

database will provide a high level of feasibility for management of PA in China.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Rescue of Function of Inactivating Mutations in Human GPCRs in the Reproductive Hypothalamic-Pituitary-Gonadal Axis

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Inactivating mutations have been described for human GPCRs at all levels of the reproductive hypothalamic-pituitary-gonadal (HPG) axis which results in reproductive incompetence. The majority of the mutations in GPCRs give rise to misfolding and a failure to traffick to the cell surface. We have interrogated data bases for cell-permeant small molecules which bind to and stabilise the GPCR as it emerges from the endoplasmic reticulum and hence facilitate trafficking of the mutant GPCR to the cell membrane and restoration of function. In this way we have successfully 'rescued' function of mutant Neurokinin B, GnRH, LH and FSH receptors using small molecule antagonists which bind orthosterically or agonists which bind allosterically. These discoveries represent an advance towards novel personalized medicine for GPCR deficiencies in the human HPG axis.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Ectopic ACTH Secretion Has Varied Presentation and Requires Individualized Treatment - One Size Does Not Fit All

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Ectopic ACTH secretion (EAS) presents in myriad ways. We present five cases of EAS to highlight similarities and differences in presentation and treatment. The first woman with known metastatic lung neuroendocrine tumour (NET) for two years presented with facial fullness, proximal weakness, worsening hypertension and hypokalaemia. Random cortisol of 2742nmol/L (99.39mcg/dL), with adrenocorticotrophic hormone (ACTH) of 201ng/L (5-50), was in keeping with EAS. She received medical treatment followed by bilateral adrenalectomy with EAS resolution and development of adrenal insufficiency. She is doing well. The second woman with proximal weakness was evaluated by neurologists. All neurological tests were normal but facial fullness and easy bruising was noted. Random cortisol was 875nmol/L (31.71mcg/dL) and ACTH was 90 ng/L. Imaging revealed metastatic liver disease with unknown primary and biopsy confirmed NET. Cortisol

rose despite medical treatment and she died within fifteen months. The third woman with significant smoking history presented with haemoptysis and breathlessness. A right lung mass was suspected on chest X-ray and confirmed with CT. Endobronchial ultrasound-guided biopsy revealed small cell lung cancer (SCLC). She developed generalised weakness and severe hypokalaemia. Random cortisol of 1645nmol/L (59.63mcg/dL) with ACTH of 282ng/L suggested EAS. Despite medical treatment, she died within two weeks. The fourth woman presented with confusion, hypertension and severe hypokalaemia. Morning cortisol of 8557nmol/L (310.19mcg/dL) and random ACTH of 73ng/L were suggestive of EAS. CT demonstrated left lung mass with widespread metastases. She deteriorated and died within 2 weeks. Our only man had incidentally discovered metastatic liver lesions on ultrasound. Further imaging revealed prostatic mass and biopsy showed small cell neuroendocrine cancer. He presented with severe hypokalaemia. Random cortisol was 1065nmol/L (38.61mcg/dL) and ACTH was 188ng/L. He was commenced on medical treatment but declined rapidly and died.

All our patients had profound hypokalaemia and metastatic disease at presentation. Many patients do not exhibit classical cushingoid features as EAS tends to develop acutely and underlying malignancy drives weight loss. A high index of suspicion is required to make a diagnosis. EAS should be considered in patients with proximal myopathy, pigmentation, resistant or severe hypokalaemia or hypertension and known or suspected malignancy. Early and quick control of cortisol excess is essential to minimise cardiometabolic abnormalities, severe infections and thromboembolic complications. Prognosis depends upon age, frailty, comorbidity, nature of neoplasm and extent of hypercortisolaemia. Adrenolytics with or without bilateral adrenalectomy, reduction in tumour burden and management of complications are the mainstay of treatment.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Necrotising Fasciitis- Importance of Glycemic Control

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Necrotising Fasciitis- Importance of glycemic control

Introduction:

Necrotising fasciitis is an infection of the deep soft tissues characterised by fulminant tissue destruction, systemic toxicity and high mortality. We report a case where accurate diagnosis, timely surgical intervention and antibiotic therapy along with strict glycemic control resulted in a favourable outcome.

Case:

A 74 year old woman with a history of type 2 diabetes mellitus, hypertension and end stage renal disease(ESRD) on peritoneal dialysis(PD) presented to the emergency department with the complaint of pain in the right lower quadrant of abdomen, right pelvis and right groin since 4 days which acutely worsened overnight. Of note the patient has Peritoneal catheter for dialysis and was last dialysed last