Acute adrenal insufficiency as a fist sign of metastatic pulmonary carcinoma

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INTRODUCTION

Adrenal insufficiency:
- **a relatively rare desease**
  - incidence – new cases ~ 0.8 cases 100.000 population per year
  - Prevalence: ~ 4-11 cases i/100.000 of population
  - the tuberculous form is most often seen in man : M/F 1.25/1 and the autoiumune in women F/M ratio 2.6-3/1
  - 60-70% of cases ar diagnosticated between 30-50 de ani years of age.
- **ethyology:** - most frequent autoimunity or infectious;
  - sometimes caused by metastatic lesions, genetic disorders and bilateral adrenal haemorrhage..

- The adrenal glands are a common sites for secondary lesions derived from malignant melanoma, lymphoma, renal, breast, colon and bronchopulmonary tumours.
- Adrenal metastasis, at the initial diagnosis of non-small cell lung cancer, occurs in less than 10% of lung cancer patients.
- Most cases involve solitary, unilateral, small asymptomatic lesions.
- Bilateral adrenal metastases are observed in less than 3% of patients with lung cancer.

CLINICAL CASES

Pacient **C L, 65 years old**

❑ Evaluated in the Emergency Department for acute episodes of :

• severe asthenia
• anorexia
• digestive disorders
• weight loss
• hypotension

• hyponatremia 125 mmol/l with
• hyperkalemia 5.3mmol/l

- no remission of symptoms after administration of macromolecular solutions raised the suspicion of ***primary adrenal insufficiency***, confirmed by functional corticotrop balance:
  - increased **ACTH = 344 pg/ml** and
  - low-normal **cortisol levels = 6.38 ug/dl.**

- Steroid replacement (hydrocortizon 15 mg/per day) determined significantly clinical improvement , normalization of blood pressure and electrolyte imbalances.

❑ In tha Endocrinology Clinic he presented with: - the absence of melanodermia.
- low-normal cortisol levels= **8.02** ug/dl.
- ACTH levels = **101** pg/ml which increased after oral steroid replacement was stopped for 48 hours - **465** pg/ml.

❖ Further investigations included **abdominal ultrasonography** *(fig. 1):*
- ***discreet enlargement of the left adrenal (21/20.7 mm)***
- ***echogenic lesion on the right adrenal (29/20 mm)***
- ***well defined hepatic nodule (22 mm).***
- **Abdominal CT** with contrast *(fig.2):*
- ***bilateral adrenal hyperplasia*** *(R: 43/22/47 mm, L: 33/24/48 mm)*
- ***observation of hepatic secondary lesion*** *(6-11mm)* and the biopsy suggested ***metastasis of lung adenocarcinoma.***

Microscopy:
▪Adenocarcioma metastasis
▪ Mildly differentiated

Immunohistochemistry:
▪synaptofizin negative
▪ chromogranin negative
▪ CK rarely positive
▪ TTF1 strongly positive

❖ **Native chest CT** (Figure 3) reveled:
- ***irregular nodular lesion (11/21/10 mm) near the oblique fissure.***
- ***medistinale lymph nodes (10-22 mm).***

* TNM classification: ***cT1bN2M1bG2***

❖ Chemotherapy was initiated (carboplatin and paclitaxel), well tolerated with favorable evolution.

Pacient **V B, 57 years old**
(heavy smoker and alcohol consumer)

❑ In july 2014, after an intervention for Dupuytren retraction, he decompensated a ***primary adrenal insuficiency***
(anamnestic, confirmed at that time by the biological data).
Steroid substituion was started with a good initial evolution.

❑ After 3 months he stopped the treatment and was hospitalized with **adrenal crisis:**

• weight loss
• important dehydration
• weakness
• anorexia
• digesive disorders

• hyponatremia 127 mmol/l
• hyperkalemia 6.76 mmol/l
• hypoglicaemia 66 mg/dl

Intensive treatment ameliorated his status but the sudden discontinuation of cortisone replacement therapy led to a new acute decompensation, hospitalized in the Endocrinology Clinic.

❑ He presented with:- diffuse hyperpigmentation
- Pancoast Tobias syndrome: enophthalmos, right eyelid ptosis, shoulder and right arm pain,
- very low levels of cortisol **<1** ug/dl and normal ACTH levels 15.2 pg/ml.

❖ **Abdominal ultrasound** *(fig. 4)* revealed ***large left adrenal lesion*** (30/26 mm).
Corticosteroid replacement therapy ameliorated the status but the persistence of anorexia, asthenia, and inflammatory syndrome (ESR 115 mm, CRP 3.59 mg/dl, fibrinogen 380 mg/dl) suggested a severe underlying cause.

❖**Pulmonary radiography** *(figure 5)* showed ***right apical lung nodule (35/45/50 mm)*** confirmed by **thoraco-abdominal CT**, which revealed a ***bilateral adrenal invasion.***

❖ **Pulmonary biopsy** confirmed ***poorly differentiated mucosecretory adenocarcinoma***

Microscopy:
▪ laterocervical adenocarcinoma metastasis
▪ with high rate of multiplication

Immunohistochemistry:
▪ CK 7 and CK 5 positive
▪ chromogranin negative
▪ TTF1 difuse positive
▪ Ki67 90%

❖ Chemotherapy was proposed as the best option of treatment at this stage, refused by the patient.

Figure 1 – Abdominal ultrasound

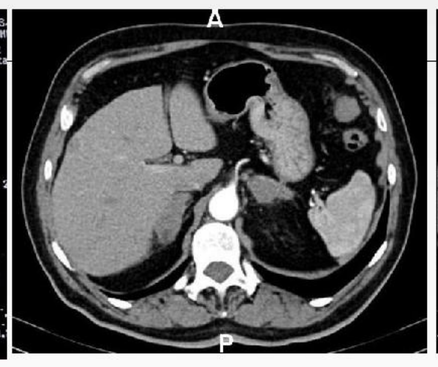
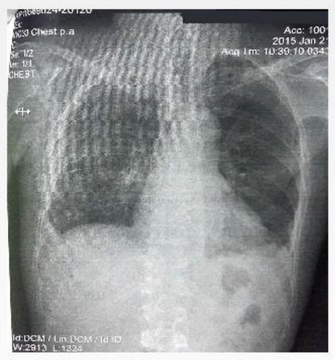


Figure 2 – Abdominal CT

Figure 3 – Thotacic CT

Figure 4 – Left drenal ultrasound



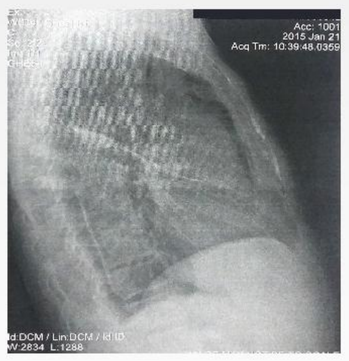


Figure 5– Thoracic radiography

CONCLUSIONS

✓ The frequency of adrenal metastasis of primary lung cancer increases with disease progression, from 10 to 40%.
✓Although adrenal metastases are usually unilateral, bilateral adrenal metastases are seen in 10% of all lung cancer patients.
✓ Clinical manifestations of adrenal insufficiency are significantly less frequent.
✓ Patients with adrenal secondary lesions are typically asymptomatic, probably because a destruction of more than 90% of adrenal cortex is needed for clinical symptoms.
✓ 1% may present with adrenal insufficiency as a first manifestation.
✓Adrenal crisis was, in our two cases, the first symptom of advanced pulmonary cancer, leading to its diagnostic and therapeutical solutions.

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