CONCLUSION

Although majority of the patients presented with symptoms related with catecholamine excess, almost one third of the patients had incidental discovery. Incidence of pheochromocytoma recurrence and metastasis in our setting has been shown to be comparable with current available studies. This study has demonstrated a low rate of genetic testing likely due to limited access to the test in our setting.

PP-A-03

HYPOKALAEMIA AND COMORBIDITIES ARE COMMON AT INITIAL PRESENTATION IN PATIENTS WITH PRIMARY HYPERALDOSTERONISM

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OBJECTIVES

Primary hyperaldosteronism (PH) is the most common endocrine cause of hypertension (HTN) and is associated with end organ damage. About 30% of cases present with hypokalemia. Studies on the presentation of PH among the Indian population is lacking. This study evaluated the presenting characteristics of patients with PH from Eastern India.

METHODOLOGY

This is a retrospective study that included Saline Suppression Test (SST) confirmed PH patients.

RESULTS

The study involved seventy-eight confirmed PH patients with mean age of 55 ± 13 years and male-to-female ratio of 1.5:1. Mean duration of HTN was 13.3 ± 7.6 years and 62% had HTN more than 10 years. Mean SBP and DBP was 165.1 ± 13.5 mm Hg and 96.2±14.4 mm Hg, respectively. The mean number of anti-hypertensive medications was 3 ± 0.7. Majority presented with hypertension and hypokalemia (78%), 52% of which were spontaneous while 26% were diuretic-induced. About 14% presented with resistant HTN and 8% with adrenal incidentaloma. Overall, 64% of subjects had resistant HTN. Approximately 16.7% of patients experienced hypokalemic periodic paralysis. Mean serum sodium and potassium levels were 139.4 ± 2.3 mmol/l and 3.08 ± 0.6 mmol/l, respectively. Mean eGFR was 71.8 ± 20.8 ml/min/1.73 m^2, with 39.7% having Stage 3 CKD. Majority (95%) had comorbidities from end organ damages, with 43% having multiple comorbidities.

CONCLUSION

Our study revealed a high proportion of hypokalemia and resistant hypertension at detection of PH suggesting delayed diagnosis. A significant number of patients had comorbid illnesses due to end organ damage at presentation, highlighting the need for awareness, early screening and appropriate management of PH.

PP-A-04

IDENTIFICATION OF ALDOSTERONE E-DRIVER SOMATIC MUTATIONS IN CELL-FREE DNA FROM ADRENAL VEIN SAMPLES OF PRIMARY ALDOSTERONISM PATIENTS

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OBJECTIVES

Cell-free DNA fragments (cf-DNA) of tumour cells are often found in the blood downstream to the tumour due to the high apoptosis/necrosis rate of the cells. Primary aldosteronism (PA), a curable cause of secondary hypertension, is commonly due to an autonomous aldosterone-producing adenoma (APA) that harbours a somatic mutation in an aldosterone-driver gene. We aimed to determine the utility of cf-DNA genotyping from adrenal vein samples (AVS) for aldosterone-driver gene mutations as a biomarker for APA.

METHODOLOGY

Genotyping of cf-DNA from AVS of PA patients was performed using the Agena MassARRAY platform. In this study, six samples of cf-DNA from three PA patients were interrogated.

RESULTS

Of the three PA patients, two had unilateral APA and one had bilateral APA. Of the six cf-DNA samples, two samples from the same patient (right adrenal and left adrenal) were found to have a mutation in an aldosterone-driver gene. Genotyping of the cf-DNA of the right AVS yielded a CTNNB1 S45P mutation whereas the cf-DNA of the left AVS had a KCNJ5 G151R mutation.

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.