

## Cutaneous Necrosis Induced by Extravasation of Arginine Monohydrochloride

Hiroo Amano<sup>1</sup>, Yayoi Nagai<sup>1</sup>, Takanori Kowase<sup>2</sup> and Osamu Ishikawa<sup>1</sup>

<sup>1</sup>Department of Dermatology and <sup>2</sup>Pediatrics and Developmental Medicine, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan. E-mail: hamano@showa.gunma-u.ac.jp  
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Sir,

Arginine is an essential amino acid, which is safely administered to infants with inborn errors of urea synthesis (1). Intravenous perfusion of arginine monohydrochloride is a standard medical procedure for testing serum growth hormone (GH) deficit. The test consists of infusing arginine monohydrochloride rapidly and measuring the GH levels of serum samples taken every 30 min up to 120 min (2). Arginine extravasation injury has been reported occasionally. We describe here a case report of a 3-year-old boy with a skin ulcer caused by arginine monohydrochloride extravasation.

### CASE REPORT

A 3-year-old Japanese boy with swelling of the right hand caused by extravasation of arginine was referred to our department on 3 April 2007. Intravenous infusion of arginine (5.5 ml arginine monohydrochloride, 10% diluted in 49.5 ml of sodium chloride 0.9%) was performed to examine the cause of his growth retardation. He visited our department immediately after a paediatrician noticed the extravasation. Physical examination revealed swelling in the right hand and fingers with reddish to purplish changes in colour. A slight erosive change was noted on the dorsal aspect of his hand (Fig. 1A). The swelling improved within a

few days; however, skin necrosis appeared on the dorsal aspect of his hand. The results of routine laboratory tests were within normal limits, including C-reactive protein. Two weeks later, despite conservative therapy with 1% silver sulfadiazine, a thumb-sized deep ulcer still remained (Fig. 1B). The same topical treatment was continued. One month after the accident the ulcer healed, leaving a slight hypertrophic scar.

### DISCUSSION

Accidental extravasation of various chemical compounds and drugs can cause tissue injuries. Leakage of certain drugs can cause severe skin necrosis or ulcerations (3). Chemotherapeutic agents, especially vesicants type, are well-recognized causes of these lesions. Other agents include calcium bicarbonate, 10% dextrose, gabexate mesilate, contrast materials and others. Arginine extravasation injury has been reported occasionally (4–7).

Intravenous perfusion of arginine monohydrochloride is a provocation test to assess GH release (2). The side-effects of arginine include cutaneous allergic reaction, anaphylaxis, hypophosphatemia and thrombocytopenia (4–8). In 1980, Massara et al. (4) described that a specific venous irritation after arginine infusion caused skin necrosis. Baker & Franklin (5) reported that the

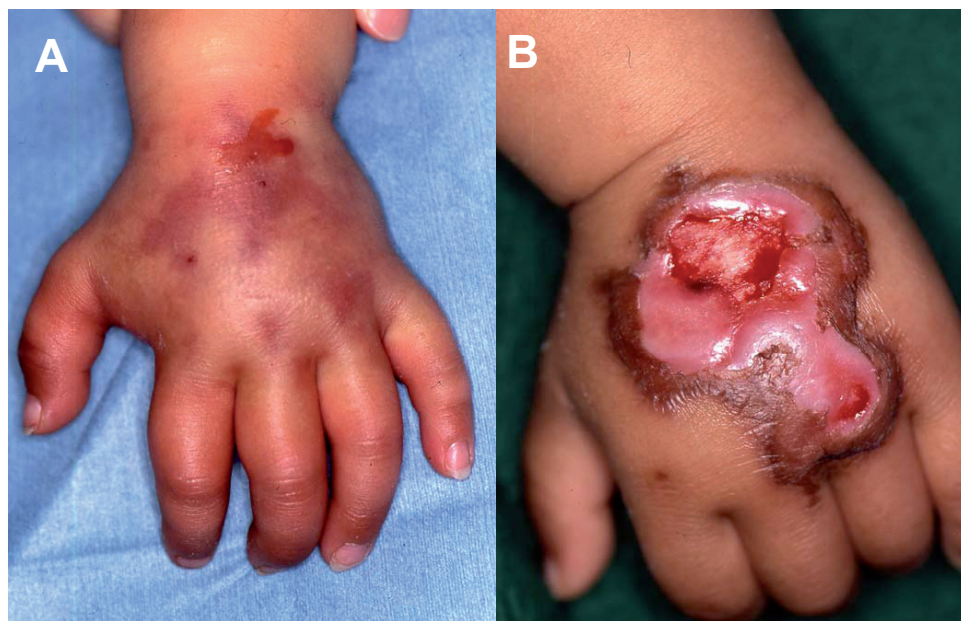


Fig. 1. (A) Swelling and purple-reddish discoloration of the right hand and fingers were noted immediately after the extravasation of arginine. (B) Two weeks later, the skin ulcer still was present.

ulceration developed several days after the extravasation. In another case with skin necrosis, consultation with the dermatologist was made 2 months after the extravasation accident (7). In our case, prominent oedema and redness with slight erosive changes were noted immediately after the extravasation, and necrotic changes became obvious a few days later. Arginine monohydrochloride may cause skin damage more slowly than some chemotherapeutic agents.

The possible pathogenic mechanisms of arginine-induced tissue injury are considered to be altered tissue pH and osmolarity. As arginine monohydrochloride is hyperosmolar, it is highly irritating to living tissues, disrupts extra-intracellular fluid compartment equilibrium, and produces local hyperkalemia. As a result, potassium ions leak out into the extracellular compartments, which leads to impaired cell function and cell death (9). To prevent extravasation it is very important to perform the procedure carefully. Nevertheless, extravasation can occur accidentally. Several treatment modalities have been suggested to limit the skin damage caused by certain agents. Namely, ice-bag application, topical steroids, local injection of dimethyl sulphoxide and steroid injections (hydrocortisone succinate) are recommended. Gault (10) reported that the injection of hyaluronidases, liposuction and saline flush-out were effective in limiting the skin damage caused by chemotherapeutic agents. Steroid injection into the surrounding area is an effective way of stopping the progress of skin damage caused by anticancer agents (11). However, the effectiveness of other drugs has not been established. In patients with deep and large ulcers, debridement and plastic surgery, such as skin flap and grafts, are required. Early and active surgical

management is recommended to prevent functional problems. In our patient, a simple conservative therapy was successful with minimal sequelae.

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