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Case Report

Nicolau Syndrome Due to Benzathine Penicillin Injection: (A Case Report)

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1. Abstract

Nicolau syndrome (NS) is a rare complication of intramuscular injections, which is manifested by pain, edema, and livedoid discoloration of the skin immediately after injection. The exact pathophysiology of it is unknown, but some studies have given the causes such as embolic vessel occlusion, sympathetic nerve stimulation, inflammation, or physical trauma. Here, we present a case of NS following penicillin Injection.

2. Introduction

Nearly 12 billion injections are performed by health care workers annually [1]. Intramuscular injections are the technique of choice for drug delivery in many cases in order to achieve an effective, quick response. The well-known and most severe complication of this procedure would be traumatic nerve injuries; however, a local collection and/or tissue necrosis may also appear at the injection site [2-6].

Nicolau syndrome (livedoid dermatitis, embolia cutis medicamentosa) is a rare complication of intramuscular injection. There is usually pain at the injection site, along with erythema, discoloration, abscess formation, and or local ischemic necrosis involving the skin and fatty tissue. The pathogenesis has not yet been clearly understood, but is thought to involve direct vascular injury, perivascular inflammatory infiltration, or vascular constriction following the injection [2-6].

The injectable drugs most commonly causing skin necrosis include phenylbutazone, local anesthetics, antihistamines, anti-inflammatory agents, corticosteroids, and penicillins [6-15]. De Sousa and colleagues have also reported a case of Nicolau syndrome proceeding to death [13].

Here, we describe a 48-year-old male with a diagnosis of Nicolau syndrome (NS) after intramuscular benzathine penicillin injection.

3. Case Presentation

A 48-year- male was referred to the emergency room with complain of pain and skin lesions on the trunk and left lower limb in Alzahra hospital in Isfahan, Iran, in September 2019. The problem had begun 24 hours after he received an IM injection of benzathine penicillin (1200000 IU) to the left buttock, for signs of an upper respiratory infection. He stated that about half an hour after the injection, his left thigh and same buttock became pale and mottled, some swelling appeared a few hours later.

He was afebrile but agitated upon admission. The vital signs were stable. The left lower limb was tender so he could not bear the weight on the same side. On inspection there were mottled, dark purplish patches on buttock, gluteal region and upper part of left thigh. There were some bulla formation, intradermal hemorrhagic areas and skin necrosis on the above-mentioned patches (Figure 1 & 2). The review of other organs including, heart, lungs, abdomen, head and neck or other extremities were normal. The pulses of both lower limbs were symmetrical and normal on palpation. CBC, ESR, Aspartate aminotransferase (AST), alanine aminotransferase (ALT), Prothrombin time (PT), Partial Thromboplastin Time(PTT), Serum Creatinine(Cr), Blood Urea Nitrogen(BUN) creatinine phosphokinase kinase (CPK), lactate dehydrogenase and C-reactive protein levels were within normal ranges. Color Doppler ultrasonography of lower limb arteries and veins were normal. The diagnosis of NS is based on the clinical features. During hospitalization, the patient's general condition improved and the mottled purplish patches faded. For our patient, as NS does not need specific treatment merely supportive care was given. Oral corticosteroid (0.5 mg/kg/day prednisolone) along with analgesics were also administered. After a week the patient had been well discharged and the lesions healed nearly completely.

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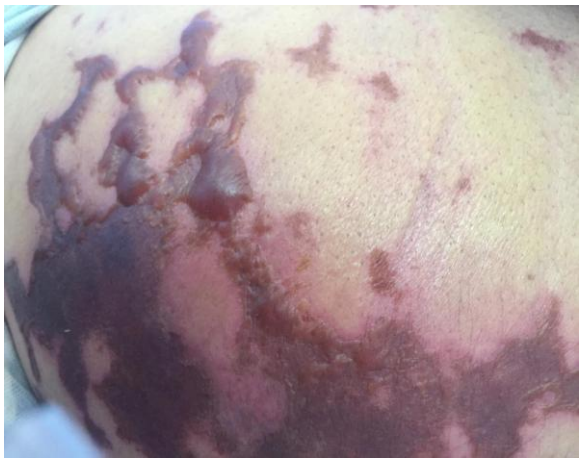

Figure 1: Close up view of left gluteal skin lesions, areas of hemorrhagic bullae superimposed on purplish livedoid patches

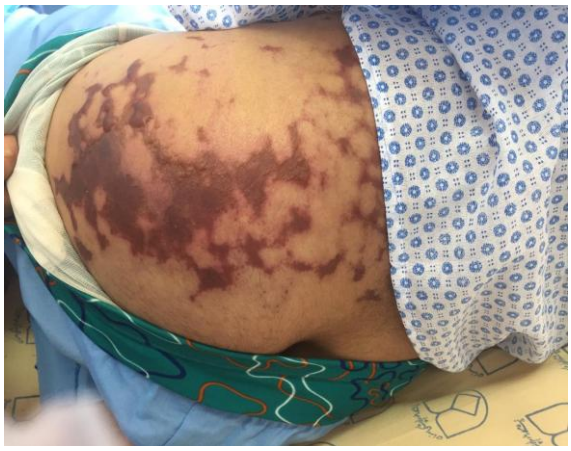

Figure 2: Distribution of tender, cool, mottled areas over left flank, buttock and upper thigh.

4. Discussion

Nicolau syndrome (also known as livedoid dermatitis) is a rare complication of intramuscular injection, which is manifested by pain, edema, and livedoid discoloration of the skin immediately after injection. It was first described in 1925 by Nicolau following intramuscular injection of bismuth salt, but it also has been reported after intramuscular or subcutaneous injection of numerous drugs [3].

Nicolau Syndrome has been reported with intramuscular injections of non-steroidal anti- inflammatory drugs (diclofenac, piroxicam, ketoprofen, ibuprofen, phenylbutazone), corticosteroids, antibiotics (penicillin derivatives, tetracycline, sulfapyridine, streptomycin, gentamicin), antipsychotics and anti-epileptics (phenobarbital, chlorpromazine), Vaccinations (diphtheria-tetanus-pertussis), antihistamines (diphenhydramine, hydroxyzine), local anesthetics (lidocaine), cyanocobalamin, interferon alpha , bismuth and vitamin K [18-19].

One theory explains, that NS happens when an intramuscular drug is injected into an artery and causes thrombosis and muscle and subcutaneous necrosis. However the pathogenesis of NS is unknown [11].

One important clinical element is the sudden onset with regard to the injection, often with no lesion at the injection site. The signs of NS are skin discoloration, intense pain, and inflammation. Necrosis usually follows hyperemia, hemorrhagic discoloration of skin, and livedoid dermatitis. Local vasospasm causes pallor. One-third of the patients may experience neurologic complications (usually transitional) which are most frequently hypoesthesia and paraplegia. NS has also been reported to cause compartment syndrome of the limb, hyperkalemia, renal failure, and death [13]. Paralysis of the lower limb can happen and can be explained by embolism in the vessels of gluteal muscle which can reach the internal iliac artery, then vertebral canal through retrograde flow. This arterial stenosis can result in peripheral neve disturbance and lower limb paralysis [20].

There is no specific treatment for NS. Treatments proposed range from local supportive care to extensive surgical debridement. Alyasin et al. reported a 7-year-old boy with NS treated with intravenous immunoglobulin (IVIG) (2 g/kg) and Pentoxyphilline. The reported patient was heparinized and after 12 days, he was discharged in an acceptable condition. Yildiz et al. utilized hyperbaric oxygen in the late stage of NS in a 3-year-old boy to prevent the progression of necrosis thus, restricting the level of amputation. An important note would be the aggravating role for application of a cold compress [21].

For preventing adverse reactions, health care providers should be informed of proper method of intramuscular injection such as Z-track method of injection, aspiration before injection, stopping the injection immediately if the patient experiences excruciating sudden pain on injection site. The needle must be long enough to reach the muscle. When multiple injections have to be given, different sites should be chosen [22].

Fortunately we have not observed any terrible complications such as electrolyte imbalance, organ failure, need to limb amputation, or disfiguring cutaneous scarring in our patient and as mentioned he has been recovered by supportive and nonspecific treatment measures in quite short period of time.

Eventually, we emphasize the importance of considering NS in differential diagnosis of any patient whose skin at the site of injection had been complicated by signs of tissue necrosis. The prompt diagnosis of this syndrome and urgent supportive care could preserve the affected limb.

References

1. World Health Organization. Safety of injections: a brief background. Fact sheet no. 231. Geneva: WHO; 1999.
2. Woo E, Chan YW, Kwong YL, Yu YL, Huang CY. A dangerous gluteal injection. J Hong Kong Medical Association. 1986; 38: 75-6.
3. Faucher L, Marcoux D. What syndrome is this? Nicolau syndrome. Pediatr Dermatol. 1995; 12: 187-90.
4. Kohler LD, Schwedler S, Worret WI. Embolia cutis medicamentosa. Int J Dermatol. 1997; 36: 197.
5. Greenblatt D, Divoll-Allen M. Intramuscular injection-site complications. JAMA. 1978; 239: 542-4.
6. Muller-Vahl H. Adverse reaction after intramuscular injections. Lancet. 1983; 1: 1050.
7. Dadaci M, Altuntas Z, Ince B, Bilgen F, Tufekci O, Poyraz N. Nicolau Syndrome after intramuscular injection of non-steroidal anti-inflammatory drugs (NSAID). Bosn J Basic Med Sci. 2015; 15: 57-60.
8. Greenblatt D, Divoll-Allen M. Intramuscular injection-site complications. JAMA. 1978; 239: 542-4.
9. Muller-Vahl H. Adverse reaction after intramuscular injections. Lancet. 1983; 1: 1050.
10. Lie C, Leung F, Chow SP. Nicolau syndrome following intramuscular diclofenac administration: a case report. J Orthop Surg. 2006; 14: 104-7.
11. Mayrink M, Mendonça AC, da Costa PR. Soft-tissue sarcoma arising from a tissue necrosis caused by an intramuscular injection of diclofenac. Plast Reconstr Surg. 2003; 112: 1970-1.
12. Lee DP, Bae GY, Lee MW, Choi JH, Moon KC, Koh JK. Nicolau syndrome caused by Piroxicam. Int J Dermatol. 2005; 44: 1069-70.
13. McGee AM, Davison PM. Skin necrosis following injection of non-steroidal antiinflammatory drug. Br J Anaesth. 2002; 88: 139-40.
14. De Sousa R, Dang A, Rataboli PV. Nicolau syndrome following intramuscular benzathine penicilin. J Postgrad Med. 2008; 54: 332-4.
15. Hay J. Complications at site of injection of depot neuroleptics. BMJ. 1995; 311: 421.
16. Nagore E, Torrelo A, Gonzalez-Mediero I, Zambrano A. Livedoid skin necrosis (Nicolau syndrome) due to triple vaccine (DTP) injection. Br J Dermatol. 1997; 137: 1030-1.
17. Noaparast M, Mirsharifi R, Elyasinia F, Parsaei R, Kondori H, Farifteh S. Nicolau Syndrome after Intramuscular Benzathine Penicillin Injection. Iran J Med Sci. 2014; 39: 577-9.
18. Okan G, Canter HI. Nicolau syndrome and perforator vessels: a new viewpoint for an old problem. Cutan Ocul Toxicol. 2010; 29: 70-2.
19. Enshaei A, Afshar A. Compartment Syndrome of the Calf Due to Nicolau Syndrome. Arch Bone Jt Surg. 2016; 4: 87-9.
20. Senel E. Nicolau Syndrome: A Review of the Literature. Clinical Medicine Insight: Dermatology. 2010; 3: 1-4.
21. Memarian S, Gharagozlou G, Alimadadi, Ahmadinejad Z, Ziaee V. Nicolau Syndrome due to Penicillin Injection: A Report of 3 Cases without Long-Term Complication. Case Rep Infect Dis. 2016; 908: 2158.
22. Karimi, Owlia MB. Nicolau Syndrome Following Intramuscular Penicillin Injection. Journal of the College of Physicians and Surgeons Pakistan. 2012; 22: 1.