

# Hand gangrene after repetitive IV midazolam injections

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**Abstract.** In the IV drug user (IVDU) population injection may inadvertently be intra-arterial or in the subcutaneous tissue causing a various range of complication ranging from simple cellulitis to artero-venous embolization. We present here a case of a full hand mummification and necrosis following repeated injection of chopped midazolam at the elbow, forearm and hand. A 36 year-old man presented to the emergency department with a 24 months history of slowly progressive necrosis to his right. Dry necrosis had progressively evolved into gangrene with almost spontaneous amputation at the level of the wrist. Surgical intervention was performed urgently with amputation at the proximal forearm level. No early complications were detected, and the patient did not show up at least follow-up. The present case represents an example of progressive microembolisation initially involving the hand and progressively affecting the whole forearm in an impressive mummification process over a 2-year period. Minimal but repetitive distal drug embolization can give silent and initially negligible symptoms, before clear signs of tissue sufferance are detected. When dealing with patients with IVDU history, anamnestic record of eventual use of chopped/pulverized should be performed. Careful examination of the limb should be always conducted, considering the risk of silent embolization and long term potentially devastating consequences. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** drug abuser, intra-arterial injection, hand gangrene, reconstructive surgery

## Introduction

Intravenous delivery of drugs is a routine anaesthesia act, with a low rate of complications. In the IV drug user (IVDU) population however, injection may inadvertently be intra-arterial or in the subcutaneous tissue causing a various range of complication ranging from simple cellulitis to artero-venous embolization, when drugs are chopped or pulverized. As the arm and the forearm are a preferred site for injection by those patients, a relatively high number of patients require hand surgery care due to acute vascular insufficiency and skin necrosis (1).

In the acute setting, intra-arterial injection of pulverized drugs is treated by preventing vasospasm and

thrombosis and promoting blood flow and vasodilatation. Medical treatment includes the use of low molecular weight heparin, steroids, ilomedin and antibiotics, while the surgical management may vary from simple surgical debridement and washout to fasciotomy when vascular compromise is present. In case of treatment failure or late presentation of the patient, treatments span from extensive debridement and reconstruction to amputation, as this may be the only possible option to prevent infection and sepsis (2), while flap reconstruction may be necessary (3).

We present here a case of a full hand mummification and necrosis following repeated injection of chopped midazolam at the elbow.

## Case report

A 36 year-old man presented to the emergency department with a 24 months history of slowly progressive necrosis to his right hand. He had a history of IV heroin drug abuse since more than 15 years which had evolved into self-injection of chopped midazolam (Dormicum®, Roche Pharma, Switzerland) due to the lower cost on the black market. The patient referred episodes of multiple injections, using the elbow, the forearm and the dorsum of the hand as preferred sites. At the time of presentation, dry necrosis had progressively evolved into gangrene with almost spontaneous amputation at the level of the wrist (Figure 1 A). Swelling and marble skin had developed in the proximal forearm (Figure 1 B).

No fever or inflammatory syndrome was present without signs of compartmental syndrome. A doppler echography was performed at admission, showing distal occlusion at the distal third of the forearm of both ulnar and radial artery.

Surgical intervention was performed urgently with amputation at the proximal forearm level (Figure 1 C).

Antibiotic therapy with Amoxicilline and Clavulanate 1.2 gr i.v. 3 times per day was started at surgical induction and prosecuted during hospital stay. The patient remained at the hospital for 4 days after surgery, afterwards he left the hospital against medical advice. He did not show up to any other follow-up examination.

Despite impressive clinical status, patient did not consider stopping IV drug abusing.

## Discussion

The pathogenesis of ischemia following intra-arterial drug injection is not yet clearly defined but is probably related to the drug as well as to the inert ingredients or excipients with which it is formulated and their effect on the microvascular physiology.

According to Lindfors et al, the distal damage may be caused by direct injury of the intima of the artery with activation of tissular thromboplastin, resulting



**Figure 1 A:** A 36 year-old man presented to the emergency department with a 24 months history of slowly progressive necrosis to his right hand. Dry necrosis had progressively evolved into gangrene with almost spontaneous amputation at the level of the wrist.

**Figure 1 B:** Swelling and marble skin had developed in the proximal forearm.



**Figure 1 C:** Surgical intervention was performed urgently with amputation at the proximal forearm level

ultimately in vascular thrombosis (4). Other mechanism described includes the noradrenaline release, platelet aggregation, embolism and toxic vasculitis (5). Goldberg et al. described the role of micro-crystalline cellulose (which is found as an excipient in the tablets), that could cause limb gangrene when injected in femoral artery of dogs (6).

In the acute setting, intra-arterial embolization of chopped/pulverized drugs may cause pallor, mottling, cyanosis, and edema. If perfusion is not reestablished to the extremity, the patient risks skin and muscle necrosis and compartment syndrome. Urgent treatment should aim to prevent vasospasm and thrombosis and promote blood flow and vasodilatation (7).

However, the present case represents an example of progressive microembolisation initially involving the hand and progressively affecting the whole forearm in an impressive mummification process over a 2-year period.

Interestingly, this never evolved to sepsis, as distal to proximal ischemia progressed at slow pace, with a supposed slow release of catabolytes and inflammatory molecules.

For such reasons the patient did not consult to A&E

for pain or septic symptoms, but rather for the smell of the limb he judged excessive.

This clinical scenario is of course related to the late hospital consultation due to the dramatic social and economic conditions of the patient. Initial signs of vascular and of soft tissue compromise would have been surely detected faster if normal social conditions were present.

Despite there are few case reports in literature presenting upper extremity necrosis due to intra-arterial drug injection, those papers describe only acute events, that develop within hours or at most days after the injection.

Nevertheless, this report represents how even minimal but repetitive distal drug embolization can give silent and initially negligible symptoms, before clear signs of tissue suffering are detected. When dealing with patients with IVUD history, anamnestic record of eventual use of chopped/pulverized should be performed. Careful examination of the limb should be always conducted, considering the risk of silent embolization and long term potentially devastating consequences.

**Statements:** Patient's informed consent was obtained for use of photos. Patient data were treated according to the declaration of Helsinki as modified in 2013.

**Ethical approval:** Not required.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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