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Bupivacaine-induced Nicolau Syndrome during Spinal Anesthesia: A Rare Presentation of Two Cases

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Purpose: We present an embolia cutis medicamentosa (Nicolau syndrome) case in a patient who received a BUPIVACANE injection with spinal anesthesia.
Summary: A pregnant woman who received a Bupivacaine injection in the OT developed a necrotic lesion at the Bupivacaine injection site on her lower back. Her chief complaints were oligohydramnios, deranged LFT, hypothyroidism, and Doppler changes. After 10 days of wound care involving topical therapy, certain medications, and frequent follow-up appointments, the patient's wound was resolved.
Conclusion: Nicolau syndrome developed in the lower back side of a patient following a parenteral injection of BUPIVACANE. A proper injection technique is recommended to reduce the risk of this idiopathic adverse effect.

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Keywords: Nicolau syndrome; livedoid dermatitis; bupivacaine injection; embolia cutis medicamentosa.

1. INTRODUCTION

Nicolau syndrome (NS) is a rare cutaneous adverse drug reaction that occurs after some drugs are administered through systemic circulation. This reaction has also been labeled as embolia cutis medicamentosa [1]. Freudenthal published the first account of it in 1924, describing how a syphilitic patient who had been given improper intramuscular injections of bismuth salts as a syphilis treatment developed the lesion [2]. It is a rare condition characterized by skin necrosis with a livedoid pattern after injections of phenylbutazones, corticosteroids, local anesthetics, antibiotics [3], and vitamin K1 [4]. In general, in 90% of the affected patients, the onset of Nicolau syndrome was followed by excruciating pain that occurred during injection, followed within a few hours by livedoid discoloration and ulceration seen on the site of injection. In approximately 55% of the cases, necrosis is seen in the afflicted area after a few days, necessitating debridement [5]. The precise pathophysiology is idiopathic [6]. A vascular origin is the most logical theory. The main processes include acute vasospasm, artery inflammation, and thromboembolic blockage of the arteriole [7]. According to the evidence, cytotoxic medication injections can also cause ischemic necrosis and perivascular inflammation. A lipophilic medication may enter the arteries and obstruct them, causing a fat embolism. In several studies on the Nicolau syndrome, sweat gland necrosis has also been noted [5]. Serious instances could progress quickly clinically and result in death [8]. Herein, we report two cases associated with spinal anesthesia with Bupivacaine.

2. CASE REPORT

2.1 Case -1

A 30-year-old patient with a 38+3-week POG (period of gestation) presented to the gynaecology department with the chief complaint of oligohydramnios, deranged LFT, hypothyroidism, and Doppler changes. There was no prior history of abdominal pain, spotting, leakage of the PV (amniotic fluid), itching, or discharge of the PV. (Foetal motions are evident.) Due to inadequate amniotic fluid, she attempted to give birth prematurely three times. And she makes her fourth try at delivery on January 27, 2023, at 5 p.m. She has moved to the operating room (OT) for an urgent caesarean due to low amniotic fluid. BUPIVACAINE, a spinal anaesthetic, was administered to the patient through the spinal route at the time of delivery (the dose of the spinal anaesthesia was 13 micrograms). She was given a prescription for treatment after delivery, including a corticosteroid, anthelmintics, NSAIDS, antibiotics, and misoprostol for healing. The patient experienced a terrible burning sensation on the backside two days after giving birth. The lesion turned into blisters in the days that followed, and finally, those blisters burst and turned black. It progressed to the buttocks and the lower half of the buttocks in 2 to 3 days. She has no known prior history of allergies or adverse drug reactions. Upon inspection, both buttocks had black eschar and extensive regions of necrosis covering the whole skin. The skin around the black eschar was erythematous, indurated, and in some spots showed pus discharge. The blanchable plaque was approximately 8 x 10 cm in size. She was then directed to the dermatology department, where she underwent an examination and was later given the Nicolau syndrome diagnosis.

Fig. 1. Black eschar and extensive regions of necrosis covering the whole skin

2.2 Case -2

A 27-year-old primigravida patient with a 37+7-week POG (period of gestation) presented to the gynaecology department with the chief complaint of lower abdominal pain radiating to the back and thighs, gradually increasing in intensity and frequency, and a history of fever three days prior. There was no history of asthma, TB, HTN, bleeding PV, burning micturition, discharge PV,

bleeding PV, or thyroid disorders. History of Alamin SN infusion six days prior, Duvadilan injection, and iron and calcium supplement consumption. At 7:10 AM, she attempts delivery on 17-2023 for the first time. She has moved to the C-section operating room. BUPIVACAINE a spinal anaesthetic, was administered to the patient through the spinal route at the time of delivery. She was given a prescription for the treatment after delivery, including antibiotics, NSAIDS, and some corticosteroids for healing. The patient experienced a lesion over the lower back and a burning sensation after one day of giving birth. The lesion turned into a solitary, well-defined, erythematous to hyperpigmented patch above the lower back measuring 3*8 cm with corrosion of approx *1 cm diameter. She was then directed to the dermatology department, where she underwent an examination and was later given the Nicolau syndrome diagnosis.

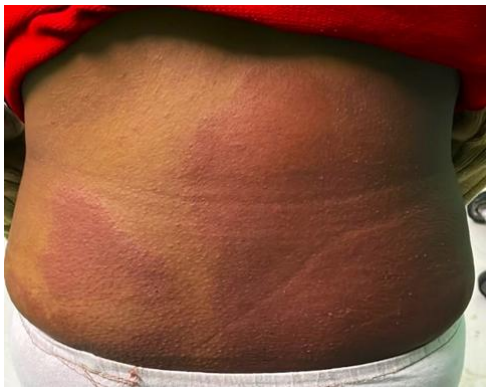

Fig. 2. Nicolau syndrome diagnosis

3. DISCUSSION

Although the exact pathogenesis of Nicolau syndrome is unclear, a theory of vascular origin is the most logical theory. In a few cases, the histologic analysis indicated reticular dermis vascular thrombosis without vasculitis and the destruction of the eccrine glands. There are other theories: An intra-arterial, peri-arterial, or peri-neural injection can first cause severe local pain and secondary vasospasm due to sympathetic nerve activation, which then causes ischemia with ensuing muscle and cutaneous necrosis. Second, accidentally injecting substances meant for intramuscular use into small cutaneous arteries could result in embolic blockage. This presumption is supported by the histologic evidence of bismuth in the afflicted skin areas' peripheral arteries in Nicolau's original instances. The third is perivascular or vascular [9,10].

In Nicolau Syndrome, the affected lesion is mostly confined to the site of injection, though in both cases presented to our hospital, there was a rapid spread of the skin lesion with involvement of an unusually large area, which included the spread to the contralateral part of the buttock and also the ipsilateral limb. The relatively favourable outcome experienced by our patients, with no residual scarring and no significant necrosis or deep ulceration at the lesion sites, implied that the major mechanism for the syndrome could not be arterial occlusion [11].

Nicolau syndrome has been linked to the injection of a variety of medications, including antibiotics (particularly sulphonamide, procaine penicillin, and benzathine penicillin), vaccines (varicella, diphtheria, tetanus, and pertussis), antihistaminic (like diphenhydramine), non-steroidal anti-inflammatory drugs (ketoprofen, diclofenac sodium, piroxicam), corticosteroids (triamcinolone), vitamin B_{12}, local anaesthetics, and sedatives [12]. In this case, the given drugs are showing concomitant effects in Nicolau syndrome. We have checked the potency of the following drugs from Medscape and Micromedex: In this case, the use of injection metron, tablet omnacortil, tablet wysolone, and tablet misoprostol is showing major suspense regarding Nicolau syndrome. But numerous accounts of comparable reactions following the injection of numerous other chemicals have shown that this phenomenon may not be connected to the drug given [13]. A review of the drugs associated with Nicolau syndrome has been reported in the literature. Nonsteroidal anti-inflammatory medications Diclofenac, piroxicam, ketoprofen, ibuprofen, and phenylbutazone are examples of medications. Antibiotics include penicillin derivatives, tetracycline, [10] sulphapyridine, streptomycin, and gentamicin. Dexamethasone, triamcinolone, paramethasone, cortivazol, and hydrocortisone are all corticosteroids. Antipsychotics and antiepileptic medications Chlorpromazine and Phenobarbital [14].

For the treatment of Nicolau syndrome, there is no specific therapy apart from prevention; parenteral injection of any drug that could be implicated should be done after aspiration of the syringe to ensure extra-vascular injection of the drug. Tissue damage is irreversible; though other modalities of treatment with favourable outcomes include plexus block, anticoagulant therapy (heparin), arteriotomy and extraction of the clot, and local care, use of vasoactive medications in

patients with Nicolau syndrome has shown a quick response to treatment with complete healing and no functional impairment or scarring at 4 weeks [10].

Further, the patient was treated with tablet wysolone, thrombophobe gel, cosvate cream, calasoft lotion, and fucidin ointment. The response was positive towards therapy but avoided the high dose of steroids. Entirely depending on the therapy is not the right way to prevent Nicolau syndrome. The major issue with Nicolau syndrome was the improper handling of parenteral injections, and the patient was given spinal anaesthesia (bupivacaine). Monitoring drugs should be the priority of the organisation because bupivacaine is a local anaesthetic drug. The site of administration of bupivacaine also influences Nicolau syndrome. The case report shows the toxicity of local anaesthetic drugs to Nicolau syndrome.

According to the prescription, BUPIVACAINE (local anaesthetic) was administered to both patients via the spinal route at a dose of 13 micrograms at a 0.5 percent heavy dose.

4. CONCLUSION

Nicolau syndrome is a rare condition that is probably underdiagnosed. It is erratic and has been linked to serious issues in the past [15]. Before injecting parenteral preparations, it is advised to aspirate, and if pain develops, the treatment should be stopped. There are currently no established standards for the management of this illness, nor is the precise etiopathogenesis of this condition recognised. The spinal anaesthesia, which was given at a dose of 13 micrograms, caused the patient to develop a significant skin problem.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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