Uploaded to VFC Website

November 2012

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a 501(c)(3) Non-Profit Corporation
Tax ID #27-3820181

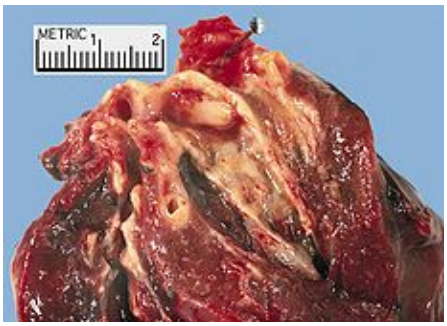
If Veteran's don't help Veteran's, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members.

Adrenocortical carcinoma



Adrenocortical carcinoma, also **adrenal cortical carcinoma** (ACC) and **adrenal cortex cancer**, is an aggressive cancer originating in the cortex (steroid hormone-producing tissue) of the adrenal gland. Adrenocortical carcinoma is a rare tumor, with incidence of 1-2 per million population annually.[1][2] Adrenocortical carcinoma has a bimodal distribution by age, with cases clustering in children under 6, and in adults 30–40 years old.[1]

Adenocortical carcinoma is remarkable for the many hormonal syndromes which can occur in patients with steroid hormone-producing ("functional") tumors, including Cushing's syndrome, Conn syndrome, virilization, and feminization. Adrenocortical carcinoma has often invaded nearby tissues or metastasized to distant organs at the time of diagnosis, and the overall 5-year survival rate is only 20-35%.[1]

Signs and Symptoms

Adrenocortical carcinoma may present differently in children and adults. Most tumors in children are functional, and virilization is by far the most common presenting symptom, followed by Cushing's syndrome and precocious puberty.[1] Among adults presenting with hormonal syndromes, Cushing's syndrome alone is most common, followed by mixed Cushing's and virilization (glucocorticoid and androgen overproduction). Feminization and Conn syndrome (mineralcorticoid excess) occur in less than 10% of cases. Rarely, pheochromocytoma-like hypersecretion of catecholamines has been reported in adrenocortical cancers.[3] Non-functional tumors (about 40%, authorities vary) usually present with abdominal or flank pain, or they may be asymptomatic and detected incidentally.[2]

All patients with suspected adrenocortical carcinoma should be carefully evaluated for signs and symptoms of hormonal syndromes. For Cushing's syndrome (glucocorticoid excess) these include weight gain, muscle wasting, purple lines on the abdomen, a fatty "buffalo hump" on the neck, a "moonlike" face, and thinning, fragile skin. Virilism (androgen excess) is most obvious in women, and may produce excess facial and body hair, acne, enlargement of the clitoris, deepening of the voice, coarsening of facial features, cessation of menstruation. Conn syndrome (mineralcorticoid excess) is marked by high blood pressure, which can result in: headache hypokalemia (low serum potassium) which can produce muscle weakness, confusion, and palpitations. low plasma renin activity, and high serum aldosterone. Feminization (estrogen excess) is most readily noted in men, and includes breast enlargement, decreased libido and impotence.[1][2][4]

Pathobiology

The main etiologic factor of adrenocortical cancer is unknown. Families with Li-Fraumeni syndrome have increased risk. The p53, retinoblastoma protein (RB) tumor suppressor genes located on chromosomes 17p, 13q respectively, may be changed. The genes h19, insulin-like growth factor II (IGF-II), $p57^{kip2}$ are important for fetal growth and development. They are located on chromosome 11p. Expression of the h19 gene is markedly reduced in both nonfunctioning and functioning adrenal cortical carcinomas, especially in tumors producing cortisol and aldosterone. There is also a loss of

activity of the $p57_{kip2}$ gene product in virilizing adenomas and adrenal cortical carcinomas. In contrast, IGF-II gene expression has been shown to be high in adrenal cortical carcinomas. Finally, c-myc gene expression is relatively high in neoplasms, and it is often linked to poor prognosis. [5]

Diagnosis

Laboratory findings

Hormonal syndromes should be confirmed with laboratory testing. Laboratory findings in Cushing syndrome include increased serum glucose (blood sugar) and increased urine cortisol. Adrenal virilism is confirmed by the finding of an excess of serum androstenedione and dehydroepiandrosterone. Findings in Conn syndrome include low serum potassium, low plasma renin activity, and high serum aldosterone. Feminization is confirmed with the finding of excess serum estrogen

Radiology

Radiological studies of the abdomen, such as CT scans and magnetic resonance imaging are useful for identifying the site of the tumor, differentiating it from other diseases, such as adrenocortical adenoma, and determining the extent of invasion of the tumor into surrounding organs and tissues. CT scans of the chest and bone scans are routinely performed to look for metastases to the lungs and bones respectively. These studies are critical in determining whether or not the tumor can be surgically removed, the only potential cure at this time. [2]

Pathology

Adrenal tumors are often not biopsied prior to surgery, so diagnosis is confirmed on examination of the surgical specimen by a pathologist. Grossly, adrenocortical carcinomas are often large, with a tan-yellow cut surface, and areas of hemorrhage and necrosis. On microscopic examination, the tumor usually displays sheets of atypical cells with some resemblance to the cells of the normal adrenal cortex. The presence of invasion and mitotic activity help differentiate small cancers from adrenocortical adenomas. [3] There are several relatively rare variants of adrenal cortical carcinoma: **Oncocytic adrenal cortical carcinoma**, **Myxoid adrenal cortical carcinoma**, **Carcinosarcoma**, **Adenosquamous adrenocortical carcinoma**, **Clear cell adrenal cortical carcinoma**.

Differential diagnosis includes: Adrenocortical adenoma, Renal cell carcinoma, Adrenal medullary tumors, Hepatocellular carcinoma.

Treatment

The only curative treatment is complete surgical excision of the tumor, which can be performed even in the case of invasion into large blood vessels, such as the renal vein or inferior vena cava. The 5-year survival rate after successful surgery is 50-60%, but unfortunately, a large percentage of patients are not surgical candidates. Radiation therapy and radiofrequency ablation may be used for palliation in patients who are not surgical candidates. [1]

Chemotherapy regimens typically include the drug mitotane, an inhibitor of steroid synthesis which is toxic to cells of the adrenal cortex, [6] as well as standard cytotoxic drugs. A retrospective analysis showed a survival benefit for mitotane in addition to surgery when compared to surgery alone. [7]

One widely used regimen consists of cisplatin, doxorubicin, etoposide) and mitotane. The endocrine cell toxin streptozotocin has also been included in some treatment protocols. Chemotherapy may be given to patients with unresectable disease, to shrink the tumor prior to surgery (neoadjuvant chemotherapy), or in an attempt to eliminate microscopic residual disease after surgery (adjuvant chemotherapy).[1]

Hormonal therapy with steroid synthesis inhibitors such as aminoglutethimide may be used in a palliative manner to reduce the symptoms of hormonal syndromes.[1]

Prognosis

ACC, generally, carries a poor prognosis[8] and is unlike most tumours of the adrenal cortex, which are benign (adenomas) and only occasionally cause Cushing's syndrome. Five-year disease-free survival for a complete resection of a stage I-III ACC is approximately 30%.[8] The most important prognostic factors are **age** of the patient and **stage** of the tumor. Poor prognostic factors: mitotic activity, venous invasion, weight of 50g+; diameter of 6.5 cm+, Ki-67/MIB1 labeling index of 4%+, p53+.

References

1. ^ [a] [b] [c] [d] [e] [f] [g] [h] edited by Vincent T. DeVita, Samuel Hellman, Steven A. Rosenberg (2005). *Cancer: principles & practice of oncology*. Philadelphia: Lippincott-Raven. ISBN 0-7817-4865-8.
2. ^ [a] [b] [c] [d] Savarese, Diane MF; Lynnette K Nieman (2006-08-08). "Clinical presentation and evaluation of adrenocortical tumors". *UpToDate Online v. 15.1*. UpToDate. http://www.uptodateonline.com/utd/content/topic.do?topicKey=adrenal/17707&type=A&selectedTitle=1~16. Retrieved 2007-06-05.
3. ^ [a] [b] Richard Cote, Saul Suster, Lawrence Weiss, Noel Weidner (Editor) (2002). *Modern Surgical Pathology (2 Volume Set)*. London: W B Saunders. ISBN 0-7216-7253-1.
4. **^** Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill, 2005. ISBN 0-07-139140-1
5. **^** Kufe D (2000). Benedict RC, Holland JF. ed. *Cancer medicine* (5th ed.). Hamilton, Ont: B.C. Decker. ISBN 1-55009-113-1. OCLC 156944448.
6. **^** Laurence L. Brunton, editor-in-chief; John S. Lazo and Keith L. Parker, Associate Editors (2006). *Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Edition*. United States of America: The McGraw-Hill Companies, Inc.. ISBN 0-07-142280-3.
7. **^** Terzolo M, Angeli A, Fassnacht M, *et al.* (June 2007). "Adjuvant mitotane treatment for adrenocortical carcinoma". *N. Engl. J. Med.* **356** (23): 2372–80. doi:10.1056/NEJMoa063360. PMID 17554118.
8. ^ [a] [b] Allolio B, Fassnacht M (2006). "Clinical review: Adrenocortical carcinoma: clinical update". *J Clin Endocrinol Metab* **91** (6): 2027–37. doi:10.1210/jc.2005-2639. PMID 16551738. Free Full Text.

External links

www.endotext.org article