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Date: Sunday, June 27, 2021 at 03:59 PM GMT+7

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Article Revision Letter for Authors - (APIC-2021-06-087)

From: Anaesthesia, Pain and Intensive Care (noreply@ejmanager.com)

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Date: Thursday, July 29, 2021 at 08:45 PM GMT+7

Dear Hanik Badriyah Hidayati,

Your manuscript entitled \"Hypopigmentation and Subcutaneous Fat Atrophy Associated with Corticosteroid Injection: A Case Report\" (Ms.Nr. APIC-2021-06-087) was reviewed by editorial board members of the Anaesthesia, Pain and Intensive Care. As initial decision, your manuscript was found interesting but some revisions have to be made before it can reach a publishable value.
Please answer all the comments below point-by-point in an accompanying response letter to your revised submission.

You should send your revised manuscript via the online system of eJManager on http://my.ejmanager.com.

Sincerely yours,

Romana S, Durrani,
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COMMENTS for Authors:

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I will have two suggestions for the authors:
-The manuscript should be revised linguistically and grammatically .
-The references should be organised according to journal rules.
Thank you.

=> Reviewer # 2

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Hypopigmentation and Subcutaneous Fat Atrophy Associated with Corticosteroid Injection: A Case Report

Abstract

Corticosteroid injection has been shown to be an effective treatment modality in musculoskeletal and rheumatological conditions. Yet, the potential adverse effects of corticosteroid injection have not been given much attention. One of the potential dermal adverse effects which should be considered by clinicians is hypopigmentation and subcutaneous fat atrophy.Although it is a rare side effect, it may cause a cosmetically unpleasant effect. The aim of this case report is to highlight the importance of providing adequate information to patients regarding these dermal adverse effects of corticosteroid injection. We report the case of 31-year-old female who suffered skin hypopigmentation and subcutaneous fat atrophy after triamcinolone injection given for de Quervain's tenosynovitis.

Keywords: de Quervain's tenosynovitis, subcutaneous fat atrophy, hypopigmentation, corticosteroid injections, adverse effects, pain, psychological well-being

Introduction

De Quervain's tenosynovitis is the most common overuse injury of the wrist resulting from repetitive microtrauma and shearing of the first dorsal compartment tendons.[1] The condition was first described by de Quervain, a Swiss surgeon in 1895.[2]The prevalence of De Quervain's tenosynovitis is reported 1.3% and 0.5% in women and men respectively.[3]Initially, it is managed conservatively with oral nonsteroidal anti-inflammatory drugs (NSAIDs), immobilization, diathermy, splinting, massage, and corticosteroid injection. Operative treatment is reserved for cases in which conservative therapy has failed. Corticosteroid injection is more favorable than other nonoperative treatments and has the highest treatment success rate compared with oral NSAID, splinting, or combination therapy.[4,5]A variety of corticosteroid formulations has the treatment success rate of 62% to 93%.[6]

Pain isa common symptomof de Quervain's tenosynovitis.[7] Pain isdefined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[8,9,10]The aim of pain management is improving the quality of life by relieving pain and help patients to gain proper functioning.[11]Unrelieved and long standing pain may substantially affects psychological well-being.[12] Corticosteroid injections are frequently administered to treat pain associated with rheumatic and musculoskeletal disorders. Corticosteroid injection has been registered as local treatment of varying conditions, such as rheumatoid arthritis, tendinopathy, bursitis, synovitis, epicondylitis, ganglion condition, neuromas, fasciitis, back pain, and entrapment syndrome.[13] Various locations of local corticosteroid injections include tendon sheath, bursal, enthesis, intraarticular, soft tissue, and epidural.[14]In spite of its common use in practice, the adverse effects associated with

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corticosteroid injection is not adequately appreciated. Wereport a case of hypopigmentation and subcutaneous fat atrophy associated with corticosteroid.

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Case Report

A 31-year-old right-handed Asian female, presented with 2 weeks history of pain in her right wrist. The pain travelled up her forearm and was substantially aggravated with movement. She reported a Numeric Rating Scale (NRS) of about 5–7 (on an 11-point scale). There was no history of prior trauma. Her past medical history was noncontributory. On examination, there were swelling and tenderness on the lateral aspect of her right hand. The Finkelstein test result was positive. Therefore, a clinical diagnosis of de Quervain's tenosynovitis was made. She was initially treated conservatively with nonsteroidal anti-inflammatory drugs (NSAIDs). After 10 days of this treatment without significant improvement, she subsequently had a single local corticosteroid injection. She received a mixture of 1 mL triamcinolone acetonide 10 mg/mL and 1 mL of 1% lidocaine hydrochloride. Injection was performed using 26 G needle, advanced at an angle of 45° angle toward the peritendinous sheath of the first dorsal compartment. The procedure was uneventful. She was also placed in a thumb spica orthosis. No infection was noted after the injection. Post-injection NRS was 3–4 and the pain resolved completely after 3 weeks. A month following the injection, she noticed a depressed, hypopigmented area around the needle insertion site on her brown-toned skin. The lesion measured 1 x 1.6 cm. Neither motor nor sensory impairment was present on her follow up examination. One and a half years later, her hypopigmented skin and subcutaneous fat atrophy resolved gradually without any specific treatment.

Discussion

Corticosteroid injection is a well established treatment modality in alleviating symptoms of de Quervain's tenosynovitis.[15] It is also increasingly used for other musculoskeletal and rheumatic conditions.[13]Yet, the adverse effects of corticosteroid injections have not been given much attention. Direct corticosteroid injections injections to the lesion site may avoid many of the potential adverse effects associated with corticosteroid systemic administration, such as suppression of hypothalamus-pituitary-adrenal axis, endocrine changes, and growth inhibition.[16] Possible major adverse effects of local corticosteroid injections ranged from minor to major manifestation. Major adverse effects include tendon ruptures, necrotizing fasciitis, severe subcutaneous fat atrophy, osteomyelitis, and skin hypo pigmentation. Minor adverse effects that could occur include disturbance in menstruation, steroid flare, milder soft tissue alteration, and skin rash.[17]

Frequently used corticosteroids are methylprednisolone, triamcinolone, dexamethasone, and betamethasone. Each preparation differs in potency, cost, corticosteroid related reactions, and duration of action.[14] The solubility of a preparation has an inverse relationship with the duration of action. The more soluble a preparation, the shorter the duration of action the preparation has, because it is absorbed from the joint faster. [17]Triamcinolone acetonide is one of corticosteroidsapproved by Food and Drugs Administration (FDA) for injection.[18]Triamcinolone acetonide is the least soluble steroid; hence it has a longer duration of action.[17] This long lasting duration of action is the reason why the majority of clinicians prefer this compound.[19] However, less soluble steroids may have more deleterious effects on adjacent soft tissues.[14,17] The size of the affected area and the length of time of such dermal adverse effects are possibly influenced by the concentration and solubility of the corticosteroid preparation.[20]

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The incidence of skin hypopigmentation is reported ranging from 1.3–4%, whereas subcutaneous fat atrophy is found ranging from 1,5%–40% in 5 studies.[13] Although the

incidence of hypopigmentation associated with corticosteroid injection was considered to be low, it could be bothersome for patients once it happens. Moreover, a recent review by Pace et al found that the incidence of soft tissue adverse effect associated with corticosteroid injection in the management of de Quervain's tenosynovitis and tennis elbow is reportedly as high as 31% and up to 40%, respectively. Patients with darker skin tone have a greater risk of developing a noticeable hypopigmentation.[17,21,22]

According to other case reports, hypopigmentation may develop 1–4 months later, following single or multiple injection.[23,24] This is similar to our experience. Our patient developed skin hypopigmentation and subcutaneous fat atrophy 3 months after a single injection with triamcinolone acetonide and resolved spontaneously within one and a half years. However, late manifestation of up to 10 months has also been reported. It then resolves after 6–30 months in the majority of cases. A few cases may be irreversible.[17,23] There is no specific treatment for hypopigmentation.[23]Application of vitamin E paste and exposure of narrow ultraviolet rays for half a year was used to treat hypopigmentation in the study by Gu et al. However, this treatment yielded a slow regression (82.50%) or consistent result (17.50%)in a year of follow up duration.[25]Fat grafting, serial normal saline infiltration, and temporal fascial implantation are a few of the treatment options that may be considered with regard to refractory subcutaneous fat atrophy.[23]

Subcutaneous fat atrophy and skin hypopigmentation associated with triamcinolone injection have been reported to affect several injection sites, depending on the location of the injection. Dhawan et al reported such dermal adverse effect after intralesional injection in 2 patients for ganglion over the wrist and a patient for lichen planus on the foot.[24]Salvatierra et al described such a lesion after triamcinolone injection for tennis elbow.[19] Another author reported atrophic and hypopigmented lesion in the postauricular region following multiple intralesional triamcinolone acetonide for the treatment of a keloid on the left ear.[26] Another

report of such a lesion was observed after intralesional injection on the eyelid of a 2-year-old girl with chalazion.[27]

The pathophysiology of subcutaneous fat atrophy and skin hypopigmentation associated with corticosteroid injection has not been clearly elucidated. A histopathological study by Gu et al revealed that the number of melanocytes was not affected in corticosteroid-induced hypopigmentation. However, their function was impaired. This might be caused by inhibition of prostaglandin or cytokine production in epidermal cells and suppression of secretorymetabolic product from melanocytes.[16,25] Concerning subcutaneous fat atrophy, it has been suggested that corticosteroid has antiproliferative effects on keratinocytes and fibroblasts. It is also known that corticosteroid alters the metabolism of extracellular matrix proteins and the synthesis of lipids in the skin.[28] The adipocytes were reduced in number and size, and in some cases, lipophages, which are macrophages engulfing adipose tissue appeared.[29]

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There are some precautions that can minimize the risk of subcutaneous fat atrophy and skin hypopigmentation. The needle should be changed after drawing up the corticosteroid preparation, and subsequently local anesthetic is used to dilute it.[30] Moreover, applying pressure using a sterile dressing at the injection site while the needle is withdrawn could avoid leakage of corticosteroid preparation into the subcutaneous tissue.[21] Superficially injecting corticosteroid may also cause leakage along the needle track and subsequently put the injection site at risk.[14]

The type of injected corticosteroid also may contribute to the risk of developing subcutaneous fat atrophy and skin hypopigmentation. Compared to methylprednisolone, the risk of dermal changes is higher with triamcinolone injection because of its increased crystal size. Accordingly, triamcinolone acetonide is preferably injected into deep soft tissue targets or large joints.[14]Injecting triamcinolone 40 mg/mL carries a substantially higher risk

compared with 10 mg/mL.[25]Dexamethasone and soluble betamethasone can be considered as a more appropriate option when subcutaneous fat atrophy and skin hypopigmentation are issues of concern.[17]

Ultrasonography guidance is commonly used in musculoskeletal pain management.[31]However, Milani et al reported a case of skin hypopigmentation and atrophy following ultrasonography-guided triamcinolone injection for de Quervain's tenosynovitis which may suggest these dermal adverse effects could still occur even under imaging modality for guidance.[28] This finding is corroborated by a prospective study conducted by Shin YH et al which compared ultrasonography-guided and blind triamcinolone injection for de Quervain's tenosynovitis and demonstrated that both groups were not significantly different in the incidence of subcutaneous fat atrophy or skin hypopigmentation.[32] In fact, even when all preventive measures have been taken, adverse effects may still emerge.

Conclusion

This report represents subcutaneous fat atrophy and skin hypopigmentation as an uncommon dermal adverse effect that may occur following corticosteroid injection. It is prudent to initially provide patients with adequate information about these dermal adverse effects before performing the procedure, particularly in dark skinned patient. Although it may resolve spontaneously without any specific treatment, it should not be belittled. Some patients may find it bothersome and may lose confidence due to its cosmetically unpleasant effect. Ultimately, clinicians should promptly recognize skin hypopigmentation and subcutaneous fat atrophy as adverse effects associated with corticosteroid injection.

Conflict Of Interest

The authors have no conflict of interest to disclose

Acknowledgement

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Figure Legends

Figure 1. Skin hypopigmentation and subcutaneous fat atrophy associated with corticosteroid injection around the injection site.

Figure 2. Resolved skin hypopigmentation and subcutaneous fat atrophy one and a half years later

October 10, 2021

Dear Fata Prihatsari, Hanik Badriyah Hidayati, Damayanti Damayanti, Trianggoro Budisulistyo

I am pleased to inform you that your manuscript titled as "Hypopigmentation and Subcutaneous Fat Atrophy Associated with Corticosteroid Injection: A Case Report" (Manuscript Number: APIC-2021-06-087 was accepted for publication in the Anaesthesia, Pain & Intensive Care. You could check your possible publication date at your author page.

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I would like to remind that you could send your future manuscripts to Anaesthesia, Pain & Intensive Care.

My best wishes and kind regards to your family and friends,
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