

Nicolau Syndrome Following Intramuscular Diclofenac Sodium Injection: A Rare Case Report

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Abstract: Nicolau syndrome is a rare local complication of intramuscular injection of Diclofenac sodium. Cases have been reported following injection of some other drugs like penicillin, antihistaminic, antiepileptic, corticosteroid and lidocaine. Avascular necrosis is attributed as etiopathogenesis and diagnosis of the condition is clinical. It is managed by debridement of necrotic tissue, wound dressing, analgesic, antibiotics and skin grafting whenever required. The ulcer may heal in months leaving a depressed scar. Incidences of disability and death have been reported in extreme cases. A 74 year old lady was treated with intramuscular injection of Diclofenac Sodium for postoperative pain on 8th postoperative day following total abdominal hysterectomy with bilateral Salpingectomy. She developed intense pain followed by a necrotic lesion over the injection site for which she was treated with debridement and wound dressing. Secondary suture was applied later. Outcome was good on removal of sutures. Though Nicolau syndrome is not completely preventable, steps can be taken to avoid this devastating pathology. We report this rare condition of Nicolau syndrome to bring about awareness of the entity and adoption of proper procedure of injection as the primary steps in its prevention.

Keywords: Vasospasm, Avascular necrosis, Debridement, scar

1. Introduction

Nicolau syndrome (NS) is a rare iatrogenic complication of intramuscular (IM) injection of Diclofenac sodium. Drugs like penicillin, lidocaine, antiepileptic drugs, diphtheria-tetanus-pertussis vaccine, corticosteroids, antihistamines and sclera therapy may also cause this pathology.¹ Though exact pathogenesis is not known; local vasospasm and tissue necrosis is the most accepted hypothesis for it. Diagnosis is usually clinical. Conservative management with antibiotics, surgical debridement, wound dressing, skin grafting in extensive lesion and surgery in case of contracture is the treatment of choice. The aim of presenting the case is to develop awareness on the pathology, to adopt preventive steps in injecting medications and avoid cold therapy; which exacerbates the tissue necrosis.

2. Case Report

A 74 years old lady had undergone total abdominal hysterectomy with bilateral salpingo oophorectomy for postmenopausal bleeding. She had simple endometrial hyperplasia on histopathological examination of endometrium. Her weight was normal for height with BMI of 27kg / m² and did not have any comorbid conditions. Injection Diclofenac sodium was given IM on the eighth postoperative night in right deltoid region for pain at surgical wound site. She complained severe burning pain at the site following injection. Next morning pain was more intense and localized black, gangrenous patch over the skin at the injection site of 04x03cm was noted (fig.1). Later blister formation occurred at the lesion within hours (Fig.2).



Figure 1: Gangrene of the overlying skin



Figure 2: Blister formation within hours over the injection site

The eschar was tender, with well demarcated margins. Debridement of the gangrenous patch was done under antibiotic cover and local anesthesia, followed by regular wound dressing with nano silver colloid gel. The ulcer on 22nd day of injection (Fig 4) was clean and without features of infection. With negative wound swab culture report and healthy granulation tissue, secondary suture was applied on 22nd day of injection. Wound healing was satisfactory following suture removal on 10th day following secondary suturing (Fig.5).



Figure 4: Healing ulcer on 22nd day



Figure 5: Healed ulcer after suture removal

3. Discussion

NS was first reported by Freudenthal in 1924.² Nicolau in 1925 attributed etiopathogenesis of the condition to vascular embolic phenomena.³ Till 2016 < 50 such cases have been reported in medical literature following intramuscular injection of Diclofenac sodium.⁴ It is more common in younger age group of <3 years of age^{5, 6} because of small caliber of vessels. Though exact etiopathogenesis is not known the accepted hypothesis of a vascular necrosis are explained by (a) perivascular injection of drug leading to vasospasm; (b) suppression of prostaglandin synthesis by inhibiting cyclooxygenase; (c) vascular obstruction by inadvertent intraarterial injection, particularly of lipophilic drugs.⁶ Sympathetic stimulation causing vasospasm is also believed by some. Clinically; patient complains of intense

burning pain at injection site followed by bluish to black discoloration of skin which gradually develops to variable degree of tissue necrosis and ulceration. Though diagnosis is clinical and based on history and evolution of lesion; ultrasound and magnetic resonance imaging may be used to assess the extent of tissue damage in certain cases. Necrotizing fasciitis, a rapidly spreading infection of the subcutaneous tissue and fascia with anaerobic organisms must be excluded as differential diagnosis. Other differential diagnoses are vasculitis and cutaneous cholesterol embolism. Management of NS depends on the extent of tissue damage. Surgical debridement, wound dressing, antibiotic and analgesic medication are the main therapeutic measures adopted for wound healing.¹ Skin grafting is required in large ulcer. In early stages of the condition vasodilators, hyperbaric oxygen and heparin therapy have been recommended by some authors.^{7- 8} It takes months for the ulcer to heal with a large depressed scar. Our patient developed the condition following intramuscular injection of Diclofenac sodium on 8th post operative day which she was taking earlier as postoperative pain management. Development of the condition was very typical of NS. After 20 days of wound dressing, we put secondary suture under local anesthesia. Sutures were removed after 10 days and the scar was healthy. This method of wound closure was also reported by Noaparast M et al.⁷ following primary treatment. Intra muscular injection of Diclofenac sodium is a very common medication in obstetrics and gynecology practice particularly for post operative pain management. Though NS is not completely avoidable the following precautions may be taken in prevention^{9, 10}:

- 1) Use of long needle for intra muscular injection. 2-3 inch needle for 90 kg patient and 1.25-1.45 inch needle for 45kg. Patient for the needle tip to reach the muscle.
- 2) Injection at the upper outer quadrant of the buttock to avoid vascular and nerve injury.
- 3) 3. Aspiration, prior to injection to avoid vessel injury or intravascular drug inoculation.
- 4) Not more than 5 ml of medication at a time in intramuscular injection.
- 5) Different sites are chosen for large amount of drug or multiple injections.

4. Conclusion

Nicolau syndrome, a rare iatrogenic pathology may be avoided to some extent with precaution. Knowledge of the pathogenesis and training of the health care personnel are important measures in the prevention of this condition. Avoiding cold therapy at the site of injection is the first step in restricting the extent of tissue damage. Secondary suturing of wound; wherever possible, may avoid the discomfort of months of wound dressing and unacceptable scar or contracture.

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