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LETTER TO THE EDITOR

Severe skin necrosis after rituximab-CHOP therapy

The cancer chemotherapeutic drug doxorubicin is known for its severe acute local complications after extravasation.[1] Rituximab is a monoclonal antibody directed against the CD20 antigen on B lymphocytes, used to treat CD20 positive non-Hodgkin lymphomas, often in combination with CHOP therapy (cyclophosphamide, doxorubicin, vincristine, prednisolone). Although it is a frequently administered drug, no severe toxic effects have been described yet after extravasation of rituximab.[2] We describe a patient with severe toxicity in the arm after extravasation of rituximab, followed by CHOP therapy in the contralateral arm.

A 76-year-old woman with a diffuse B-cell non-Hodgkin's lymphoma started her first treatment with R-CHOP (rituximab combined with CHOP). During infusion of rituximab, extravasation of rituximab was observed at the infusion site and local erythema and oedema developed. The following day, CHOP therapy was administered via the opposite arm. However, the lesion was progressive and ulceration and necrosis developed over time, complicated by subcutaneous and muscular necrosis. Therefore, surgery was needed with resection of necrosis and skin grafting (*figure 1*).

To our knowledge, no severe local toxic effects have been described after extravasation of rituximab. However, a case of Stevens-Johnson syndrome (erythema exsudativum multiforme major) has been reported after treatment with rituximab in a patient with relapsed follicular lymphoma.[3] Nevertheless, this case describes a diffuse dermatological condition, not related to extravasation.

Doxorubicin is a highly vesicant anthracycline anticancer drug. Extravasation can lead to severe necrosis of the skin and soft tissues.[1] Vincristine is a non-DNA binding vesicant drug, which belongs to the group of vinca alkaloids. These agents are cleared more easily from extravasation sites and cause less tissue damage than DNA-binding agents (such as doxorubicin).[1] Cyclophosphamide belongs to the group of alkylating agents and is an irritant drug, which means it is not a vesicant drug.[1]

Figure 1. *Skin lesion right arm, 64 days after extravasation and after treatment by resection of necrosis, skin grafting and vacuum assisted closure therapy*

Only extravasation of rituximab occurred in this patient, and a new side effect of rituximab can therefore not be excluded. However, the clinical presentation and development of the arm lesion closely resemble the toxicity of doxorubicin. This may point towards a recall phenomenon.[4] Extravasation of rituximab caused local inflammation. The following administration of doxorubicin in the contralateral arm might have resulted in increased levels of doxorubicin locally at the site of inflammation, leading to subcutaneous and muscular necrosis. Toxic recall effects of doxorubicin have been described earlier after previous use of doxorubicin, after radiotherapy and diffuse sunburn.[4-6]

In conclusion, caution is advised when the administration of doxorubicin is considered in patients with local inflammation due to previous extravasation.

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