Revisiting prophylactic hydrocortisone in Mitotane therapy

Hypertensive emergency in cortisol- secreting adrenocortical carcinoma treated with Mitotane and prophylactic hydrocortisone

Swetha Rayaroth, MD; Rashid Cheema, MD; Anuraj Mambazhathu Sudhakaran, MD
Geisinger Medical Center, Danville, PA

Geisinger

Introduction

- Adrenocortical carcinoma (ACC) is a rare malignancy.
- Mitotane is widely used in treating ACC due to its inhibition of steroidogenesis enzymes and direct adrenal cortex toxicity.
- This case presents hypertensive emergency in a patient with cortisol-secreting adrenal carcinoma on mitotane therapy with prophylactic hydrocortisone.

Case description

- A 70-year-old male was admitted for acute decompensated heart failure due to hypertensive emergency.
- Two months prior to presentation the patient was diagnosed with recurrent cortisol secreting ACC, and was treated with Pembrolizumab and Mitotane with prophylactic hydrocortisone.
- On admission, he was hypertensive to 186/84 mmHg, with hypokalemia and normal aldosterone/plasma renin activity ratio (ARR). No further hormonal workup was done due to being on hydrocortisone.
- The patient was treated with IV diuretics and antihypertensives, and hydrocortisone was held due to worsening hypokalemia and uncontrolled hypertension.
- Outpatient workup after holding hydrocortisone further confirmed Cushing's syndrome.
- On further monitoring, his cortisol levels remained high and additional therapy was recommended with Metyrapone, but was not initiated due to pursuing comfort care.

Initial labs at cancer diagnosis	
8 AM cortisol [2.5-19.5 µg/dL]	19.9
24-hour urine free cortisol [4-50 µg/24hr]	168
ACTH [7.2-63.3 pg/mL]	<3
ARR </= 28	3.7

Admission labs	
Potassium [3.5-5.1 mmol/L]	3.5
ARR </= 28	1.5

Labs after holding hydrocortisone	
Late night salivary cortisol x 3 [<0.9mcg/dl]	0.6, 0.4, 0.58
24-hour urine free cortisol [4-50 µg/24hr]	93.1

Periodic monitoring of mitotane levels showed subtherapeutic levels despite dose increment

Discussion

- Mitotane can cause adrenal insufficiency (AI), leading to the common practice of prophylactic glucocorticoid use with mitotane. Evidence indicates some patients require higher-than-physiological glucocorticoid doses, often necessitating lifelong corticosteroid and mineralocorticoid replacement.
- In this case the patient developed hypertensive emergency due to hypercortisolism from ACC and exogeneous supplementation.
- Hypercortisolism persisted even after discontinuing hydrocortisone, and therapeutic mitotane levels were never achieved despite a dose of 5 grams per day.
- This highlights the challenge of balancing hormonal excess from ACC and deficiency from mitotane therapy, with both potentially leading to life threatening complications

Conclusion

- This case emphasizes the need to reassess the practice of prophylactic glucocorticoid therapy with mitotane, particularly in cortisol-secreting cancers.
- Developing standardized glucocorticoid replacement regimens based on mitotane levels and hormonal workup is crucial to avoid fatal complications associated with both hormonal excess and deficiency.