Primary bilateral diffuse large B-cell lymphoma of adrenals presenting as incidental adrenal masses

Cristina Alina Silaghi[1,2], Delia Dima[3], Carmen Georgiu[4], Delia Lupu[5], Ionela Lungu[1], Anca Elena Crăciun[6], Daniel Tudor Cosma[6], Cristina Sorina Cătană[7], Horațiu Silaghi[8], Carmen Emanuela Georgescu[2], Romeo Chira[9]

[1] County Emergency Hospital, Cluj-Napoca, Romania; [2] Department of Endocrinology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3] Departament of Hematology, Institute of Oncology "Prof. Dr. Ion Chiricuta" Cluj-Napoca, Romania, [4] Discipline of Pathology, Department of Morphological Sciences, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [5] IInd Internal Medecine Departament "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [6] Diabet, Nutrition and Metabolic Diseases Clinical Center Cluj-Napoca, Romania; [7] Department of Medical Biochemistry "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania, [8] 5th Departament of Surgery "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [9] Ist Internal Medecine Departament, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Introduction

Primary adrenal lymphoma is defined as a histologically proven malignant proliferation of lymphoid cells, which may involve one or both adrenal glands and has the following features: there is no history of lymphoma with another location and and the lesions of the adrenal glands are clearly dominant. The frequency of primary adrenal non Hodgkin lymphoma (PANHL) is rare, being described in less than 1% of all non-Hodgkin lymphomas and 3% of extranodal lymphomas, occurs usually in the 6th and 7th decades, and the male:female ratio is 2:1. Between 50% and 70% of patients with bilateral PANHL have clinical or biochemical evidence of primary adrenal insufficiency. There is no correlation with tumor size. Diffuse large lymphomas of B-cell origin (DLBCL) histology is reported in 70% of PANHL cases.

Clinical case

The present case is a primary, bilateral DLBCL of adrenals in 75-year-old male patient admitted for abdominal pain, weight loss and fatigue. Abdominal CT scan revealed an incidental, bilateral, marked, homogenous adrenal gland enlargement, measuring 15 × 8 cm on the right and 9 × 4.8 cm on the left (both masses > 10 HU), with no lymphadenopathy or visceral involvement (Fig1 A and B). Past medical history included hypertension, mitral regurgitation, tricuspid regurgitation, pulmonary arterial hypertension, chronic pulmonary heart disease, congestive heart failure NYHA class II and COPD, stage GOLD II.

Physical examination reveals body height: 157cm, weight: 65,7kg, afebrile, regular heart rate: 75 beats/minute, blood presure 120/70 mmHg, nontender abdomen with hepatosplenomegaly, right axillary and inguinal lymphadenopaty. There was no skin/mucosal hyperpigmentation. Mild bilateral leg edema was seen. He had no known past history of lymphoma or other carcinoma.

The hormonal assessments

Adrenal function	Results	Normal range
Basal serum cortisol	15.2 µg/dl	5-25 µg/dl
Plasma ACTH	↑112.7 pg/ml	7.2-63.3 pg/ml
Serum cortisol 4 hours after ACTH (Synacthen) stimulation test	↓17.8 µg/dl	> 3-5 X basal value
DHEA-S	↓0.21 µg/ml	0.9-3.6 µg/ml
17-OH progesterone	0.96 ng/ml	0.5-2.1 ng/ml
17-OH progesterone 4 hours after (Synacthen) stimulation test	3.22 ng/ml	< 10 ng/ml
Testosterone	11 nmol/l	9.9-37.8 nmol/l
Aldosterone	3.09 ng/dl	1.6-23.2 ng/dl
Renin	7.1 µIU/ml	2.8-39.9 µIU/ml
Aldosterone/renin ratio	0.4	< 3.7
Plasma metanephrines	14.8 pg/ml	< 90pg/ml
Plasma normetaneprhrines	40.2 pg/ml	< 180 pg/ml
Adrenal antibodies	Negative (<1.10)	<1/10

Serum lactate dehydrogenase (LDH) and ferritine were increased.

Chest CT scan

- enlarged inflammatory axillary and mediastinum lymph nodes.
-no evidence of pulmonary tumors or further pathological findings

Abdominal ultrasounds revealed a bilateral bilobate heterogeneous mass, which measured 10/7.5 cm on the right side and 9.5/4.8 cm on the left side. (Fig. 2 A and B)

Percutaneous ultrasound-guided / Histological examination

Diffuse large B-cell non Hodgkin lymphoma (DLBCL), Fig.3 A and B

Immunohistochemistry study - Markers	Results
CD20	Strongly positive (on 100% of cells)
CD10, CD99, Synaptophysyna, Hep Bar	Negative
Ki- 67 index proliferation 90%	

Treatment

6 cycles of imunochemotherapy type R-CHOP (rituximab, cyclophosphamide, epirubicine, vincristine, metilprednisolone) + 2 cycle of rituximab monotherapy; hydrocortisone substitution therapy: 10 mg/day, starting from the 6th day of each cycle, until the next one.

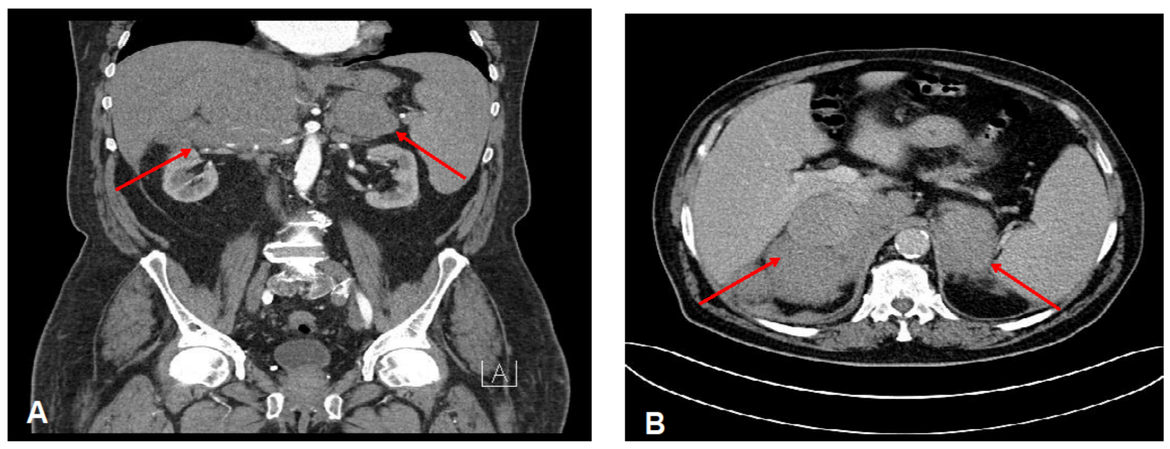

Fig 1. **Abdominal CT scan:** showed large bilateral adrenal masses . **A**: frontal section, **B**: transversal section

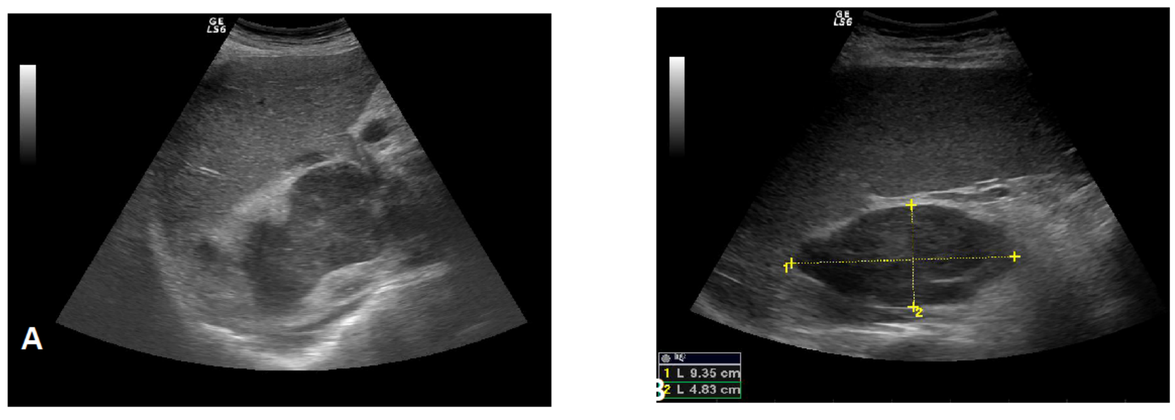

Figure 2: **Abdominal ultrasound : A- right adrenal region:** bilobate heterogeneous mass, which measured 10/7.5 cm, with increased vascularity, near the inferior caval vein, spreading to the right renal hilum and extending to the liver parenchyma **B- left adrenal region:** heterogeneous tumora 9.5/4.8 cm, extending to the posterior side.

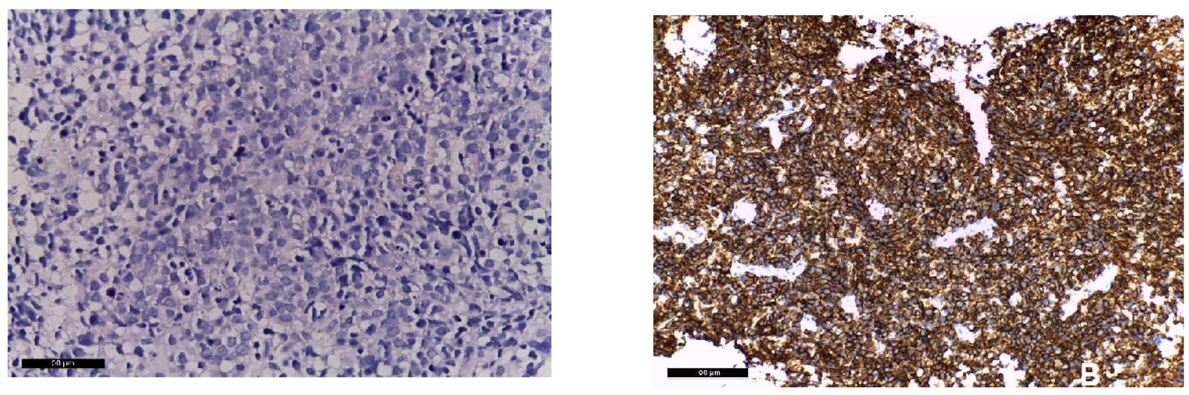

Fig 3: A (Hematoxilina eosina x 400) „small blue cells" with low eosinophilic cytoplasm, large, irregular, hipercrome nucleus, with a prominent central nucleolus or 2-3 nucleolus near membrane, many apoptotic bodies; B: (Immunohistochemical staining x 200), diffuse large B-cell lymphoma strong staining for B-cell marker CD20 on the membrane and cytoplasm.

Discussions :

In contrast with the hight frequency of the adrenal metastases, fewer than 200 cases of PANHL have been reported in the English literature until 2013.

Background autoimmune adrenalitis is a frequent mechanism proposed in the pathogenesis and may explain the fact that 70% of PANHL are bilateral and 60-70% have adrenal insufficiency (AI). Although in our case the both adrenal glands were involved and the patient developed mild AI, the adrenal antibodies were negative.

Imaging investigations include: abdominal ultrasound, CT, MRI and FDG PET / CT.

CT or ultrasound guided biopsy are the preferred diagnostic procedures and this should only be performed after the exclusion of pheochromocytomas.

DLBCL is the most common histological type of PAL, and it was confirmed in this case.

Treatment modalities includes surgery, multi agent combination chemotherapy, radiotherapy and corticosteroid replacement therapy. Complete remission can be achieved using a regimen R-CHOP. The prognosis is poor and is worsened by increased LDH, increased age, AI, and initial large tumor size.

The follow up PET scan study showed complete remision after 4 cycles of CHOP chemotherapy and 1 cycle of rituximab. Seven months after substitution therapy the patient presented improved health status, low basal cortisol (4.71µg/dl), while ACTH was within the normal range (49.9 pg/ml) and the response was appropriate upon the ACTH stimulation test (Cortisol = 31.6 µg/dl). Abdominal ultrasounds revealed no tumor progression.

Conclusions:

This case should remind clinicians that PANHL may be a cause of bilateral adrenal incidentaloma with or without AI