Case Report

Late-Onset Fluorouracil Extravasation in a Patient with Nasopharyngeal Carcinoma: A Case Report from Persahabatan Hospital

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Abstract

Background: Extravasation in chemotherapy remains one of the serious complications of chemotherapy administration and can result in patient injury with an incidence of 0.09%. Management of extravasation in cancer patients requires interprofessional collaboration. Pharmacists can also play a role in the management of extravasation.

Case: In this article, we report the case of a 46-year-old patient diagnosed with advanced-stage nasopharyngeal carcinoma of the squamous cell carcinoma type. The patient had undergone radiotherapy 35 times. Subsequently, the doctor planned adjuvant chemotherapy with a regimen of cisplatin 150 mg on the first day and fluorouracil 1500 mg from the first to the fifth day. Five days after the second cycle of chemotherapy, the patient complained of dark red discoloration and heat along the venous line. The pharmacist managed the patient by identifying the cause, recording and reporting the drug side effects to the hospital and pharmacovigilance, recommending a protocol change by adding dilution to fluorouracil, recommending the application of hydrocortisone ointment for the scar, and monitoring the patient's condition at home after treatment. The recommendations were accepted, and the patient's condition improved in the subsequent chemotherapy cycle after the above management.

Conclusion: The role of pharmacists is crucial in identifying and recommending appropriate treatments to doctors regarding medications and patient therapy management to ensure patient safety is always maintained.

Keywords: Extravasation, chemotheraphy, pharmacist, fluorouracil.

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Nasopharyngeal Carcinoma (NPC) is a malignancy that occurs in the nasopharynx region (the area above the throat and behind the nose). This cancer is predominantly of the squamous cell type. NPC is the sixth most common type of cancer in Indonesia with 4.6% from all new case in 2022.[1] In the treatment of NPC, several modalities are used, such as chemotherapy, radiotherapy, and chemoradiation. Intravenous chemotherapy is one of the main modalities in the treatment of NPC, with an adjuvant chemotherapy regimen using cisplatin 100 mg/m² on the first day and fluorouracil 1000 mg/m² from the first to the fifth day.[2]

The administration of chemotherapy can pose safety issues for both patients and medical teams. One of the concerns is chemotherapy extravasation, which is defined as the accidental infiltration of chemotherapy into subcutaneous or sub-dermal tissue at the injection site, potentially resulting in tissue necrosis.[3]

Ehmke et al. (2017) evaluated the incidence of extravasation in chemotherapy. Out of a total of 739,812 infusions evaluated, 673 extravasation events were identified. The incidence for all extravasation events was 0.09%.[4]

Effective management of extravasation is crucial to ensure patient safety. According to the European Society for Medical Oncology - European Oncology Nursing Society (ESMO-EONS), cisplatin and fluorouracil (5-FU) are classified as irritants. However, case reports of fluorouracil causing extravasation, particularly those with delayed onset, are very rare. Literature indicates that irritant agents do not cause permanent damage.[5] To manage extravasation, every effort must be made to minimize the resulting complications. All healthcare professionals involved with chemotherapy patients share the responsibility of ensuring safe chemotherapy administration. One of the healthcare professionals involved is the pharmacist.[6] According to the Ministry of Health Regulation No. 72 of 2016, one of the clinical pharmacy services is Drug Therapy Monitoring (MESO). MESO involves monitoring every unwanted response to drugs that occurs at usual doses used in humans for prophylaxis, diagnosis, and therapy purposes.[7] Adverse Drug Reactions are unwanted drug reactions related to pharmacological action. The goal of MESO is to identify, minimize, and prevent unwanted drug reactions.[8] We report the case of a 46-year-old man diagnosed with NPC who experienced severe extravasation due to 5-FU, with symptoms of pain, erythema, and darkened veins that appeared five days after chemotherapy. The pharmacist played a role in managing this case to prevent similar incidents in other patients.

METHODS

This case report details the intervention of a clinical pharmacist in the management of extravasation in a 46-year-old male patient at Persahabatan Hospital on 2023. Upon identification of the extravasation incident, the pharmacist conducted a thorough assessment, including the evaluation of the extravasated agent, the volume of infusion, and the site of extravasation. The pharmacist collaborated with the multidisciplinary team to develop a comprehensive management plan, which included monitoring for potential complications and providing patient education on signs and symptoms of extravasation. All procedures were performed in accordance with institutional protocols.

CASE

A 46-year-old male presented in June 2022 with a marble-sized lump on the right side of his neck, which had not increased in size. The patient had not sought medical attention at that time. In February 2023, he began experiencing nasal congestion, particularly in the right nostril, and a sensation of fullness in the right ear, accompanied by hearing loss. The patient consulted an ENT specialist, and a biopsy of the nasopharynx was performed. Pathological examination revealed nasopharyngeal carcinoma. The patient underwent 35 sessions of head radiation therapy. Post-radiation evaluation

showed the lump was still palpable at level 2 (2x1x1 cm). The patient has a history of hepatitis B, for which he has received treatment. He denies any history of hypertension, diabetes mellitus, asthma, or allergies. His mother has a history of thyroid cancer. The patient has a history of smoking one pack per day but has since quit.

The patient was referred to the hematology-oncology clinic and was scheduled for adjuvant chemotherapy with a TF regimen consisting of 4 cycles of cisplatin (150 mg on day 1) and fluorouracil (1500 mg on days 1-5) every 3 weeks. The TF regimen was administered in the inpatient ward through a peripheral venous access in the hand. During the first cycle, cisplatin (150 mg) was infused in 250 mL of 0.9% NaCl over 2 hours, and 5FU (1500 mg) was administered in 500 mL of 5% dextrose on the first day. The 5FU administration was repeated daily until day 5. Extravasation, as shown in Figure 1, was detected 5 days after the completion of the second chemotherapy cycle. The patient exhibited skin spotting, pigmentation along the venous pathway, accompanied by pain and erythema.

The pharmacist intervened by reviewing the patient's medication usage to identify potential drug-related side effects. A causality analysis using the Naranjo scale indicated that fluorouracil, an irritant, was suspected to cause the extravasation. The pharmacist promptly reported the adverse drug reaction to the pharmacovigilance department of the manufacturing company. Upon identifying the causative agent, the pharmacist recommended to the physician, based on literature, to revise the chemotherapy protocol by increasing the diluent volume for fluorouracil from 500 mL to 900 mL of 5% dextrose to reduce its concentration. This recommendation was accepted by the physician. Additionally, the pharmacist suggested prescribing hydrocortisone upon discharge to minimize extravasation effects, which was also accepted. The pharmacist monitored the patient's condition at home via text messages. During the patient's subsequent chemotherapy admission, the previously extravasated venous route was not used.

Following the pharmacist's recommendation to dilute fluorouracil and the application of hydrocortisone ointment, there was a noticeable improvement. No severe extravasation was observed in the venous route used during the subsequent chemotherapy cycle, as shown in Figure 2.

Figure 1. Fluorouracil Extravasation in patient

Figure 2. Improvement After Intervention

DISCUSSION

Antineoplastic drugs can cause toxic local tissue reactions due to extravasation. Extravasation is the accidental leakage or infiltration of cytotoxic drugs into the subcutaneous tissue around the

infusion site. The resulting injury can range from mild erythema to severe skin necrosis mimicking infection.[9] The damage can extend to surrounding nerves, tendons, and joints. If left untreated or ignored, the injury may necessitate surgical debridement, skin grafting, or even amputation.[3]

A similar experience was reported by Reddy et al. regarding fluorouracil extravasation during chemotherapy with the DCF regimen (Docetaxel-Cisplatin-Fluorouracil). Based on their findings, several preventive measures were recommended. First, chemotherapy requiring short infusions should ideally use peripheral venous access. Second, the use of the back of the hand and wrist areas should be avoided.[10] However, in our hospital, peripheral lines are more commonly used, while central lines are rarely utilized due to the additional costs and procedures required before chemotherapy. For chemotherapeutic agents with a high risk of causing severe tissue damage, using central lines through larger blood vessels is a better preventive measure.[11]

The pharmacist recommended the use of corticosteroid cream and dilution of the infusion concentration to prevent infusion-related reactions, particularly those affecting the skin and blood vessels, given the lack of a specific antidote for fluorouracil extravasation.[12] A causality analysis conducted by the pharmacist using the Naranjo algorithm yielded a score of 6, indicating a probable adverse drug reaction. Reporting adverse drug reactions is crucial for clinical pharmacy services in hospital settings.

LIMITATION

As this study is a single case report, the findings cannot be generalized to all patients. In addition, monitoring was conducted via text messages, which may not provide as accurate an assessment as direct clinical evaluation. Further multicenter studies with larger sample sizes and more objective evaluation methods are needed to strengthen the findings of this report.

CONCLUSION

The case presented highlights the role of pharmacists in managing chemotherapy extravasation as part of an interprofessional team caring for cancer patients. For comprehensive management, further investigation into medical and nursing aspects is necessary. In this case, the pharmacist managed the patient by reporting the adverse drug reaction, recommending additional preventive therapy with hydrocortisone cream, and suggesting changes to the chemotherapy protocol's diluent.

As a result, the chemotherapy protocol at Rumah Sakit Persahabatan was revised for patients receiving fluorouracil chemotherapy to ensure patient safety.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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