Cancer Association of South Africa (CANSA)

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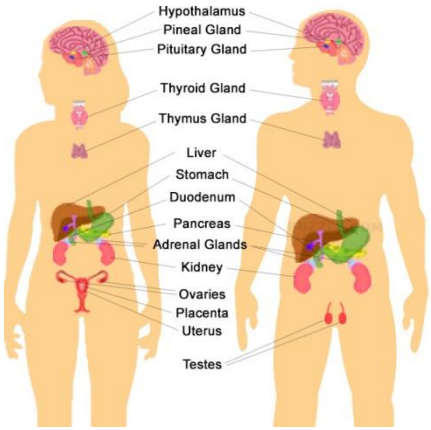
Fact Sheet on Adrenal Gland Cancer

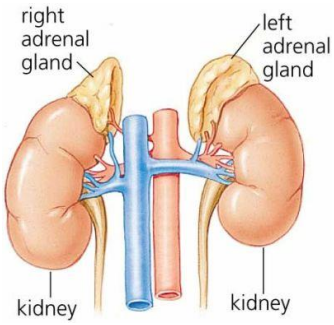
Introduction

A cancerous tumour of the adrenal gland is called an adrenal cortical carcinoma and is a condition where there is abnormal multiplication of cells. A noncancerous tumour of the adrenal gland is called a benign adenoma.



[Picture Credit: Major Endocrine Organs]

A tumour begins when normal cells change and grow uncontrollably, forming a mass. A tumour can be benign (noncancerous) or malignant (cancerous, meaning it can spread to other parts of the body).



Each person has two adrenal glands - one located on top of each of the body's two kidneys. These glands are important to the body's endocrine (hormonal) system. Each adrenal gland has two main parts that function separately:

[Picture Credit: Adrenal Gland]

Torti, J.F. & Correa, R. 2020.

"The adrenal is an endocrine organ that has two physiological functions. The outer adrenal cortex produces steroid hormones, including glucocorticoids such as cortisol, and mineralocorticoids (aldosterone, and the androgen dehydroepiandrosterone. The glucocorticoids play a role in carbohydrate, protein, and fat metabolism. The mineralocorticoids are essential for the sodium (Na) and potassium (K) balance and the maintenance of fluid homeostasis. Glucocorticoids and mineralocorticoids are critical for survival. The inner adrenal medulla produces catecholamines (dopamine, epinephrine, and norepinephrine). Occasionally one does encounter adrenal masses during a routine study. These lesions can categorize as either functional (hormone-secreting) or silent (either benign or malignant). Overall, less than 1% of these tumors are cancerous. The Fourth Edition of the World Health Organization (WHO) classification of endocrine tumors published in 2017 has classified adrenal cancer in two groups. The first includes tumors of the adrenal cortex, and the second group includes tumors of the adrenal medulla and extra-adrenal paraganglia. The key feature of the

WHO classification is the role of genetics that may be involved in adrenal cortical carcinoma and pheochromocytoma/ paraganglioma as well as the inclusion of a few rare malignancies of the adrenal cortex and medulla. The following are tumors of the adrenal cortex: Adrenocortical adenoma (ACA), Adrenal myelolipoma (mesenchymal and stromal tumors) and adrenal adenomatoid tumor are benign neoplasms of the adrenal cortex. The sex cord-stromal tumor of the adrenal gland is rare, and there are only six reports in the literature. Primary hematological tumors are mostly lymphomas and rarely plasmacytoma. Secondary tumors of the adrenal cortex are usually metastatic lesions due to direct infiltration by adjacent cancer or more commonly via hematogenous spread from a distant site. Adrenal metastases are common in patients with advanced cancer. Adrenocortical carcinomas (ACC) are very uncommon; these lesions are less common than cortical adenomas and pheochromocytoma. The worldwide incidence of ACC is 0.5 to 2 per 1 million people annually. However, this neoplasia accounts for 0.02 to 0.2% of all cancer-related deaths. Adrenocortical carcinomas are very aggressive lesions and in some cases may be functional and present with Cushing syndrome and/or virilization. In most cases, ACC is non-functional and presents as an abdominal mass or an incidental finding. As with all adrenal tumors, the presence of local or distant spread defines their malignancy. No absolute criteria of malignancy exist for lesions confined to the adrenal gland, but a Weiss score of 3 or higher, which is determined by histopathological features, is generally an indicator of malignancy."

Long, S.E. & Miller, B.S. 2019.
"Adrenocortical cancer is a rare disease. Prognosis remains poor but is improving. In this article, initial presentation, biochemical and imaging evaluation, surgical approach to resection, and postoperative care are reviewed. Prognosis, patterns of recurrence, treatment of metastatic disease using medical therapy and other surgical and nonsurgical therapies are discussed."

Incidence of Adrenal Gland Cancer in South Africa
The outdated National Cancer Register of 2017 does not provide any statistics regarding the incidence of adrenal gland cancer in South Africa.

Shashank, R.C., Shiva, K.R.M. & Harsha, K. 2020.
"Adrenal metastases are the most common malignant lesions involving the adrenal gland and the second most common tumor of the adrenal gland after benign adenomas. These metastases were primarily found on autopsy. However, with the increasing role of CT, MRI, and PET in diagnosing, staging, and follow-up of malignancies, adrenal metastases are increasingly found incidentally."

Signs and Symptoms of Adrenal Gland Cancer
Some other symptoms of adrenal cancer that produce excess cortisol and aldosterone in adults can include:

- high blood pressure
- high blood sugar
- low potassium levels
- weight gain
- irregular periods
- changes in genitalia
- easy bruising
- nervousness

- feeling of anxiety
- depression
- headache
- excessive perspiration
- frequent urination
- muscle cramps
- excessive hair growth
- changes in libido

Diagnosis of Adrenal Gland Cancer
One or more of the following may be employed in the diagnosis of adrenal gland cancer:

Laparoscopy - this procedure uses a laparoscope, a thin, flexible tube with a tiny video camera on the end. It is inserted through a small surgical opening in the patient's side to allow the surgeon to see where the cancer is growing.

[Picture Credit: Laparoscope]

Biopsy - imaging tests may find tumours, but often the only way to know for sure that a tumour is cancerous is to remove a sample of tumour tissue to look at under the microscope. This is called a *biopsy*.

Tests for adrenal hormones - blood and urine tests to measure levels of adrenal hormones are important in deciding whether a patient with signs and symptoms of adrenal cancer has the disease.
Tests for high cortisol levels - the tests used in this case include measuring levels of cortisol in the blood and in the urine.

Tests for high aldosterone levels - the level of aldosterone will be measured and will be high if the tumour is making aldosterone.

Tests for high androgen or oestrogen

Chest X-ray - this can show if the cancer has spread to the lungs. It may also be useful to determine if there are any serious lung or heart diseases.

Ultrasound - ultrasound tests use sound waves to take pictures of parts of the body.

Molecular markers - studies analysing the role of genes and proteins in a person's tumour are underway. The focus of these studies is to help fine-tune the diagnosis of adrenal gland tumours and predict treatment results.

Computed tomography (CT) - the CT scan is an x-ray procedure that produces detailed cross-sectional images of your body

Positron emission tomography (PET) - in this test, radioactive glucose (sugar) is injected into the patient's vein.

Magnetic resonance imaging (MRI) - MRI scans use radio waves and strong magnets instead of x-rays

Yalniz, C., Morani, A.C., Waguespack, S.G. & Elsayes, K.M. 2020.
"Endocrine disorders associated with adrenal pathologies can be caused by insufficient adrenal gland function or excess hormone secretion. Excess hormone secretion may result from adrenal hyperplasia or hormone-secreting (ie, functioning) adrenal masses. Based on the hormone type, functioning adrenal masses can be classified as cortisol-producing tumors, aldosterone producing tumors, and androgen-producing tumors, which originate in the adrenal cortex, as well as catecholamine-producing pheochromocytomas, which originate in the medulla. Nonfunctioning lesions can cause adrenal gland enlargement without causing hormonal imbalance. Evaluation of adrenal-related endocrine disorders requires clinical and biochemical workup associated with imaging evaluation to reach a diagnosis and guide management."

Igaz, P. 2019.
Purpose of review: Circulating microRNAs represent promising minimally invasive markers of several diseases including tumors. As the preoperative diagnosis of different adrenal tumors is difficult, for example, diagnosis of adrenocortical or adrenomedullary malignancy, circulating microRNAs might be helpful in their clinical management.
Recent findings: Observations regarding the applicability of circulating microRNAs isolated both from unfractionated plasma or serum and from extracellular vesicle preparations for the diagnosis of adrenocortical malignancy have been published. Data show that circulating microRNA might be exploited for monitoring adrenocortical cancer progression. Circulating microRNA profiles of adrenal myelolipoma have also been published that might be useful for differentiating adrenocortical cancer and adrenal myelolipoma in dubious cases.
Summary: In this review, recent advances in the field of circulating microRNAs in adrenal tumors are discussed.

Staging of Adrenal Gland Cancer
Staging is a way of describing where the tumour is located, if or where it has spread and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the tumour's stage.

One tool that doctors use to describe the stage is the TNM system. TNM is an abbreviation for tumour (**T**), node (**N**), and metastasis (**M**). Doctors look at these three factors to determine the stage of cancer. The TNM system tells the doctor:

- How large the primary tumour is and where is it located **(Tumour, T)**
- Whether the tumour has spread to the lymph nodes **(Node, N)**
- Whether the cancer has metastasised to other parts of the body **(Metastasis, M)**

Treatment of Adrenal Gland Cancer
Different types of treatments are available for patients with adrenocortical carcinoma. Some treatments are standard (the currently used treatment), while some are being tested in clinical trials.

Treatment may include:

- Surgery - surgery to remove the adrenal gland (adrenalectomy) is often used to treat adrenocortical carcinoma.
- Radiation therapy - radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing.
- Chemotherapy - chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.
- Biologic therapy - biologic therapy is a treatment that uses the patient's immune system to fight cancer.
- Targeted therapy - is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.

Rosenberg, R., Köberle, R., Becker, P.M. & Meienberg, F. 2020.
"Adrenal tumors **Abstract.** The term 'adrenal tumor' describes benign and malignant mass lesions of the adrenal gland, including primary adrenal tumors and metastases from extra-adrenal origin. With the widespread use of imaging technique, adrenal tumors have become increasingly detected as 'incidentalomas'. The detection of an adrenal tumor raises two questions: Is the mass malignant? Is the mass hormonally active? Whereas the evaluation for malignancy is based on specific imaging characteristics (imaging phenotype), a targeted clinical examination and specific biochemical tests are required to assess for hormonal secretion. An adrenal mass < 4 cm with clear benign features on imaging and with a normal hormonal workup does not require treatment. If malignancy is suspected further diagnostic procedures and / or adrenalectomy are indicated. For hormonally active tumors surgery is generally considered the treatment of choice; however, the decision for surgery has to be individualized for aldosterone-secreting tumors and for cortisol-secreting tumors with only mild cushing's syndrome. Also in patients with large tumors (> 4 cm), and in cases with non-conclusive evaluation for malignancy or hormonal activity, the decision for further management has to be made on an individual basis. A minimally invasive surgical approach may be considered in adrenal tumors < 6 cm and without local infiltration of adjacent structures. Both laparoscopic (transabdominal) and retroperitoneoscopic techniques are possible. The surgical outcome depends on the surgeon's experience. A close interdisciplinary collaboration is mandatory in the evaluation and treatment of adrenal tumors."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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