

are important for comparison and understanding of the spectrum of DTC worldwide. In Saudi Arabia, DTC is the 3<sup>rd</sup> most common cancer in general and the second most common in females after breast cancer. King Faisal Specialist Hospital and Research Centre is the main tertiary care referral center that manages the vast majority of DTC in the country. In this study, we describe the clinical and histopathological features and the management and outcome of a large series of 814 patients (pts) managed during the period Jan. 2004-Dec. 2006. Data were collected from electronic medical records. Thirty-seven pts were medullary and anaplastic thyroid cancers and 31 pts had incomplete data and were excluded from further analysis. The remaining 746 pts of DTC were studied in detail. There were 154 males (20.6%) and 592 females (79.4%). The median (range) age at the time of diagnosis was 38 years (6-83). Total thyroidectomy was performed in 719 pts (96.4%) while the other 27 pts had partial thyroid surgery. Central and/or lateral lymph node dissection was performed in 545 pts (73%).

The tumors were classic papillary thyroid cancer (PTC) in 539 (72.3%) pts, follicular variant PTC in 103 (13.8%), tall cell variant PTC in 22 (2.9%), diffuse sclerosing type PTC in 10 (1.3%), follicular thyroid cancer (FTC) in 22 (2.9%), Hurthle cell cancer in 10 pts (1.3%) and 35 (4.7%) pts with other types of TC. The median tumor size is 2.0 cm (range 0.1-13). The tumors were multifocal in 307 (41.2%), had extrathyroidal extension in 299 (40%) and lymphovascular invasion in 161 pts (21.6%). Minimal to extensive lymph node resection/dissection was performed in 545 pts (73%) and was positive in 323 pts (43.3% of total pts and 59% of those who underwent LN dissection). Distant metastases were found in 96 pts (12.9%). Using TNM staging system version 8, 602 pts (80.7%) had stage 1, 73 (9.8%) stage 2, 11 (1.5%) stage 3, 1 (0.1%) stage 4a, 37 (4.9%) stage 4b and 22 (1.9%) unstageable. Radioactive iodine (I-131) ablation/therapy was given to 646 pts (86.6%) with a median administered activity of 147 mCi (range 14-302). Additional therapies were given to 187 pts and included additional RAI, surgeries and/or external irradiation. Over a median follow up of 7.6 yrs (0.5-13.2), the final outcome was as follows: 432 (58%) were in excellent status, 92 pts (12.3%) in an indeterminate status, 23 pts (3.1%) with biochemically incomplete status, 63 pts (8.4%) with structurally incomplete disease. Death due to DTC occurred in 31 pts (4.2%) while 103 pts (13.8%) were lost for follow up and their status is not clear.

Conclusions: Compared with data from North America and Europe, DTC in Saudi Arabia occurs at a much earlier age, is frequently metastatic at presentation and is associated with a higher mortality.

## Adrenal

### ADRENAL CASE REPORTS I

#### **Management of VHL-Associated Pheochromocytoma in Pregnancy**

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#### SAT-212

Management of Pheochromocytoma and Von-Hippel Lindau Syndrome in Pregnancy

**Background:** The appropriate treatment of pheochromocytoma during pregnancy is crucial because, while its incidence is rare (0.007%), it is associated with increased maternal and fetal mortality<sup>1</sup>.

**Clinical Case:** A 32 year old Caucasian primigravida female presented with intrauterine pregnancy at 25 weeks for evaluation and management of a 9 mm left adrenal mass. The patient was previously diagnosed at age 10 with Von-Hippel Lindau (VHL) syndrome and genetic testing was positive for a VHL gene mutation (Type 2C VHL). At age 14, she underwent laparoscopic adrenalectomy to excise a right sided pheochromocytoma. At age 20, imaging revealed an enhancing left adrenal mass with imaging characteristics consistent with pheochromocytoma and with catecholaminergic labs that were normal or only mildly increased to 1.5 times upper normal range. Pre-partum the patient had been experiencing periodic episodes of headaches and palpitations. She reported experiencing baseline levels of palpitations and sweating with new onset of pre-syncope and hypotension during her pregnancy. Labs revealed normal serum levels of fractionated free metanephrines. Alpha adrenergic blockade, beta adrenergic blockade, and surgery were considered but deemed unnecessary as the patient was asymptomatic, imaging indicated the left adrenal mass was stable in size, and the patient wished to avoid lifelong adrenal replacement therapy. The patient's blood pressure and heart rate were monitored closely throughout pregnancy and the use of alpha blockade or beta blockade was not needed. The patient had an uncomplicated induced delivery at 39 weeks. MRI with contrast of abdomen performed 10 months postpartum confirmed the presence of an enhancing 8 mm lesion on the inferior pole of the left adrenal gland with imaging characteristics again consistent with pheochromocytoma.

**Conclusion:** This case demonstrates that a conservative approach of monitoring blood pressure and heart rate can be sufficient and appropriate for management of some patients with pheochromocytoma and VHL during pregnancy.

Citation:

1. ENDOCRINOLOGY IN PREGNANCY: Pheochromocytoma in pregnancy: case series and review of literature in: European Journal of Endocrinology Volume 177 Issue 2 (2017).

## Neuroendocrinology and Pituitary PITUITARY TUMORS II

### **Acute, Life-Threatening and Perioperative Complications in Cushing's Syndrome: Predictors and Outcomes**

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#### MON-318

Introduction

Cushing's syndrome is associated with significant chronic and acute comorbidities including acute thromboembolic

and cardiovascular events. To date, there are no data on the prevalence and predictors of acute and perioperative complications in patients with active Cushing's syndrome.

#### Methods

In a single-center cohort analysis we evaluate predictors and outcomes of acute, life-threatening and perioperative complications in patients with active biochemically verified Cushing's syndrome attending our endocrine department between 1978 and 2016. Any medical complications necessitating hospitalization, including admission to intensive care units (ICUs), from the time of appearance of first symptoms of hypercortisolism until one year after biochemical remission by surgery (or where surgical remission was not achieved, during continuing follow-up) were recorded and classified. Baseline factors related to and predicting acute complications were tested using uni- and multivariate analysis.

#### Results

The study included 242 patients (m/f n=54/188) with Cushing's syndrome (pituitary n=99, adrenal n=116, ectopic n=27), 14.0% of which had malignant disease.

At least one acute complication was observed in 54.5% of patients; these included electrolyte disturbances (24.4%), infections (27.7%), thromboembolic events (14.9%), cardiac arrhythmias necessitating medical intervention (5.4%), hypertensive crises (8.7%), acute coronary events (3.3%) and cerebrovascular events (4.1%). At least one ICU admission (excluding post-surgical observance) was required in 13.2% of patients. The majority of complications occurred prior to surgery (60-90%); infections occurred pre- and postoperatively (51.7% vs 48.3%, respectively).

Patients with ectopic Cushing's syndrome demonstrated a higher likelihood of infection ( $p<0.001$ ), hypokalemia ( $p<0.001$ ) and ICU stays ( $p=0.009$ ) compared to patients with pituitary or adrenal Cushing's syndrome. Patients with diabetes mellitus at diagnosis (n=81) had a significantly higher frequency of infection ( $p<0.001$ ), hypokalemia ( $p<0.001$ ), hypertensive crises ( $p=0.004$ ), acute coronary events ( $p=0.029$ ), arrhythmias ( $p=0.025$ ) and a higher likelihood of an ICU stay ( $p<0.001$ ).

The total number of acute complications and the number of days at ICU correlated positively with parameters of cortisol excess including urinary free cortisol and the time of hypercortisolism.

#### Conclusion

This cohort analysis identifies a significantly high prevalence of acute and perioperative complications in Cushing's syndrome, with one in eight patients suffering a life-threatening situation necessitating ICU admission. These acute complications are positively predicted by the degree of hypercortisolism, emphasizing the necessity for acute interventions aiming to reduce cortisol excess even before definitive disease cure is achieved.

## Adrenal

### ADRENAL CASE REPORTS I

#### *Parotid Carcinoma Ex Pleomorphic Adenoma Can Produce Ectopic ACTH Too*

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### SAT-213

**Background:** Ectopic ACTH syndrome accounts for about 14% of Cushing syndrome cases. Small cell lung cancer is the most common cause. A few case reports described ectopic ACTH syndrome in patients with parotid acinic cell carcinoma. Parotid carcinoma ex pleomorphic adenoma is a malignant transformation within a pleomorphic adenoma, which is mostly adenocarcinoma not otherwise specified, but other subtypes can occur.

**Clinical Case:** A 41-year old man with parotid cancer and hypothyroidism was admitted to the hospital for hypokalemia (2.1 mmol/L, n: 3.5-5 mmol/L). Parotid cancer was diagnosed a year before admission. At that time, he underwent left parotidectomy, and pathology showed carcinoma ex pleomorphic adenoma with areas of acinic cell carcinoma. Despite chemoradiation, he was diagnosed with metastasis in the lungs, for which pembrolizumab was started. Over the two months prior to admission, he gained 20 lb, and developed lower extremity weakness, acne, erectile dysfunction and loss of libido. He was also diagnosed with hypertension and started to have mild hypokalemia. Suspecting hyperaldosteronism, oncology team ordered labs just prior to admission, which showed the hypokalemia of 2.1 mmol/L, hyponatremia (147 mmol/L, n: 133-143 mmol/L), normal aldosterone and renin, and high cortisol (59.12 mcg/dL, n: 3-22 mcg/dL) and ACTH (121 pg/mL, n: 9-50 pg/mL).

In the hospital, potassium was slowly improving despite aggressive replacement, and blood pressure was still elevated despite increasing his lisinopril dose. Screening for Cushing syndrome revealed an abnormal 1 mg dexamethasone suppression test (cortisol 51.9 mcg/dL, n: <1.8 mcg/dL), and high 24-hour urinary free cortisol (6495 mcg/24h, n: 3.5-45 mcg/24h) and midnight salivary cortisol (2610 ng/dL and 4250 ng/dL, n: <100 ng/dL). Cortisol was not suppressed after 8 mg dexamethasone (cortisol 47.85 mcg/dL, pretest cortisol 48.73 mcg/dL) pointing toward ectopic ACTH syndrome. Spironolactone was started and titrated up to 100 mg BID with better control of hypertension and normalization of potassium. Ketoconazole was started at 200 mg TID and increased gradually as outpatient to 400 mg TID within three weeks. A repeat 24-hour urinary free cortisol was done five weeks after ketoconazole was started showing significant improvement (110 mcg/24h, n: 3.5-45 mcg/24h). Potassium requirements remarkably decreased from 80 mEq TID to 40 mEq daily. Of note, chest CT done during hospitalization showed new lung lesions despite treatment with pembrolizumab.

**Conclusion:** This is the first case of ectopic ACTH syndrome to be described in a patient with parotid carcinoma ex pleomorphic adenoma, though areas of acinic cell carcinoma within the tumor can be the source of ACTH. Hypercortisolism due to ectopic ACTH secretion is usually of rapid onset, and can present with severe hypokalemia. Steroid synthesis inhibitors seem to be an effective therapy.

## Genetics and Development (including Gene Regulation)

### ENDOCRINE DISRUPTING CHEMICALS

#### *Bisphenol-A Alters Pancreatic B-Cell Proliferation and Mass in an Estrogen Receptor Beta-Dependent Manner*

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