SUN-484

Levoketoconazole Use Prior to Adrenalectomy

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BACKGROUND

Current Endocrine Society clinical practice guidelines indicate initial resection of the primary lesion as first line treatment for adrenal adenomas.[1]

A patient presented with mild hypercortisolismand a 2.6 cm adrenal adenoma was scheduled for adrenalectomy. Patient was given levoketoconazole (Recorlev®, Xeris Pharmaceuticals, Inc., Chicago, IL, USA) pre-operatively to minimize surgical complications related to elevated cortisol levels,a use not previously reported.

PRESENTATION

A 35-year-old female presented in December 2020 complaining of a four-year history of 40 lbs. weight gain. Her medical history included hyperlipidemia, metabolic syndrome consisting of central obesity, and asthma. At presentation, her weight was 191 lbs. Due to rising fasting blood glucose levels, metformin 850 mg twice daily was initiated in March 2021 alongside dulaglutide (Trulicity®, Lilly, Indianapolis, IN, USA) 0.75 mg titrated to 3 mg weekly.

Table 1: Biochemical workup

Labs	Normal range	June 2023	March 2024	December 2024 (Post-operative)
ARR (ng/dL)/(ng/mL/hr)	0.9 - 28.9	42	Normal	
Plasma renin (ng/mL/hr)	0.25 - 5.82	0.19	Normal	
Aldosterone (ng/dL)	≤ 28	8.0	Normal	
DST (µg/dL)	≤ 1.8	2.0	—	
LNSC (µg/dL)	≤ 0.09	0.16	—	
Morning cortisol (µg/dL)	0.04 - 0.56	0.72	Normal	
DHEAS (µg/dL)	45 - 270		Normal	
ACTH (pg/mL)	10 - 60			Undetectable
Serum cortisol post-operative (µg/dL)	4.0 - 22.0			1.2
Cosyntropin stimulated cortisol (µg/dL)	> 18			30 min: 20.5
				60 min: 26.5

ARR: aldosterone-to-renin ratio; DST: dexamethasone suppression test; LNSC: late night salivary cortisol; DHEAS: dehydroepiandrosterone sulfate; ACTH: adrenocorticotropic hormone

CLINICAL CASE

At follow-up in March 2023, cross-sectional imaging identified a 1.9 × 1.9 cm adrenal tumor. Biochemical workup showed no initial abnormalities. However, repeat tests inJune 2023 (Table 1) revealed an elevated aldosterone-to-renin ratio (ARR) of42 (ng/dL)/(ng/mL/hr), plasma renin of 0.19 ng/mL/hr, and aldosterone of 8.0 ng/dL. A one milligram overnight dexamethasone suppression test (DST) was abnormal at 2.0 µg/dL. The late night salivary cortisol (LNSC) test was 0.16 µg/dL and morning cortisol was 0.72 µg/dL. A repeat CT scan (Table 2) showed a 1.9 cm low attenuation lesion inthe right adrenal gland, consistent with an adenoma producing aldosterone and cortisol. Levoketoconazole 150 mg daily was started in December 2023 with Trulicity and metformin discontinued.

Table 2: Adrenal Tumor Size on CT scan

	Mar 2023	June 2023	July 2024	Dec 2024
Tumor size (cm)	1.9 x 1.9	1.9	2.0	2.6

At a January 2024 follow-up, the levoketoconazole dose was increased to 150 twice daily. By March 2024, all biochemical parameters, including DHEAS, cortisol, aldosterone, plasma renin, and ARR were within normal ranges. By July 2024, seven months after starting levoketoconazole, the patient weighed 162 lbs., representing a29 lbs. weight loss.

A repeat CT scan (Figure 1) revealed a 2 cm adenoma with -2HU. Given the patient's age and tumor progression, surgery was chosen. Levoketoconazole was continued and laparoscopic adrenalectomy was performed in December 2024. The final pathology was of an adrenal cortical adenoma measuring 2.6 cm confirming the interval growth of the tumor. Prior to surgery, levoketoconazole was immediately discontinued. Post-operative testing on day one showed: undetectable ACTH, baseline cortisol of 1.2 µg/dL, and a 30- and 60-minute Cosyntropin stimulated cortisol level of 20.5 µg/dL and 26.5 µg/dL respectively. Outpatient post-operative biochemical follow-up showed all labs within normal range.

Figure 1: CT scan



CONCLUSION

This is the first documented case of pre-operative use of levoketoconazole in a patient undergoing unilateral adrenalectomy. The tumor was foundto secrete both cortisol and aldosterone. Pre-operative administration of levoketoconazole successfully attenuated these hormones, facilitating a smooth surgical procedure and favorable postoperative outcome.

REFERENCES

1. Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2015;100(8):2807-2831. doi:10.1210/jc.2015-1818.

MED-US-LEV-25-00024