



Case Report

Steroid as double edged sword; a catastrophic event in the rural part of Nepal

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ABSTRACT

Introduction and Importance: Cushing's syndrome is a rare condition caused by the long-term glucocorticoid exposure. The clinical picture is variable in severity and presentation. All form of steroid use (parenteral, topical, inhalational as well as additive in herbal and other formulations) are responsible for causing iatrogenic Cushing syndrome.

Case: We present a case of 59 year male from rural Nepal who initiated prednisolone 10mg per day for trivial joint pain over the counter (OTC) for 14 years presented with acute cellulitis of arm and long term changes of steroid overuse. This study is directed to alarm the importance of medical history review and management.

Clinical findings and investigations: Patient had features of florid Cushing syndrome and joint line tenderness of bilateral knee along with lumbar vertebral tenderness. ACTH level, Abdominal ultrasonography, imaging of knee and thoracolumbar spine was sent for diagnosis.

Intervention and outcome: Patient was managed with analgesics, antibiotics, alternate day dressings and referred to orthopaedics for further management of osteoarthritic changes.

Conclusion: To prevent such catastrophic event topical steroids and their mixtures must be sold as "prescription-only" medications and physicians must take detailed history prior to management and correct the irrational use of drugs like Steroids.

1. Introduction

1.1. Background and rationale

Nepal is a developing country in south Asia where health care system is run by both public and private sectors and yet considered unable to maintain international standard. And there is huge health care disparities in rural and urban area regarding resources which led to sub-standard treatment in various time period.

Corticosteroid is a magic bullet discovered in modern medicine. It is widely used for many diseases as anti-inflammatory. However, irrational use of corticosteroid has been increasing every day. According to 2001 report, one percentage of general population was on systemic corticosteroid [1] and among which about two third exhibits iatrogenic Cushing syndrome due to excessive use of the drugs [2]. Sadly, we have multiple unauthorized prescriptions and OTC availability of steroids in

rural part of our country. So, it is absolute necessary for treating physicians to look over the patient medical and drug history. We present a case of preventable adverse drugs reaction in a patient.

2. Case report

2.1. Patient information

2.1.1. Demographics and presentation

59 year old male, from rural part of country who is farmer by occupation and have no formal education (cannot read and write any language) presented to out-patient department with the complaints of painful swelling of right fingers since five days. He also mentioned that similar wounds developed with trivial prick or abrasion as well. On further evaluation he said he had gain weight, started severe back and knee pain bilaterally and proximal muscle weakness gradually over

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time.

2.1.2. Past history

Similar wounds developed on trivial injury on past.

2.1.3. Family history

Non significant family history.

2.1.4. Drug and allergy history

patient reveal taking aceclofenac 100mg and prednisolone 10mg, twice a day since 14 years for non-specific knee pain. It was prescribed by some pharmacist and has been taking till date over the counter (OTC).

2.2. Clinical findings

On examination the patient had features of florid Cushing syndrome (Fig. 1) and joint line tenderness of bilateral knee along with lumbar vertebral tenderness. The right hand is swollen and there was necrotic tissue at the base of middle finger (Figs. 2 and 3). The dorsum of hand also had swallow ulcers which developed after trivial injury in the area. The skin look thin and shiny with normal pulse at radial.

2.3. Diagnostic assessment and interpretation

Laboratory finding revealed low adrenocorticotrophic hormone (ACTH) level in the blood measuring 6 pg/ml and low 8 a.m. cortisol level measuring 1.6mcg/dl. Abdominal ultrasonography shows slightly atrophic bilateral adrenal gland. He also had slight liver function derangement and hyperlipidemia but normal blood sugar level. Patient



Fig. 2. Swollen hand and necrotic skin at the base of middle finger.



Fig. 3. Ventral surface of right hand showing necrotic tissue at the base of middle finger.



Fig. 1. Patient from rural part of Nepal with Cushingoid facies.



Fig. 4. Osteoarthritis of both knee due to steroid overuse.

had lymphopenia (5%), neutrophilia (97%) and anemia (11g/dl).

Imaging of knee shows bilateral osteoarthritic changes (Fig. 4) and thoracolumbar imaging also show osteoporotic changes, scoliosis and osteoarthritic changes of steroid. (Figs. 5 and 6).

Hence diagnosis of iatrogenic Cushing syndrome with complicated cellulitis was made and dressing of wound was done. The patient was counseled regarding steroid misuse but patient pain has increased more so patient was reluctant to change the drug. Dressing of wound reveals sloughs and draining pus which was sent for culture. Gram stain reveals gram positive cocci in clusters and few gram negative rods. Patient was kept in tramadol 50mg prn along with Ampicillin-cloxacillin four times daily for 5days.

2.4. Outcome and followup

On the alternate dressing the wound was drastically improved and granulation tissue started already. Patient is referred for orthopedics and physiotherapist consultation for further management of osteoarthritis.

3. Discussion

Cushing's syndrome is a rare condition caused by the long-term glucocorticoid exposure. The clinical picture is noticeably different [3]. The clinical manifestations of Cushing's syndrome differ depending on the gender. Men with Cushing Disease (CD) are more prone to show with more florid clinical symptoms at a younger age. Much more common are striae, muscular weakness and atrophy, osteoporosis, and kidney stones [4], which was present in our study as well except renal stone.

In both men and women, gonadal dysfunction manifests as a loss of libido, infertility, monthly irregularity or amenorrhea in women, and erectile dysfunction in men [5]. Testicular atrophy was present in our



Fig. 5. Anteroposterior view of X-ray of dorsolateral spine showing osteoporotic changes, scoliosis and osteoarthritic changes.



Fig. 6. X ray of lateral view of dorsolateral spine showing osteoporotic and osteoarthritic changes.

patient as well.

Patients with ectopic Cushing's syndrome typically have significant hypercortisolemia, hypokalemia, and acute or opportunistic infections, as well as a quick start of symptoms and a florid appearance [5,6, and 7]. These characteristics, on the other hand, suggest the severity of hypercortisolism. But endogenous use of steroid for such a long period has presented with these features which is a tragedy.

In 50%–80% of Cushing's syndrome patients, decreased bone mineral density, osteoporosis, and fractures are prevalent. Bone mineral density improves after cure, although ongoing therapy for fractures and discomfort may be required [8]. Our patient who initiated steroid out of misdiagnosis of joint pain led up into osteoporotic changes and fracture of spine and osteoarthritis of knee joints.

Psychiatric and cognitive dysfunction is present in 70%–85% of patients with Cushing's syndrome [9], which was not seen in our patient. Excess glucocorticoids cause skeletal muscles, skin, and connective tissue to break down. Increased protein wasting and type II muscle-fiber atrophy are linked to considerable muscular weakening, with the pelvic girdle musculature being the most affected [10,11]. Disuse muscular atrophy and decreased mobility are further exacerbated by vertebral fractures, back discomfort, and depression. Even several years after remission, a consistently decreased quality of life, mainly in the physical area, and permanent muscle weakness have been described [12,13,14, and 15].

Dyslipidemia (increased low-density lipoprotein, decreased high-density lipoprotein) and glucose intolerance occur in 45%–70% of patients [16–18]. Although not usually present, hypertension (cortisol-mediated augmentation of vascular reactivity to vasoconstrictors and cortisol's mineralocorticoid effects) is common in people with Cushing's syndrome, with an estimated frequency of 80% [17,19].

Endogenous Cushing's syndrome has traditionally been characterized as either ACTH-dependent or ACTH-independent. Cushing's syndrome caused by ACTH is responsible for 80–85% of cases. 75–80% of these are caused by ACTH production from a pituitary adenoma (Cushing's disease [CD]), 15%–20% are caused by ACTH production from non-pituitary tumors (ectopic ACTH syndrome [EAS]), and 1% are caused by corticotrophin-releasing hormone (CRH)-producing tumors [20,21]. The most common cause of Cushing's syndrome (exogenous or iatrogenic Cushing's syndrome) is the use of supraphysiologic dosages of glucocorticoids [22].

A complete medication history is required because glucocorticoids

are used to treat inflammatory, autoimmune, and neoplastic illnesses. Although oral glucocorticoids are the most typically associated with iatrogenic Cushing's disease, any form of delivery should be considered, including inhalation, topical, or injectable glucocorticoids [23,24, and 25]. Mepredolone acetate or high dosage medroxy progesterone, a progestin with considerable inherent glucocorticoid activity, can also cause it [26]. Ritonavir causes Cushing syndrome by delaying the clearance of some inhaled steroids [27]. The use of glucocorticoid-containing lotions or herbal medicines can potentially produce Cushing syndrome [28,29].

Community pharmacists play an essential role in Nepalese health care, handling prescriptions, providing primary support, and referring patients to higher levels of care. Patients visit community pharmacies before and after their doctor visits to receive drugs and drug information because they are a convenient location to obtain medications [30].

In Nepal, all residents do not have access to comprehensive health insurance coverage. Instead of going to the doctor early and preventing problems, patients choose the pre-doctor trial technique. As a result, steroid use and steroid-related diseases have increased. Many OTC medications are prescribed without a doctor's prescription in Nepal, and there are no clear distinctions between OTC and prescription drugs [31]. The lack of a proper law, as well as the lack of qualified pharmacists and paramedics providing drugs, are two of the most prevalent causes of steroid use [31]. Another factor is a scarcity of professionals and public understanding, particularly in Nepal's rural areas [32]. Steroids are available in a variety of forms, either alone or in combination with antibiotics and antifungals, all of which are commonly available over-the-counter at pharmacies [32].

In a sample of 19,464 dermatology OPD patients, 614 (3.15 percent), similar to an Indian study [33], indicated a history of using steroid-containing or other creams (ayurvedic/herbal/cosmetic) suspected of containing steroid without justification [32]. Sixty-six percent of patients were prescribed steroids by pharmacists. TCS was recommended by relatives/friends/neighbors in 19% of cases [32].

The easy availability of steroid over the counter at pharmacist shops across the country without a valid prescription in countries like Nepal and India is exacerbating the problem of abuse, as evidenced by various research [34–40].

4. Take away lesson

In recent years, steroid abuse has become increasingly common. Pharmaceutical industry manufacturing and promoting inappropriate fixed drug combinations containing steroids, unregulated over-the-counter supply and unrestricted sale of steroids, professional obliviousness (qualified and unqualified persons prescribing steroid), and general ignorance (layperson using steroid or advising friends/family to use it) are all factors contributing to this epidemic. As a result, it is past time to raise public awareness and educate prescribers (chemists and medical practitioners). Another important step would be to raise awareness of the problem with the government authorities and have them control the manufacture and over-the-counter selling of certain steroid mixtures. Topical steroids and their mixtures must be sold as "prescription-only" medications. Physician should opt to do medical history taking and correct irrational use of medicine. Chemist or pharmacist should avoid prescribing steroid without physician prescription. We all are responsible for such preventable mishaps and it's time to be accountable.

Ethical approval

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Author contributions

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Registration of research studies

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Declaration of competing interest

There is no any conflicts of interest with this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104697>.

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