

Discontinuation of Antihypertensives and Insulin in a Patient With Difficult-to-Control Type 2 Diabetes and Hypertension After Treatment With Levoketoconazole

Poster # 19

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Background

Hypercortisolism is defined as a clinical state of prolonged exposure to excess cortisol from exogenous or endogenous sources, the latter being Cushing's Syndrome (CS).^{1,2} The most common cause is an ACTH-secreting pituitary adenoma (Cushing Disease); less common sources are the adrenal gland or an ectopic ACTH-secreting tumor. Endogenous CS is a rare disorder with classic features consisting of "buffalo hump," moon facies, purple striae, thinning skin, and central obesity.³ More recently, patients with less severe hypercortisolism have been observed to have mild autonomous cortisol secretion (MACS) due to adrenal adenomas or hyperplasia but without typical external characteristics.⁴ Patients with hypercortisolism present with a higher prevalence of cardiovascular risk factors including hypertension (HTN), hyperlipidemia, diabetes mellitus (DM), obesity, and comorbidities such as osteoporosis, mood disorders, and immunosuppression.^{1,2} Furthermore, CS and MACS have been associated with an increased risk of cardiovascular events and mortality.⁵ Hypercortisolism has reportedly been present in 5-10% of patients with seemingly uncontrolled HTN and DM.⁴ Studies have also indicated that a large proportion of patients with poorly controlled DM, despite treatment with multiple antidiabetic medications, have hypersecretion of cortisol as a causative factor.⁴ Therefore, patients with poorly controlled HTN and DM warrant further investigation into possible causes.

Purpose

Prompt diagnosis and treatment is critically important due to the increased morbidity and mortality.^{1,2} MACS is diagnosed based on an abnormal early morning serum level of cortisol >1.8 µg/dL utilizing the 1 mg overnight dexamethasone suppression test (1 mg-DST). This is followed by adrenocorticotrophic hormone (ACTH) and dehydroepiandrosterone sulfate (DHEAS) levels which confirm the adrenal gland as an ACTH independent source.⁶ Patients may not always have a culprit lesion on imaging which makes medical, rather than surgical intervention, the appropriate treatment approach. Current guidelines suggest that comorbidities not meeting standard target numbers warrant further intervention.⁷ Presented here is a patient with uncontrolled HTN and DM with multiple comorbidities treated with levoketoconazole (LKZ), a cortisol synthesis inhibitor approved to treat CS, with subsequent cardiometabolic improvement.

Table 1: Labs evaluating HPA axis

Labs	NML range	Sept 2024	Mar 2025	Feb 2026
DST (µg/dL)	≤1.8	1.78	3.22	2.21
DEX (ng/dL)	140-550	484		
DHEAS (µg/dL)	42-290	175		60
ACTH (pg/mL)	10-60	35		20

ACTH, adrenocorticotrophic hormone; DEX, serum dexamethasone; DHEAS, dehydroepiandrosterone sulfate; DST, dexamethasone suppression test; NML, normal.

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Methods

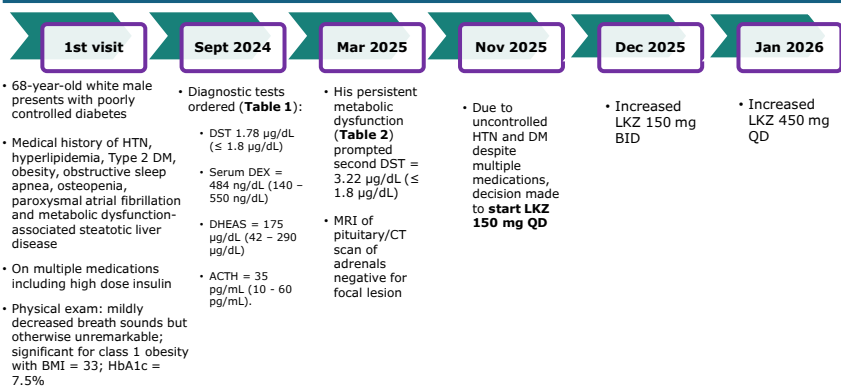


Table 2: Vital signs and metabolic labs

Labs	NML range	Sept 2024	Mar 2025	June 2025	Sept 2025	Nov 2025	Dec 2025	Feb 2026	Mar 2026	Apr 2026	July 2026
BP (mm Hg)	< 130/80	148/72	157/89	113/73	104/71		101/69	109/72	127/84		125/79
HR (bpm)	60-100	109	84	106	101		84	78	81		
HbA1c (%)	<6.5	7.1	7.5	7.5		6.9				6.0	
Wt (lb)		228	223	223	220	223	211	206	197		188

BP, blood pressure; HbA1c, hemoglobin A1c; HR, heart rate; NML, normal; Wt, weight.

Results

1 mo after LKZ	2 mo after LKZ	4 mo after LKZ	5 mo after LKZ	8 mo after LKZ
- LKZ increased to 150 mg twice daily (Table 3) - Insulin glargine decreased from 90 units to 72 units - Olmesartan decreased to 20 mg QD	- LKZ increased to 450 mg daily - D/C HCTZ - Insulin glargine decreased from 72 units to 30 units	D/C insulin glargine & amlodipine	- D/C olmesartan - HbA1c decreased from 6.9% to 6.0%	- Metoprolol decreased from 75 mg to 25 mg BID - Metformin ER decreased from 2000 mg to 1500 mg QD - Started on irbesartan 75 mg QD - All other medications continued - Wt decreased to 188 lbs and BP was at 125/79 mm Hg

Conclusion

This case study suggests that LKZ is an effective treatment option for patients with poorly controlled Type 2 DM and HTN and documented hypercortisolism or MACS. Our patient did not exhibit a lesion upon imaging but otherwise met the criteria for "textbook MACS" and benefited from treatment with LKZ with the discontinuation of 3 antihypertensives along with high dose insulin. Hypercortisolism and MACS may be more common in high-risk metabolic conditions than originally thought.¹ A review by Defronzo RA, et al. has even added hypercortisolism as a contributor to Type 2 DM and terming the organ systems involved as the "Noxious Nine."⁴ One might speculate that although MACS is rather new, it more than likely has not been recognized since many of its comorbidities of HTN, DM, central obesity, infections, cardiac disease, mood disorders, osteoporosis/osteopenia and cognitive dysfunction were seen as age-related phenomena. The prevalence of MACS associated with adrenal incidentalomas increases with aging and is up to 7% in those over age 70.⁸ The potential incidence may be much higher, and recognition and treatment of MACS may have a vital role in the future of Geriatric Medicine.

Table 3: Medications

Medications ^a	Dosage									
	Sept 2024	Mar 2025	June 2025	Sept 2025	Nov 2025	Dec 2025	Jan 2026	Mar 2026	Apr 2026	July 2026
insulin glargine	64 U QAM	+ 90 U QD	NC	NC	NC	- 72 U QD	- 30 U QD	D/C		
metformin ER	2000 QD	NC	NC	NC	NC	NC	NC	NC	NC	-1500 QD
empagliflozin	25 QD	NC	NC	NC	NC	NC	NC	NC	NC	25 QD
semaglutide	2 QWK	NC	NC	D/C						
tirzepatide				15 QWK	NC	NC	NC	NC	NC	15 QWK
apixaban	5 BID	NC	NC	NC	- 2.5 BID	NC	NC	NC	NC	2.5 BID
metoprolol tartrate	75 BID	NC	NC	NC	NC	NC	NC	NC	NC	- 25 BID
amlodipine	5 QD	NC	NC	NC	NC	NC	NC	D/C		
HCTZ	12.5 QD	NC	NC	NC	NC	NC	D/C			
olmesartan	40 QD	NC	NC	NC	NC	- 20 QD	NC	NC	D/C	
irbesartan										75 QD
atorvastatin	20 QD	NC	D/C							
rosuvastatin			20 QD	NC	NC	NC	NC	NC	NC	20 QD
icosapent ethyl		2 gm BID	NC	NC	NC	NC	NC	NC	NC	2 gm BID
LKZ					150 QD	+ 150 BID	+ 450 QD	NC	NC	450 QD

^a in milligrams unless otherwise noted; (+), increased dose; (-), decreased dose; BID, twice daily; D/C, discontinued; ER, extended release; HCTZ, hydrochlorothiazide; LKZ, levoketoconazole; NC, no change; QD, each day; QWK, once weekly.

