Case Report

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Surgery Section

Healing against the Odds by Prompt Recognition and Management of Chemotherapy Extravasation Injury: A Case Report

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ABSTRACT

Chemotherapeutic agent extravasation is an acute complication which may lead to tissue necrosis, ulceration, and functional deficits specifically amongst immunocompromised patients. Managing such cases, especially in the paediatric age group is challenging, given the risk of spreading infection and long-term functional deformity of tissues surrounding the intravenous cannulation site. Emergency prompt management of such injury is of paramount importance to get good functional results. This case report demonstrates how a progressive, necrotic ulcer of an intravenous site in a five-year-old girl with B-cell ALL and sickle cell disease was successfully managed through multidisciplinary collaboration using debridement, negative-pressure wound therapy, and split-thickness skin grafting to heal the wound and restore the hand function in otherwise severely immunocompromised paediatric patient.

Keywords: Debridement, Intravenous extravasation, Negative-pressure wound therapy, Plastic surgery, Skin grafting

CASE REPORT

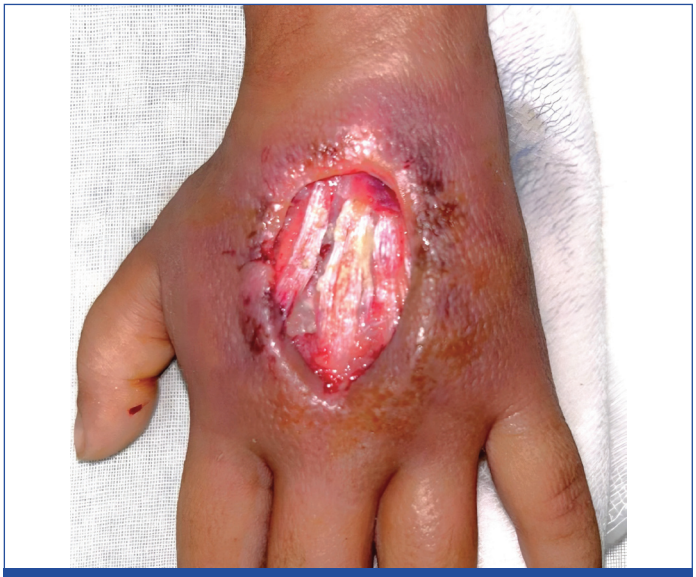
A five-year-old female child, diagnosed case of B-cell acute lymphoblastic leukaemia with sickle cell disease, was admitted to a tertiary care hospital in central India for continuation of induction chemotherapy during an ongoing treatment course. Initial induction chemotherapy included vincristine, daunorubicin, and intrathecal methotrexate.

During the current admission, the patient required Intensive Care Unit (ICU) management due to severe anaemia (haemoglobin of 3.2 g/dL), thrombocytopenia (platelets: $12\times10^3/\mu L$), and also leucocytosis. She received packed red cell, platelet transfusions, intravenous antibiotics, antipyretics, and supportive care. She was re-initiated on the chemotherapy protocol.

During the course of her hospitalisation, the child developed a wound over the dorsum of her left hand at the intravenous cannula site following cytarabine infusion as shown in [Table/Fig-1]. Initially, it was superficial but later it progressed rapidly over approximately 24 hours. On clinical examination, there was an ulcer measuring 2×2×1 cm having necrotic margins and, slough.

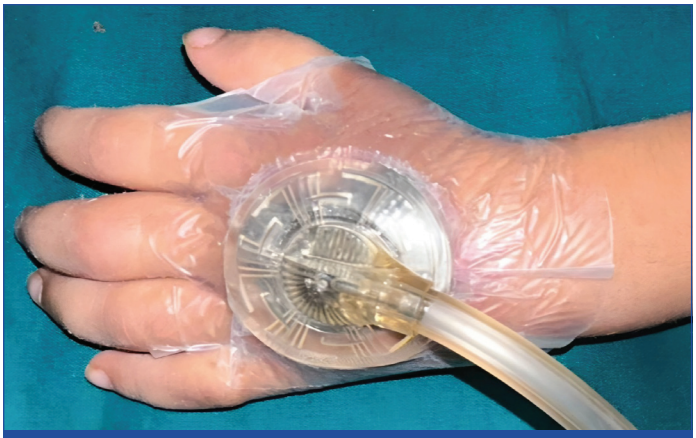
Given the extent of damaged tissue and lack of response of the patient to conservative management inclusive of immediate removal of the intravenous cannula, application of sterile dressings, local wound care with topical mupirocin ointment, she was referred to plastic surgery department. Surgical debridement under sedation was performed approximately 24 hours after the extravasation injury to prevent further tissue damage. Excision of necrotic tissue and slough was carried out, followed by application of a sterile moist dressing and a functional hand-position splint postoperatively as shown in [Table/Fig-2]. Despite this, suboptimal granulation was observed in wound, which prompted a second debridement, seven days after the initial debridement with initiation of negative pressure wound therapy i.e., Vacuum-Assisted Closure (VAC) dressing as shown in [Table/Fig-3].

After achieving a clean wound bed, child underwent a split-thickness skin grafting. The skin graft was harvested from the anterior-medial aspect of left thigh and affixed to the raw area on the dorsum of



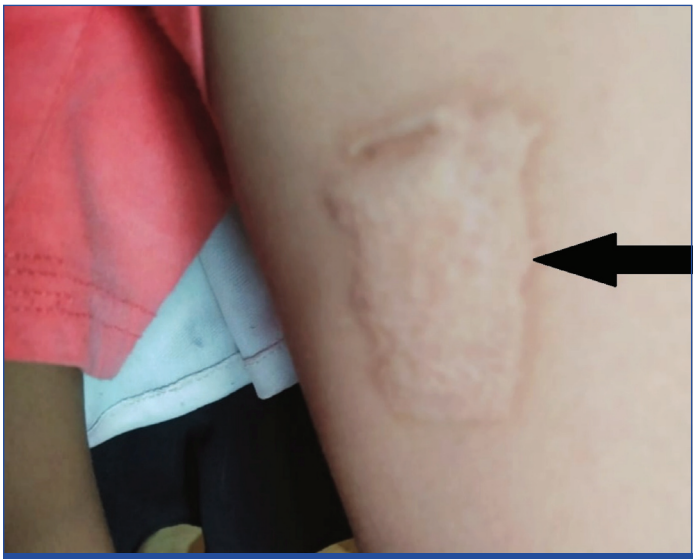
[Table/Fig-1]: Non-healing ulcer on the dorsum of left hand at the site of intravenous cannula placement.

[Table/Fig-2]: Postoperative sterile dressing application after excision of necrotic tissue, slough, proper wound irrigation.

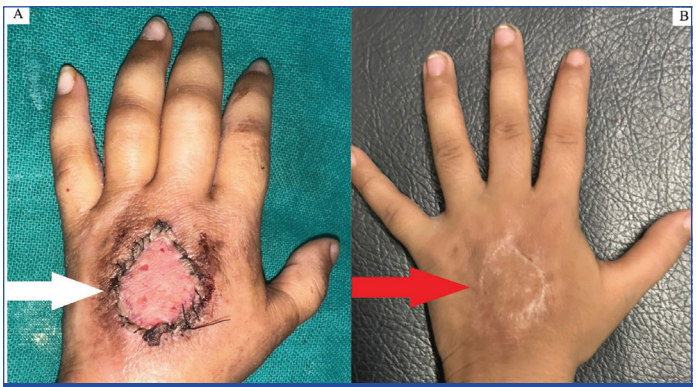


[Table/Fig-3]: Second debridement with Vacuum-Assisted Closure (VAC) dressing due to suboptimal granulation of wound.

the hand. The hand was immobilised in functional hand position. The given procedure was uneventful, and the graft harvested was also satisfactory and donor site healed without any obvious scar as shown in [Table/Fig-4]. Suturing at site of wound immediately after grafting is shown in [Table/Fig-5a]. Complete wound healing with good graft uptake was observed at five months of follow-up as shown in [Table/Fig-5b]. Postoperative care of the patient included continuation of hand physiotherapy to maintain range of motion.



[Table/Fig-4]: Donor site healed without any obvious scar.
(Anterior-medial aspect of the left thigh from where graft was taken healed properly without any obvious scar is highlighted with black arrow).



[Table/Fig-5]: a) Suturing at the site of wound just after grafting pointed with white arrow; b) After 5 months of grafting, properly healed site of wound shown with red arrow.

DISCUSSION

Extravasation is an inadvertent leakage of intravenously administered agents into surrounding tissues, which is a devastating complication more commonly associated with cancer therapy [1]. Extravasation is capable of inducing tissue necrosis, ulceration, and functional impairment, especially when vesicant chemotherapeutic drugs such as vincristine and anthracyclines (e.g., daunorubicin) are involved [2,3]. These agents are used widely in induction regimens for B-cell Acute Lymphoblastic Leukaemia (B-ALL), can cause damage of cutaneous and subcutaneous structures [1,4]. When extravasation occurs with anthracyclines, it can cause deeper and more prolonged tissue injury due to its DNA-binding properties [2]. Timely diagnosis and proper intervention, including surgical debridement and reconstructive strategies, are thus important for preserving viability of tissue along with its function in extravasation type of injury [5].

The most common agents causing IV extravasation site necrosis include anthracyclines (doxorubicin, epirubicin), which bind DNA and persist in tissues leading to progressive ulceration; mitomycin-C, known for delayed necrosis; and vinca alkaloids (vincristine, vinblastine, vinorelbine), which cause direct cytotoxic injury [2]. Among non-cytotoxic drugs, vasopressors (norepinephrine, dopamine) induce ischaemic necrosis via vasoconstriction, while calcium salts, potassium chloride, and phenytoin produce caustic or hyperosmolar damage leading to tissue sloughing [6].

Cytarabine (Ara-C) is a synthetic pyrimidine nucleoside analogue that is phosphorylated intracellularly to its active form, Ara-CTP, which inhibits DNA polymerase, blocks repair and ligation mechanisms thus leads to a premature termination of DNA chains [7]. The high local concentration of cytarabine, when extravasated into soft tissues causes direct cytotoxicity of endothelial cells, fibroblasts, and keratinocytes, triggers cell death, inflammation, and microvascular injury [7,8]. The outcomes of this cascade include ischaemia, poor tissue perfusion, and progressive necrosis and slow healing of wounds [8]. The chemical composition, strong antimetabolite effect, and endothelial dysfunction are the reasons why cytarabine extravasation results in ulceration and tissue injury, and surgical interventions are required to stabilise the wound and maintain the functionality [7].

Similar cases of chemotherapeutic and antibiotic extravasation injuries are reported in the literature. Mieczkowska K et al., reported a 77-year-old woman with anal cancer who had erythematous, indurated ulcers with central necrosis on the dorsum of the hand and forearm following infusion with mitomycin, and histopathology showed dermal necrosis and fibrosis; the patient only recovered after a prolonged topical treatment [9]. A 46-year-old female patient with breast cancer reported by Edwards JJ et al., developed rapid swelling, ecchymosis, and crystalline deposits following intraoperative vancomycin and gentamicin infusion through dorsal hand cannula, which resulted in a temporary obstruction of the brachial artery which was resolved with conservative measures [10]. Hale O et al., described a similar case of 77-year-old female patient who developed progressive necrosis of dorsum of right hand after epirubicin extravasation and consequently had to undergo a staged debridement and radial forearm flap reconstruction for tendon exposure and tissue loss [11]. Comparative analysis between the case report and reports, which are published in the past is presented in the [Table/Fig-6].

Management Strategies for IV Extravasation Injuries

The immediate management of IV extravasation includes halting of the infusion, aspirating the infiltrated drug, elevation of the limb, and local thermal therapy, i.e., cold compresses for DNA-binding drugs and warm compresses for non-DNA-binding drugs [12,13]. Drug-specific antidotes should be administered, including hyaluronidase for vinca alkaloid extravasation, sodium thiosulfate for mechlorethamine, and systemic dexrazoxane for anthracycline extravasation [13]. Most of the cases react positively to the conservative measures (elevation, observation, and topical corticosteroids), although moderate and severe injuries require prompt assessment [13,14]. Timely surgical interventions by the

Author and year	Patient demographics	Causative drug(s) / infusate	Clinical features	Management	Outcome
Mieczkowska K et al., [9]	American female, 77 y, anal cancer	Mitomycin	Erythematous, indurated ulcers with central necrosis on dorsum of hand and forearm after "pinching" sensation at infusion site	Initial antibiotics; wound healing only with prolonged topical therapy over several months	Gradual wound healing, but highlights *insidious, infection-mimicking course*
Edwards JJ et al., [10]	American female, 46 y, ASA II breast cancer with brain metastasis	Gentamycin + Vancomycin (20-G cannula, dorsum of hand)	Rapid swelling, purplish ecchymosis, crystalline deposits, brachial artery obstruction with weak pulses	Conservative: limb elevation, dry heat, nitroglycerin patches; arteriography showed obstruction, but spontaneous recovery; ICU monitoring	Swelling subsided, brachial pulsations restored spontaneously, discharged next day
Hale O et al., [11]	Female from United Kingdom, 77 y, oesophageal cancer	Epirubicin	Mild swelling and blistering initially; progressed to extensive necrosis with tendon exposure and foul discharge (by day 20)	Initially conservative (hydrocortisone + DMSO), then surgical: staged debridement + radial forearm flap + split-thickness skin grafting	Flap viable, functional recovery preserved, minor dehiscence healed conservatively
Present case	Indian female, 5 y, immunocompromised (severe anemia, thrombocytopenia, leukocytosis)	Vincristine + Daunorubicin + Methotrexate, but wound appeared shortly after infusion of Cytarabine (at second phase of chemotherapy)	Non-healing ulcer on dorsum of left hand at IV cannula site; ulcer of size 2×2×1 cm with necrotic margins, slough, tendon exposure; rapidly progressive despite conservative measures	1. Initial debridement + moist sterile dressings 2. Repeat debridement + Negative Pressure Wound Therapy (VAC) 3. Split-thickness skin graft from left thigh; immobilisation, antibiotics, pain control, multidisciplinary care	Successful graft take, donor site healed without major scar; child achieved wound healing despite severe immunosuppression

[Table/Fig-6]: Comparative analysis between the case report and reports, which are published in the past.

specialist plastic surgeon are essential to perform surgical flush-out procedures, which may prevent necrosis of tissues along with preserving hand function [15]. However, delayed management in such cases may cause further irreversible damage necessitating grafts or flap reconstruction [14].

CONCLUSION(S)

The accurate diagnosis and treatment are important to avoid any loss of function along with prevention of progressive tissue necrosis in intravenous extravasation injury cases. A stepwise method of debridement, negative pressure wound therapy, and split-thickness skin grafting with multidisciplinary support helped the patient in given case. Effective recovery within this environment underscores the value of timely surgical decision-making, close observation and coordinated team efforts to maximise functional and cosmetic results.

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