GIANT ADRENAL CARCINOMA ASSOCIATED WITH RENAL VEIN AND INFERIOR VENA CAVA THROMBUS. CASE REPORT AND LITERATURE REVIEW


Summary.- OBJECTIVE: To present a case of giant adrenal carcinoma associated with renal vein and inferior vena cava (IVC) thrombus. Up to now, there is no similar case reported in the national literature.

METHODS: 75 year old woman with signs of virilization. CT-scan showed an 18 cm adrenal mass with venous thrombus and possible pulmonary metastases. The working diagnosis was primary suprarenal carcinoma.

RESULT: Due to elderly age and advanced stage, including metastasis, we decided not to perform surgery, and initiate chemotherapy.

CONCLUSIONS: Adrenal Cancer is an infrequent and very aggressive tumor. Surgery is the only curative treatment. In advanced stages chemotherapy is recommended, but with poor results.

Keywords: Cancer. Adrenal. Thrombus. Vein.

INTRODUCTION

AC is an extremely unfrequent tumor, with an incidence of 1 case/1.7 millions. Only represents 0.02% of all cancers.

AC shows a bimodal pattern of age distribution, with higher incidence in the first and the fifth decade of life. Affects more often to women vs men (1.5:1). Approximately 60% of cases presents with symptoms related to higher hormone production (corticoids y less frequently oestrogens and androgens). Virilizing presentation is very rare (1-3).

It has a very aggressive behaviour, being the second more aggressive endocrine malignancy after anaplastic
thyroid carcinoma. Up to 70-80% of cases present disseminated stage at the time of diagnosis. Higher adrenal masses (>6 cms) tumors usually are carcinomas (1-3).

The objective of this paper is to report a giant AC case with venous thrombus associated, up to now not reported in the national literature.

**CASE REPORT**

75 year old woman referred to our department with a left adrenal mass. Patient showed hoarseness, facial fine downy hair and alopecia added to a very difficult control of blood pressure and glucose level. In the Medical History, several TUR for non-invasive bladder tumours, Complete thyroid gland resection caused by nodular hiperplasia and malign melanoma removed more than 20 years ago. In analytic, important elevation of LDH (1266 U/L), alkaline phosphatase (150 U/L), testosterone (8.55 ng/ml), free testosteronae (119 pg/ml), DHEA (1527 µg/dl), with normal blood levels of aldosterone and cortisol, and normal urine levels of catecholamines. No suppression in cortisol levels after 1 mg Dexametasone test.

In abdominopelvic CT is described a 18 cm left adrenal mass with thrombotic tumor in renal vein, ovaric vein and IVC. In thoracic CT hilium nodes aummented and possible pulmonary metastases. Suspected diagnosis was primary adrenal carcinoma: T4N1M1 (stage IV), but metastatic adrenal involvement should not be ruled out, related to tumoral findings in the past.
We discuss this case in an uro-oncological session, and due to advanced age and clinical stage (including possible pulmonary metastases), we decided not to perform any surgical procedure. Patient is referred to Oncology to start Chemotherapy treatment with Mitotane.

**DISCUSSION**

Adrenal gland pathology is divided into:

1) Adrenal cortex pathology:
   a. Diffuse adrenal Hyperplasia
   b. Nodular adrenal Hyperplasia
      i. Adrenal adenoma:
         1. Not functioning
         2. Functioning:
            a. Glucocorticoid; Cushing syndrome.
            b. Mineralocorticoid.
            c. Virilizing
      ii. Adrenal Carcinoma: Functioning and not functioning.

2) Adrenal medulla pathology:
   a. Ganglioneuroma
   b. Neuroblastoma
   c. Pheochromocytoma

3) Adrenal stroma pathology:
   a. Mielolipoma
   b. Cysts-Pseudocysts
   c. Haemorrhage
   d. Abscess
   e. Fibroma, Linfangioma
   f. Sarcoma

4) Metastases

Adrenal incidentaloma incidence represents between 1.4 and 8.7%, with a media of 2.3%. Some authors report higher prevalence in women and in older than 50 years patients. Most of them are benign adenomas with no hormonal activity. However, it is important to rule out other potentially lethal causes like adrenal carcinoma (0.3-12%) and functioning adrenal tumors (2.6-13%). Percutaneous fine needle aspiration cytology under CT on USG-guided aspiration biopsy is unreliable in preoperative diagnosis, as it is unable to differentiate AC from adenoma (3,4).

AC aetiology keep unknown. Perhaps, the heterozygosity in chromosomes 11P, 13Q or 17P have a role. p53 anomalies are also described. (5).

An AC practical classification is based on adrenal hormone production capacity. Among functioning:

Case described is an AC, primary or metastatic. In fact, adrenal gland is the unit of weight/organ that is more often affected from other organ metastases. 50% derived from melanomas, breast and pulmonary cancer. (We must not forget melanoma treated in the past in this patient) (2).

AC grows very quickly, and 82% of cases have already metastatic development at presentation. Spontaneous tumoral regression have been described. AC usually cause metastasis in lung (71%), lymph nodes (68%), liver (42%) and bone (26%) (6).

This kind of tumors extends earlier to surrounding structures, specially the kidney. They can also affect to the renal vein, IVC, and in some special cases SVC and right atrium. Vena cava infiltration can develop through direct extension or more often by intraluminal extension from renal or adrenal veins. 20% of tumoral vein affection is estimated. Among 121 adrenalectomies with vein thrombus reported up to now, 71% were carcinomas, 15.8% pheochromocytomas, 5.5% neuroblastomas, 2.5% leiomyosarcomas and 5% metastatic. Usually shows high recurrence rates (70-80% after surgical resection). Spread happens in 82% of cases (local recurrence is common). In 1889 Thorton practiced the first adrenalectomy with nephrectomy for a virilizing tumor, and Castleman et al reported in 1972, the first tumoral thrombotic affection (7,8).

Computerized tomography (CT) and magnetic resonance (MRI) are the election imaging techniques, MRI allows us to distinguish between tumoral and fibrinogenic thrombus. AC radiological typical findings are: Irregular borders, heterogenic density, tumoral calcification, diameter > 4 cm, unilateral, local invasion and attenuation after endovenous contrast in CT.

Adrenal functionant mass percentage is between 15-20%; 10% secrete cortisol and cause Cushing syndrome, 5-6% secrete catecolamines (pheochromocytoma) and 2% secrete aldosteron (hyperaldosteronism). Proportion of functioning masses depends on mass size, very unfrequent if < 1 cm, however 40% of tumors > 6cms are functioning (4).

Several poor AC prognosis factors are classically described:

1) Advanced stage.
2) Incomplete surgical resection.
3) High grade.
4) Elderly age.
5) Hormonal hypersecretion.
6) Size higher than 10 cm.
Surgery is the treatment of choice, even, for some authors in the advanced stages. However we think that, as an exception, we do not recommend surgical treatment in some metastatic AC in elderly patients. Surgical treatment includes complete resection of whole mass, including surrounding organs if necessary. It shows several advantages:

1) Reduce pulmonary emolism risk,
2) Reduce symptoms related to adrenal hyperfunction
3) Reduce symptoms related to local organ compression.

Classically open technics were recommended. Bilateral subcostal incision (Chevron), Sometimes associated with medial incision, thoracotomy and/or sternotomy. Lymph node dissection is mandatory. Actually, in experimented centers, laparoscopic adrenalectomy are performed (even without nephrectomy), either using transperitoneal than retroperitoneal access, with results and survival rates comparable with open surgery. Recently a german group reported a 152 adrenalectomy serie comparing open vs laparoscopic access, with the final recommendation of not perform laparoscopic adrenalectomy in masses higher than 10 cm (9).

In the venous thrombotic cases we must proceed to vascular control clamping of (depend on level of affectionation):
1) renal vein if thrombus in subhepatic IVC,
2) Hepatic vascular exclusion if thrombus in retro or suprahepatic IVC, and
3) Cardiopulmonary by-pass if thrombus is in IVC supradiaphragmatic and/or in the right atrium (10).

The most frequently used chemotheraphy regimen is based on Mitotane, producing only 35% remissions, moreover in the majority of cases without response, no relapse free survival increasing and with high toxicity (specially gastrointestinal, neurological and cutaneous).

For some authors the most effective treatment is the combination of Etoposide, Cisplatin y Doxorubicin associated with Mitotane (3-12 gr/day), with respond rates up to 55%. Also has been used protocols with DDT, ketoconazole, metirapone and aminoglutetimide with modest respond rates (8)

Radiotherapy role in AC is yet not well defined, now limited to bone metastases (treatment of choice).

Altough extremely rare, spontaneous tumoral adrenal and metastasis regressions are described.

Prognosis of AC is poor if untreated, with less than 35% survival at 5 years. (2,5).

**CONCLUSIONS**

AC is an infrequent tumor with a very aggressive behaviour. Often occurs with local invasion or metastases at presentation. The only curative treatment is surgical resection. In advanced stages chemotherapy is recommended, if surgery is not an option, but with poor response and survival rates.

**REFERENCES AND RECOMMENDED READINGS**

(*of special interest, **of outstanding interest)