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Case Report

The Nicolau Syndrome: A case report and a review of the literature

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Abstract

Nicolau syndrome (NS) is a rare aseptic cutaneous adverse reaction and necrosis caused by intra-muscular, subcutaneous, intravenous, or intra-articular injection of various drugs. We report a case of this syndrome. A 20-year-old male who developed intense pressure pain, the local sensation of heat, and reddish discoloration of the skin after receiving an intramuscular injection of diclofenac for renal colic. The complaints started two days after the injection. The patient was managed at peripheral health care center as a case of post-injection site abscess. However, the patient developed gluteal necrosis and was referred to our tertiary care center for further management. The patient was treated with antibiotics, and aggressive multiple debridements, and healed with secondary intention with an ugly scar. The observed syndrome was due to the injection of the drug into subcutaneous tissue instead of proper muscular planes. Medical and paramedical personnel must be properly educated and sensitized to such a complication that can occur during drug administration. They should follow the standard and appropriate injection techniques and take all necessary precautions to avoid this severe complication, which increases the patient's morbidity. Proper teachings of injection techniques to junior medical and paramedical staff should be exercised at the apex and peripheral centers for the prevention of this syndrome.

Keywords: Embolia Cutis Medicamentosa, Nicolau Syndrome, Diclofenac, Renal Colic

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Introduction

Nicolau Syndrome (NS) is a rare aseptic cutaneous adverse reaction and necrosis caused by intra-muscular, subcutaneous,intravenous, or intra-articular injection of various drugs (1-4). The condition, also known as Embolia Cutis Medicamentosa or Livedoid Dermatitis, should be considered if there is an acute onset of severe pain and erythemato-ecchymotic reticular lesions at the injection site. The pathophysiology of this syndrome is unclear, but thrombotic occlusion, vasospasm followed by ischemia, and tissue necrosis has been hypothesized (3-5). This potentially avoidable iatrogenic severe condition can be avoided by using proper injection techniques and auto-injectors. We report a patient with Nicolau syndrome after diclofenac injection and a review of the literature.

Case

Mr. Y, a 20-year-old male patient, normotensive, non-diabetic, euthyroid, and non-smoker, was given an intramuscular injection of diclofenac in the right gluteal region by a local healthcare worker for renal colic at a peripheral health care center. Two days after the injection, the patient developed local pain, erythema, and painful swelling. The patient was subjected to incision and drainage without any improvement.

The patient was transferred to our tertiary care center for further treatment due to worsening gangrenous changes and overall deteriorating general conditions. A workup, including, thorough history taking, baseline biochemical tests, radiograph, and local ultrasonography to rule out any collection was performed. Except for hypoalbuminemia (3.1 g/dl), elevated C-reactive protein level (CRP) (58mg/l), and microcytic hypochromic anemia (7.9g/dl), the rest of the investigations were normal.

There was no history of trauma, systemic or topical medication, or spontaneous bleeding from the gingiva or mucosa. On examination, a well-defined, nontender, large violaceous patch measuring 20 cm×12 cm with sharp gangrenous geographic margins was discovered over the right gluteal region, with an incision and drainage site in the centre (Figure 1).

Figure 1: Nicolau Syndrome in 20-year-old patient.

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The patient and attendants were counselled about the nature of the disease and future management after the diagnosis of Nicolau's syndrome was made. The patient was kept under observation and started on broad-spectrum antibiotics after sending wound swab culture. The culture yields E.coli that was sensitive to Meropenem. Meropenem injections (25mg/kg/dose) were given three times a day for ten days, along with anaerobic cover with Metronidazole (7.5mg/kg/dose) and twice daily wound debridement and antiseptic dressings. On a daily basis, the patient was also given multivitamins, iron supplements, a high-protein diet, and vitamin C. Clinically, the patient improved, and the wound was covered with healthy granulation in about three weeks. The wound healed gradually by secondary intention.

Discussion

In 1925, the first case of Nicolau Syndrome was reported in a patient with syphilis after an intramuscular injection of bismuth salt (6). The reaction has been linked not only to intramuscular injections, but also to subcutaneous, intravenous, and intra-articular injections (7-9). The reaction has been reported with range of drugs including, Penicillin, NSAIDS, corticosteroids, vaccines, and many others, indicating that the class of drug administered is unrelated (10).

In a recent review of case studies of Nicolau syndrome, females had higher chances of developing the disease as compared to males. Furthermore, children in their first decade of life and adults in their fourth decade of life have a higher incidence of this disease (19.26% 1nd 20% respectively) (11). Clinically, the syndrome is distinguished by sudden, intense pain, pallor, and the development of a well-defined lived like violaceous patch, which eventually leads to necrotic ulcers and scarring involving the subcutis and the muscular layer (12,13).

The aetiology of this iatrogenic syndrome is attributed to vasospasm caused by a needle prick, embolization of injected material, or pressure caused by the material placed around the vessel, which leads to necrosis of the skin and deeper tissues (14). History of drug administration, clinical differentiation, laboratory tests , and imaging, assists in the diagnosis of this syndrome. Increased serum ESR and C-Reactive Protein (CRP) levels due to inflammation and histopathological examination of a skin biopsy shows characteristic necrosis, associated with extensive perivascular leucocytic infiltration, thrombosis of medium and small-sized vessels of the reticular dermis, and no evidence of vasculitis, support the diagnosis (15).

Ultrasonography of the skin and magnetic resonance imaging help in delineating the extent of damage. Ultrasonography shows evidence of an area of diffuse edema and hyperechoic area, as well as inflammation of the subcutaneous area and the muscles (16).

There is no specific treatment therapy for Nicolau Syndrome and doesn't differ from the management of other wounds. The extent of the lesion determines treatment, which can range from conservative to surgical. For minor cases, the mainstay of therapy is local wound debridement with analgesia and daily anti-septic dressings. Negative pressure wound therapy, local Lacto calamine lotion in combination with anti-inflammatory drugs, subcutaneous heparin, intravenous steroids, and pentoxifylline have yielded promising results (17-20).

This case report draws attention to a potentially fatal complication that can occur during routine intramuscular diclofenac administration and the precautions that should be taken to avoid this mishap.

Conclusion

Nicolau syndrome is potentially avoidable with proper injection techniques and the use of auto-injectors. Proper awareness of this syndrome, as well as appropriate injection techniques during drug administration, can aid in the prevention of this severe complication. Medical and paramedical personnel must be properly educated and sensitized to such a complication that can occur during drug administration. They must use standard and appropriate injection techniques and take all necessary precautions to avoid this mishap, which increases the patient's morbidity.

For the prevention of this syndrome, proper

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injection technique teaching to junior medical and paramedical staff should be practiced at the apex and peripheral centers.

Conflicts of interest

The authors declare that they have no conflict of interest.

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