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Severe Bacterial and Opportunistic Infections in Endogenous Cushing's Syndrome: A Case Series

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INTRODUCTION
Cushing's syndrome is a clinical condition characterised by elevated serum cortisol levels from either exogenous or endogenous glucocorticoids. Hypercortisolemia impairs immune function and increases host susceptibility to bacterial, viral and fungal infections. We report two cases of endogenous Cushing's that succumbed to severe bacterial and opportunistic infections.

CASE 1:
A 69-year-old lady with diabetes and hypertension presented with lower limb weakness, easy bruising and severe hypokalemic alkalosis. Biochemical investigations confirmed Cushing's as demonstrated by elevated 24-hour urine cortisol and non-suppressible cortisol after overnight and low dose dexamethasone suppression test. Adrenocorticotropic hormone (ACTH) was suppressed while dehydroepiandrosterone sulfate (DHEAS) and androstenedione were elevated. Magnetic resonance imaging of the abdomen revealed an adrenocortical carcinoma with liver and lung metastases. She required high doses of insulin, potassium and ketoconazole to control her disease. She developed severe Klebsiella pneumonia with aspergillosis and finally expired.

CASE 2:
A 59-year-old lady was diagnosed with ACTH-dependent Cushing's syndrome when she presented with weight gain, hirsutism and persistent hypokalemia. Initial workup revealed a mediastinal mass which was reported as a neuroendocrine tumour by biopsy. Biochemical investigations were consistent with Cushing's, with elevated serum ACTH. She was given ketoconazole and metyrapone and was subsequently admitted for hospital-acquired and opportunistic fungal pneumonia. She underwent removal of the mediastinal tumour. Post-surgery, her disease was still active with a residual tumour. Ketoconazole was restarted but she succumbed to Salmonella sepsis despite aggressive treatment.

CONCLUSION
Patient's with Cushing's syndrome are susceptible to severe and life-threatening infections. The diagnosis of infections is often made late because the signs and symptoms are often masked by hypercortisolemia. Treatment with anti-cortisol drugs often unmasks infections. Hence, there is a need for a high index of suspicion in order to diagnose opportunistic infections early.

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Treatment Modalities for Advanced Metastatic VIPoma: A Case Report

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INTRODUCTION
Pancreatic neuroendocrine tumors (pNET) secreting vasoactive intestinal peptide (VIP) are rare tumors, with an annual incidence of 1 per 10 million individuals. The diagnosis is made based on a combination of laboratory evaluation (serum VIP level), imaging findings [functional positron emission tomography-computed tomography (PET-CT)] and histological analysis. The first line of treatment is still surgical excision in benign and non-metastatic disease. However, there is no accepted standard management for patients with metastatic disease, which is seen in 60 to 80% of cases.

METHODOLOGY
We present a case that highlights the challenges in managing metastatic unresectable VIPoma. This is also the first case report in Malaysia using peptide receptor radionuclide therapy (PRRT) as the treatment for metastatic unresectable VIPoma.

RESULTS
We present a case of 62-year-old Chinese gentleman who presented with chronic diarrhoea since 2014. Initial investigation revealed a pancreatic mass at the tail of the pancreas measuring 6.5 cm x 5.2 cm. He underwent distal pancreatectomy and splenectomy. Histopathology report showed a grade 1 pNET with a Ki67 index of <2% and negative margins. He remained asymptomatic post-surgery until 2017, when surveillance CT scan showed a local recurrence at the body of pancreas measuring 2.0 cm x 2.2 cm with multicentric liver lesions, the largest of which measured 4.5 cm x 3.1 cm in segment VIII and 3.6. cm x 3.9 cm in segment IVa. Trans-arterial hepatic chemo-embolization was deemed unsuitable. Since March 2018, the patient had multiple hospitalisations for profuse watery diarrhoea, severe electrolyte imbalance and

metabolic acidosis. A trial of short-acting Sandostatin was able to alleviate the symptoms temporarily. He was then started on Octreotide LAR 30 mg every 4 weeks, which dramatically improved his diarrhoea. Unfortunately, the effect of Octreotide LAR was transient. In view of refractory diarrhoea despite the combination of short- and long-acting somatostatin analogues, systemic therapy via PRRT was started in October 2018.

CONCLUSION

PRRT offers a step-change in the therapeutic options for functioning pancreatic neuroendocrine tumour. However, data on the efficacy of this treatment on individual functional pNET secreting VIP is still lacking.

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Characteristics of Primary Hyperparathyroidism in a Tertiary Referral Centre and Incidence of Hungry Bone Syndrome

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INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrine disorder discovered by routine biochemical screening. The most commonly reported aetiologies are parathyroid adenoma (80 to 85%), parathyroid hyperplasia (15%) and parathyroid cancer (5%). This condition is associated with excess morbidity and mortality.

METHODOLOGY

We described the clinical characteristics, biochemical findings and treatments that influence the outcome of parathyroidectomy and the incidence of hungry bone syndrome in our PHPT patients. We conducted a retrospective review of confirmed PHPT cases who underwent parathyroidectomy in Hospital Putrajaya, an endocrine referral centre, from January 2002 to February 2018. Electronic medical records were reviewed and patient details such as clinical data, laboratory results, medications, imaging, surgical treatment and post-operative outcomes were analysed using SPSS 17.

RESULTS

Of the 345 patients included for analysis, majority were female (n=228, 66.1%) with a mean age of 52.15 years (±14.78), with 141 subjects (41%) younger than 50 years. Majority were Malays (41.4%), followed by Chinese (38.8%) and Indian (17.7%). Hypercalcemic manifestations were seen in 82.8%, presenting as renal calculi (46.4%), bone pain (30.1%), fatigue (17.1%), gastritis (14.2%) and fracture (5.5%). While mean serum calcium at presentation was 3.10 mmol/L (±0.61), 82.6% had serum calcium more than 2.85 mmol/L and 17.2% had severe hypercalcemia (≥3.5 mmol/L). Mean levels of serum phosphate, intact parathyroid hormone and alkaline phosphatase were 0.79 mmol/L (±0.25), 27.95 pmol/L (range 5.5 to 616) and 126 IU/L (range 28 to 2879), respectively. The mean estimated glomerular filtration rate (eGFR) was 38.3 mL/min/1.73 m^2, with renal impairment (eGFR <60 mL/min/1.73 m^2) in 38.6%. Nearly two-thirds received at least one medical therapy preoperatively (saline diuresis, bisphosphonate or subcutaneous calcitonin). Majority of the cases were histologically confirmed adenoma (76.7%), with the rest being hyperplasia, normal or carcinoma. Hungry bone syndrome postoperatively was seen in 10.8%.

CONCLUSION

PHPT cases in our setting were more symptomatic, with higher serum calcium levels and more frequent findings of nephrolithiasis and renal impairment.

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Catecholamine Requests in Malaysia: Hospital Kuala Lumpur's Experience

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INTRODUCTION

The Chemical Pathology Unit in Hospital Kuala Lumpur is one of the centres that offer 24-hour urinary catecholamines in Malaysia. Urinary catecholamine determination is a specialised and expensive test offered in limited centres in Malaysia. It is important to reduce inappropriate requests as they can make up a large proportion of laboratory workload leading to unnecessarily increased cost. We review the clinical indications and the significance of results obtained for each catecholamine request sent to our laboratory.

METHODOLOGY

This is a retrospective study involving all requests for 24-hour urinary catecholamine tests sent from all over Malaysia that were available from 2014 until 2016. Clinical indications for requesting the test were reviewed based on information provided in the request forms. Catecholamine results were gathered from the laboratory information system. Clinical indications were classified into 5 categories. Results were tabulated into 3 groups: normal, borderline and abnormal.