

# Extravasation Injury: What is the Appropriate Management of Extravasated Skin Ulcer?

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## Abstract

**Background:** Extravasation injury can cause a serious problem from significant soft tissue necrosis. The proper treatment is always being delayed before being referred to surgeons.

**Objective:** To study the appropriate surgical management of the extravasated skin ulcer.

**Patients and Methods:** During August 2001 and January 2003, there were seven patients (5 males, 2 females) suffering from extravasation injuries; 5 cases from chemotherapeutic agents (Doxorubicin HCL, Epirubicin) and 2 cases from calcium. Early radical debridement of necrotic tissues and either immediate or delayed reconstruction were successfully performed using either skin flaps or skin grafts if direct closure is impossible.

**Results:** There were one partial flap necrosis and one minimal wound dehiscence. They healed after secondary minor surgery.

**Conclusions:** Prevention of extravasation injury is the best policy because once this serious injury develops it will be difficult to heal by conservative treatment. Early radical debridement of the necrotic or non-healthy tissues with immediate or delayed skin coverage is recommended.

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## INTRODUCTION

Extravasation is the leakage of agent from the vein. An extravenuous leakage of cytotoxic drugs is known to cause significant tissue necrosis. The extravasation injury and its sequelae can be more serious than the condition which originally brings the patient to hospital, an amputation for example. Cancer patients who receive intravenous chemotherapy are prone to extravasation because their veins are often fragile, mobile and difficult to cannulate. On the dorsum of the hand or in the antecubital fossa where there is little cutaneous fat, the extravasated agent may

cause damage to the underlying nerve, tendon and joint.

The incidence of extravasation injury is between 0.1-6%.<sup>1-6</sup> Patients receiving a course of cytotoxic injections run a 4.65% risk of extravasation injury.<sup>1,6</sup> In children, the incidence of extravasation injury is 11%.<sup>2,6</sup> Once the extravasation occurs, it may be difficult to predict whether a serious soft tissue complication will occur or not. The toxicity of the drug, the site of the extravasation, the amount of the agent and general condition of the patient all influence the outcome.

This paper presents seven patients who had skin necroses and ulcers from extravasated agents and were

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referred for surgical treatment in our Department.

4 patients with immediate reconstruction and 3 patients with delayed reconstruction.

### MATERIALS AND METHODS

Between August 2001 and January 2003, seven patients (5 females, 2 males) were referred to the Division of Plastic and Maxillofacial Surgery, Department of Surgery, Ramathibodi Hospital. Each patient had a skin necrosis and ulcer caused by extravasation injury. Four patients suffered from hematological malignancies (3 cases of acute leukemia, 1 case of lymphoma), two patients had infectious diseases (1 case of encephalitis, 1 case of tuberculosis), and one patient suffered from stage III breast cancer. All of them were treated conservatively by dressing only for more than 3 weeks (ranged between 3 weeks and 4 months) before being referred to our Department. We treated all patients with surgery (radical debridement and soft tissue reconstruction);

### RESULTS

The details of all patients suffering from extravasation injury are described in Table 1 and 2.

#### Case Reports

**Patient No.1** A 3-year-old girl, known case of acute lymphocytic leukemia (ALL), had a chronic wound at the dorsum of right wrist from leakage of chemotherapeutic agent (doxorubicin HCl) 4 months previously. She received conservative treatment by wet dressing for 4 months without signs of healing. She was then referred to our Department. The wound, measuring 2 × 2 cm, was covered with eschar with surrounding inflammation. She had limited range of motion of the right wrist joint and metacarpophalangeal

**Table 1** Age, sex, underlying diseases and extravasated agents

Patient No.	Age	Sex	Underlying disease	Extravasated agent
1	3	Female	Acute lymphocytic leukemia	Doxorubicin HCl
2	17	Female	Acute lymphocytic leukemia	Acyclovir
3	65	Male	Non-Hodgkin's lymphoma	Doxorubicin HCl
4	18	Female	Acute lymphocytic leukemia	Doxorubicin HCl
5	30	Male	Tuberculosis	Calcium
6	8	Female	Encephalitis	Calcium
7	57	Female	CA breast	Epirubicin

**Table 2** Site of injury, size of wound, duration, reconstruction and complications

Patient No.	Site of injury	Size of wound (cm)	Duration of wound	Reconstruction	Complication
1	Dorsum of right wrist	2 × 2	4 months	Immediate with local flap	Partial flap necrosis
2	Proximal forearm	4 × 4	3 weeks	Delay with split-thickness skin graft	None
3	Dorsum of right hand	4 × 4	1 month	Delay with local flap	Minimal wound dehiscence
4	Dorsum of left hand	2 × 3	3 weeks	Primary closure	None
5	Left knee and leg	10 × 18	1 month	Delay with split-thickness skin graft	None
6	Left foot and ankle	5 × 15	3 weeks	Immediate with split-thickness skin graft	Donor site minor infection
7	Dorsum of right hand	4 × 8	7 weeks	Immediate with reversed radial forearm island flap	None

(MP) joints. In our service, she was treated with radical debridement and immediate coverage with local flap from dorsum of the hand. Post-operatively, the flap was partially necrotic and was debrided. The wound healed by secondary intention in 2 weeks (Figure 1-3).

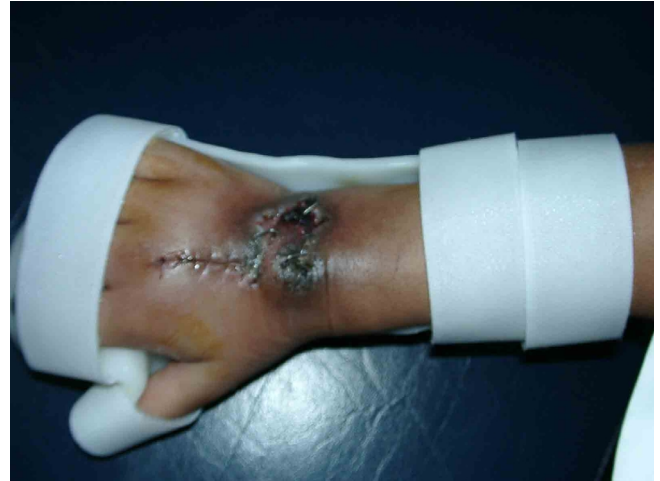
**Patient No. 2** A 17-year-old girl, known case of acute lymphocytic leukemia (ALL), had an extravasated wound at posterior aspect of left elbow. The wound was due to leakage of acyclovir 3 weeks previously. She was treated conservatively with wet dressing and antibiotics for 3 weeks without improvement. She was

in severe pain and was referred to us. The wound, 4x5 cm. in size, was covered with eschar and surrounded with inflammation and induration. The wound was debrided and delayed for coverage 1 week later by split-thickness skin graft. (Figure 4-7)

**Patient No. 3** A 65-year-old man, known case of lymphoma, had an ulcer on the dorsum of his right hand 1 month previously. The ulcer was due to leakage of chemotherapeutic drug (doxorubicin HCl). He was treated conservatively by wet dressing and antibiotic for 3-4 weeks but the ulcer did not improve and the



**Fig. 1** A 3-year-old girl with acute lymphocytic leukemia (ALL) had a 2 × 2 cm. dry eschar wound (full-thickness skin necrosis) at the dorsum of right wrist from leakage of oxorubicin HCl 4 months previously.



**Fig. 2** The wound 1 week after debridement and immediate reconstruction with proximally based local flap from dorsum of right hand. The tip of the flap was partially necrotic.



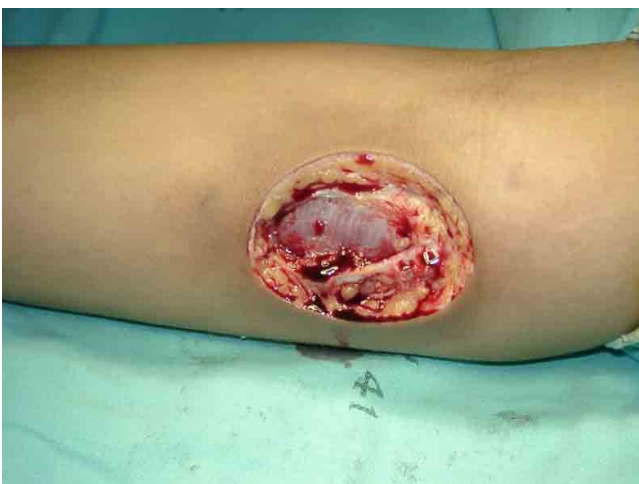
**Fig. 3** The wound 3 weeks after surgery with a scab at the tip of the flap. It completely healed by secondary intention in 2 weeks. The hand function was restored.



**Fig. 4** A 17-year-old female with a wound, 4 × 4 cm. in size, on the posterior aspect of left elbow caused by leakage of acyclovir 3 weeks previously. The central eschar was surrounded by inflammation and induration.



**Fig. 6** The wound at 1 week after radical debridement. It was managed with wet dressing twice a day until healthy granulation tissue was seen in the wound bed.



**Fig. 5** The eschar and the inflammatory area were radically excised until bleeding was observed with no exposed tendon or bone.



**Fig. 7** The wound, after coverage with split-thickness skin graft 2 weeks earlier, healed satisfactorily with complete take of the skin graft.

hand was stiff. He was then referred to our Department. Radical debridement of the ulcer and delayed coverage 2 weeks later with local V-Y advancement flap had been successfully performed. Post-operatively, minimal wound dehiscence at the distal part of the flap was noted and secondary suture was done one week later. (Figure 8-10)

**Patient No. 4** An 18-year-old girl, known case of acute lymphocytic leukemia (ALL), had an ulcer on the dorsum of left hand for three weeks from leakage of doxorubicin HCl. She had been treated with topical antibiotic and dressing for three weeks before being

referred. The ulcer was debrided completely and primary closure was performed with simple suture of the defect which measured 2 × 3 cm. There were no complications.

**Patient No. 5** A 30-year-old man, known case of tuberculosis, had a large full-thickness skin necrosis (eschar) at left knee and upper leg one month previously. The eschar was due to calcium solution leakage. He was treated by wet dressing and systemic antibiotic before being referred to our Department. He also had stiffness of the knee joint. The eschar was debrided completely and delay coverage with split-





**Fig. 8** A 65-year old man with chronic ulcer at the dorsum of the right hand caused by leakage of doxorubicin HCl 1 month previously. The extensor tendons were exposed and the ulcer was surrounded by induration.



**Fig. 9** The wound, 4 × 4 cm. in size, after radical debridement of all necrotic and induration tissue until bleeding from normal tissue was observed. The extensor tendons were exposed.



**Fig. 10** The wound healed completely after coverage with local V-Y advancement flap 3 weeks previously.

thickness skin graft was performed 2 weeks later. Post-operative result was uneventful. After the graft had taken well, she underwent rehabilitation program of the knee joint.

**Patient No. 6** An 8-year-old girl, known case of encephalitis, had a full-thickness skin necrosis (eschar) due to calcium solution leakage at left foot and ankle three weeks earlier. She was treated by topical antibiotic dressing before being referred to our Department. We excised the eschar completely with carbon dioxide laser and covered the defect which measured 5 × 15 cm. immediately with split-thickness skin graft. Unfortunately, during the post-operative period she developed minor wound infection at the donor site. The infected wound was treated with wet dressing and proper antibiotic until there was complete epithelialization 2 weeks later.

**Patient No. 7** A 57-year-old woman suffered from stage III carcinoma of left breast. She underwent radical mastectomy, post-operative radiotherapy, and adjuvant chemotherapy. There was leakage of epirubicin HCl at the dorsum of the right hand. The wound was treated with wet dressing for 7 weeks before being referred to us. The eschar and its indurated area, measuring 4 × 8 cm. in size, was radically excised and immediately covered with a reversed radial forearm island flap. The secondary defect was covered with split-thickness skin graft. Post-operative result was uneventful and the hand function was restored.

## DISCUSSION

Extravasation injury is due to leakage of agent from the puncture site at which a cannula enters the vein. This accidental extravasation injury has unpleasant complications such as ulcer, skin necrosis, stiffness of joint, damage to nerve, tendon and prolonged hospital stay. Various solutions have been described as the causal agent in extravasation injury,<sup>7</sup> such as cytotoxic drugs, intravenous nutrition, calcium, potassium, 10% dextrose solution, vasopressors, and other radiographic contrast agents. The extravasated agents can cause pain, erythema, discoloration of the overlying dermis and tissue necrosis. The degree of soft tissue damage depends on the physiologic and chemical properties of the agents, particular type of agent, osmolarity, pH and molecular weight.<sup>2</sup> When extravasation occurs, there is no certain way of knowing

which case will result in significant tissue damage (skin necrosis, ulcer).

Millam<sup>8</sup> proposed clinical staging based on 1 to 4 clinical stages of the extravasation injury. In stage 1 and 2, no signs of skin damage and loss are observed, whereas in stage 3 and 4, the soft tissue damage is more extensive and may include skin and underlying tissue necrosis. There is no standard treatment for the acute phase of this extravasation injury. However, once it is detected, emergency management must be taken immediately. The infusion should be stopped and any agents that remain in the blood vessels should be aspirated. Any collection or palpable effusion in the subcutaneous tissues should be drained and the limb should be immobilized and elevated above the heart level. Many authors prefer the conservative treatment until lesions evolve for at least 1 week.<sup>1,3,4,6</sup> Some authors advocate the use of specific antidotes as the mainstay of early treatment, such as hyaluronidase that acts by hydrolysing hyaluronic acid in the extracellular matrices and thus increases tissue permeability and dilutes the toxic agent trapped in the tissue.<sup>9</sup> Hyaluronidase has been shown to be effective with many toxins<sup>9,10</sup> and its injection can reduce the skin necrosis.<sup>11</sup> Gault reported the emergency treatment by injection of hyaluronidase into the extravasated site and gentle aspiration of the site with an atraumatic liposuction cannula. His study showed 86% good results with these treatments when implemented within 24 hours of the leakage.<sup>1</sup> On the other hand, with full-thickness skin necrosis, ulcer or persistent pain, many surgeons suggest early aggressive debridement because the chronicity and the nature of the wound can cause patients to suffer delayed treatment of primary disease (ie. carcinoma) and morphofunctional damage.<sup>3,4,6</sup> In these situations, surgical intervention with radical debridement and wound coverage would be required.<sup>12</sup>

This study presents seven patients who had full-thickness skin necroses or ulcers from extravasation injury. All patients had prolonged conservative wound management (dressing only) before being referred to us. Every patient suffered for more than 3 weeks and the patients No.1 and 3 also had decreased hand function. Two patients (No. 5 and 6) had large area of full-thickness skin necroses due to calcium solution leakage when they were unconscious in the intensive care unit. We treated all patients with radical debridement and immediate or delayed coverage with skin

grafts or skin flaps and all wounds completely healed. Unfortunately, one patient (No. 1) had partial skin flap necrosis and another (No. 3) had minimal wound dehiscence. The latter was due to incomplete excision of the ulcer because doxorubicin HCl is DNA-binding chemotherapeutic agent that can be retained in the tissue for five months.<sup>6</sup> Shenaq suggested that complete excision should be performed by excising the ulcer until the wound margins bleeds.<sup>6</sup> Some authors use the intra-operative fluorescent dye injection to detect the doxorubicin HCl in the tissue for complete excision.<sup>13</sup>

The indications for surgery in an extravasation injury patient include full-thickness skin necrosis, chronic ulcer and persistent pain.<sup>3,6</sup> When the patient has fulfilled the indication for surgery, it is necessary for as early a surgical treatment as possible to decrease the morbidity, suffering, and delayed treatment of primary disease of the patient. It is imperative that complete or radical excision of all necrotic tissues must be performed until the bleeding is observed and only healthy tissue is left for wound coverage. Immediate or delayed surgical reconstruction could then be successfully performed.<sup>6</sup>

## SUMMARY

Extravasation injury is very dangerous. It increases morbidity and may be more disabling in long term and causes delayed treatment of the primary disease. Unfortunately, these patients are poor in terms of their general conditions and are suffering from primary diseases, so prevention is the best thing to do.

The presence of skin ulcers, full-thickness skin necrosis and persistent pain make it necessary to perform early surgery. Reconstructive surgery involves excision of all necrotic tissues and the use of plastic surgical armamentarium.

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