

Cutaneous Complications of Direct Intra-arterial Injections in Drug Addicts

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Sir,

After several years of addiction, the peripheral veins, the usual route for drug injection, become sclerosed and injection is difficult. Drug addicts may then deliberately or incidentally use direct intra-arterial injections. This route of injection may result in severe complications where mainly skin and underlying structures are affected. We report here five patients with cutaneous manifestations after direct intra-arterial injection of a suspension of boprenorphine crushed tablets, including two patients who had clinical features that have not been reported previously.

CASE REPORTS

In all five subjects the skin manifestation followed the same initial course. Immediately after intra-arterial injection the patients felt a burning pain in the area supplied by the artery. The pain was intense and lasted for several days. Swelling and a cold cyanosis were rapidly present.

Patient 1 was a 33-year-old man who had inadvertently injected himself in the radial artery. Cyanosis and oedema predominated in the palm area. He was lost to follow-up after 3 days of hospitalization.

Patient 2 was a 34-year-old man who had injected in the brachial artery. Local examination showed livedoid purpuric plaques over the dorsal hand and wrist. Histological examination showed focal necrosis in epidermis, a perivascular lymphohistiocytic infiltrate, with some neutrophils, without leucocytoclasia vasculitis and empty vacuoles in some deep capillary vessels. Superficial skin necrosis occurred but the outcome was favourable after 2 weeks.

Patient 3 had unusual manifestations. He was a 25-year-old man who had injected in the radial artery. The pain and the swelling of the hand were intense. He could not move his fingers actively and passive mobilization was extremely painful. Local examination showed disseminated dome-shaped firm erythematous and purpuric papules (Fig. 1). The papules were present over both the palmar and dorsal surface, 2–5 mm in size, some with a central pustule, others with central necrosis. The general health examination was unremarkable. He had neither fever nor lymphadenopathy. No other cutaneous lesion was seen elsewhere. Both clinical and ultrasonographic cardiac examinations were normal. The cutaneous biopsy of two papules showed similar features: subcorneum pustule, with a fibrino-leucocytic aggregate, a perivascular inflammatory infiltrate and some empty vacuoles within capillary vessels, but no visible foreign body even after a polarized light microscopic examination. Cultures of both the pustule content and the cutaneous biopsy were negative. The patient received parenteral empirical antibiotic therapy with rifampicin, ofloxacin and oxacillin, antalgic and dalteparin (5000 UI/daily) for 10 days. The outcome was favourable in 2 weeks.

Patient 4 was a 20-year-old man who had injected himself in the femoral artery. Cyanosis and purpuric plaque occurred over the upper part of the left thigh, with petechiae over the foot. After 3 days of surveillance the patient was lost to follow-up.

Patient 5 was a 25-year-old woman who had unusual features. She had injected in the groin. She had a significant oedema of the external genital area. Cyanosis and necrosis occurred in the pubic area (Fig. 2). After 2 weeks of local care, she was lost to follow-up.

DISCUSSION

The first reports of direct intra-arterial injections were accidental injections during induction of anaesthesia (1).



Fig. 1. Papulo-pustular and purpuric lesions of the palm resulting from micro-emboli after radial artery injection (see the site of injection on the wrist).



Fig. 2. Cutaneous necrosis corresponding to the territory of the pubic artery.

During recent decades the majority of reports referred to the intra-arterial administration of illicit drugs. In some instances intravenous drug users inject a mixture of dissolved oral drugs. The complications resulting from this misuse affect mainly skin and underlying structures. But to our knowledge, such manifestations have not been reported in the dermatological literature.

The majority of intra-arterial injections are in the upper limbs. The spectrum of clinical signs is common to the various drugs injected (2–6). Direct intra-arterial injection of drugs may cause severe ischaemia and necrosis. Immediately after a direct intra-arterial injection, the patient feels an intense ‘burning’ pain in the injected artery area. Within a few hours a marked oedema of the affected limb appears. Peripheral pulses are usually normal. Cyanosis and livedoid patches appear in the affected territory. Distal necrosis occurs in the most severe cases.

It is likely that the rate of complications may differ according to the drug injected. Nott et al. (7) observed that after radial artery injection of temazepam, tissue loss occurred in 100% of cases. The drug was administered after breaking open the gelatin capsule and heating it in water to form a solution for injection (7, 8). In the patients reported by Maxwell et al. (9), barbiturates were responsible for most complications. Many drugs used by addicts have been responsible for distal limb ischaemia – such as cocaine, heroin, pentazocine, diazepam, amphetamine and others (2–10). Buprenorphine (Subutex™) is a semisynthetic partial opioid agonist used in Europe as an oral treatment for opioid dependence (11). Subutex™ tablets are designed for sublingual administration, but some addicts, in drug maintenance programmes, inject a water suspension of crushed tablets heated in a spoon. Gouny et al. (11) reported a similar case of embolic complication in a man following intra-arterial injection of a suspension of Subutex™.

Several mechanisms have been suggested to explain the tissue ischaemia. Some drugs such as cocaine act as a powerful adrenergic agent and may cause a direct local vasoconstriction. In addition the local cytotoxicity of a drug may cause vascular injury, namely a chemical endarteritis resulting in vasospasm and thrombosis. Using a rabbit model of ear intra-arterial penthotal injection, Buckspan et al. (12) showed that the primary injury was a direct toxic effect of the drug on the vessels with secondary oedema, vasospasm and thrombosis with tissue ischaemia and necrosis. Finally an oral drug suspension may contain microparticles which act as microemboli. The peripheral ischaemia results in oedema. When this oedema affects a limb a compartment syndrome may occur, which in turn worsens the ischaemia. Finally superficial and deep tissue necrosis occurs in the ischaemic territory. Prolonged postural

pressure on the limb after drug-induced coma can worsen the ischaemia.

Two of the present cases had unusual manifestations. Patient 3 had purpuric and pustular nodules. Probably as a result of distal embolization of insufficiently solubilized and filtered particles. The histopathological study showed empty vacuoles obturating vascular lumen, which are suspected to be micro-emboli of Subutex™. Patient 5 had cutaneous necrosis of the genital area. Injection in the groin may result in incidental intra-arterial injection of the femoral artery or its branches. Rare reports exist of incidental pubental artery injection, resulting in scrotal and penile skin necrosis (13–15) but no female cases have been published.

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