Unique Diagnostic Challenges of Cushings From Large Bilateral Adrenal Adenoma and Mifepristone Utilization for Hypercortisolism Prior to Surgery

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ABSTRACT

A 47 year old female was found to have a 1.8 x 4.9 cm right adrenal nodule and 3.8 x 4.3 cm left adrenal nodule with calcification on her 12 month pain evaluation. Extensive workup was done that was negative for pheochromocytoma and Cushing syndrome. Her work up showed hypothyroidism with laboratory studies revealing high urine free cortisol, unpressed cortisol on 1mg DST and low morning cortisol suppression test (OCTH), 70.1 pmol cortisol with aldosterone 117.9 pmol/L suggestive of Cushing syndrome. CT scan with contrast showed a 1.8 x 4 cm nodule right adrenal with possible invasion. Initial step was right adrenalectomy but was deferred due to the size of the nodule and undetectable ACTH. She had normal Sheehan-S, plasma adrenocorticotropic hormone, adrenocorticotropin levels and aldosterone levels.

Since her adenomas were > 4cm bilaterally, adrenal surgery was indicated due to increased risk of adrenal carcinoma. Adrenal venous sampling (AVS) done with hepatic vein to right adrenal ratio > 5 and right adrenal to left adrenal ratio < 2 suggested bilateral Cushing's based on literature from Mayo Clinic . The evaluation of response is based on clinical evaluation and not laboratory measurements. Side effects include hypokalemia, worsening blood pressure and increase risk for infectious complications and delayed tissue healing. The options of subtotal management of hypercortisolism include ketoconazole, metyrapone and mifepristone. Ketoconazole could not be used due to drug interactions with atorvastatin, and mifepristone is not readily available. Mifepristone has been FDA approved and studied in the SEISMIC trial with positive clinical reports with bilateral cortisol hypersecretion. It was determined patient should undergo resection as it was >100 pg/ml suggesting successful localization of the catheter. Adrenal vein to peripheral cortisol ratio > 4 was consistent with bilateral adrenal secretion. Ratio of left to right adrenal cortisol levels < 2 again was consistent with bilateral cortisol hypersecretion. It was determined patient should undergo unilateral adrenalectomy as it was larger in size compared to the left adrenal adenoma.

CASE & CLINICAL COURSE

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The procedure was deferred as patient needed carotid artery surgery. Patient needed medical management for hypercortisolism during the interim. She also had several comorbidities including uncontrolled hypertension on Metoprolol 65lb(240lbs to 175lb) weight loss, hypertension improved, had complete healing of cellulitis, glucose intolerance, and poor functional status requiring antiobiotics for 10 months, glucose intolerance, and poor functional status requiring atorvastatin which could not discontinued due to her vascular disease.

Following her right adrenal resection, her work up showed suppressed ACTH and suggestive of persistent Cushing’s despite unilateral adrenal resection. She will be evaluated for continued Cushing’s symptoms and will obtain a repeat 11pm salivary cortisol level x 2. She has the left adrenal adenoma intact, measuring >4cm which will need resection in the future. Mifepristone could potentially be used as bridge therapy when surgery needs to be deferred.

Unique Diagnostic Challenges of Cushing’s From Large Bilateral Adrenal Adenoma and Mifepristone for Hypercortisolism Prior to Surgery

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This case had unique diagnostic and management dilemmas. Aldosterone in AVS, reportedly used in case reports, might have helped in diagnosis, given the subtly low right adrenal cortisol and low left adrenal epinephrine levels (likely from phrenic vein dilution) but based on size, bilateral adrenal secretory activity. Mifepristone utilization for hypercortisolism assessment has been used in cases of adrenals venous sampling and this would have provided additional information but was not used in our case. The patient needed medical management for hypercortisolism during the interim before adrenalectomy. Mifepristone is a glucocorticoid receptor antagonist that affinity 18 times greater than that of endogenous cortisol and has been FDA approved for inoperable Cushing’s. The evaluation of response is based on clinical evaluation and not laboratory measurements. Side effects include hypokalemia, worsening blood pressure and increase risk for infectious complications. Persistent hypercortisolism increases the risk of perioperative morbidity by increasing infectious complications and delayed tissue healing. The options of subtotal management of hypercortisolism include ketoconazole, metyrapone and mifepristone. Ketoconazole could not be used due to drug interactions with atorvastatin, and mifepristone is not readily available. Mifepristone has been FDA approved and studied in the SEISMIC trial with positive clinical reports in managing specific signs and symptoms of Cushing’s. The drug was utilized in this case to antagonize the hypercortisolism, which facilitated healing of her chronic cellulitis, optimized her functional status, improved her blood pressure and reduced her weight by greater than 50lbs.

Following her right adrenalectomy, her work up showed suppressed ACTH and suggestive of persistent Cushing’s. She will be evaluated for continued Cushing’s symptoms and will obtain a repeat 11pm salivary cortisol level x 2. She has the left adrenal adenoma intact, measuring >4cm which will need resection in the future. Mifepristone could potentially be used as bridge therapy when surgery needs to be deferred.

Mifepristone Utilization for Hypercortisolism Prior to Surgery

Despite the success of bilateral adrenalectomy, persistant cushing. She will be evaluated for continued Cushing’s symptoms and will obtain a repeat 11pm salivary cortisol level x 2. She has the left adrenal adenoma intact, measuring >4cm which will need resection in the future. Mifepristone could potentially be used as bridge therapy when surgery needs to be deferred.

REFERENCES