

NICOLAU SYNDROME DUE TO INTRAMUSCULAR DICLOFENAC SODIUM INJECTION

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Abstract

Nicolau syndrome (NS) is a rare complication characterized by tissue necrosis that occurs after parenteral injection of drugs. The exact pathogenesis is uncertain, but there are several hypotheses, including direct damage to the end artery, acute vasospasm and cytotoxic effects of the drug. Severe pain in the immediate post injection period and purplish discoloration of the skin with reticulate pigmentary pattern is characteristic of this syndrome. Diagnosis is mainly clinical and there is no standard treatment for the disease. Herein, we present a rare case of NS due to Diclofenac Sodium (Voltaren®) injection in an 80-year-old female suffering from Lower Respiratory Tract Infection (LRTI) who was managed conservatively.

Keywords: Nicolau Syndrome, Embolia cutis medicamentosa, Voltaren, Diclofenac sodium

Introduction

Nicolau syndrome (NS) is a rare complication caused by parenteral injection of various medications. Necrosis at the injection site is a characteristic feature of this syndrome. The development of acute vasospasm following intra-arterial or peri-arterial injection is the most widely accepted hypothesis in its pathogenesis. The occurrence of NS following Diclofenac Sodium injection is rare and to the best of our knowledge has been mentioned only in eight previously published reports^[8].

Case Report

An 80-year-old obese female presented to the emergency department with the complaints of dyspnea, cough, wheezing and abdominal pain for seven days. Upon thorough clinical examination and investigations, a diagnosis of Acute Exacerbation of COPD with Lower Respiratory Tract Infection (LRTI) was made and the patient was shifted to the medical ICU for further management. A complete blood count, coagulation profile, urine examination, renal and liver function tests were within normal limits. Chest X-Ray showed diffuse interstitial inflammatory infiltrates consistent with the diagnosis of LRTI. The patient was started on Inj. Cephalexin 1gm BD and given an intragluteal injection of Diclofenac Sodium (Voltaren®) for pain relief. After receiving diclofenac sodium, she immediately experienced severe pain and erythematous swelling at the injection site followed by blistering and ulceration. On day 3 of

admission, cutaneous examination revealed ulceration in the lateral part of her right gluteal region (Figure 1) and erosions with a hemorrhagic patch in the right cubital fossa (Figure 2) measuring approximately 6x3 cm and 2x2 cm in diameter respectively. There was a 5x4 cm ecchymotic patch over the epigastrium in the periumbilical region (Figure 3). Lesional biopsy was not obtained to avoid the risk of worsening necrosis. The patient was treated with sterile dressings and Mupirocin ointment (topical 2%). During admission, she showed gradual clinical improvement the signs and symptoms improved gradually. On the follow-up visit after one month, the lesions had completely resolved.



Figure 1: Ulceration over gluteal region



Figure 2: Erosions and hemorrhagic patch over cubital fossa



Figure 3: Ecchymotic patch over the epigastrium

Discussion

Nicolau Syndrome (NS), also known as “livedo-like dermatitis” and “embolia cutis medicamentosa” was first described by Freudenthal and Nicolau following an injection of bismuth for the treatment of syphilis^[1,2]. It is a rare condition caused by intramuscular or intra-articular injection of various medications. Penicillin, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids, and local anesthetics have been reported as the causative agents of NS^[3-5]. Saputo and Bruni (1998)^[6] reviewed 102 cases of NS and showed that 78.43% of cases occurred under the age of 12 years. However, according to Senel et al. (2008)^[7], the majority of the cases were adults.

The pathogenesis of NS remains unknown; however, several hypotheses have been postulated to explain the process. It is presumed that intra-arterial or peri-arterial injection of drugs leads to sympathetic nerve overstimulation giving rise to severe pain due to embolic occlusion and ischemic necrosis.

The diagnosis of NS is mainly clinical which typically begins

with sudden onset of pain around the injection site soon after drug administration. Necrosis follows hyperemia, discoloration of skin, formation of hemorrhagic patch at the site of injection and livedoid dermatitis. About 33% cases present with transient neurological complaints like hypoesthesia and paraplegia^[8]. Several studies have shown the occurrence of secondary infections following NS^[9]. Our patient presented with classical necrotic lesions and ecchymotic patches over intramuscular injection sites which extended to the abdomen. Histological examination of the affected region shows necrosis of dermis and subcutaneous fat along with vascular thrombosis due acute inflammation.

NS has no definitive treatment. During the early stage of the disease, the main goal of therapy is to prevent the development of necrosis. According to Murthy et al. (2007)^[8], conservative management with pain control is the mainstay of therapy. However, surgical debridement should be performed in the case of necrosis.

NS is an avoidable complication and its onset cannot be predicted. However, precautionary measures like, Z-track technique of intramuscular injection into the superolateral quadrant of the gluteal muscle, choosing different sites in case of a larger drug dose (>5 ml) or multiple injections, must be undertaken in order to prevent this syndrome^[10].

To conclude, NS is an important cause for morbidity in bed ridden patients with life threatening infections. These patients turn out to be poor candidates for establishing an intravenous access, thereby requiring a central line insertion for further management which could subsequently add to the morbidity. Intramuscular injections appear to be a simple procedure; however, all precautions must be undertaken during the procedure to prevent the onset of this rare complication. The present case highlights the need for increased awareness about NS and the need to exercise utmost care during the administration of any parenteral drugs by health care workers.

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