Cushing's syndrome

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Cushing's syndrome (CS) results from chronic exposure to excess glucocorticoids, which can be from either exogenous supraphysiologic doses of corticosteroids (exogenous or iatrogenic CS, the most common cause of CS) or from an endogenous source of cortisol (endogenous or spontaneous CS). It is a severe disease due to the complications of glucocorticoid excess. The increased morbidity and mortality in these patients is due to the cardiovascular, thrombotic, metabolic, infectious and musculoskeletal complications. Mortality in CS (non-malignant causes) is increased, with a standard mortality ratio roughly between 2.0 and 4.0; cardiovascular deaths are most common. Most studies indicate that early diagnosis is important to reduce mortality and morbidity.

Endogenous CS is rare, with an incidence of 0.7 − 2.4 per million population per year. Median age of onset/diagnosis was 41.4 years with a female to male ratio of 3:1. Endogenous CS is divided between ACTH-independent (unilateral or bilateral adrenal adenoma or carcinoma, primary pigmented nodular adrenocortical disease, ACTH-independent bilateral macronodular adrenocortical hyperplasia) and ACTH-dependent (Cushing's disease, ectopic ACTH or CRH syndrome) causes. In Caucasians, ACTH-independent and ACTH-dependent CS accounts for 15% − 20% and 80% − 85%, respectively. In Taiwan (Kaohsiung CGMH and NTUH), ACTH-independent and ACTH-dependent CS accounts for 59% − 75% and 25% − 41%, respectively. The clinical presentation of CS is variable. It is influenced by age and sex and the severity and duration of the disease. No single sign or symptom is pathognomonic. More common signs and symptoms of CS include obesity or weight gain, moon face, facial plethora, buffalo hump, violaceous/pinkish striae, ecchymosis, hirsutism, menstrual irregularity, decrease libido, muscle weakness, osteopenia or osteoporosis, hypertension, dyslipidemia, and glucose intolerance.

Detection of CS relies first on clinical suspicion and then on biochemical confirmation. The following screening tests should be used for the definitive diagnosis of CS: plasma cortisol circadian rhythm, 24-h urinary free cortisol, midnight serum or salivary cortisol, and overnight or 2-day low-dose dexamethasone suppression test. Once the diagnosis of CS has been established, the next step is to differentiate between the ACTH-independent and ACTH-dependent CS. Measurement of plasma ACTH levels is the initial step in the differential diagnosis of the two causes of CS. The high-dose dexamethasone suppression test is based on the concept that corticotrope adenomas retain some sensitivity to glucocorticoid negative feedback, which ectopic-secreting tumors and adrenal CS do not.

Surgical resection of the source of glucocorticoid excess (pituitary adenoma, nonpituitary ectopic ACTH-secreting tumor, or adrenal tumor) remains the first-line treatment of all forms of CS. Transsphenoidal selective tumor resection (TSS) is the optimum initial treatment of Cushing's disease. Second pituitary surgery is a good option when residual tumor is visible or has regrown but is not invasive. Pituitary radiotherapy is a good primary therapy for non-surgical candidates and is a second-line approach persistent or recurrent disease after TSS, particularly when the tumor is invasive and not surgically resectable. Minimally invasive unilateral adrenalectomy is the standard of care for cortisol-secreting unilateral adenoma. Laparoscopic procedures are safe, effective, and less expensive

than open adrenalectomy. Open adrenalectomy is recommended if adrenocortical cancer is suspected. Medical treatments include steroidogenesis inhibitors, tumor-directed drugs, and glucocorticoid receptor antagonists.

Cases report will be presented in the session.