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Short Running Title: Cushingoid facies from one time Intra-articular joint Kenalog Injection
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ABSTRACT

Introduction
Kenalog (triamcinolone acetonide) corticosteroid injection is a standard procedure for approaching intra-articular joint pain due to mild and severe debilitation and degeneration. A focal intra-articular steroid injection effect is mostly localized in the capsular space. Given the slow absorbance of corticosteroid injection in intra-articular area into the intravascular system, systemic effects are usually not manifested.

Case report
We report a case of secondary cushingoid features after a one time intra-articular injection of Kenalog (triamcinolone acetonide) preparation in an HIV patient. The patient’s HIV medication included a protease Inhibitor, which can inhibit the metabolism of the corticosteroid and may contribute to a cushingoid presentation.

Conclusion
Intra-articular corticosteroid injection is not a benign procedure and may lead to extra-articular dysregulation of other organ systems.

Keywords: Kenalog, corticosteroid, intra-articular injection, cushingoid facies
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INTRODUCTION
There are various modalities for the treatment of chronic joint pain; however, intra-articular steroid injection is accepted as a standard treatment. It is considered as the best conservative treatment of lateral epicondylitis by Tonks et al [1]. Corticosteroid reduces the inflammation and the level of degeneration in the cartilage and the soft tissue that surround the joint space when used in appropriate doses for a limited period of time. Studies have shown that the release of cytokines and other inflammatory substance that destroy the soft tissues of the joint are modulated by steroids [2, 4, 9]. There is a significant decrease in inflammatory cytokines after corticosteroid injection [3]. Steroid injection in the extra-articular and vascular system can cause multiple side effects on different organ systems including the integumentary, nervous, endocrine and cardiovascular systems among others [4, 5]. Some of the typical physical manifestations from the systemic administration of steroids include moon facies, weight gain, elevated blood glucose, menstrual dysregulation and buffalo hump. However, there are reported cases of reported extra-articular manifestation of intra-articular steroid injections due to the absorption of the steroid into the central circulation system [5, 8, 10]. We report in this paper, cushingoid manifestations and the suppression of the HPA axis after a one-time intra-articular steroid injection.

CASE REPORT
A 60 year old male with diagnosis of HIV presented to the HIV clinic for a routine follow up visit. He reported persistent right shoulder pain and was referred to PMR clinic for better pain control. Diagnostic imaging revealed mild degenerative change of the right acromioclavicular and glenohumeral joints. One time dose of Kenalog (triamcinolone acetonide) 40mg steroid preparation was injected into the right subacromial space. The injection was prepared with Kenalog (triamcinolone acetonide) 1cc and 2 cc each of lidocaine and bupivicaine. The patient reported back to the HIV clinic 44 days after his initial IACI with complaints of facial swelling for three to four weeks after Kenalog (triamcinolone acetonide) injection. He also
reported mild tremors, cramping and stiffness in his hands. On his 2 weeks follow up
visit to the HIV clinic he reported facial and chin swelling, neck hump and new onset
of bilateral hand tremors. He noted an increase in shirt neck size from 16 cm to 17.5
cm two weeks after the injection. Table 1 illustrates serum cortisol and DHEAS of the
patient 2 weeks after the Kenalog (triamcinolone acetonide) injection were 2 mcg/dl
(0-25 mcg/dl) and 48 mcg/dl (10-619 mcg/dl) respectively. Of note, the patient was
on HIV medications, which are noted to cause lipodystrophy. However, the patient
had been taking these medications for several years and he denied any moon facies,
buffalo neck hump or increased neck girth in the past. The patient reported that the
facial swelling and neck puffiness were resolving on the follow up visit two months
after his inatra-articular corticosteroid injection (IACI). Cotrosyn test was done on
July 25 with AM serum cortisol baseline of 0.9 mcg/dl (7-28 mcg/dl). The serum
cortisol level 1 hour after Cosyntropin 0.25mg intramuscular injection was 6.5 mcg/dl.

DISCUSSION

Intra-articular steroid injections are used by different medical specialties for patients
who fail various pain medications as modality of pain control for moderate to severe
arthritis. It has been shown that Intra-articular or intramuscular steroid injections can
cause suppression of the adrenocortical and Hypothalamic-Pituitary Axis (HPA) [5,
9]. Intra-articular steroid injections are slowly absorbed into the systemic circulation
as compared to IV steroid therapy; hence, there is potential for longer exposure to
the external source of steroids intra-articular joint injections [5]. Patients subjected to
intra-articular steroid injections may therefore demonstrate symptoms of Cushingoid
features such as moon face and neck humps. Similar symptoms are seen in patients
with Cushing’s syndrome, which characteristically is diagnosed with an elevated
level of serum cortisol. In this patient, however, the serum cortisol levels were
depressed. The level of serum cortisol has shown to decrease significantly within
hours of intra-articular injection [5]. This demonstrates the suppression of the HPA
axis due to the direct consequence of the negative feedback of exogenous steroid in
the systemic circulation [6].
The patient was discussed with an endocrinologist who suspected secondary Cushing’s syndrome based on patient’s presentation. The low serum cortisol of 2 mcg/dl implied non-endogenous corticosteroid exposure or adrenal insufficiency. Normal levels of DHEAS made adrenal insufficiency less likely. Cotrosyn test was done per endocrinology recommendation. Baseline serum cortisol was 0.9 cg/dl and serum cortisol after Cosyntropin 0.25 mg injection IM was 6.5 mcg/dl. The results of the test rules out the primary adrenal insufficiency and confirms secondary adrenal suppression from HPA from exogenous corticosteroid exposure.

There a few reported cases where patients developed Cushingoid facies after intra-articular corticosteroid injections (AICI). Jansen et al reported four cases of Cushingoid state following local triamcinolone injection [8]. All the patients in this report were female. Three received 40 mg of TCA (Kenacort) with 4 ml of lignocaine 2% and the remaining patient received 40 mg of TCA (Kenacort) with 5 ml lignocaine 2%. All of the patients reported increase in weight ranging 5 to 8 kg, moon facies, and dysregulation in their menstrual cycle. Three of the four women also noted significant buffalo hump. The signs and symptoms of Cushingoid state resolved after 6 months.

Lazarevic et al studied the reduction of cortisol levels after single intra-articular and intramuscular steroid injection [5]. They reported that a significant decrease in endogenous adrenocortical secretion after single IACI is due to the HPA axis suppression. They suggested that the duration of the endogenous corticosteroid suppression is dependent on the solubility and the dose of the corticosteroid. Triamcinolone is noted to have a lower solubility and therefore less likely to be absorbed; however, Hameed et al reported 2 pediatric cases of adrenal suppression and Cushingoid features after Triamcinolone acetonide IACI [9]. Both patients were reported to have fully recovered from the Cushingoid state with normalization of serum cortisol in about 7 months. The manifestation of the Cushingoid state has been demonstrated to occur due the endocrine system imbalance [8].

Fat distributions have been shown to occur in patients other than those with hypercortisolism [10]. There are reports of lipodystrophy in type 2 diabetic patients and HIV patients with antiviral therapy [10, 11, 12]. The case discussed here involves a patient with HIV diagnosis who had been on antiviral therapy for several
years. The patient has been on ritonavir, lamivudine, raltegavir and darunavir prior to IACI. Lipodystrophy is one of the main side effects shown in patients with antiviral therapy specifically, protease inhibitors [13, 14]. HIV patients with lipodystrophy may present with neck fat distribution that might appear as neck hump. However, the patient described here denied similar finding prior to the IACI [13, 14]. The patient discussed in this paper received ICAI; however, there is evidence suggesting that the half-life of prednisolone is prolonged in HIV-infected patient, which may partially be attributable to a pharmacokinetic drug interaction between HIV protease inhibitors and corticosteroids [15]. This drug interaction between protease inhibitors and corticosteroid may result in Cushing’s syndrome [15].

**CONCLUSION**

It has been shown that intra-articular corticosteroid injection is not a benign procedure and may lead to extra-articular dysregulation of other organ systems. Due to the potential deleterious effects of ICAI, serum cortisol level should be monitored prior to and after the injections. Physicians should not wait on the appearance of Cushingoid features before taking appropriate measures. Serum cortisol monitoring will enable the physician to detect HPA axis suppression and perhaps minimize the systemic effects of ICAI.

**CONFLICT OF INTEREST**

There is no conflict of interest among the authors of this paper.

**AUTHOR’S CONTRIBUTIONS**

Justice Otchere, MD

Group 1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Chitra Damodaran, MD
Group 1 - Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2 - Drafting the article, Critical revision of the article
Group 3 - Final approval of the version to be published

Scott Russel Strum, MD
Group 3 - Final approval of the version to be published

REFERENCES
8. Jansen T, Roon E. Four cases of a secondary Cushingoid state following local triamcinolone acetonide (Kenacort) injection. The Netherlands Journal of Medicine, 2002; 60 (3):151-153


### Table 1: Blood cortisol levels after Kenalog intra-articular injection

<table>
<thead>
<tr>
<th>Cortisol levels</th>
<th>6 weeks after IACI</th>
<th>8 weeks after IACI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 units in mcg/dl</td>
<td>0.9 units in mcg/dl</td>
<td></td>
</tr>
</tbody>
</table>

Units in mcg/dl
FIGURE LEGENDS

Figure 1: Frontal view showing cushingoid facies 2 months post injection with Kenalog preparation

Figure 2: Frontal view showing resolution of cushingoid facies 19 months post injection with Kenalog preparation

Figure 3: Lateral view showing cushingoid facies 2 months post injection with Kenalog preparation

Figure 4: Lateral view showing resolution of cushingoid facies 19 months post injection with Kenalog preparation
FIGURES

Figure 1: Frontal view showing cushingoid facies 2 months post injection with Kenalog preparation.
Figure 2: Frontal view showing resolution of cushingoid facies 19 months post injection with Kenalog preparation.
Figure 3: Lateral view showing cushingoid facies 2 months post injection with Kenalog preparation.
Figure 4: Lateral view showing resolution of cushingoid facies 19 months post injection with Kenalog preparation