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Case Report

Opioid Induced Adrenal Insufficiency Complicated by Adrenal Crisis-A Case Report

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Abstract

Introduction: 1 in 5 people experience chronic pain that limits their ability to carry out activities of daily living. Opioid analgesics are one of the pharmaceutical interventions utilized to treat chronic pain. In fact, chronic pain is one of the most common reasons opioids are prescribed. Although many of the secondary effects of opioids are well known, a lesser-known side effect is opioid induced adrenal insufficiency (OIAI). OIAI can cause significant morbidity and has the potential to result in adrenal crisis, profound hypotension, and potential cardiovascular collapse, resulting in death. With sparse literature on OIAI, we present a case of OIAI complicated by adrenal crisis to expand awareness and discussion on the topic.

Methods: The patient was a 65-year-old female on chronic opioid therapy for back pain who presented to the emergency room for syncope. On presentation, patient was hypotensive, bradycardic, and had an inadequate fluid response requiring pressors. Traditional etiologies of shock were ruled out, but interestingly morning cortisol and adrenocorticotropic hormone (ACTH) levels were low. Additionally, the cosyntropin stimulation test was suboptimal. Results suggested central hypothalamic pituitary axis suppression, which after discussion with Endocrinology indicated OIAI given the patient's history.

Results: Shortly after steroid regimen initiation the patient was weaned off pressors, and after multiple taper trials was successfully sent home on a steroid taper with Endocrinology follow up.

Conclusion: Long term opioid use to treat chronic pain can decrease cortisol production via HPA axis suppression resulting in OIAI. To date, there is limited investigation into OIAI despite its increased prevalence and widespread use of opioids. The case adds to the available literature on OIAI, and sheds light on adrenal crisis as its initial presentation.

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Keywords: Chronic pain; Opioid; Joint; Steroid; Back pain; Analgesics.

Introduction

Chronic pain remains one of the most common conditions within the United States, with estimates suggesting 1 in 5 people experience chronic pain that limits patient ability to carry out activities of daily living [1]. Due to its pervasiveness, it is no surprise that there is a variety of therapeutic modalities available to treat it [2]. Pharmaceuticals remain a mainstay in the treatment of chronic pain and generally are classified as non-opioid analgesics and opioid analgesics [2].

In fact, chronic pain is one of the most common reasons opioids are prescribed [3]. With the prevalence of chronic pain and the utilization of opioid analgesics, it is imperative that health care providers are aware of and know how to manage the various side effects and conditions caused by these medications. Many of the potential side effects are well known (tolerance, constipation, sedation, etc.) but one that is less recognized and has the potential to cause significant morbidity and mortality is opioid induced adrenal insufficiency (OIAI) [3]. OIAI presents with nonspecific signs and symptoms that can overlap with chronic pain, making it a challenging diagnosis to make [4].

One retrospective study of 40 OIAI patients found that fatigue (73%) and musculoskeletal pain (53%) were the two most common symptoms experienced by this specific subset of patients with weight loss, headache, and nausea being experienced to a lesser degree [5]. Uncontrolled OIAI can ultimately result in adrenal crisis which is characterized by profound hypotension and potential cardiovascular collapse [6].

To expand the recognition of OIAI in order to optimize patient care, we present a case of OIAI that was complicated by adrenal crisis and successfully managed with exogenous corticosteroids.

Case presentation

A 65-year-old female presented to the emergency department for syncope. On arrival, the patient was somnolent, hypotensive, and bradycardic. Patient past medical history was notable for type II diabetes mellitus, gastroparesis, multiple episodes of diabetic ketoacidosis, hypothyroidism, depression, postural orthostatic tachycardia syndrome, and chronic back pain with opioid dependence. Despite fluid intervention, the patient had ongoing pressor requirements requiring MICU admittance. Workup revealed non-anion gap acidosis, glucosuria without ketonuria. Traditional shock etiologies including cardiac, pulmonary, neurologic, and infectious workup had no significant findings. Interestingly, morning cortisol levels were low-normal at 4.7mcg/dL at 5 AM and 2.6mcg/dL at 11 AM. Additionally, cosyntropin stim tests were suboptimal at <20mcg/dL with a peak of 18.6mcg/dL, adrenocorticotropic hormone (ACTH) was low at <5pg/mL and Renin: Aldosterone was within normal limits at 0.6. Endocrinology was consulted, who proposed these results suggested central HPA axis suppression, likely indicating OIAI given the patient's

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history. The patient was started on a hydrocortisone regimen as shown in (Table 1). Within hours the patient was weaned off of pressors, and after 48-hour monitoring was transferred to stepdown.

Results

Hospital Day	AM	PM	Total/ Day
1 (MICU)	50 mg	25 mg Q6h (2doses)	100 mg
2	25 mg	10 mg	35 mg
3 (Stepdown unit)	50 mg IV	50 mg IV	100 mg
4	50 mg	25 mg	75 mg
5 (Hypoglycemia)	25 mg	25 mg	50 mg
6	50 mg	40 mg	90 mg
7	40 mg	40 mg	80 mg
8	40 mg	30 mg	70 mg
9 (Day of Discharge)	30 mg	30 mg	60 mg

Table 1: Initial Hospital Course.

In stepdown on day 3, the patient developed hypotension following the day 2 taper, which improved with IV hydrocortisone 50 mg BID seen in (Table 1). When reduced to a 25mg/25mg regimen on day 5, the patient developed recurrent episodes of hypoglycemia, requiring a 50mg/40mg regimen started on day 6.

With sugars and pressures stable days 6-9, the patient was sent home on (Table 2) post-discharge taper plan.

Post-discharge Day	Planned AM dose	Planned PM dose	Total/day
1	30 mg	20 mg	50 mg
2	20 mg	20 mg	40 mg
3 until follow up with Endocrinology	20 mg	10 mg	30 mg

Table 2: Initial Planned Outpatient Regimen.

Unfortunately, the patient was admitted 3 weeks later for worsening hypotension. The patient reported taking 20mg/20mg doses of hydrocortisone instead of the 20mg/10mg maintenance dose recommended at discharge due to progressive hypotension.

During this admission, pressures improved Day 1 with IV Hydrocortisone (Table 3). Patient was transitioned to PO hydrocortisone day 2 and discharged day 3 on the regimen described in (Table 3), which allowed patient to follow up with Endocrinology.

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Hospital Day	AM Dose	PM Dose	Total/Day
1 (Admission)	100 mg IV	50mg IV_{x2}	200 mg
2	40 mg	40 mg	80 mg
3 and 4	30 mg	30 mg	60 mg
5 and 6	30 mg	20 mg	50 mg
7 and 8	20 mg	20 mg	40 mg
9 until follow up with Endocrinology	20 mg	10 mg	30 mg

Table 3: New Hydrocortisone Regimen.

Discussion

50.2 million U.S. adults report having pain daily, or most days of the week, with opioids being a commonly utilized pharmacologic intervention in chronic pain management [1-8]. Despite a 9%-29% prevalence of OIAI amongst chronic opioid users, it remains poorly recognized by clinicians [4,5]. Opioids target peripherally and centrally located nervous system receptors and are theorized to suppress the hypothalamic-pituitary-adrenal (HPA) axis centrally [7,8]. With the HPA's involvement in vascular, cognitive, metabolic, and immune system regulation, suppression can lead to impaired blood pressures, inflammatory responses, mood dysregulation, metabolic derangement, and cardiovascular disease [7-12].

Adrenal insufficiency from HPA axis suppression generally presents with fatigue, headache, hypotension, nausea, and loss of libido [7]. Similarly, in a retrospective study of 40 OIAI patients, fatigue (73%) and musculoskeletal pain (53%) were the two most common symptoms experienced in addition to weight loss, headache, and nausea [5]. With the symptomatology of OIAI being largely nonspecific and similar to chronic pain, this contributes to why it takes on average 12 months to be diagnosed after symptom onset [4,5]. Larger opioid dosages and longer opioid duration of action are assumed to be two primary risk factors for OIAI development [4,6]. By more promptly identifying risk factors like this, OIAI can be diagnosed and managed more effectively [5]. Another major barrier to prompt identification is the lack of a standardized diagnostic approach [4]. To date, the best recommended diagnostic approach involves measuring baseline ACTH, morning cortisol, and dehydroepiandrosterone (DHEA) [6]. If these values are inconclusive, proceed to cosyntropin stimulation test or an insulin tolerance test [6]. The implementation of a standardized diagnostic approach such as this in conjunction with more research to identify specific risk factors for developing OIAI can allow for more prompt diagnosis with decreased morbidity/mortality risk. Ultimately, prevention of OIAI is the best treatment, but prompt recognition of OIAI can decrease the incidence of potentially fatal sequela like adrenal crisis [6].

Conclusion

Chronic pain is a debilitating condition for which opioids remain a commonly prescribed medication. Long-term opioid use decreases

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cortisol production via HPA axis suppression, impeding the body's inflammatory and metabolic response to stress.

This case demonstrates an individual on chronic opioids and found to have OIAI while in adrenal crisis, which resolved with glucocorticoid administration. To date, there is limited investigation into OIAI despite the widespread use of opioid analgesics and prevalence of OIAI. Our case adds to the available literature on OIAI and adds data on the management of OIAI complicated by adrenal crisis.

References

1. Yong RJ, Mullins PM, Bhattacharyya N. Prevalence of Chronic Pain Among Adults in the United States. Pain. 2022;163(2):328-32. PubMed | CrossRef
2. Hylands-White N, Duarte RV, Raphael JH. An Overview of Treatment Approaches for Chronic Pain Management. Rheumatol Int. 2017;37:29-42. PubMed | CrossRef
3. Gazelka HM, Leal JC, Lapid MI, Rummans TA. Opioids in Older Adults: Indications, Prescribing, Complications, and Alternative Therapies for Primary Care. Mayo Clin Proc. 2020;95(4):793-800. Elsevier. PubMed | CrossRef
4. Coluzzi F, LeQuang JA, Sciacchitano S, Scerpa MS, Rocco M, Pergolizzi J. A Closer Look at Opioid-Induced Adrenal Insufficiency: A Narrative Review. Int J Mol Sci. 2023;24(5):45-75. PubMed | CrossRef
5. Li T, Donegan D, Hooten WM, Bancos I. Clinical Presentation and Outcomes of Opioid-Induced Adrenal Insufficiency. Endocr Pract. 2020;26(11):1291-7. PubMed | CrossRef
6. Donegan D, Bancos I. Opioid-Induced Adrenal Insufficiency. Mayo Clin Proc. 2018;93(7):937-44. Elsevier. PubMed | CrossRef
7. Bleicken B, Ventz M, Quinkler M, Hahner S. Delayed Diagnosis of Adrenal Insufficiency is Common: A Cross-Sectional Study in 216 Patients. Am J Med Sci. 2010;339(6):525-31. PubMed | CrossRef
8. Schwan J, Sclafani J, Tawfik VL. Chronic Pain Management in the Elderly. Anesthesiol Clin. 2019;37(3):547-60. PubMed | CrossRef
9. Farooqi NA, Scotti M, Lew JM, Botteron KN, Karama S, McCracken JT, et al. Role of DHEA and Cortisol in Prefrontal-Amygdalar Development and Working Memory. Psychoneuroendocrinology. 2018;98:86-94. PubMed | CrossRef
10. Ha T, Granger DA. Family Relations, Stress, and Vulnerability: Biobehavioral Implications for Prevention and Practice. Fam Relat. 2016;65(1):9-23. PubMed | CrossRef
11. Sheng JA, Bales NJ, Myers SA, Bautista AI, Roueinfar M, et al. The Hypothalamic-Pituitary-Adrenal Axis: Development, Programming Actions of Hormones, and Maternal-Fetal Interactions. Front Behav Neurosci. 2021;14:601939. PubMed | CrossRef
12. Rensen N, Gemke RJ, Van Dalen EC, Rotteveel J, Kaspers GJ. Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression After Treatment with Glucocorticoid Therapy for Childhood Acute Lymphoblastic Leukaemia. Cochrane Database Syst Rev. 2017(11). PubMed | CrossRef

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