CONCLUSION

These results suggest that the genotyping of cf-DNA of APA from AVS samples is promising to detect the somatic mutations present in the APA. However, as AVS is an invasive procedure, genotyping of cf-DNA from peripheral blood may be investigated as an alternative. Therefore, further work is needed to ensure this strategy can be non-invasive as then it can be used as a screening method before AVS.

PP-A-05

ELUCIDATING THE EFFECTS OF MUTATIONS IN Q209 OF GNA11 ON CELL APOPTOSIS IN HUMAN ADRENOCORTICAL CELLS

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OBJECTIVES

Gain-of-function mutations, Q209H, Q209P and Q209L, of GNA11 were recently found to occur in CTNNB1 mutant aldosterone-producing adenomas (APAs). These mutations were also found to be present in the hyperplastic zona glomerulosa adjacent to the double-mutant APAs. This study aims to investigate the effects of GNA11 Q209 mutations on tumorigenesis through measurement of cell apoptosis in the human adrenocortical cell line, HAC15.

METHODOLOGY

HAC15 was transfected with GFP-tagged GNA11 Q209H, Q209L, Q209P or wild-type (WT) plasmids. To note, HAC15, a subclone of H295R cells, inherently has the CTNNB1 S45P mutation. 48 hours post-transfection, cell apoptosis was assessed using the Pacific Blue™ Annexin V/SYTOX™ AADvanced™ apoptosis assay (BD Biosciences, USA). The supernatants and cells were harvested for aldosterone and cortisol determination, and RNA isolation.

RESULTS

HAC15 cells transfected with GNA11 mutants, Q209H, Q209L and Q209P, had elevated aldosterone production compared to WT at 62.4% (p=0.001), 71.2% (p=0.001) and 59.5% (p=0.001), respectively. Cortisol production was only slightly elevated in HAC15 cells transfected with Q209H (19.7%, p=0.01) and Q209L (24.6%, p=0.01), compared to WT. CYP11B2 mRNA expression was also upregulated compared to WT by 3.5 folds (p=0.001) for Q209H, and around 8 folds (p=0.001) for Q209L and Q209P. Analysis of flow cytometric apoptosis assay showed GNA11 mutants did not affect cell apoptosis.

CONCLUSION

The findings suggests that GNA11 Q209 mutation increases aldosterone secretion of adrenocortical cells with no or little effect on apoptosis rate. Further experiments on cell proliferation are needed to rule out whether GNA11 Q209 mutations affects tumorigenesis.

PP-A-06

UTILITY OF ADRENAL VENOUS SAMPLING IN ACTH-INDEPENDENT CUSHING'S SYNDROME PRESENTING WITH BILATERAL ADRENAL ADENOMA

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BACKGROUND

Adrenocorticotropic Hormone (ACTH)-independent Cushing's syndrome in a patient with bilateral adenoma poses a management challenge to clinicians. Utilization of adrenal venous sampling (AVS), as in this case, is instrumental in the precise localization of the functioning adenoma which will ensure the best management for these patients.

CASE

We report the case of a 67-year-old Filipino who presented with gradual weight gain for 3 months described as rounding of the face and increasing abdominal girth. The diagnosis of ACTH-independent Cushing's syndrome was based on undetectable ACTH and an unsuppressed cortisol level by dexamethasone suppression test. CT scan revealed bilateral adrenal adenomas measuring 1.1 x 0.9 cm (APxT) in the right and 1.1 x 1.3 cm (APxT) in the left. AVS was done using cortisol levels adjusted by plasma aldosterone. This successfully lateralized the hypersecretion of cortisol to the left adrenal gland, hence a unilateral laparoscopic left adrenalectomy was done.

Treatment was successful with post-operative laboratory confirmation of adrenal insufficiency. The patient was subsequently placed on glucocorticoid replacement until HPA axis recovery.

CONCLUSION

AVS adjusted by plasma aldosterone is a useful technique in localizing ACTH-independent CS in patients with bilateral adenoma to lateralize the lesion before planned surgery where unilateral adrenalectomy may be performed. Successful lateralization of the lesion may potentially spare the patient from lifetime or continuous corticosteroid replacement. In the unavailability of catecholamine or epinephrine, aldosterone ratio can be used to confirm success of adrenal vein cannulation.

PP-A-07

A CASE OF ECTOPIC CUSHING'S SYNDROME FROM AN OCCULT SOURCE IN A PATIENT WITH DIABETES, HYPERTENSION AND ACUTE PSYCHOSIS: THE DILEMMA IN PLANNING A CURE

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BACKGROUND

A 40-year-old patient with diabetes and hypertension, prior alcohol use and psychotic episodes, presented with accelerated hypertension associated with agitation and erratic behavior. Biochemical assessment revealed normal renal and hepatic function, elevated hepatic enzymes, spontaneous hypokalemia, poor glycemic control and central hypothyroidism.

In view of the patient's facial plethora, obesity, subtle striae and subtle pigmentation of periungual areas, Cushing's syndrome was considered. The baseline cortisol was significantly elevated while the adrenocorticotropic hormone (ACTH) was in the low-normal range. A two-day high-dose dexamethasone suppression test (HDDST) showed around 50% suppression. Imaging studies revealed a normal pituitary structure on MRI and bilaterally enlarged adrenal glands on adrenal CT. Inferior Petrosal Sinus Sampling (IPSS) revealed no gradient. The chest imaging did not reveal any suspicious nodules. Hence, we considered the patient to have an Ectopic Cushing's syndrome with an occult source. Medical therapy using ketoconazole was deferred in view of the elevated hepatic enzymes and psychological status. Following an educated decision with the family, bilateral adrenalectomy was done. The patient had an uneventful post-operative status with improvement of hyperglycemia, hypertension and behavior. Routine adrenal hormone replacement, anti-hyperglycemic and anti-hypertension therapies were continued with no untoward consequences.

CONCLUSION

In cases of clinically symptomatic ectopic Cushing's syndrome where the source remains occult despite expeditious work-up, aggressive management through bilateral adrenalectomy is a beneficial therapeutic option to selected patients such as in this case.