

CASE REPORT

TUBERCULOUS ADDISONS DISEASES : A DIAGNOSTIC DILEMMA

Sohail Akhtar, FRCP
Professor of Medicine and Consultant Pulmonologist
Baqai University Hospital, Karachi

CASE REPORT

YW, a 65 years old male of Chinese origin presented as out patient with a three month history of malaise, anorexia and weight loss of 14 kg. He denied any significant cough, dyspnea, fever, diarrhea, joint pains or rashes.

His past history included having pulmonary Tuberculosis 30 years ago and a left pleural effusion 8 years ago.

He smoked pipe and consumed approximately half an ounce of tobacco per week. He drank alcohol socially.

He was on no medications.

There was no family history of note. He was married and had two children.

On examination he looked ill with evidence of recent weight loss. There was no lymphadenopathy, jaundice, clubbing or edema. His temperature was 37.4° C, Blood Pressure was 110/70 supine; chest examination revealed reduced air entry at left base. The rest of the systemic examination was unremarkable.

His initial investigations revealed Hemoglobin of 11.9 gm per dl, normocytic blood picture, normal white cell count, total and differential, and platelets; Erythrocyte Sedimentation Rate of 54 mm in first hour and normal glucose, urea, creatinine, electrolytes, liver and thyroid function tests, serum calcium and hemoglobin electrophoresis. Chest X-ray showed atelectasis at left costophrenic angle (unchanged since 1983). Pleural aspiration was attempted twice but no fluid was aspirated.

Ultrasound of abdomen was normal. Fiberoptic bronchoscopy revealed changes of chronic bronchitis only. Brush cytology was negative for any pathology.

An upper G.I. Endoscopy was also normal.

Tomogram of chest showed elliptical opacity at left base and pleural thickening at left costophrenic angle. Similar findings were seen on computed tomography (CT) scan of chest. A suspicion of tumour was made and CT guided fine needle aspiration (FNA), and later true cut biopsy of the mass was done. Histology simply showed fibrosis and chronic inflammatory cells and no malignancy.

These investigations were done over ten weeks and during follow-up the patient showed no improvement in his initial complaints. He complained of inability to eat rice, lost weight further and thought his skin color especially back of hands had turned darker.

He was admitted and empirical anti-tuberculous therapy (ATT) including Rifampicin, Isoniazid and Pyrazinamide was started.

After 7 days he was even worse, in fact completely anorectic. His B.P. was 100/70mm Hg supine (and 90/60 erect). His serum biochemistry was deranged; sodium 126 meq/l, potassium 5.5 meq/l, urea 12.8 mmol/l, creatinine 132 mmol/l.

His ATT was stopped after one week and CT scan was reviewed. In the abdominal films there was suggestion of 'bulky' adrenal glands. Keeping this along with his clinical and laboratory picture, a suspicion of Adrenocortical Insufficiency was made and he was commenced on intravenous hydrocortisone 100 mg 6 hourly after taking a stat sample of blood for Cortisol.

Within 24 hours, he showed dramatic improvement, started eating and drinking normally and was fully mobile in 48 hours. His blood pressure was normal and his urea, creatinine and electrolytes returned to normal in a week. Serum Cortisol level prior to steroids was 53 nmol/l at 2 PM (N: 180-600). He was discharged home 10 days later on Hydrocortisone 20mg in morning and 10mg in evening, and Fludrocortisone 100 microgram per day. He was followed up for another four years and remained well on these drugs.

DISCUSSION

Addison's disease or Adrenocortical Insufficiency is an uncommon disease. Prevalence is reported as 93-140 per million and incidence 4.7-6.2 per million in white population^{1, 2}. The etiology is quoted as 75% auto-immune, 20% tuberculosis and 5% others including fungal infection, hemorrhage, infiltrative disorders and infarction¹¹. In areas with high prevalence of TB, the incidence is higher.

Signs and symptoms are non-specific (lethargy, anorexia, abdominal pain, pigmentation) and hence a delay in diagnosis can occur unless a high index of suspicion is made. It can present several years after tuberculosis infection even after apparently successful treatment. Slow destruction of adrenal glands is thought to be responsible. Up to 90% of adrenals have to be destroyed for manifestation of symptoms³. Sub-clinical disease may manifest as acute crises at time of stress. Asymptomatic and borderline cases are not infrequent. In a study of Tanzania⁴, 32% of 50 patients with chronic pulmonary tuberculosis who had only subtle symptoms, had an impaired synacthen response. Other studies from Australia and Africa have found abnormal response in active tuberculosis patients at 8% and 55% respectively^{5, 6}.

In our case, there was a past history of pulmonary tuberculosis and another illness with pleural effusion perhaps of the same etiology. The latter was 8 years ago after which he remained well. The insidious illness of anorexia, weight loss, and low grade pyrexia along with the CT scan findings lead to a suspicion of reactivation of TB or malignancy. But investigations were repeatedly negative including true cut and FNA biopsies. The incidental finding of adrenal enlargement on CT scan was later appraised in view of his serum biochemistry (high urea & potassium and low sodium), hypotension and skin pigmentation. The latter is due to enhanced stimulation of skin MC1 receptors by high circulating Adrenocorticotrophic hormone (ACTH) in Addison's disease¹.

Another notable feature was the rapid deterioration when he was put on anti tuberculosis treatment. All borderline features then became prominent, so much so that the treatment had to be stopped after one week. This was most likely due to the fact that Rifampicin is a potent inducer of hepatic cytochrome P450-dependent mixed oxidase system, a pathway through which cortisol is metabolized as well. Hence in a person given both the drugs, the availability of cortisol can be reduced by 40-50% making borderline deficient cases go into Addisonian crisis^{7,8,9}. While Rifampicin is an enzyme inducer, Isoniazid is an inhibitor; the balance of effect is always in favour of Rifampicin. In patients receiving Anti TB treatment, in particular Rifampicin, as well as Cortisol, the dose of latter should be increased to at least double^{9,10}.

In our case short synecthen test could not be done; however the serum cortisol value at 2 pm was significantly below the normal afternoon values. Moreover, the dramatic resolution in symptoms within 48 hours when he was only receiving cortisone leaves no doubt as to the etiology.

Our patient did not receive anti TB treatment while on adrenal replacement despite having evidence of weight loss, raised ESR and a previous TB history. Although being non specific and present in Addison's cases too, this can be debated, as corticosteroids alone in a patient with high risk of TB can precipitate reactivation or spread of TB. But in our case, this did not occur and in a follow up of four years the patient remained free of tuberculosis. This was perhaps because Tuberculous Addison's disease occurs due to destruction of adrenal glands rather than infection, and hence in these cases does not require anti TB treatment.

Conclusion

In patients with current or past history of tuberculosis, Addison's disease should be in the differential diagnosis of unexplained ill health, weight loss and skin pigmentation. Especially in areas with high prevalence of TB there should be a high index of suspicion for it. This is important as it is a potentially lethal yet easily treatable disease with simple replacement therapy. Moreover, when Rifampicin containing anti tuberculous therapy is given, consideration should be given for its enzyme inducing capacity when cortisol is given simultaneously.

REFERENCES

1. Wiebke Arlt, Bruno Allolio. Adrenal insufficiency. Lancet 2003; 361: 1881-93.
2. Laureti S, Vecchi L, Santeusano F, Falorni A. Is the prevalence of Addison's disease underestimated? J Clin Endocrinol Metab 1999; 84:1762.
3. Davenport J, Kellerman C, Reiss D, Harrison L. Addison's Disease: AFP 1991 : 43:1338-1342.
4. Mugussi F, Swai ABM, Turner SJ, Alberti KGMM, McLarty DG. Hypoadrenalism in patients with pulmonary tuberculosis in Tanzania; an undiagnosed complication? Transaction of the royal Society of Tropical Medicine and Hygiene 1990; 84: 849-851.

5. Barnes DJ, Naraqi S, Temu P, Turtle JR. Adrenal function in patients with active tuberculosis. *Thorax* 1989; 44: 422-4.
6. Ellis, ME, Tayoub F. Adrenal function in Tuberculosis. *British J. of Diseases of the Chest* 1986; 80: 7-10.
7. Wilkins EGL, Hnizdo E, Cope A. Addisonian crisis induced by treatment with Rifampicin. *Tubercle* 1989; 70: 69-73.
8. Mc Allister WAC, Thompson PJ, Al-Habet SM, Rogers HJ. Rifampicin reduces effectiveness and bioavailability of prednisolone. *BMJ* 1983; 286: 285-5
9. Mc Allister WAC, Thompson PJ Al-Habet S, Rogers HJ. Adverse effects of Rifampicin on prednisolone disposition. *Thorax* 1982 ; 37: 792.
10. Benini F., Savarin T., Senna G.E., Durigato s., Vettore L.,
Diagnostic and therapeutic problems in a case of adrenal tuberculosis and acute Addison's disease. *J. Endocrinol. Invest.* 1990; 13: 597-600.
11. Wilson J.D., Foster D.W.
Williams Text book of Endocrinology, 1992: 8th. Ed. Page 525.