Freestyle Perforator-Based Fasciocutaneous Flap Reconstruction in Nicolau Syndrome-Related Tissue Necrosis

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Abstract The actual pathology of the Nicolau syndrome (NS) is still unknown. It is thought to involve direct vascular damage and vasospasm. Many NS cases were reported in the literature but a treatment protocol is still not established. However, after demarcation of the necrotic tissue, surgical intervention is mandatory. Five NS cases with extensive tissue necrosis on the upper lateral gluteal region were analyzed retrospectively. Operative technique was described in details for freestyle perforator-based fasciocutaneous flaps from the gluteal region to reconstruct defects of NS-related tissue necrosis. Freestyle perforator-based fasciocutaneous flaps were used for defect closure in all patients. All flaps survived totally. No complications occurred during the follow-up period. Although rare, NS is a serious complication of inadvertent intramuscular injections. Prevention is the best treatment. However, in case of large-tissue necrosis, freestyle perforator-based fasciocutaneous flaps harvested from the gluteal region is a satisfactory option for reconstruction.

Keywords Nicolau syndrome · Inadvertent drug injection · Freestyle perforator-based fasciocutaneous flap · V-Y flaps

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Introduction

Intramuscular administration of various drugs is a safe method that is widely used in clinical practice. However, inappropriate injections of drugs (i.e., inadvertent subcutaneous or intra-arterial injections) may cause locoregional tissue damage which is known as Nicolau syndrome (NS), synonymously livedo-like dermatitis or embolia cutis medicamentosa [1]. The actual physiopathology of the NS is yet unknown; it has been proposed that the direct arterial damage and vasoconstrictive effects of various drugs may induce inflammation and subsequently cause skin necrosis [2, 3]. Agents, such as nonsteroidal anti-inflammatory drugs, steroids, vitamins, benzathine penicillin, hydroxyzine, vaccines i.e., are reported to be potential triggering factors of this clinical entity [2, 4–13]. There is no consensus on the treatment protocol of the disease. If it is diagnosed during early onset, treatment may be conservative [3]. However, if skin necrosis occurs; surgical intervention including debridement and reconstruction is mandatory [1]. Although clinical features of NS have been reported in many case reports, NS-related skin defects are often underestimated and are not studied in detail. Proposed reconstruction methods in the literature are skin grafts or random fasciocutaneous flaps which usually result in unsightly and depressed scars. In the present article, we reported five cases of skin defects due to NS-related necrosis in the upper outer gluteal region, which were treated with freestyle perforator-based V-Y flaps immediately after debridement.

Material and Methods

From April 2008 to November 2011, five patients with diagnosis of NS who were treated with freestyle perforator-based V-Y flaps were analyzed retrospectively. The patients were diagnosed with NS on the basis of medical history of locoregional skin changes in the upper outer gluteal regions

and subsequent necrosis shortly after gluteal injections. Verbal and written consents for both treatment and scientific presentations were taken from all patients or their relatives. The patients' demographic data, location and size of defects, underlying diseases, drugs responsible for the pathology, and treatment methods were recorded. Surgical technique for free-style perforator-based fasciocutaneous flaps from the gluteal region was described in details [14]. The data of the patients were summarized in Table 1.

Surgical Technique for Freestyle Perforator-Based Fasciocutaneous Flap Harvest

Patients underwent surgery under general anesthesia and in prone position. After adequate debridement of the necrotic gluteal soft tissue and being certain that the necrosis were confined within the subcutaneous fat tissue without an extension to the muscle, an appropriate area adjacent to the tissue defect was selected (Fig. 1a). With handheld Doppler, reliable and well-pulsating perforators are mapped within the area of interest followed by marking the flap sign in a V-Y fashion, designed vertically or horizontally according to the long axis of the wound (Fig. 1b). The flap was raised including the gluteal muscle fascia and the dissection proceeded until the chosen perforator was encountered. The flap was islanded on the perforator, leaving an amount of soft tissue around the pedicle to prevent kinking and twisting (Fig. 1c). It was not necessary to trace the perforator vessel to the source artery because the sufficient flap mobility was obtained. Then, the tension-free flap was adapted to the defect and the donor site was closed without tension (Fig. 1d).

Results

All patients except one were female. The mean age of the patients was 74 (ranged between 69 and 79). All patients were

mobile at the time of surgery. Patients received intramuscular injections for pain control due to sacroiliitis in one patient and chronic osteoarthritis in the others. All patients experienced intense burning pain and erythematous, ecchymotic to purpuric patches which developed into necrotic lesions in about a week. None of the patients noticed systemic manifestations. All patients were referred to the department of plastic surgery after demarcation of necrosis. The etiological agent of NS was diclofenac in three cases; however, the administered drugs were unknown in the other two patients. Three wounds were localized on the left, where two on the right gluteal region. No clinical infection was seen in all wounds. Patients were treated with immediate debridement and flap reconstruction. Freestyle perforator-based fasciocutaneous flaps were used for defect closure in all patients as described. Patients were followed 6 months postoperatively. No complications such as hematoma, infection, or wound dehiscence occurred during the follow-up period. All wounds healed uneventfully.

Discussion

In the present study, we showed that replacing a damaged perforator site with a freestyle perforator-based flap harvested from an adjacent region is beneficial in the management of large defects after debridement in NS.

Recently, it has been demonstrated that vascular events in NS are correlated with angiosome-perforator vessels concept [7, 15]. This explains the ischemic skin changes and further necrosis in NS with damaged vascular sites which are supplied by affected vessels. Marangi et al. showed this macroscopically by dissecting the necrotic area on a thrombotic vessel [16]. This viewpoint was also supported by sonographic findings of Park et al. and mirror Doppler mapping of nonaffected cutaneous territories by Uri and Arad in NS cases [7, 17]. Focal thrombosis in associated vessels was also observed in

Table 1 Summary of the patients' data

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age	69	78	79	75	73
Gender	Male	Female	Female	Female	Female
Underlying disease	Sacroiliitis, DM	COA	COA, DM	COA	COA
Associated drug	Diclofenac	Diclofenac	Diclofenac	Unknown	Unknown
Localisation	Left superolateral gluteal region	Left superolateral gluteal region	Right superolateral gluteal region	Left superolateral gluteal region	Left superolateral gluteal region
	<i>Mezun</i>				
Defect size (length × width)	10×13 cm	12×7 cm	13×9 cm	7×8 cm	5×7 cm
Adjuvant interventions	Debridement	Abcess drainage, Debridement	Debridement	Debridement	Debridement

COA chronic osteoarthritis, DM diabetes mellitus

Fig. 1 Operative sequences of freestyle local perforator flap. Obtaining the actual defect size after debridement, perforator location, and flap planning (a). Incising outer lines of the flap (b). Harvesting flap based on a perforator without dissecting the source artery (c). Advancing the flap in V-Y fashion and direct closure of the donor site (d)

histological sections [4]. These findings support that the theory of end artery damage induced by inadvertent drug injection plays a role in the pathogenesis of NS [7]. This so-called perforosome concept gave us the inspiration of replacing a damaged perforator site with a perforator-based flap harvested from an adjacent region [15].

Diclofenac is one of the most commonly reported nonsteroidal anti-inflammatory drugs to cause NS [2, 5, 7, 18–20]. Vasoconstructive effect of diclofenac is attributed to reduction of prostaglandin synthesis via cyclooxygenase inhibition in NS pathogenesis [21]. In three of our five patients, the etiological agent was also diclofenac. However, this adverse reaction should not be associated with a specific drug; it depends mostly on the inadvertent subcutaneous administration.

No clinical guidelines have been established for the conservative treatment of acute NS before demarcation of the necrotic area appears. Rapid administration of steroids, anticoagulants, and vasoactive agents has been emphasized for clinical improvement and regression of the livedoid lesions whereas it has been demonstrated that heparin and pentoxifylline are useless in preventing the development of necrosis [1, 3, 10, 22]. Hyperbaric oxygen treatment may be beneficial at the early onset of disease [10]. If NS is regarded as an unintended intra-arterial injection injury and recognized at early stages, treatment guidelines preceded by Sen et al. from the Mayo Clinic may be beneficial [23]. Even if it is controversial, cold application which contributes to skin necrosis by aggravating the effect of vasospasm should also be avoided [21, 24]. Sometimes, skin lesions of NS may regress without intervention. Charesse et al. mentioned about five cases, in three of them, lesions resolved spontaneously and two of them expressed no skin changes [8]. In brief, there are no generally accepted therapeutic rules for acute NS. Do's or don'ts are still controversial.

At the end of the acute phase of NS when necrosis have demarcated, no alternative to debridement and reconstruction is available. Many reconstructive options have been proposed to cover the defects when the necrotic tissues were removed. Best aesthetic results are almost always obtained by primary closure. However, this may not be suitable for large defects. Some reporters leave the tissue to secondary healing, which always takes several months and results in atrophic scars and hyperpigmentation; while the others use skin grafting which causes unsatisfactory depressed scars [1, 2, 6, 18]. For large gluteal defects, flaps are probably the best reconstructive option which enables the wounds to heal faster without depression by decreasing the tension on the wound edges. Especially freestyle perforator-based fasciocutaneous flaps which include refined techniques of flap surgery take the advantage of less donor site morbidity [14]. Previously, gluteal perforator-based flaps were used to cover pressure sores on the gluteal region, to increase flap mobility for better aesthetic shape without tissue foldings and dog ears [25–28]. In the present study, the gluteal flaps were harvested based on one perforator in a V-Y fashion for closure of the gluteal upper quadrant defects caused by NS for the first time. The flaps were described as freestyle because flap selection was based solely on the detection of an audible Doppler signal [14]. The flaps were sufficiently mobile on their pedicles. Recipient and donor sites were closed primarily without tension. Thus, the advantage of perforator-based flaps and V-Y flaps were combined as stated by Yildirim et al. [27]. In the presence of various vascular sources (inferior and superior gluteal, pudental, lumbal, and lateral sacral arteries) freestyle local perforator-based flaps can be planned anywhere on the gluteal region, where Doppler signals of a sizable perforator vessel are determined [28].

Still, the best treatment remains to be prevention. Using longer needles for drug delivery or stretching the skin to decrease fatty tissue thickness and inserting the needle at 90 ° angle, choosing different injection sites in case of repeated administrations, aspiration before injection, may be advised for prevention of local complications such as NS, granuloma formation, or abscesses [2, 6, 29]. Besides Z-track method for intramuscular injection, a maneuver of skin stretching, which enables the drugs diluted in the subcutaneous levels should be adopted to apply routinely by nursing staff [2]. It can minimize cumulative irritation by blocking the needle track after injection.

Conclusion

NS is a rare adverse reaction including ischemic necrosis of skin and deeper tissues which occurs after inadvertent parenteral drug administrations. The etiopathogenesis is not well understood, thus standard guidelines for its management is not established. However, debridement and reconstructive surgery play a role after demarcation of necrosis. In the present article, the versatility of freestyle perforator-based local flaps from gluteal region is reported in the management of defects after debridement in NS. If a suitable perforator vessel is not found for flap harvest, other flap options can be reserved as plan B.

Conflict of Interest Emre A. Kocman, Fatih N. Yaşar, Aydan A. Kose, Yakup Cil, Yakup Karabagli, and Cengiz Çetin declare that they have no conflict of interest.

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