Standard Safety Procedure Before Therapeutic Administration of $^{223}$Ra-Dichloride

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$^{223}$Ra-dichloride is an $\alpha$-emitter therapy approved for the treatment of castration-resistant prostate cancer with symptomatic bone metastases. $^{223}$Ra-dichloride is the first targeted $\alpha$-therapy for this indication with evidence of benefit in overall survival. The administration is intravenous, and extravasation can cause severe injuries such as tissue necrosis. To prevent this side effect, some procedures can be performed according to the guideline of the European Association of Nuclear Medicine. Ionizing radiation is a well-established risk factor for the development of cutaneous squamous cell carcinoma, but surprisingly there are few reports of local adverse effects related to extravasation of radiotherapies at the injection sites. Recently, a possible case of cutaneous cancer was observed after $^{223}$Ra-dichloride extravasation at the injection sites. To prevent this side effect, some procedures can be performed according to the guideline of the European Association of Nuclear Medicine. Ionizing radiation is a well-established risk factor for the development of cutaneous squamous cell carcinoma, but surprisingly there are few reports of local adverse effects related to extravasation of radiotherapies at the injection sites. Recently, a possible case of cutaneous cancer was observed after $^{223}$Ra-dichloride extravasation.

**Methods:** To complement the prevention of extravasation, we developed a standardized technique to be performed before the injection of $^{223}$Ra. **Results:** Our technique was successfully applied to the study population, and no apparent extravasation was seen. **Conclusion:** Our study suggests that use of this standardized technique before administration of $^{223}$Ra is helpful in preventing extravasation during this treatment.

**Key Words:** extravasation; prostate cancer; $^{223}$Ra; technique; Xofigo

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For castration-resistant prostate cancer with symptomatic bone metastases, $^{223}$Ra-dichloride (Xofigo; Bayer) is an approved $\alpha$-emitter therapy (1). $^{223}$Ra-dichloride is the first targeted $\alpha$-therapy for this indication with evidence of benefit in overall survival (2). The administration is intravenous, and the dosage is 55 kBq per kilogram of body weight, administered in 6 injections at 4-wk intervals. The administration should be stopped in the case of suspected extravasation, which can cause severe injuries such as tissue necrosis (3). To complement the prevention of extravasation, we have developed a standardized technique to be performed before the injection of $^{223}$Ra-dichloride.

**MATERIALS AND METHODS**

The study protocol was approved by the Research Ethics Committee of Fundação Antonio Prudente–A.C. Camargo Cancer Center, and all subjects gave written informed consent.

**RESULTS**

We studied 13 male patients (age, 56–76 y) between 2020 and 2023. Our technique was systematically implemented in the study population, and the results yielded a demonstration of its effectiveness in preventing extravasation during the administration of $^{223}$Ra-dichloride. Notably, no apparent extravasation was observed, indicating the useful application of the proposed methodology. The successful execution of the technique reinforces its potential as a reliable preventive measure against the risk of extravasation, aligning with the overarching goal of enhancing patient outcomes and safety in nuclear medicine procedures. Moreover, the absence of observed extravasation in our study population suggests that the proposed methodology could serve as a valuable addition to existing preventive measures. In summary, the results affirm the efficacy of the proposed technique in preventing extravasation during the...
administration of $^{223}$Ra-dichloride, marking a significant step forward in the refinement of safety protocols within the realm of nuclear medicine.

DISCUSSION

Some procedures that can prevent extravasation include ensuring that the staff are properly trained, administering the injection slowly through a permanent cannula, confirming proper placement of the cannula/venous access directly before injection and monitoring during the injection, and flushing the access with saline solution before and at the end of the administration (3–5). If extravasation occurs, the guideline of the European Association of Nuclear Medicine recommends using a clean syringe to aspirate as much $^{223}$Ra-dichloride as possible from the tissue through the cannula. Inducing local hyperthermia, elevating the affected limb, and massaging gently can promote lymphatic drainage, reducing the dose of local radiation (3). Exposure to high doses of radiation can potentially cause severe tissue damage, such as skin desquamation, necrosis, and cutaneous squamous cell carcinoma, but surprisingly there are few reports of local adverse effects related to extravasation of radiotherapies at the injection sites (6,7). A systematic review found that radiopharmaceutical extravasation had been reported in 44 publications; 8 of these extravasations involved therapeutic radiopharmaceuticals, and the most severe symptom was ulceration (6). Additionally, a possible case of cutaneous cancer was observed after $^{223}$Ra-dichloride extravasation (7). Our proposed technique, although developed for $^{223}$Ra-dichloride, could also be applied to any radiotherapeutic administration (e.g., $^{177}$Lu-DOTATATE, $^{177}$Lu-PSMA, or $^{131}$I-metaiodobenzylguanidin).

CONCLUSION

Our study suggests that use of this standardized technique before administration of $^{223}$Ra-dichloride is helpful in preventing extravasation during this treatment.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Would it be possible to adopt a standardized protocol to prevent extravasation during $^{223}$Ra-dichloride treatment?

PERTINENT FINDINGS: The prior administration of a small amount of $^{99m}$Tc into the venous access helps in assessing its patency.

IMPLICATIONS FOR PATIENT CARE: This procedure may prevent a patient from experiencing extravasation during $^{223}$Ra-dichloride administration.

REFERENCES


FIGURE 1. Sequential images acquired at rate of 1 per second after injection of $^{99m}$Tc in left upper limb, showing progression of radiopharmaceutical through superficial and deep venous pathways until it reaches lungs and heart, demonstrating that there was no extravasation or retention.