Diagnostic and Management of Patient with Adrenocortical Carcinoma

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ABSTRACT
Endogenous Cushing’s syndrome is a rare case, and about 8% is due to adrenocortical carcinoma. We report a case of a 31-year-old woman with complaints of weight gain, round face, brown lines, menstrual disorders, and limb weakness. On physical examination, there were hypertension, moon face, central obesity, and stroke. On laboratory examination, there were morning serum cortisol levels were 46.87 and ACTH levels 5. On CT scan. It was found that the right adrenal gland solid mass enhancement was +/- 6.6x4.9x7.3 cm, with suspicion of adrenal carcinoma. On histopathological examination, adrenocortical carcinoma was obtained, and capsule invasion was obtained. Patients underwent surgery to remove the tumor, radiotherapy and chemotherapy. The patient was alive and had no residual mass at the surgical bed.

Keywords: Adrenal Carcinoma, Cushing’s Syndrome, Adrenal mass

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INTRODUCTION
Cushing’s syndrome is a syndrome that results from chronic exposure to excess glucocorticoid hormones in the blood. Both endogenous and exogenous factors can cause Cushing’s syndrome. Exogenous factors that cause Cushing’s syndrome are exposure to glucocorticoids from outside the body, while endogenous factors that cause Cushing’s syndrome can be divided into ACTH-dependent and ACTH-independent. ACTH-independent occurs in about 20% of people with endogenous Cushing’s syndrome and about 8% due to adrenocortical carcinoma. Adrenocortical carcinoma is found in many young patients and children, so it needs proper diagnosis and aggressive management. It has been found that further management of adrenocortical carcinoma but with limited efficacy and significant side effects can reduce patients’ quality of life (Rajput, 2013; Terzolo et al, 2013).

CASE REPORT
Mrs. R, 31 years old, female, Batak ethnicity, Catholic, married, residing in Sidoarjo, East Java, BPJS financing. Come to the Endocrine Clinic, dr. Soetomo on May 1, 2017, with a chief complaint of brownish lines on the skin.

From the history, it was found that brown streaks appeared on the body’s skin six months before the patient came to the hospital. Initially, brown streaks appeared on both legs, then appeared on the patient’s stomach. The patient also complained of gaining weight with relatively smaller legs for six months before the patient came to the hospital. The patient’s face also felt increasingly swollen. The patient complained that the skin on the body was getting whiter, thinner, and drier. The patient also felt tired quickly, and the body was often weak. The patient also complained that acne often appeared for seven months before coming to the hospital so that the patient took acne medication from the pharmacy, and the patient forgot the name of the medicine. The patient denied the frequent complaint of swelling in both legs. She also denied the history of frequent fever, shortness of breath. Complaints of frequent hair loss and easy removal were experienced for six months before coming to the hospital. The patient has not had her period for five months. There were no complaints on urination and defecation. The patient had no history of diabetes mellitus, hypertension, asthma, heart disease, tumors, and had never been hospitalized before. The patient’s family did not have the same history of pain as the patient.

The patient had a history of using monthly injectable contraceptives since 2014 and stopped one year ago. The patient denied the history of taking any other drugs. The patient married in 2013 and has one child who was currently 3 years old. The patient was currently working as a kindergarten teacher. The patient did not smoke.

On physical examination, the general condition is good, with GCS 456, blood pressure 139/89, pulse 92x/minute, breathing 16x per minute, and axillary temperature 36.7°C. The examination of the head and neck showed moon face, hyperpigmentation of the lip mucosa, no anemia, jaundice,
The patient was evaluated with an abdominal CT scan, and the results showed no visible mass in the abdominal cavity, no residual or residual mass on the surgical bed.

**DISCUSSION**

Cushing’s syndrome is a syndrome that results from chronic exposure to excess glucocorticoid hormones in the blood. Both endogenous and exogenous factors can cause Cushing’s syndrome. Cushing’s syndrome due to endogenous factors is very rare and is divided into ACTH-dependent and ACTH-independent. ACTH-dependent Cushing’s syndrome can result from excess ACTH secretion from the pituitary gland or ectopic ACTH production, which is usually the result of a neuroendocrine tumor. The ACTH hormone produced by pituitary tumors and those produced by non-pituitary tumors can stimulate the hormone cortisol production from the adrenal glands. ACTH-independent Cushing’s syndrome is caused by excess production of cortisol by the adrenal glands, usually due to benign adrenal tumors or adrenocortical adenomas, while those caused by adrenocortical carcinoma are rare. This excess cortisol production will inhibit CRH and ACTH’s secretion from the pituitary gland (Niemann & Swearingen, 2013; Raff et al, 2014). The mechanism of Cushing’s syndrome can be seen in the image below.

Figure 1. mechanism of Cushing’s syndrome (Niemann & Swearingen, 2013)

The diagnostic criteria for Cushing’s syndrome are obtained from history, physical examination, and laboratory examination. In Cushing’s syndrome, high levels of glucocorticoids in the blood for a long time can cause abnormalities in the metabolic system such as central obesity, weight gain, hyperglycemia, dyslipidemia, hypokalemia, hormonal disorders (menstrual disorders or amenorrhea, delayed puberty), disorders of the musculoskeletal system. (muscle weakness and osteoporosis), disorders of the cardiovascular system (hypertension, venous thromboembolism) and skin manifestations (striae, facial plethora), and neuropsychological manifestations (insomnia, depression, and irritability). Radiological examination in patients with Cushing’s syndrome is useful to determine the tumor’s location as a cause. In laboratory tests, several tests are needed to help make a diagnosis of Cushing’s syndrome. Three laboratory tests required to diagnose Cushing’s syndrome are a 24-hour urine cortisol test, morning serum cortisol, and a low-dose dexamethasone suppression test. To see the cause of Cushing’s syndrome, several tests can be performed, namely, the CRH stimulation
test, High dose dexamethasone suppression test (HDDST), and radiological examinations to see first hand the picture of the endocrine glands (Nieman et al, 2005). The steps to find out the cause of Cushing’s syndrome can be seen in the image below.

To determine the cause of Cushing’s syndrome, the first step that must be done is to check the ACTH levels in the blood. If the ACTH level in the blood is below 15pg/ml, these results indicate ACTH-independent Cushing’s syndrome, and in the next step, a CT or MRI scan of the adrenal glands should be performed. If the ACTH level is above 15pg/ml then these results indicate an ACTH-dependent Cushing’s syndrome, and in the next step, a CT scan or MRI examination of the pituitary gland is performed, a CRH test, and a high-dose dexamethasone suppression test (HDDST). If the ACTH plasma level is above 5 to 15 then careful interpretation and further examination with the CRH test is needed (Price & Grossman, 2007).

The patient complained of weight gain, rounded face, brownish lines on the skin, menstrual disorders, and limb weakness. On physical examination, hypertension, moon face, central obesity, and stroke were found. On laboratory tests, GD2JPP 253, total cholesterol 315, LDL 179, morning serum cortisol levels 46.87, and ACTH 11 levels. A solid mass (34HU), firm boundaries, lobulated edges, size +/- 6,6x4,9x7,3 cm were found in the right adrenal gland with contrast administration on the CT scan. It appears that the contrast enhancement in the right adrenal gland with a size of >11 cm, while cortical adenoma generally has a size of <5 cm. There is currently no single radiological examination that can be used to help establish adrenocortical carcinoma. An abdominal CT scan should be performed in patients with suspected adrenocortical carcinoma. If the abdominal CT scan shows a basal density ≤ 10 HU, it can be suspected that it is a benign lesion. If the basal density is >10 HU and the administration of contrast media in the washout phase helps differentiate benign lesions from adrenocortical carcinoma. If the washout phase is >50%, a benign lesion can be suspected. In addition to an abdominal CT scan, other radiological examinations are also important to show the process of the spread of the tumor. In addition to the radiological examination, an important examination to establish adrenocortical carcinoma diagnosis is histopathological examination. Histopathological examination is used to determine a definite diagnosis of adrenocortical carcinoma. Examination using the FNAB for the biopsy is rarely used because of the risk for needle track metastases, and it is difficult to distinguish whether the lesion is benign or malignant. All patients with adrenal tumors should rule out pheochromocytoma in preparation for surgery (Libe, 2015; Zini L I, 2011).

The patient showed symptoms of Cushing’s syndrome and ACTH 11 levels. A solid mass (34HU), firm boundaries, lobulated edges, size +/- 6,6x4,9x7,3 cm were found in the right adrenal gland with contrast administration on the CT scan. It appears that the contrast enhancement in the venous phase (85HU), delay (63HU) (relative percentage washout) appears to be a small part through the capsule. On histopathological examination, adrenocortical carcinoma and capsule invasion were obtained.

After someone is diagnosed with adrenocortical carcinoma, the next step is to determine the tumor stage. One of the classifications that use the metastatic nodule tumor (TNM) system to determine adrenocortical carcinoma patients’ stage is the ENSAT system. In stage 1, there was a tumor with a size of ≤5cm, and in stage 2, there was a tumor size of > 5 cm, both without finding any spread to the surrounding tissue or far. In stage 3, there is infiltration to the surrounding tissue, lymph nodes, or thrombus in the vena cava and/or renal veins, while in stage 4 there are distant metastases from the tumor. The prognosis of adrenocortical carcinoma is determined by tumor stage, resection status, and tumor grading. The survival rate of adrenocortical carcinoma is divided into 3 groups. First, localized tumors, namely tumors that do not invade the surrounding tissue, obtained a 5-year relative survival of 65%. The second group is regional tumors, namely tumors that invade the surrounding tissue (stage 3), with a 5-years survival rate of 44%, and the third group is tumors that have distant spread or metastasis, with 5 years survival rates of 7% (Libe, 2015). In this patient, on abdominal ultrasound examination, there were multiple nodules on the liver. The
chest x-ray showed no abnormalities.

Treatment of adrenocortical carcinoma consists of surgery, radiation, and chemotherapy. Adrenocortical carcinoma management requires cooperation from various divisions, namely endocrinologists, surgeons, interventional radiologists, and oncologists. The management of patients with adrenocortical carcinoma can be seen in the picture below.

In patients with adrenocortical carcinoma with localized tumors, surgery with total tumor removal is still the primary therapy. Adrenalectomy is also indicated in patients with stage I and II adrenocortical carcinomas, according to ENSAT. Besides, resection is indicated in ENSAT stage III if evidence of loco-regional invasion, including the extension to adjacent organs or the vena cava, is indicated. Another therapy for adrenocortical carcinoma is radiotherapy. Radiation therapy in patients with adrenocortical carcinoma aims to reduce the risk of local recurrence of the tumor. In stage 4, adrenocortical carcinoma with oligometastatic (metastasis in 1 organ) and >80% of the tumor can still be resected, tumor resection can be done, radiotherapy and chemotherapy with mitotane are given, whereas, in patients with multiple metastases, mitotane chemotherapy can be given only. Then the patient is evaluated every 2 months, and if progressive results are obtained, then first-line chemotherapy with etoposide, doxorubicin, and cisplatin can be given. If there is stable disease or response, then chemotherapy with mitotane can be continued (Libe, 2015).

In this patient, surgical removal of the tumor was carried out, followed by 25 radiotherapies and chemotherapy with etoposide, doxorubicin, and cisplatin 8 times.

CONCLUSION
It has been reported that a female patient presents with complaints of weight gain, round face, brownish lines, menstrual disorders, and limb weakness. On physical examination, hypertension, moon face, central obesity, and stroke were found. On laboratory tests, GD2JP 253, total cholesterol 315, LDL 179, morning serum cortisol levels 46.87, and ACTH 5 levels. On CT scan, it was obtained solid mass enhancement of right adrenal gland with a size of +/- 6.6x4.9x7.3 cm. with a relative percentage when washing out, a small portion penetrated the capsule, suspecting adrenal carcinoma. On histopathological examination, adrenocortical carcinoma and capsule invasion were obtained. Patients undergo surgery to remove the tumor, radiotherapy, and chemotherapy.

CONFLICT OF INTEREST
The author declare there is no conflict of interest of this study.

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