseases [2-4].

PVNS is a rare, aggressive, non-malignant proliferative histiocytic joint lesion that causes swelling, pain and loss of mobility in the affected joint [5]. The disease poses challenges in the management. It is primarily treated by open or orthroscopic synovectomy with reasonable success rates but there is a high risk of recurrence ranging from 8-46% depending on extent and severity of disease [6, 7].

In such conditions, RSO plays an appealing role in that it selectively irradiates the proliferating synovium without any significant radiation burden to the rest of the body [8]. Radiopharmaceuticals with strong ß emissions and soft-tissue penetration are ideal for RSO [4, 9]. The most commonly used radio pharmaceuticals for RSO along with their physical properties are presented in Table 1.

^{188}Re has excellent nuclear and chemical properties, therefore its potentials are being explored in a variety of clinical settings. ^{188}Re is available from ^{188}W/^{188}Re generator which offers significant advantages in terms of in-house availability and convenience with low cost as compared to other therapeutic radionuclides [10]. Owing to its deep tissue penetration (10 mm), ^{188}Re is considered suitable for treatment of large and some time medium joint diseases. In this study, ^{188}Re Tin colloid was prepared and its biodistribution was assessed after intra articular injection into the knee joint affected by PVNS under ultrasound guidance.

Case Report

A 17-year-old girl was referred to the nuclear medicine department of Institute of Radiotherapy and Nuclear Medicine (IRNUM) for treatment of PVNS. She had undergone multiple open surgical synovectomies over the last 18 months. On examination, she had a large swollen right knee joint with multiple scars of past surgical synovectomies [Figure 1]. The joint had a limited mobility and was tense and tender. The patient had undergone de-bulking surgery and removal of septations prior to ^{188}Re-RSO. After four weeks of the debulking synovectomy, the patient underwent RSO. 185 MBq (5 mCi) of ^{188}Re tin colloid was injected into the right knee joint under ultrasound guidance at 2 sites. After 1 hour, an image of the knee was acquired to look for biodistribution of the radiopharmaceutical (Figure 2).

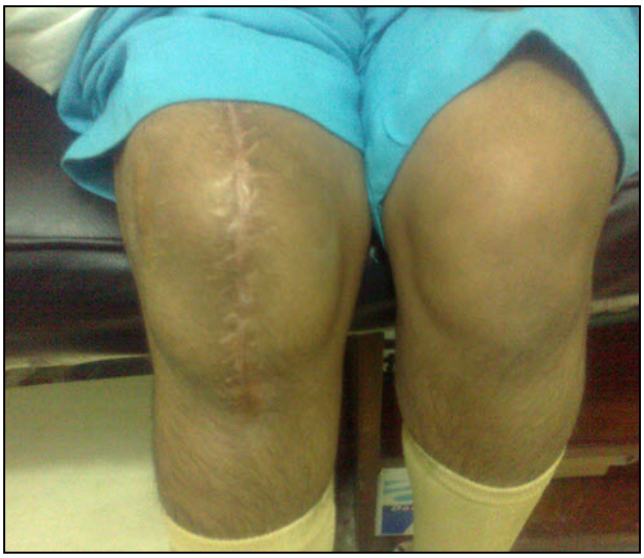

Figure 1

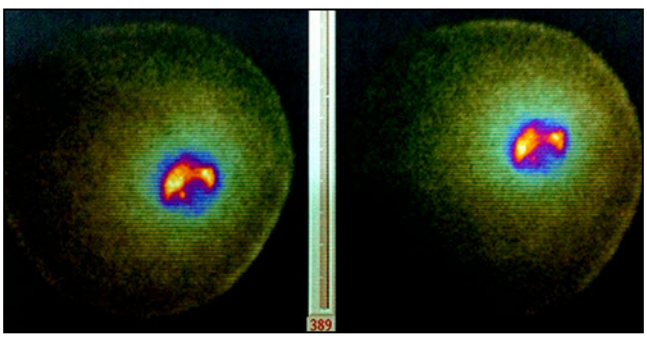

Figure 2 *1-hour images of the knee showing the distribution of the radio pharmaceutical in the knee joint*

To see any leakage, imaging was also performed at 24 and 48 hours (Figure 3). The patient was assessed for pain, swelling and mobility, every two weeks from the date of injection for two months and then on every two months for one year.

Quality control of radiopharmaceutical

Radiochemical purity (RCP) of the radio pharmaceutical was determined by paper chromatography using Whatman paper 1 in normal saline and acetone. RCP was found to be 98.0+0.2%, which was then brought to 100% through centrifugation. Particle size was also determined through electron microscopy from Centralized Resource Laboratory, Peshawar University.

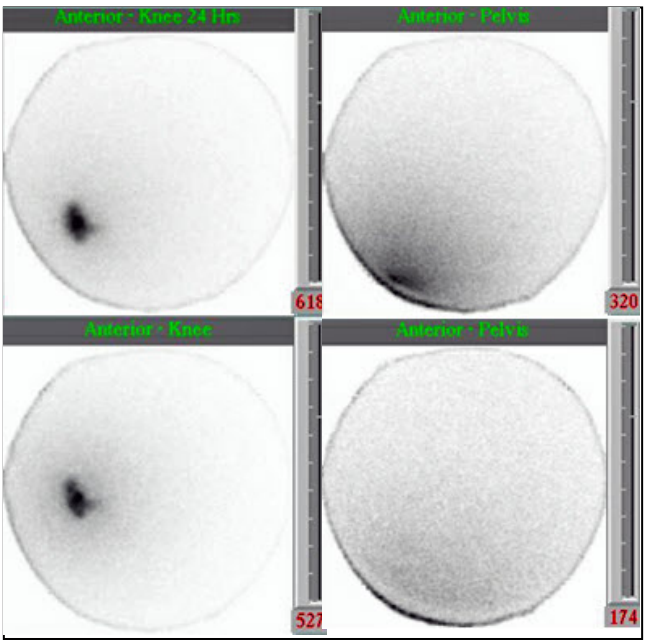

Figure 3 *Delayed images of the knees (left) and pelvis (right) at 24 (top) and 48 hours (bottom)*

Injection technique

The involved joint was draped and prepared according to standard sterile techniques. A 185 Mbq dose was then injected into the affected knee joint of the patient under ultrasound guidance using a 20-gauge needle. The joint was brought through a full range of motion to improve distribution of the radiopharmaceutical and was then splinted for comfort and for limiting the extra articular leakage of the radiopharmaceutical.

Follow-up procedure

We evaluated our patient for pain relief, swelling and quality of life at 2, 4, 6 and 8 weeks, and then after every 2 months until one year. At the time of injection, the patient complained of tolerable pain, which subsided after the needle was removed. After 2 weeks, the patient had mild reduction in the pain, effusion and size of the joint swelling. After 4 weeks, the knee circumference was markedly reduced from 30.9 cm to 27.3 cm (Figure 3). The joint mobility was also improved from completely immobile to flexion of about 450 at the affected knee joint. After eight weeks the patient was completely asymptomatic (pain free)

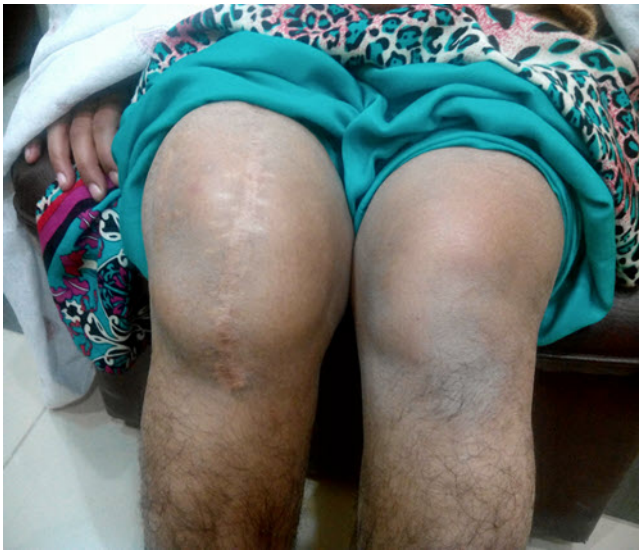

Figure 3

without taking any analgesics and the swelling subsided over the next six months. The patient is still free of symptoms and at times complains of slight pain which subsides after some rest.

Biodistribution

Early 1-hr and delayed 24-hr & 48-hr anterior and posterior images of the knee joint and pelvis (Figure 2) were acquired to see if there was any leakage of the radiocolloid especially into the regional lymph nodes. The biodistribution study was performed on Siemens Orbiter gamma camera with low-energy all-purpose (LEAP) collimator with energy window of 15% centered at 155 KeV photo peak. We found no focal area of abnormal tracer accumulation and all the ^{188}Re labelled colloid was found localized to the injected joint space.

Discussion

PVNS is a rare, aggressive but benign proliferative histocytic joint lesion, which results in various degrees of villous and/or nodular changes in the affected joint structure [2, 11]. It poses serious challenges in the management because surgical attempts are not successful in most of the cases and frequent recurrences are common. Repeated surgeries are associated with greater morbidity and may result in complications like infections and limitation of movement [12]. With recent advances in the field of therapeutic nuclear medicine, in such scenarios, RSO offers a quick and economical solution [3, 10].

In this process mostly ß-emitting radionuclides labelled with particulate compounds are introduced into the affected joints. As there is presumably no leakage outside the joint cavity, the radiolabelled colloid deposits most of its ß-energy on the internal lining of the joints when these are phagocytosed by the free floating fluid macrophages [4, 13].

RSO is regularly practiced in Australia and Canada as well as in other Western European countries but it is very common in Germany. According to an estimate, RSO is performed in about 70,000 joints per year in Germany [4]. However, it hasn't gained widespread acceptance in the developing or under developing countries where its clinical benefits can be better utilized, mainly due to the non-availability of the isotopes and resulting lack of expertise in the field.

The physical and chemical properties of the radionuclide as well as the particle size of the labelled colloid, are important factors considered for RSO. The availability of ^{188}Re from ^{188}W/^{188}Re generator, has made the nuclear medicine community take interest in this isotope because of its favourable physical properties. ^{188}Re ($T_{1/2}$=16.9 hrs) is the decay product of its parent ^{188}W ($T_{1/2}$=69.4 d). It has a β energy of 2.12MeV (70%) accompanied by a 155 KeV γrays. The additional 155 KeV γray emission can be helpful for imaging or biodistribution studies. It has a deep tissue penetration of 10 mm as compared to other isotopes. These physical properties and its potential low cost associated with a long-lived parent makes it a suitable candidate for radionuclide therapies in large joint RSO.

Similarly various size particles ranging from 11000 µm has been applied for RSO in the literature. But for homogenous distribution and to be phagocytosed easily by the lining

cells of the synovium, particles with small size are preferred [13]. However, they have an associated high risk of leakage from the treated joints resulting in a higher radiation dose to the non-target organs. To overcome this problem, radiolabelled particle of 210µm size are considered suitable [14].

In this case, we selected tin colloid as a carrier with particle size 0.1–2±0.2 µm. To avoid leakage, the larger labelled particles were isolated from the smaller ones through centrifugation. The biodistribution studies (imaging at 1, 24 & 48 hours) showed that following intra-articular injection, ^{188}Re tin colloid is retained in the knee joint throughout the study. The 24-hr and 48-hrs postinjection images prove the efficacy of ^{188}Re tin colloid as a better radiation synovectomy agent.

This particular patient had undergone multiple repeated surgical interventions, which had caused some degree of scarring and pocket formation in the joint space that was treated by pre RSO surgical de-bulking and removal of intervening septa. The double site of injection ensured adequate distribution of the tracer. The clinical response at two years of follow-up is satisfactory. The patient married after one year of treatment and has recently given birth to a healthy male child. She has slight limitations of movements with no swelling and occasional slight pain. The limitation of movement is attributed to scarring due to previous surgery.

The clinical outcome, ease of administration and comparatively lower cost than surgical synovectomy, make RSO a reasonable option in the therapy of PVNS. This is however a single case and further studies are needed to better define the role of ^{188}Re labelled tin colloid in PVNS.

Conclusion

PVNS is a slow growing but challenging joint lesion and RSO remains a viable option for its management [15]. In this connection ^{188}Re labelled tin colloid is an economical and readily available radiopharmaceutical for patients with recurrent PVNS who are unresponsive to traditional therapy.

References

1. Mödder G. Radiosynoviorthesis. In: Biersack H J, Freeman LM, editors. Clinical Nuclear Medicine. Berlin Heidelberg: Springer-Verlag; 2007.p. 512-518.

2. Karavida N and Notopoulos A. Radiation Synovectomy: An effective alternative treatment for inflamed small joints: Hippokratia 2010; 14(1): 22-27.

3. Clunie G, Fischer M. European Association of Nuclear Medicine procedure guidelines for radiosynovectomy. Eur J Nucl Med Mol Imaging. 2003; 30 BP 12- 16.

4. Modder G, Modder-Reese R. Radiosynoviorthesis. In: Aktolun C, Goldsmith SJ. Nuclear Medicine therapy-principles and clinical applications, New York: Springer; 2012.p. 315-355.

5. Wu CC, Pritsch T, Bickels J, Wienberg T, Malawer MM. Two incision synovectomy and radiation treatment for diffuse pigmented villonodular synovitis of the knee with extra articular component. Knee, 2007; 14: 99 - 106.

6. Schweitzer ME, Laredo JD. New Techniques in Interventional Musculoskeletal Radiology. Informa Healthcare, 2007. p.195-203. eBook ISBN: 978-1-4200-1430-3

7. Kat S, Elbracht T et al. Radiosynovectomy in pigmented villonodular synovitis. J Nucl Med 2000; 39(7): 209-213.

8. Elgazzar, Abdelhamid H. Basis of Therapeutic Nuclear Medicine. In: Synopsis of Pathophysiology in Nuclear Medicine; New York: Springer International Publishing; 2014.p. 322-324.

9. Kampen WU, Fischer M. Local Treatment of Inflammatory Joint Diseases, Benefits and Risks; Springer, New York, 2015.p. 81-90.

10. Kampen WU, Brenner W, Kroeger S. Long-term results of radiation synorectomy: a clinical follow-up study. Nucl Med Commun. 2001; 22: 239-246.

11. Nassar WAM, Bassiony AA, and Elghazaly HA. Treatment of Pigmented Villonodular Synovitis of the knee with combined surgical and radiosynovectomy. HSS J. 2009; 5(1):19-13.

12. Siegel HJ, Luck VJ Jr, Siegel ME. Advances in radionuclide therapeutics. J Am Acad Orthop Surg. 2004; 12: 55-64.

13. Valotassiou V, Wozniak G, Demakopoulos N, Georgoulias P. Radiosynoviorthesis - indications, side effects. Hell J Nucl Med. 2006; 9: 187-188.

14. Schneider P, Farahati J, Reiners C. Radiosynovectomy in Rheumatology, Orthopedics, and Hemophilia. J Nucl Med 2005; 46: 48S-54S.

15. Tyler WK, Vidal AF, Williams RJ and Healey JH. Pigmented Villonodular Synovitis. J Am Acad Orthop Surg. 2006; 14(6):376-85.