Turkish Journal of Endocrinology and Metabolism, (2006) 3 : 73-77 **CASE REPORT**

A Surrenal Tuberculosis Presented Itself As Metastasis

Sürrenal Metastazmış Gibi Kendisini Gösteren Bir Adrenal Tuberkülozis

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52 year-old female patient seen at to our outpatient clinic had severe fatigue, weight loss and darkening of skin color. Patient's clinical manifestations and laboratory findings were found to be compatible with Addison's disease and malignancy. Ultrasonographic examination was performed to investigate the etiology of adrenal insufficiency, and revealed bilateral suprarenal mass. Further investigation with CT and MRI scans favored malignancy. However, search for the primary lesion revealed no sign of systemic metastasis apart from the suprarenal masses. Pathological analysis of the suprarenal mass revealed signs of tuberculosis adenitis. The patient was diagnosed as adrenal insufficiency due to suprarenal tuberculosis and four-drug anti-tuberculosis regimen and steroid replacement therapy were started. Patient's complaints diminished and clinically significant improvement was observed.

Keywords: Adrenal mass, Malignancy, Adrenal tuberculosis, Addison's disease

52 Yaşında ki bayan hasta kliniğimize; ileri derecede halsizlik, kilo kaybı, cilt renginde koyulaşma nedeniyle başvurdu. Hastanın kliniği ve labaratuar incelemeleri Addison Hastalığı ve maliğnite ile uyumlu bulundu. Adrenal yetmezliğin etiyolojisi için yapılan tetkiklerinde ultrasonda bilateral surrenal kitle saptandı. BT ve MR ile yapılan ileri incelemelerinde kitleler malignite lehine yorumlandı. Maliğnite için yapılan primer odak araştırmasında Sürrenaldeki kitleler dışında, başka bir odak veya sistemik metastaz bulgusu saptanmadı. Surrenaldeki kitlenin patolojik incelenmesi sonucu: tüberküloz adrenalitis olarak rapor edildi. Bunun üzerine olgu sürrenal tüberküloza bağlı Adrenal yetmezlik tanısı aldı. Hastaya adrenal tüberkülozu için 4'lü antitüberküloz tedavi ve sürrenal yetmezliği için steroid tedavisi başlandı. Hastanın şikayetleri azaldı, belirgin klinik düzelme gözlendi.

Anahtar Kelimeler: Adrenal kitle, Malignite, Adrenal tüberküloz, Addison hastalığı

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Introduction

Tuberculosis may affect many endocrine glands including hypothalamus, pituitary, thyroid and adrenals. The most commonly involved endocrine organ in tuberculosis is adrenal glands. Adrenal glands may be directly or indirectly affected in tuberculosis. Tuberculous Addison's disease is still

an important cause of primary adrenocortical insufficiency particularly in the developing countries (1). Tuberculosis might result not only in chronic adrenocortical insufficiency but also in acute adrenal failure (2). During the last 4 decades, prevalence of tuberculosis as an etiological factor in Addison's disease reduced from 79 % to 7%, yet it continues to be among top etiologies in the developing countries (3,11).

CT scans showed glandular enlargement associated with necrosis and in some cases, calcification. The presence of lesions reminding a mass, were ruled out in order not to exclude the diagnosis (4). Kawashima et al. reported that CT was useful for diagnosis of subacute forms of to tuberculosis or histoplasmocytic Addison's disease. Typical CT findings were bilateral adrenal enlargement, central necrosis and distinct contours (5).

In a study encompassing 12 abdominal tuberculosis patients, Yılmaz et al. have presented bilateral adrenal calcification (6). Tajdine et al. have stated that tuberculous pseudotumor of the adrenals is rarely seen without extra-adrenal involvement. They have examined a 24 year-old woman with a mass in her right adrenal gland by ultrasound and CT, dissected the gland laparoscopically and diagnosed tuberculosis upon histological examination (7). In another study, all 9 Addison's disease patients showed adrenal enlargement accompanied by irregularity or thickening of the glandular margins in 7 cases, and calcifications in 5 patients (8).

Case

A 52 year-old female patient was admitted to our clinic in August 2003 with complaints of discoloration of the skin, weight loss, weakness and an overall feeling of discomfort for the past 5 months. Patient was hospitalized, after an adrenal mass was determined via abdominal ultrasound for further investigation.

Medical history of the patient: ovariectomy due to an ovarian cyst and exploration of the other ovary due to perfusion deficiency has been performed 30 years ago. Patient has been in menopause since surgery.

Physical examination: Patient's arterial blood pressure was 90/60 mmHg; pulse rate, 90/min, body temperature: 37 °C; body weight: 67 kg; body mass index (BMI): 26.8. Hyperpigmentation was observed, predominantly on face, between breasts, at palmar linings, and in oral mucosa. Cardiovascular and other systems were considered normal. PPD test was positive (25 x 15 mm).

The result of the laboratory examination were as follows: Erythrocyte sedimentation rate 26 mm/h, Na:132 (135-150) mEq/L, K: 5,3 (3,5-5) mEq/L, Free T3: 3,9 (1,8-4,6) pg/ml, Free T4 1,1(0,9-1,7) ng/dl, TSH: 1,1 (0,2-4,2) µIU/ml, Cortizol 3 (5-25) µg/dl, ACTH 922 (10-70) pg/ml, DHAS 37 (35-450) µg/dl, tumor markers were within the normal limits; AFP: 1,44 (<7) u/l, CEA: 1,02 (0-5) u/l, Ca19,9: 11,9 (<25) u/l, Ca15,3: 15 (<=25) u/l, Ca 125: 2,32 (<35) u/l. FSH and LH were compatible with menopause. FSH: 106 (21,7-153) mIU/ml, LH 42 (11,3-50) mIU/ml.

Standard dose ACTH (250 microg) stimulation test was subnormal.

Radiological examination: No finding compatible with tuberculosis or malignancy was detected on chest X-ray. No sign of metastasis was detected on vertebral bone scan. Abdominal CT revealed two nodules; one originating from the medial crus in the right suprarenal gland (42 x 28 mm,), and a second one located in the crus adjoining region of the left suprarenal gland measuring 12 mm (Figures 1). Abdominal MRI scan, a lesion measuring 42 x 28 mm was detected originating from the lateral crus in the right suprarenal gland. The lesion exhibited an increase in the signal intensity following fat suppression sequence, and suggested suprarenal metastasis due to its fat content being close to 0% (Figures 2,3). MRI of pituitary gland were normal. Thorax CT was evaluated as normal apart from the nodules of 2 mm. Whole body bone scan was evaluated as normal apart from the degenerative changes in L4.

Pathological analysis of the suprarenal masses revealed signs of tuberculosis adenitis (Figure 4).

The patient was diagnosed as adrenal insufficiency due to suprarenal tuberculosis. Four-drug anti-tuberculosis regimen and steroid replacement therapy were started. Patient's complaints diminished and clinically significant improvement was observed.

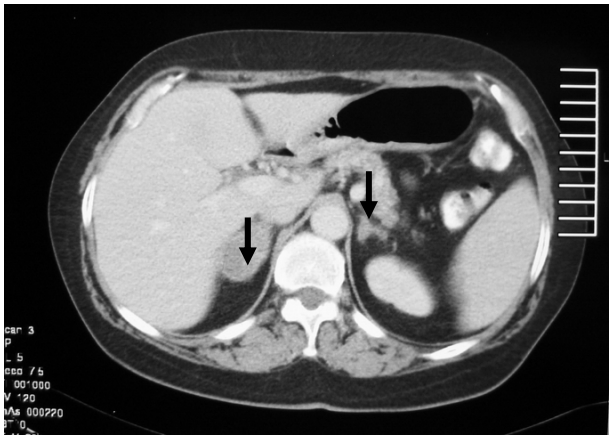

Figure 1. Abdominal CT: two nodules were detected; one originating from the medial crus in the right suprarenal gland measuring 42 x 28 mm, and a second one located in the crus adjoining region of the left suprarenal gland measuring 12 mm

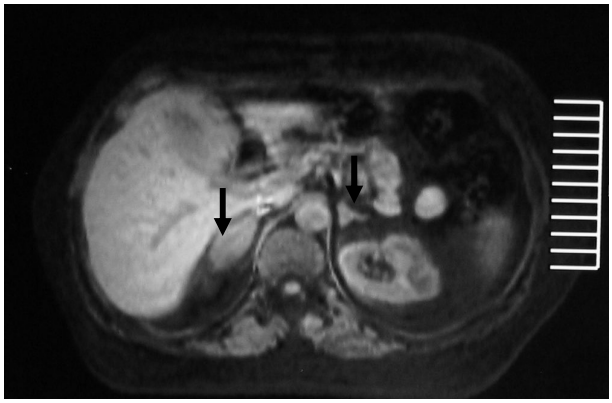

Figure 2. Pre-contrast T1W fat-saturation MRI

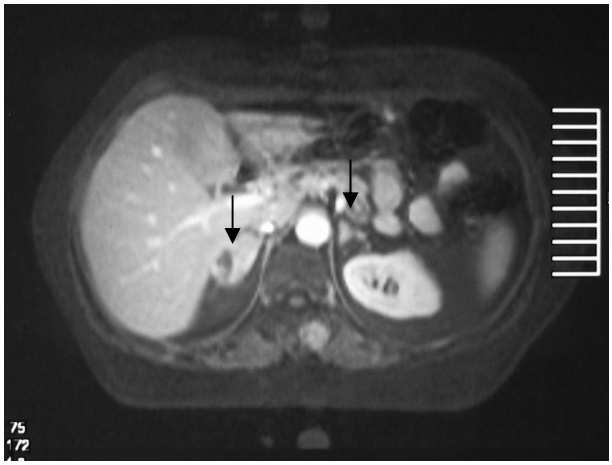

Figure 3. Post-contrast T1W fat-saturation MRI

Figure 2 and Figure 3: Abdominal MRI scan, a lesion measuring 42 x 28 mm was detected originating from the lateral crus in the right suprarenal gland. The lesion exhibited an increase in the signal intensity following fat suppression sequence, and suggested suprarenal metastasis due to its fat content being close to 0%.

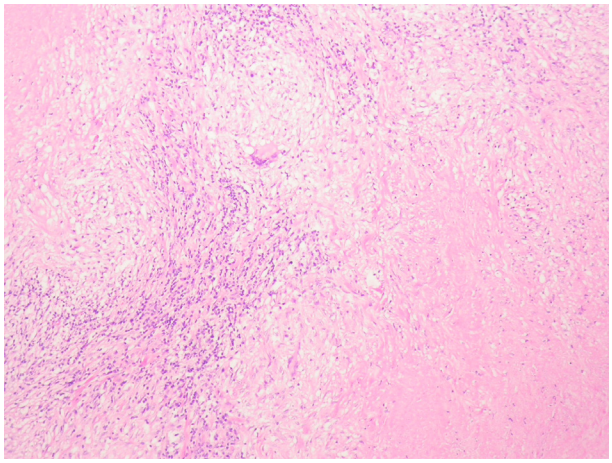

Figure 4. Granulomas with central area of caseous necrosis surrounded by Langhans giant cells, epitheloid cells, lymphocytes and plasma cells (HE).

Discussion

Bilateral adrenal enlargement is much less common. The various causes can be classified as malignant tumors, either primary or metastatic; endocrinopathies, usually associated with corticotropin stimulation; and infectious diseases. Adrenal insufficiency may occur due to a dysfunction in any part of the hypothalamic-pituitary-adrenal axis. Tuberculosis is one of the well-known causes of adrenal insufficiency.

Since laboratory tests, performed for this case revealed low basal cortisol and significantly high ACTH levels accompanied with notable hyperpigmentation, primary adrenal insufficiency and malignancy was considered. Standard dose ACTH (250 microg) stimulation test was subnormal.

Investigations were performed to determine the etiology, where by abdominal CT (Figure 1) and ultrasound examinations revealed a 42x28mm mass in the right suprarenal and a 12 mm mass in the left suprarenal gland. Hyperplasia was not considered since no increase was detected in dimensions of the glands. Further investigation using MRI (Figure 2-3). MRI revealed slight curving in the left adrenal crus adjoinment area and a lesion of 42 x 28 mm, originating from crus in the right adrenal gland. The lesion was isodense with liver in T2-W sequences and hypodense in T1-W sequences; and since there was an increase in signals after fat suppression, it was concluded that its fat content is very low. All of the above

findings led us to diagnose bilateral adrenal metastasis in this patient. Thorax CT scan, body bone scan, mammography, gynecological examination and smears Occult blood test result, Tumor markers and etc... directed to investigate primary cancer were normal.

Since no finding suggesting primary cancer was detected, biopsy from the suprarenal gland was planned. laparotomy and left adrenalectomy were performed. Wide necrotic area and tuberculous adenitis were reported as a result of the pathological investigation (Figure 4). The patient was diagnosed with adrenal insufficiency due to tuberculosis.

Most common causes of adrenal mass are metastatic or primary malignancies, endocrine diseases, infectious causes and other reasons such as incidentaloma. Al Hadi et al. explored a 47 year-old patient who complained of loss of appetite, weight reduction and fatigue for the past 6 months and had a right adrenal mass diagnosed via ultrasound and CT, with a prediagnosis of malignancy; and tuberculosis was determined to be the cause (9). Villabona et al observed extra-adrenal tuberculosis foci in all cases in a study with 5 tuberculous Addison's disease patients, there was glandular calcification in 2 patients during initial diagnosis process. Upon 4-30 month follow-up, reduction in enlarged glandular sizes was observed (10). Tuberculosis may attack adrenal glands endemically and is a common cause of Addison's disease in developing countries. Mostly, it appears together with pulmonary lesions. On the other hand, in acute tuberculous adrenalitis, bilateral adrenal enlargement without calcification predominates (11).

If a metastatic adrenal mass is suspected; other systems, namely breasts, gastrointestinal system, ovaries, and thorax should be screened (12, 13). Although primary adrenal lymphoma is a rare condition, it is found in 25% of patients with diffuse B cell non-Hodgkin Lymphoma (NHL) upon postmortem biopsies. Lymphoma patients with bilateral adrenal involvement generally present with adrenal insufficiency (14,15,16). Adrenal tumors >6cm are rare, usually nonfunctional, and about 38% are reported to be malign. Carcinomas lead to massive bilateral enlargement infrequently. In a study, >6cm bilateral massive enlargement was found in only 2 of 18 cases (one macronodular adrenal enlargement and one adrenal lymphoma) with adrenal tumor (17,18). Adrenal incidentaloma are usually found during screening for other pathologies. They may be bilateral, but rarely enlarge the gland, and do not cause systemic findings. Other rare adrenal mass causes are myolipomas, hemorrhage and amyloidosis (19,20).

Among infectious causes of adrenal mass, the most common ones are tuberculosis and fungal infections such as histoplasmosis. Tuberculosis is particularly common in developing countries. In general, pulmonary involvement is observed. Calcification in adrenal glands is a common finding. However, in acute tuberculous adrenalitis, bilateral enlarged glands might be seen (21). Histoplasmosis is endemic in USA. Its prevalence is 1/1000 cases, 79% with adrenal involvement and 40-50% with adrenal insufficiency. Serological markers might be positive or negative, and diagnosis is usually performed by aspiration biopsy (22,23).

In our case, CT and MRI examinations strongly indicated malignancy. In addition, there were no extraadrenal tuberculosis symptoms, and no adrenal calcifications or enlargement were observed, both of which are considered to be findings of adrenal tuberculosis. Instead, we found a mass which seemed to be separate from the adrenal gland. Since this is a very rare condition in tuberculous adrenalitis, we hope that our experience might help fellow physicians in their future diagnoses.

References

1. Kelestimur F. The endocrinology of adrenal tuberculosis: the effects of tuberculosis on the hypothalamo-pituitary-adrenal axis and adrenocortical function. *J Endocrinol Invest* **27**(4): 380-6. Review, 2004.
2. Kelestimur F, Ozbakır O, Saglam A, Ozturk F, Yucesoy M. Acute adrenocortical failure due to tuberculosis. *J Endocrinol Invest* **16**(4): 281-4, 1993.
3. Nerup J. Addison's disease: Clinical studies. A report of 108 cases. *Acta Endoc* **76:** 127-141, 1974.
4. Wang YX, Chen CR, He GX, Tang AR. CT findings of adrenal glands in patients with tuberculous Addison's disease. *J Radiol* **81**(5):226-8, 1998.

5. Kawashima A, Sandler CM, Fishman EK et al. Spectrum of CT findings in nonmalignant disease of the adrenal gland. *Radiographics* **18**(2): 393-412, 1998.

6. Yilmaz T, Sever A, Gur S, Killi RM, Elmas N. CT findings of abdominal tuberculosis in 12 patients. *Comput Med Imaging Graph* **26**(5): 321-5, 2002.

7. Tajdine MT, Ait Taleb K, Amahzoune M et al. Adrenal tuberculous pseudotumour. *Prog Urol* **12**(3): 462-4, 2002.

8. Mani S, Cunha N, Sachdev R, Sheth S.Tuberculosis and Addison's disease the role of CT in diagnosis and follow up. *The Indian Practitioner* **50**(2): 170-2, 1997.

9. Al Hadi HI, Hadi MA, Ali SM. The incidentally discovered asymptomatic adrenal tuberculous mass mimicking malignancy. *Bangladesh Med Res Counc Bull* **25**(1): 24-6, 1999.

10. Villabona CM, Sahun M, Ricart W, Serres X et al. Tuberculous Addison's disease. Utility of CT in diagnosis and follow up. *Eur J Radiol* **17**(3): 210-3, 1993.

11. Dunlop D. Eighty six cases of Addison's disease. *Br Med J* **2:** 887-891, 1963.

12. Carey RW, Harris N, Kliman B. Addison's disease secondary to lymphomatous infiltration of adrenal glands. Recovery of adrenocortical function after chemotherapy. *Cancer* **59**(6): 1087-1090, 1987.

13. Huminer D, Garty M, Lapidot M, Leiba S, Borohov H, Rosenfeld JB. Lymphoma presenting with adrenal insufficiency: adrenal enlargement on computed tomographic scanning as a clue to diagnosis. *Am J Med* **84**(1): 169-172, 1988.

14. Rosenberg SA, Diamond HD, Jaslowitz B, Craver LF. Lymphosarcoma: a review of 1269 cases. *Medicine (Baltimore)* 40:31-84, 1961.

15. Hsu CW, Ho CL, Sheu WH, Harn HJ, Chao TY. Adrenal insufficiency caused by primary aggressive non-Hodgkin's lymphoma of bilateral adrenal glands: report of a case and literature review. *Ann Hematol* **78**(3):151-154, 1999.

16. Wang J, Sun NCJ, Renslo R, et al. Clinically silent primary adrenal lymphoma: a case report and review of the literature. *Am J Hematol* **58**(2):130-136, 1998.

17. Lopez JM, Fardella C, Arteaga E, Michaud P, Rodriguez JA, Cruz F. Adrenal macrotumors diagnosed by computed tomography. *J Endocrinol Invest* 13: 581-585, 1990.

18. Lucon AM, Pompeo AC, Rodrigues PR, Mitre AI, Saldanha LB, Arap S. Synchronous bilateral carcinoma of the adrenal gland: 2 case reports. *J Urol* **149**(6): 1527-1529, 1993.

19. Udelsman R, Fishman EK. Radiology of the adrenal. *Endocrinol Metab Clin North Am* **29**(1): 27-42, 2000.

20. Pear BL. Other organs and other amyloids. *Semin Roentgenol* **21**(2): 150-161, 1986.

21. Doppman JL, Gill JR Jr, Nienhuis AW, Earll JM, Long JA Jr. CT findings in Addison's disease. *J Comput Assist Tomogr* **6**(4): 757-761, 1982.

22. Schonfeld AD, Jackson JA, Smith DJ, Hurley DL. Disseminated histoplasmosis with bilateral adrenal enlargement: diagnosis by computed tomography-directed needle biopsy. *Tex Med* **87**(4): 88-90, 1991.

23. Wilson DA, Muchmore HG, Tisdal RG, Fahmy A, Pitha JV. Histoplasmosis of the adrenal glands studied by CT. *Radiology* **150**(3): 779-783, 1994.