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Case Report

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Skin Necrosis After Ketorolac Intravascular Administration

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ABSTRACT

Skin necrosis is considered as a rare but severe complication of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) injections. Symptoms comprise intense pain around the injection site, evolving into erythema, livedoid violaceous patch, hemorrhagic patch, and eventually necrosis of the skin. The pathogenesis is not fully clear. However, it is presumed that damage to an end artery and the cytotoxic effects of the drug are main causes. We present a patient who developed skin necrosis after ketorolac intravascular administration for the treatment of renal colic. To the best of our knowledge, this is the first report describing skin necrosis after ketorolac intravascular injection.

Introduction

Skin necrosis is recognized as a rare but severe complication of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) injections [1]. The most accepted hypotheses in the pathogenesis of skin necrosis is damage to an end artery, the cytotoxic effects of the drug and the additives in the injectate [1].

Ketorolac, a member of NSAIDs, is an effective analgesic in the short-term management of acute pain. It is

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comparable to that of narcotics in analgesic potency, but without any narcotic side effects. These advantages have resulted in the use of ketorolac for the management of acute pain [2]. We present a patient who developed skin necrosis after ketorolac intravascular administration for the treatment of her renal colic. To the best of our knowledge, this is the first report describing skin necrosis after ketorolac intravascular injection.

Case Presentation

A 68-year-old female patient referred to our hospital with one episode of fever and shaking chills, nausea, vomiting, dysuria, frequency and urgency since 7 days ago. Two days before, she received a ketorolac intravascular injection to cubital vein for renal colic pain relief. On admission, she had a red to purple discoloration at the injection site with some blisters on the distal of the left forearm that gradually extended to the arm within next days (Figures 1 and 2).

In the emergency room, her BMI was close to 24 and vital signs were as follows: blood pressure=80/p, pulse rate=120 and axillary temperature=38.5°C. The patient was conscious and her laboratory test results showed leukocytosis, metabolic acidosis, prolonged PT & INR, decreased platelet count and pyuria in urine analysis. Upper extremity plain radiography was normal without any evidence of gas in soft tissue, and ultrasound of the upper limb did not show an abscess or collection.

First she was admitted to infectious disease ward with regard to urosepsis and soft tissue infection, and received intravascular antibiotics including imipenem and vancomycin. Based on surgical consultation, only daily dressing of the skin lesions was recommended. A few days later, skin lesions developed into necrosis in some regions and the patient experienced more pain in her left arm (Figure 3). On examination, the patient was afebrile and looked well.

The patient underwent a second surgery consultation for debridement and biopsy. Histology report of the necrotic site comprised exudates mixed with fibrin and leukocytes in inflammatory cells with infiltration, necrosis and fibrosis. Actually, focal dermal necrosis, inflammation and transepidermal elimination were observed. Two weeks later, wound break down resulted in several surgical procedures. After multiple surgical debridement, the skin of the upper limb became clean without any necro-

Figure 1. Red to purple discoloration of the injection site and upper extremity

Figure 2. Some blisters around the injection site

Figure 3. Black discoloration and necrosis of the skin on the patient's arm

sis and discharge; subsequently, the patient was referred to another hospital for a skin graft.

Discussion

The term Nicolau syndrome, also known as embolia cutis medicamentosa, has been coined to describe skin necrosis as a rare, but severe complication after injection [1]. Clinically, the typical presentation is intense pain around the injection site, followed by erythema that develops into a livedoid violaceous patch, then hemorrhagic patch, and eventually necrosis of the skin [1, 3].

Nicolau syndrome is often described in association with intramuscular injections. However, several cases have been recently reported after intravenous, intraarticular, and subcutaneous injection [4]. This case is special since it highlights a potentially serious complication of ketorolac intravascular injection. This observation is in line with other findings by Kosaraju et al. and Begin et al., that reported purpura fulminans after ketorolac intramuscular injection and Nicolau syndrome following intravascular vaccine injection, respectively [5, 6]. In our patient, the IV injection to cubital vein was performed, and tissue necrosis occurred on upper limb. The authors presume that such an extensive necrosis is due to the extravasation of intravenous fluid into the subcutaneous tissue.

The pathogenesis of the disease is poorly understood. However, it is presumed that direct vascular damage, perivascular inflammation and vascular contraction are involved in the pathogenesis. It is thought that the stimulation of sympathetic nerve caused by pain from the intra-arterial or peri-arterial injection of drugs induces vasospasms and resulting in ischemia. The other causes to consider are the properties of the drug injected; for instance, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) inhibit the enzyme cyclooxygenase, leading to prevention of prostaglandin synthesis, thereby inducing vascular spasm, and blocking local circulation [3, 7].

The recommendations for the best treatment depend mostly on the time of diagnosis. In the early period, a medical resolution can be achieved through hyperbaric, antibiotics, dressing and heparin injection. Surgical debridement and skin graft should be considered as the main treatments in a case of late diagnosis [3, 4, 8]. The suggestions to prevent unwanted side effects of NSAIDs injections include adding specific warnings to drug information sheet, discontinuing injection if pain occurs, applying proper injection techniques and aspirating just before injecting medication [1, 4].

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article. The participant was informed about the purpose of the research and its implementation stages.

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Conflict of interest

The authors declare no conflict of interest.

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