Skin necrosis after self-administered intramuscular diclofenac

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Summary Intramuscular diclofenac is used extensively for pain relief in medical practice. Tissue necrosis is a rare but serious complication of intramuscular injections. The pathogenetic mechanism is still not completely understood. A case of tissue necrosis following self-administration of diclofenac inadvertently injected into an arterial perforator branch of the superficial femoral artery is reported, supporting a vascular pathogenesis.

CASE REPORT

Tissue necrosis is a rare complication of intramuscular drug injection and may involve the skin, subcutaneous tissue and muscular layer. The pathogenesis of the necrotic process is not completely understood. Reported is a case of skin necrosis following self administration of intramuscular diclofenac inadvertently injected into an arterial perforator branch of the superficial femoral artery, supporting an end artery damage pathogenesis.

Case report

A 52-year-old healthy male was referred to our emergency room by his general practitioner due to painful skin necrosis of the anterior aspect of his thigh, which had gradually progressed over the previous week. He had undergone a series of intramuscular diclofenac injections for alleviation of low back pain two weeks earlier. The injections were self-administered at a dose of 75 mg once daily over five days. The last injection was administrated into the anterior left thigh muscle, ten days prior to presentation. The patient reported having noticed a backflow of blood into the syringe which he ignored and continued to inject the substance. A painful red rash soon appeared around the injected area, which developed into true necrosis over the following week. Physical examination revealed a 15 × 5 cm necrotic eschar over the anterior aspect of his thigh with no signs of cellulitis or infection (Figure 1). Complete blood tests revealed no indications of infection. Ultrasound examination of the involved thigh showed no signs of cellulitis.
often leaving an atrophic scar. Complications, such as debridement. Recovery usually occurs over a few months, leave an underlying ulcer or it may require surgical result in a thick eschar that may either slough off and cation of the necrotic area appears after several days, the skin, subcutaneous tissue and muscular layer. Demar-

Figure 1 Necrotic eschar and cellulitis over the anterior aspect of the patient’s thigh observed on admission.

collection or abscess. Doppler examination of both thighs demonstrated a perforator branch of the superficial femoral artery in the contralateral thigh at a point that exactly mirrored the necrotic injection site.
The patient was admitted to the plastic and reconstructive surgery department and underwent surgical wound debridement with primary closure of the wound. The necrosis was confined to the skin and subcutaneous fat. No pathological specimens were sent. A superficial wound infection with partial wound dehiscence developed post-operatively, and wound cultures were positive for Staphylococcus aureus. The patient was treated with intravenous antibiotics and standard wound dressings which led to full recovery and his discharge from hospital. On ambulatory follow-up, the wound was noted to have healed well and uneventfully.

Discussion

Tissue necrosis as a serious complication of intramuscular drug injection was first observed in the 1920’s by Freudenthal and Nicolau after administration of bismuth salts for syphilis treatment, and has been referred to since then as Nicolau’s syndrome (NS), livedo-like dermatitis or embolia cutis medicamentosa. The syndrome typically begins as an immediate intense pain and pallor at the injection site, followed by erythema that evolves within hours into a livedoid bluish reticular patch which becomes hemorrhagic and then necrotic. The necrosis may involve the skin, subcutaneous tissue and muscular layer. Demarcation of the necrotic area appears after several days, resulting in a thick eschar that may either slough off and leave an underlying ulcer or it may require surgical debridement. Recovery usually occurs over a few months, often leaving an atrophic scar. Complications, such as neurological injury, extensive necrosis, limb ischemia, sepsis due to superimposed infection and even death in children, have been reported. In addition to bismuth salts, injection of several other drugs has been reported to cause necrosis, including non-steroidal anti-inflammatory drugs, local anesthetics, corticosteroids, antihista-
mes, penicillin and other types of antibiotics, interferon, vitamin B complexes, iodine and several vaccine preparations.

The pathogenesis of post-injection necrosis is not completely understood, however damage to an end artery by massive inflammatory reaction induced by intra-arterial or para-arterial drug injection seems as the leading hypothesis. Allergic, immunologic and mechanical vascular occlusion theories have been disproved.

Considering the fact that there is no established treatment for NS, it is important to employ a proper injecting technique for minimizing risk factors, such as subcutaneous and intra-arterial injection. The preferred technique for intramuscular drug administration is injection into the upper outer quadrant of the gluteal region perpendicular to the tissue, using a needle with adequate length to avoid subcutaneous injection. Aspiration prior to injection is important to preclude intravascular injection.

Several studies have mentioned clinical improvement with prompt administration of anticoagulation treatment (e.g. subcutaneous heparin), intravenous steroids (e.g. intravenous betamethasone, dexamethasone or methylprednisolone), and vasoactive therapy (e.g. pentoxyfylline). However, data regarding treatment of acute NS is available only from sporadic case report, and no established guidelines exist. There may not be any alternative to debridement and reconstructive surgery after necrosis and ulceration have evolved.

In our above-described case diclofenac was injected into an arterial vessel, probably a perforator branch of the superficial femoral artery, as was precisely mirrored by Doppler mapping of the patient’s contralateral thigh. The necrotic area coincided with the vascular territory of soft tissue supplied by this artery. These findings support the theory of end artery damage induced by intra-arterial drug injection as the pathogenesis of NS.

Conflict of interest

The authors warrant that they have no financial interest in the subject matter or materials discussed, and have no conflict of interests regarding the content of this article.