Fluoroscopy-induced radiation dermatitis: A pitfall complication of percutaneous cardiac interventions

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Received: July 28, 2016
Published online: September 12, 2016

Fluoroscopy-assisted procedures are widely used and commonly utilized for percutaneous cardiac interventions (PCIs). Radiation dermatitis after fluoroscopy-guided procedures could become mild to serious, however, it may remain misdiagnosed or unnoticed. Clinical presentations of fluoroscopy-induced radiation dermatitis include location-specific erythema, dry and moist desquamation, ulceration and even skin necrosis. Diagnosis should always be based on history of radiation exposure. Treatments for radiation dermatitis depend on clinical severity. Once symptoms such as itching or pain present, consultation of dermatologists should be taken into consideration. For the late stage of skin damage such as refractory ulcerations, surgical interventions or skin grafts may be considered. Decreasing the radiation dose and procedure time are beneficial for preventing and minimizing radiation skin injury. Self-monitoring and long-term follow-ups of skin conditions are necessary for early detection of skin damage and possible radiation-associated malignancies.

Keywords: Fluoroscopic intervention; percutaneous cardiac intervention (PCI); radiation dermatitis; radiation ulcer


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Introduction

Nowadays, coronary interventions are commonly applied in medical practices, with about 1 million cardiac fluoroscopic interventions per year in the United States and about 35,000 cases in Taiwan [1]. However, these fluoroscopy-assisted procedures may be accompanied by some side effects, caused by ionizing radiation during the procedure.

Radiation dermatitis after cardiac catheterization was first reported in 1996 with four patients developing atrophic telangiectatic plaques on the back and axilla about 2 to 10 years after the first intervention was performed, with cumulative radiation doses ranging from 11.4 to 34.9 Gy [2]. The severity of cutaneous side effects is correlated with procedure time and cumulative radiation doses. Erythema, desquamation, telangiectasia, and most severe, ulcers may be present days to months after procedures. It is an overlooked complication due to its nonspecific and variable clinical presentation. This article aimed to give an overview of radiation dermatitis related to cardiac fluoroscopic
interventions.

Prevalence

The incidence of radiation dermatitis after cardiac fluoroscopic interventions has been estimated to be as low as between 0.01% and 0.001% [3-6]. The extremely low incidence might be attributed to several reasons. Lack of awareness by the patients, physicians, and even dermatologists could be a cause of under-reporting [7]. Patients may not turn to doctors for help immediately when initial symptoms occur. They may wait until more severe conditions present several months or years after the cardiac intervention. The complicated cutaneous conditions may lead to misdiagnosis, especially when doctors are unfamiliar with patients’ previous history. All these causes may lead to incorrect diagnosis in patients’ medical records, resulting in an underestimated prevalence. However, PCI-induced skin damage is probably no longer as rare as before, and the number of case reports is increasing [7-10]. The estimated incidence rate was more than 0.42% in our recent study [11].

Risk factors

Several conditions lead to higher incidence of skin injury for patients after procedures. Obesity is an important factor since larger radiation doses are required or a closer distance from the radiation source is needed to achieve the same image quality during procedures, compared to non-obese patients. Patients with autoimmune or connective tissue disease such as systemic lupus erythematosus are thought to be prone to developing skin injury after irradiation [11]. Diabetes mellitus may also predispose radiation skin damage due to poor vessel conditions. Some genetic disorders such as defects in abilities of DNA repair may increase radiation sensitivities. Other disorders which have been reported to increase radiation sensitivities include familial polyposis, Gardner syndrome and dysplastic nevus syndrome [11]. Patients using certain medications, for instance, doxorubicin, methotrexate, or taxanes, may be more sensitive to ionizing radiation and can present drug-induced radiation recall reactions [5, 12].

Clinical presentation

Fluoroscopy-related radiation dermatitis can be divided into acute and chronic types. Local erythema is the most common and earliest type of acute skin reaction. It appears as early as immediately or hours later after receiving a relative higher radiation dose (>2-8 Gy radiation dose [8]). It often spontaneously subsides in hours to days. Most of these cases are asymptomatic while some subjects may have pain, pruritus, burning and tingling sensations. Because it is self-limited and asymptomatic, many patients are not aware of its existence.

Subacute to chronic radiation skin damage may present with polymorphous characteristics such as erythema, edema, blistering, epilation, and dry and/or moist desquamation within days to weeks after radiation exposure. The most bothersome point is the delay of the onset of the first clinical symptom, and chronic radiation dermatitis can present as late as weeks to even years later. Patients may seek for help from non-specialists without providing information about previous PCIs. The injury to skin may cause itching and intolerable pain and thus cause a considerable impact on affected patients. Insidious and late onset features include telangiectasia, atrophy, hyperpigmentation, fibrosis, skin necrosis and ulceration.

Though the clinical presentations of radiation dermatitis can mimic other diseases such as fix drug eruption and contact dermatitis, it has important clinical features, manifesting as a well-demarcated lesion radiation entrance site [8, 13]. Due to the different directions of the radiation beams during fluoroscopy-assisted intervention, the affected sites may depend on the coronary arteries being explored. The right axillar area, right dorsal subscapular region and upper back are the most commonly involved, resulting from the frequent highest dose exposure of the left and right anterior oblique projections.

Dosage

Ideally, the peak skin entrance radiation dose should be recorded when performing fluoroscopy intervention. However, real-time measurement of accurate patient skin radiation doses is difficult. Instead, skin radiation doses have usually been estimated by indirectly taking procedure time and fluoroscopy time into consideration. Previous studies [5, 14, 15] have tried to investigate maximum skin doses during PCI by using certain quantities such as reference point air kerma or dose area product. Chida K. et al [16] proposed that the formula of maximum skin dose= 0.5 * of the total entrance skin dose. With advances in radiation dose measurement facilities, Kato M et al [17] found correlation between maximum skin absorbed dose and cumulative air kerma in real time, which may aid in radiation dose measurement. Though there is no consensus about the best way to evaluate skin dose accurately, these findings can still be helpful for avoiding skin injury during PCI in clinical practices.

During a cardiac fluoroscopy procedure, radiation exposure is usually from 0.02 to 0.05 Gy/min, while in some
In extreme cases the dose may be as high as 0.2 to 0.5 Gy/min. In general, an average dose of 2.5 Gy is required for patient receiving a cardiac catheterization procedure, while some situations, such as chronic total occlusion or difficult cases, may require larger dose \[^{13}\].
Generally speaking, patients who receive peak entrance skin radiation doses above 2 Gy may develop cutaneous radiation injuries. Previous reports showed that it may require single dose of 2-5 Gy for epilation, 5-10 Gy for prolonged erythema, 10-15 Gy for dry desquamation, dermal atrophy and telangiectasia. Larger radiation doses could produce greater skin injury, for instance, in radiation doses above 25 Gy, patients may develop skin necrosis. For cumulative doses larger than 10 Gy, patients may develop chronic and insidious courses of radiodermatitis.

Grading

A grading system is required for evaluating the severity of radiation dermatitis and this kind of system is important for medical records and communications. The grading system of the National Cancer Institute Common Toxicity Criteria-Adverse Event (NCI CTCAE) for radiation dermatitis is most commonly used in current clinical practices for radiation therapy induced skin damage. However, there is no satisfactory grading system for fluoroscopy-related radiation dermatitis. Modification of NCI CTCAE grading for this kind of radiation dermatitis has been proposed and used in clinical practice. This system includes 5 grades. Grade 1 radiation dermatitis is characterized by faint erythema (Figure 1) and dry desquamation hours or days after a single dose of radiation and the condition may subside weeks later, spontaneously or with some topical agents. Grade 2 dermatitis features moderate to brisk erythema, which may progress to patchy moist desquamation (usually localized to skin folds) and edema is often present. When the moist desquamation progresses to wider areas other than the skin folds or creases, grade 3 radiation dermatitis is defined (Figure 3). Weak skin integrity and easily wound formation caused by minor trauma could also occur. In grade 4 radiation dermatitis, skin necrosis, ulcerations (Figure 4) and spontaneous bleeding are observed. Grade 5 radiation dermatitis is defined as mortality attributed to radiation.

Although dermatologists and physicians common used the NCI CTCAE grading system in radiotherapy-induced radiation dermatitis, it still has shortcomings in evaluation of fluoroscopy-related radiation dermatitis. For instance, the volume of radiation exposure may be different in affected areas due to diverse fluoroscopy angles during intervention, causing various severities in single involved areas. More than one grade could be contained simultaneously. Further correction of grading systems specified to fluoroscopy-induced radiation dermatitis is required and may include the surface areas, while records of each specific irradiation angles with corresponding severity of cutaneous reaction should be noted.
Histology

The histology features of radiation dermatitis include epidermal atrophy, superficial dermal vessels dilation, dermal/epidermal edema, and dermal lymphocytes infiltration. Under a high radiation dose, epidermal necrosis and bullae formation can be seen. When the condition progresses to the chronic stage, thick, homogenous and pink collagen fibers deposits through reticular dermis. Moreover, adnexal structure loss occurs, and increasing atypical fibroblasts aggregation (Figure 5), and vascular changes are found [13, 22]. Small-vessel thrombosis and endothelial damage result in hypoperfusion, leading to poor wound healing [23]. The presence of atypical fibroblasts featuring a satellite shape is distinct to radiation dermatitis and can thus be differentiated from scleroderma [3].

Diagnosis

The diagnosis of radiation dermatitis is primarily based on clinical presentation and previous history of radiation exposure. Well-demarcated skin lesions manifesting either erythema, desquamation, or ulceration located on the back may indicate radiation damage. History of past radiation-required procedures is necessary. When taking a history from this kind of patient, one should pay attention to radiation sources, procedure position, procedure time, radiation dose, and radiation exposure rate. Patients’ comorbidities or genetic diseases such as ataxia-telangiectasia mutated gene (ATM gene) abnormality [5] should be clarified since some diseases may present severe skin manifestations even after receiving brief, low dose irradiation. This could disguise the diagnosis due to a mismatch between the procedure time interval and clinical condition.

Differential diagnoses include contact dermatitis, scleroderma and fixed drug eruption. Patients with radiation dermatitis may seek some topical agents to relieve symptoms. History of topical agent use is helpful for diagnosis of contact dermatitis, but the diagnosis could still be difficult since physicians may confuse contact dermatitis and radiation dermatitis. Recurrent similar skin lesions over the same site after taking specific kinds of medication indicate fix drug eruption.

Scleroderma and radiation dermatitis could have many clinical and pathologic features in common. Generally speaking, radiation dermatitis causes severe pain and pruritus in some cases, while scleroderma does not. Histopathology can help diagnosis. As mentioned above, atypical fibroblasts differentiate radiation dermatitis from scleroderma. However, atypical fibroblasts may present only focally and thus could be easily missed by pathologists [1].
Radiation induced-morphea can be mistaken for radiation dermatitis. However, radiation induced-morphea is usually seen in women receiving breast irradiation and, in patients in the acute stage, and radiation induced-morphea may extend beyond the radiation field. The histopathological findings of radiation dermatitis in the acute stage include edema, vasodilation, and erythrocytes extravasation, whereas radiation induced-morphea does not present such findings. Radiation induced-morphea seldom results in ulceration and also lacks of atypical fibroblasts, in contrast to chronic radiation dermatitis [22, 24].

Though histopathology may help establish a diagnosis, skin biopsy on radiation damaged skin should only be taken into consideration until malignancy occurs or when is difficult to confirm diagnosis by the clinical condition and history. This is because that damaged skin may cause poor wound healing over the biopsy site and can result in a secondary infection. In addition, the histological findings of radiation ulcers can sometimes be similar and nonspecific when compared with scleroderma and other sclerotic process.

Treatment

Most cases of early stage radiation dermatitis (grade 1) are self-limiting, so there is no recommended treatment. The cutaneous reaction of erythema, itching or irritation may spontaneously disappear after 2-3 weeks after symptoms occur. One can consider the use of topical mid- to high-potency corticosteroid for symptom relief [25]. Patients can apply moisture in areas of dry desquamations.

For higher grades of radiation dermatitis (grade 2 and grade 3), prevention of further irritation or minor injury (such as topical irritant agents and skin incisional biopsy), secondary infection and re-exposure of radiation to the affected areas are most important. If there are wounds present, wound care with topical antibiotics should be considered and moreover, systemic antibiotics can be given if cellulitis occurs. Some studies suggest hydrogel, hydrocolloid or silicone-coated foam dressings, but offer no specific recommendations among these dressing methods [1, 13, 26-29].

The late (or worst) stage of radiation dermatitis presents with refractory ulcerations and skin necrosis. Hyperbaric oxygen therapy is thought to promote wound healing in radiation-induced ulcers by increasing the oxygen pressure and blood flow of the wound bed, which in turn enhances leukocyte activities, and stimulates new collagen formation.
and angiogenesis. However, this way was not effective in our case series. If combination of hyperbaric oxygen therapy and wound care shows little effect on wound healing, surgical debridement should be applied. Wider excision exceeding into the normal tissue is necessary and a full-thickness skin graft, myocutaneous or pedicle flaps can be considered.

Prevention

Prevention is always more efficient than treatment for radiation dermatitis. The key to prevention is to minimize the radiation dose. Recommendations have been established for dose management and patient protection in fluoroscopy-assisted procedures. For patients who are at high risk (such as obesity, repeated procedures, chronic total occlusion of right coronary artery disease) of developing radiation dermatitis, health education about skin care and protection is necessary for patients receiving cardiac catheterization. Physicians should inform patients of possible cutaneous side effects so that patients can self-monitor their skin condition. This may aid in proper diagnosis of radiation dermatitis and thus earlier treatment can be applied. Prophylactic pre-procedure well hydration, post-procedure management with gentle washing with water with or without mild soap and topical corticosteroid use are recommended. If symptoms such as itching or pain present after receiving fluoroscopy-assisted procedures, referring patients to a dermatologist should be considered. Regular follow up by dermatologists is also essential for patients with high risk of radiation dermatitis, for example, patients with complicated comorbidities or receiving higher radiation dose. Due to potential risks of malignancies, close examination and long-term follow-ups related to skin condition either by clinical physicians or dermatologists as well as patients’ self-monitoring are important.

Carcinogenicity

Radiation-induced cancer after fluoroscopy-assisted procedures has been reported. These cases mostly involve bone marrow, lung, and, in women, breast cancer. Breast cancer is thought to be dose-dependent while lung cancer is not. Younger patients are thought to have higher risks of suspicious malignancy due to their longer life expectancies. Squamous cell carcinomas and basal cell epitheliomas have been reported in chronic radiation dermatitis sites after diagnostic X-ray. Due to the potential carcinogenicity of ionizing radiation, doctors should closely monitor the damaged skin in patients receiving fluoroscopy procedures, especially when a higher radiation dose has been applied. Moreover, carcinogenicity in association with radiation fluoroscopy may be a concern for both patients and interventionists.

Conclusion

Radiation dermatitis can be a serious complication after cardiac fluoroscopy-guided interventions. Prolonged procedure time, high dose irradiation and underlying comorbidities (i.e. diabetes mellitus, obesity, repeated procedures) put patients at high risk of higher stages of radiation dermatitis. The disease may be overlooked due to unawareness or misdiagnosis because its presentation can be highly various and patients’ histories are usually misleading. Thus, it is important for cardiologists to educate patients about self-examination and it is cardiologists’ responsibility to adjust radiation doses once cutaneous reactions are observed. Physicians who encounter patients with suspicious skin lesions should be highly alert about examining patients’ previous irradiation histories, the specific lesion shape as well as corresponding location of the skin lesions. Skin biopsy should be reserved only for when the diagnosis cannot be made clinically. Treatments should be modified according to different severities. Surgery is imperative for refractory radiation ulcerations, but designing a wide excision zone exceeding to a healthier area and negotiation with patients are prerequisites to the success of surgery. Reconstruction with local flaps or skin grafts following wide excision is recommended. For prevention of fluoroscopy-induced radiation dermatitis, reduction of the radiation dose is necessary and skin care with self-monitoring by patients is indispensable for early detection of radiation dermatitis and possible malignancies. For patients presenting with clinical symptoms such as pain or itching, transferring the patient to a dermatologist for further evaluation and management should be considered.

Conflicting interests

The authors have declared that no conflict of interests exist.

Author contributions

Y.A. Wei and K.C. Wei designed the review, searched and reviewed the literatures as well as drafted the manuscript. W.H. Wang was the consultant of cardiology practice and helped in clinical cases collection. P.C. Lai designed the review and drafted the manuscript.

Abbreviations

PCIs: Percutaneous cardiac interventions; DNA: Deoxyribonucleic acid; Gy: Gray; NCI CTCAE: National Cancer Institute Common Toxicity Criteria-Adverse Event; ATM gene: Ataxia-telangiectasia mutated gene.
References


