

Adrenal insufficiency and bowel obstruction: An overlooked association

Ryan A. Kunjal^{1*}, Ria R. Ramadoo¹, Surujpal Teelucksingh¹, Vijay Naraynsingh²

¹Department of Clinical Medical Sciences, University of the West Indies, St. Augustine, Trinidad and Tobago;

*Corresponding Author: ryankunjal@hotmail.com

²Department of Clinical Surgical Sciences, University of the West Indies, St. Augustine, Trinidad and Tobago

Received 16 March 2013; revised 20 April 2013; accepted 4 May 2013

Copyright © 2013 Ryan A. Kunjal *et al.* This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Bowel obstruction is a documented but rare presentation of adrenal insufficiency (AI). We report a case of acute AI manifesting as intestinal pseudo-obstruction (IPO) in a patient with underlying iatrogenic adrenal suppression. An 83 years old female was admitted for partial small bowel obstruction that failed to resolve with conservative management. She then underwent exploratory laparotomy where no mechanical obstruction was found and the small bowel was manually decompressed. Postoperatively she developed acute swelling of her right ankle which was similar to mono-articular attacks in the past. This was diagnosed clinically as gout. Her obstruction failed to settle and a second laparotomy was done which yielded the same as the first. Given her past account of arthritic pain, direct questioning of steroid use unearthed a history of multiple intra-articular corticosteroid injections for analgesia. She also described several short courses of high dose oral steroids for respiratory tract infections, including a recent course which was abruptly stopped two days prior to presentation. Clinical suspicion of AI was supported by biochemical testing of stress cortisol levels and change in the serum cortisol in response to 250 µg of synthetic adrenocorticotrophic hormone. Moreover, her improvement following a therapeutic trial of steroid replacement was dramatic and strongly supports this diagnosis. It is therefore worthwhile to consider a diagnosis of AI in cases of bowel obstruction in patients with comorbidities that predispose to steroid use and especially in settings where steroid abuse is prevalent.

Keywords: Pseudo-Obstruction; Steroids; Adrenal Insufficiency

1. INTRODUCTION

Adrenal insufficiency (AI) commonly presents with gastrointestinal effects such as nausea, vomiting and abdominal pain; so severe, that it can appear to be an acute abdomen. These symptoms also overlap considerably with those of bowel obstruction. However, on review of the literature, bowel obstruction has been described as a presenting feature of AI in sick preterm neonates [1] and oncology patients [2]. Furthermore, postoperative ileus has been reported in patients with glucocorticoid induced AI who decompensated after surgical stress [3-5]. In this light, we report a case of acute AI manifesting as intestinal pseudo-obstruction (IPO) in a patient with underlying iatrogenic adrenal suppression.

2. CASE REPORT

An 83 years old female was admitted with partial small bowel obstruction after presenting with an acute onset of severe vomiting and worsening abdominal pain. Vital signs were stable and her abdomen was diffusely tender but not distended. She had no previous surgery and hernial orifices were normal. Laboratory investigations revealed normal electrolytes and a mild microcytic anaemia. CT radiography showed mid- to distal small bowel dilatation, fluid filled and with multiple air-fluid levels. There was no evidence of focal bowel thickening, intramural air or intraluminal masses. She was managed conservatively but failed to improve and underwent an exploratory laparotomy 3 days later. At laparotomy, collapsed ileum was traced back to distended jejunum but no mechanical obstruction was identified. The bowel was viable and manual decompression (milking) was done.

Two days post laparotomy, she was referred to our

medical team for the sudden painful swelling of her right ankle. She gave a 10-year history of similar acute intermittent mono-articular swelling of knees and ankles for which she used acetaminophen and topical non-steroidal analgesics. On examination, the right ankle was noted to be, hot, swollen and painful whilst no other joints were affected or deformed. Uric acid levels were normal; nevertheless, a clinical diagnosis of gout was made.

However, her obstruction had not resolved and on the subsequent day a second laparotomy was performed. Again, no mechanical obstruction was found and manual decompression of dilated small bowel was done. At this time the medical team was again consulted.

Upon more careful examination, her skin was noted to be very thin with a few scattered petechiae. This finding coupled with a long history of arthritides prompted direct questioning of steroid use. It was revealed that she had multiple intra-articular steroid injections spanning over ten years for palliation of arthritic pain. Her last injection was two years prior. She also had intermittent short term courses of high dose prednisolone for respiratory tract infections in the past few years. Most unexpected however, was that she had presented just two days after completing an eighteen day course of adjuvant inhaled corticosteroids and high dose prednisolone, of at least 30 mg daily prescribed for a likely severe lower respiratory tract infection.

In light of this, a diagnosis of acute AI presenting as bowel obstruction was considered and a synthetic adrenocorticotrophic hormone stimulation (Synacthen®) test was done. This was immediately followed by a therapeutic trial of glucocorticoids with 100 mg of Hydrocortisone intravenously. Clinical improvement was dramatic; within 12 hours her nasogastric tube was discontinued and a bowel action occurred the next day. She was maintained on hydrocortisone 50 mg every 8 hours until discharge 2 days later, when a tapering course of oral prednisolone was instituted. Synacthen® test results were: basal cortisol—27.7 µg/dL and stimulated cortisol—37.4 µg/dL.

3. DISCUSSION

Therapeutic glucocorticoid administration is thought to be the most common cause of secondary AI, since exogenous steroids suppress the hypothalamic-pituitary-adrenal (HPA) axis [6]. As such, either a sudden withdrawal of steroid therapy or stressful stimuli, such as an infection or surgery, may precipitate acute AI due to inadequate adrenal reserve [3]. In this case, we believe that it is a combination of such precipitants (steroid withdrawal and lower respiratory tract infection) against a background of chronic steroid use, which accounted for the acute insufficiency; presenting as IPO.

The cumulative effect of recent short courses of high dose oral steroids and multiple intra-articular injections must be considered in assessing the likelihood of iatrogenic AI in our patient. The association between AI and oral steroid therapy has been recognized for decades and typically any patient who has received the equivalent of 15 mg/day of prednisolone for more than 3 weeks should be suspected of having HPA suppression [7]. It has also been reported that even short term courses, as in our patient, can increase the risk of AI [8] and that HPA suppression could take up to one year to recover fully [9]. Additionally, whilst intra-articular steroids comprise compartmental therapy, the systemic suppressive effects on the HPA axis have been widely described [10-13], but the maximum duration of those effects, have not. It is, however, most important to note that there is a great deal of individual variability in susceptibility to suppression of the HPA axis. Thus it is not possible to predict with confidence how patients will be affected even when factors such as dose, duration and delivery route are taken into account [14-17].

Given this unpredictability, biochemical evidence of AI gains great importance in this case. However, the diagnosis of AI is problematic in the presence of acute illness and there are many controversies as well as limitations to all of the tests used. Nevertheless, the diagnosis has been based on the measurement of a random total “stress” cortisol level < 10 µg/dL or the change in the serum cortisol in response to a 250 µg Synacthen® test, the so-called delta cortisol < 9 µg/dL [18]. While our patient’s delta cortisol of 9.7 µg/dL closely approximates those recommendations, there is a marked discrepancy with the stress cortisol level of 27.7 µg/dL.

As mentioned, much controversy exists in this area and we strongly believe that the serum cortisol levels in the initial postoperative period were thought to be less than expected for the degree of the patient’s illness and in keeping with AI. Surgery is one of the most potent activators of the HPA axis and cortisol secretion is high in the immediate postoperative recovery period, when this sample was taken [19,20]. Marik and Zaloga, in their review suggested that the magnitude of the postoperative increase in serum cortisol is correlated with the extent of the surgery, with a peak of 30 - 45 µg/dL [21], while levels of 15 - 34 µg/dL have been advocated by others in response to stress [22]. We, therefore, concur with Marik that the delta and stress cortisol levels, the clinical features and the severity of the illness be considered complementary in the diagnosis of AI [23].

Perhaps, it is the dramatic and rapid resolution of IPO after glucocorticoid administration that is most significant for the diagnosis. Causes of IPO can be categorized into primary and secondary causes. Smooth muscle disorders constitute rare primary causes. Secondary causes

of IPO include Parkinson's disease, myxoedema and opiate drugs [24,25]. Based on clinical and physical findings, the patient did not fill criteria for these and other inflammatory diseases such as systemic lupus erythematosus and scleroderma, which have been associated with IPO.

This diagnosis may not have been made and the patient's outcome, uncertain, if there was not a high clinical suspicion of steroid use. In our experience the injudicious use of steroids; whether by self-medication or over prescription, is not uncommon particularly in patients with arthritides. More importantly, many patients do not always volunteer information regarding steroid use since most perceive it as innocuous given the widespread use and ease of obtaining steroids over-the-counter. It is therefore worthwhile to consider AI in cases of bowel obstruction of indeterminate cause, especially in patients with conditions predisposing to steroid use and in settings where steroid abuse is prevalent.

REFERENCES

- [1] Lavoie, P.M., Pelligra, G., Lupton, B. and Osiovich, H. (2007) Gastrointestinal presentation of relative adrenal insufficiency in a sick preterm neonate. *American Journal of Perinatology*, **24**, 493-495. [doi:10.1055/s-2007-986694](https://doi.org/10.1055/s-2007-986694)
- [2] Poon, D., Cheung, Y.B., Tay, M.H., Lim, W.T., Lim, S.T., Wong, N.S., et al. (2005) Adrenal insufficiency in intestinal obstruction from carcinomatosis peritonei—A factor of potential importance in symptom palliation. *Journal of Pain and Symptom Management*, **29**, 411-418. [doi:10.1016/j.jpainsymman.2004.07.012](https://doi.org/10.1016/j.jpainsymman.2004.07.012)
- [3] Rai, S. and Hemingway, D. (2003) Acute adrenal insufficiency presenting as high output ileostomy. *Annals of the Royal College of Surgeons of England*, **85**, 105-106. [doi:10.1308/003588403321219876](https://doi.org/10.1308/003588403321219876)
- [4] Sharma, A., Naraynsingh, V., Goalan, R. and Teelucksingh, S.T. (2011) Severe intestinal pseudo-obstruction following withdrawal from over-the-counter steroid abuse. *Journal of Postgraduate Medicine*, **57**, 218-220. [doi:10.4103/0022-3859.85212](https://doi.org/10.4103/0022-3859.85212)
- [5] Stelzner, M., Phillips, J.D. and Fonkalsrud, E.W. (1990) Acute ileus from steroid withdrawal simulating intestinal obstruction after surgery for ulcerative colitis. *Archives of Surgery*, **125**, 914-917. [doi:10.1001/archsurg.1990.01410190112018](https://doi.org/10.1001/archsurg.1990.01410190112018)
- [6] Arlt, W. and Allolio B. (2003) Adrenal insufficiency. *Lancet*, **361**, 1881-1189. [doi:10.1016/S0140-6736\(03\)13492-7](https://doi.org/10.1016/S0140-6736(03)13492-7)
- [7] Stewart, P.M. (2003) The adrenal cortex. In: Larsen, P.R., Kronenberg, H.M., Melmed, S. and Polonsky, K.S., Ed., *Williams Textbook of Endocrinology*. 10th Edition, Saunders, Philadelphia, 491-551.
- [8] Schuetz, P., Christ-Crain, M., Schild, U., Süess, E., Facompre, M., Baty, F., et al. (2008) Effect of a 14-day course of systemic corticosteroids on the hypothalamic pituitary-adrenal-axis in patients with acute exacerbation of chronic obstructive pulmonary disease. *BMC Pulmonary Medicine*, **8**, 1. [doi:10.1186/1471-2466-8-1](https://doi.org/10.1186/1471-2466-8-1)
- [9] Livanou, T., Ferriman, D. and James, V.H. (1967) Recovery of hypothalamo-pituitary-adrenal function after corticosteroid therapy. *Lancet*, **2**, 856-859. [doi:10.1016/S0140-6736\(67\)92592-5](https://doi.org/10.1016/S0140-6736(67)92592-5)
- [10] Lazarevic, M.B., Skosey, J.L., Djordjevic-Denic, G., Swedler, W.I., Zgradic, I. and Myones, B.L. (1995) Reduction of cortisol levels after single intra-articular and intramuscular steroid injection. *American Journal of Medicine*, **99**, 370-373. [doi:10.1016/S0002-9343\(99\)80183-1](https://doi.org/10.1016/S0002-9343(99)80183-1)
- [11] Habib, G.S. (2009) Systemic effects of intra-articular corticosteroids. *Clinical Rheumatology*, **28**, 749-756. [doi:10.1007/s10067-009-1135-x](https://doi.org/10.1007/s10067-009-1135-x)
- [12] Reid, D.M., Patel, S., Reid, I.W., Eastmond, C.J. and Rennie, J.A.N. (1983) Hypothalamic-pituitary-adrenal (HPA) axis function in patients receiving long-term intra-articular corticosteroids. *Clinical Rheumatology*, **2**, 159-161. [doi:10.1007/BF02032173](https://doi.org/10.1007/BF02032173)
- [13] Duclos, M., Guinot, M., Colsy, M., Merle, F., Baudot, C., Corcuff, J.B., et al. (2007) High risk of adrenal insufficiency after a single articular steroid injection in athletes. *Medicine & Science in Sports & Exercise*, **39**, 1036-1043. [doi:10.1249/mss.0b013e31805468d6](https://doi.org/10.1249/mss.0b013e31805468d6)
- [14] Alves, C., Robazzi, T.C.V. and Mendoca, M. (2008) Withdrawal from glucocorticosteroid therapy: Clinical practice recommendations. *Journal of Pediatrics*, **84**, 192-202. [doi:10.2223/JPED.1773](https://doi.org/10.2223/JPED.1773)
- [15] Lamberts, S.W., Bruining, H.A. and de Jong, F.H. (1997) Corticosteroid therapy in severe illness. *New England Journal of Medicine*, **337**, 1285-1292. [doi:10.1056/NEJM199710303371807](https://doi.org/10.1056/NEJM199710303371807)
- [16] Schlaghecke, R., Kornely, E., Santen, R.T. and Ridderkamp, P. (1992) The effect of long-term glucocorticoid therapy on pituitary-adrenal responses to exogenous corticotropin-releasing hormone. *New England Journal of Medicine*, **326**, 226-230. [doi:10.1056/NEJM199201233260403](https://doi.org/10.1056/NEJM199201233260403)
- [17] Henzen, C., Suter, A., Lerch, E., Urbinelli, R., Schorno, X.H. and Briner, V.A. (2000) Suppression and recovery of adrenal response after short-term, high-dose glucocorticoid treatment. *Lancet*, **355**, 542-545. [doi:10.1016/S0140-6736\(99\)06290-X](https://doi.org/10.1016/S0140-6736(99)06290-X)
- [18] Marik, P.E., Pastores, S.M., Annane, D., Meduri, G.U., Sprung, C.L., Arlt, W., et al. (2008) Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: Consensus statements from an international task force by the American College of Critical Care Medicine. *Critical Care Medicine*, **36**, 1937-1949. [doi:10.1097/CCM.0b013e31817603ba](https://doi.org/10.1097/CCM.0b013e31817603ba)
- [19] Udelsman, R., Norton, J.A., Jelenich, S.E., et al. (1987) Responses of the hypothalamic-pituitary-adrenal and renin-angiotensin axes and the sympathetic system during controlled surgical and anesthetic stress. *Journal of Clinical Endocrinology & Metabolism*, **64**, 986. [doi:10.1210/jcem-64-5-986](https://doi.org/10.1210/jcem-64-5-986)
- [20] Raff, H., Norton, A.J., Flemma, R.J. and Findling, J.W.

- (1987) Inhibition of the adrenocorticotropin response to surgery in humans: Interaction between dexamethasone and fentanyl. *Journal of Clinical Endocrinology & Metabolism*, **65**, 295. [doi:10.1210/jcem-65-2-295](https://doi.org/10.1210/jcem-65-2-295)
- [21] Marik, P.E. and Zaloga, G.P. (2002) Adrenal insufficiency in the critically ill: A new look at an old problem. *Chest*, **122**, 1784-1796. [doi:10.1378/chest.122.5.1784](https://doi.org/10.1378/chest.122.5.1784)
- [22] Arafah, B.M. (2006) Hypothalamic pituitary adrenal function during critical illness: Limitations of current assessment methods. *Journal of Clinical Endocrinology & Metabolism*, **91**, 3725-3745. [doi:10.1210/jc.2006-0674](https://doi.org/10.1210/jc.2006-0674)
- [23] Marik, P.E. (2004) Unraveling the mystery of adrenal failure in the critically ill. *Critical Care Medicine*, **32**, 596-597. [doi:10.1097/01.CCM.0000110729.73061.4B](https://doi.org/10.1097/01.CCM.0000110729.73061.4B)
- [24] Mok, M.Y., Wong, R.W. and Lau, C.S. (2000) Intestinal pseudo-obstruction in systemic lupus erythematosus: An uncommon but important clinical manifestation. *Lupus*, **9**, 11-18. [doi:10.1177/096120330000900104](https://doi.org/10.1177/096120330000900104)
- [25] Nguyen, H. and Khanna, N. (2004) Intestinal pseudo-obstruction as a presenting manifestation of systemic lupus erythematosus: Case report and review of the literature. *Southern Medical Journal*, **97**, 186-189. [doi:10.1097/01.SMJ.0000087197.59817.AF](https://doi.org/10.1097/01.SMJ.0000087197.59817.AF)