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CLINICAL VIGNETTE

Skin Graft Site Recall Reaction after Transarterial Chemoembolization (TACE) with Doxorubicin

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Case Presentation

A 70-year-old male with a remote history of severe burns with skin grafts was scheduled for treatment for hepatocellular carcinoma. He underwent planned transarterial chemoembolization (TACE) with injection of doxorubicin into carcinoma lesion. He was admitted after the injection for close monitoring for complications as well as symptom control. He tolerated the procedure well with no issues overnight and had no pain, nausea, or evidence of post TACE syndrome on labs the next morning. As he was preparing to leave, he developed blanching, red pruritic patches on his facial skin graft sites. They were initially present in some of the facial graft sites, but over the next hour, the patches coalesced and cascaded down the graft sites of his shoulders, upper trunk, and arms. We were concerned for a rapidly developing toxic skin syndrome such as Stevens-Johnson (as he had in the past) or toxic epidermal necrolysis, but there was no mucosal involvement nor skin sloughing, and the graft sites were the only involved areas. His pruritus and erythema both improved quickly after diphenhydramine. Dermatology was consulted and after monitoring closely without recurrence or worsening, the patient was discharged home the following day.

Discussion

HCC is a common complication of liver cirrhosis. Due to a multitude of factors that limit curative resective/ablative treatment options to fewer than 20% of patients, transarterial chemoembolization (TACE) has become a mainstay of therapy.[1] This procedure involves local infusion of a chemotherapeutic agent via catheter directly into the artery that supplies a tumor in order to induce ischemic necrosis. There is no current consensus on best chemotherapeutic agent from comparison trials, but doxorubicin is the most commonly used for TACE procedures.[1]

Drug recall reactions manifest as acute inflammatory dermatitis and were first described in the late 50s or early 60s in the setting of radiation therapy and actinomycin D.[2,3] Post radiation therapy areas remain the most frequent location for development of these recall reactions, and hence another more common name for this syndrome is radiation recall dermatitis (RRD). The pathophysiology of recall phenomena is not well characterized, but believed to be secondary to local immune system dysregulation in the area of the prior skin injury or insult, a so-called immunocompromised district which may appear to have completely healed, where an exaggerated immune response is elicited to the chemotherapeutic agent and no response is elicited in non-injured skin areas.[2,4] These reactions are by far most commonly seen with antineoplastic agents with other medications only rarely being implicated.[3] Diagnosis can be difficult not only due to rarity but also that days to years can lapse between when the offending agent is introduced and development of the skin recall reaction, though a biopsy of the affected area can confirm the diagnosis if necessary.[5] There are no proven interventions to speed recuperation or relieve symptoms, but in general the reaction is self-limited, and NSAIDs and steroids (topical or systemic) can be considered depending on severity.[6] Recall reactions are not considered allergic in nature, and a rechallenge may or may not re-elicit the skin reaction.[3]

In review of the medical literature we found no similar reported cases of recall reactions after TACE with doxorubicin administration. Although catheter directed administration directly into the target vessel limits its distribution, some of the drug becomes available systemically. We suspect our patient's grafted skin sites still constitute an immunocompromised district, and the restriction of his erythema to only the previously burned and grafted skin areas support the immunocompromised district theory in relation to recall phenomena. Interestingly, whereas our patient's reaction was limited to the grafted areas, in the literature we found another case where skin grafts done after breast radiation treatment helped to actually confirm the diagnosis of radiation recall as the grafted areas didn't develop lesions like the non-grafted (and previously irradiated) areas.[5]

Conclusion

Recall reactions (elsewhere generally described as radiation recall dermatitis) are well described, though not well understood. They remain uncommon in general medical practice, but are often seen in oncology. They may occur in the setting of any prior skin injury most commonly previous radiation therapy, and use of inciting medications such as doxorubicin or other antineoplastic agents. They are not allergic reactions and should be recognized as generally self-limited complications of these medications, but if diagnosis is in doubt either dermatology consultation or biopsy should be considered.

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