



Tuberculous Lymphadenitis and Adrenalitis with Concomitant Addison's Disease: A Need to Diagnose and Treat Early

Ya-Li Chang¹, Shi-Wen Kuo¹, Leay-Kiaw Er¹

¹Department of Endocrinology, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan, R.O.C

Extrapulmonary tuberculosis often proceeds with an indolent course until a substantially infected organ is destroyed. This fact creates a great diagnostic challenge for clinicians. We report a rare case of tuberculous lymphadenitis and bilateral tuberculous adrenalitis with concomitant Addison's disease successfully treated with antitubercular drugs and steroid replacement.

Key words: Addison's disease, extrapulmonary tuberculosis, primary adrenal insufficiency, tuberculous lymphadenitis, tuberculous adrenalitis

INTRODUCTION

Since the 1950s, as therapies for tuberculosis (TB) have emerged, autoimmune adrenalitis has exceeded TB as the leading cause of adrenal insufficiency in Western countries. Nevertheless, TB remains an important cause in developing countries. Primary adrenal insufficiency secondary to adrenal TB is rare in current practice, and the clinical manifestations are mostly nonspecific, so it is often overlooked. Herein, we report a case of tuberculous lymphadenitis and bilateral tuberculous adrenalitis with a typical presentation of primary adrenal insufficiency successfully treated with antitubercular drugs and steroid replacement.

CASE REPORT

A 71-year-old female presented to our Emergency Department with nausea, vomiting and dizziness that had progressively worsened over the last 2 months. Two months ago, she sought advice from general practitioners several times. However, her symptoms did not lead to a diagnosis.

The patient had a history of left nephrectomy for renal stones, and excision of a right cervical lymph node with a pathology report of chronic granulomatous inflammation without further

management 2 years ago. She denied any history of TB infection or malignancy. On admission, her vital signs were stable. She denied having a cough, abdominal pain, weight loss, fever, or night sweating. Laboratory studies showed normal white blood cell counts. Biochemistry tests including alanine transaminase, lipase, and plasma glucose were normal. The serum sodium was extremely low, 109 mmol/L, and potassium was 4.7 mmol/L. Serum osmolality was 236 mOsm/kg, urine osmolality was 402 mOsm/kg, and the urinary sodium concentration was 109 mmol/L. Physical examination revealed hyperpigmentation in the patient's palmar creases, knuckles, face (freckles), lips and gums [Figure 1a], and longitudinal lines on the nails [Figure 1b]. We found three enlarged lymph nodes in the right neck. Further laboratory workup for hyponatremia revealed high morning plasma adrenocorticotrophic hormone, at 716 pg/ml (reference range 5-77 pg/ml), and low morning serum cortisol, at 6.18 µg/dl (reference range 5-25 µg/dl). Results of the endocrinological test and skin hyperpigmentation strongly suggested chronic primary adrenal insufficiency. Mineralocorticoid deficiency was also proved by low-normal plasma aldosterone, at 7.86 ng/dl (reference range 7-35 ng/dl) and elevated plasma renin activity, at 8.93 ng/ml/h (reference range 1.31-3.95 ng/ml/h).

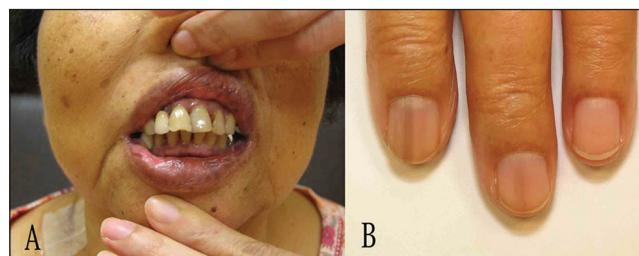


Figure 1: (a) Hyperpigmentation in the patient's face (freckles), lips and gums, and (b) Longitudinal hyperpigmentation on the nails

Received: April 24, 2015; Revised: June 14 2015 Accepted: July 28, 2015

Corresponding Author: Dr. Leay-Kiaw Er, Department of Endocrinology, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, No. 289, Jianguo Road, Xindian District, New Taipei City 231, Taiwan, R.O.C. Tel: +886 2 6628 9779 ext. 5767; Fax: +886 2 6628 9009. E-mail: erleaykiaw@yahoo.com.tw

TB lymphadenitis and adrenalitis with Addison's disease

Right cervical lymph node excisional biopsy was then performed and pathology revealed caseous granuloma [Figure 2a], yet no acid-fast bacilli in the special stain. No acid-fast bacilli were found in the special stain or culture of sputum. Chest X-ray was unremarkable. However, the abdominal contrasted computed tomography (CT) scan revealed a heterogeneous right adrenal tumor measuring 3.66 cm × 2.26 cm, soft tissue with dense calcification measuring 1.59 cm × 0.76 cm in the left suprarenal space and enlarged lymph nodes in the left iliac and paraaortic region [Figure 2b and c]. Extrapulmonary TB, involving bilateral adrenal glands, right cervical, and multiple intra-abdominal lymph nodes was highly suspected. The patient refused adrenal CT-guided needle biopsy.

The patient's general symptoms dramatically improved after initiation of steroid treatment (glucocorticoid and fludrocortisone) which was adjusted based on the clinical symptoms and electrolyte concentration. We started empiric anti-TB treatment, including rifampicin, isoniazid, pyrazinamide, and ethambutol that was maintained for 18 months. Sequential abdominal CT scans during and after complete anti-TB treatment revealed a significant reduction of the bilateral adrenal gland tumor within the 18 months [Figure 2d]. The enlarged cervical, paraaortic, and iliac lymph nodes disappeared after 6 months of anti-TB treatment. The hyperpigmentation also gradually faded 6 months following steroid replacement; the disappearance of longitudinal hyperpigmentation on the nails was especially impressive. At present, 6 years after diagnosis, the patient feels well and maintains on steroid replacement.

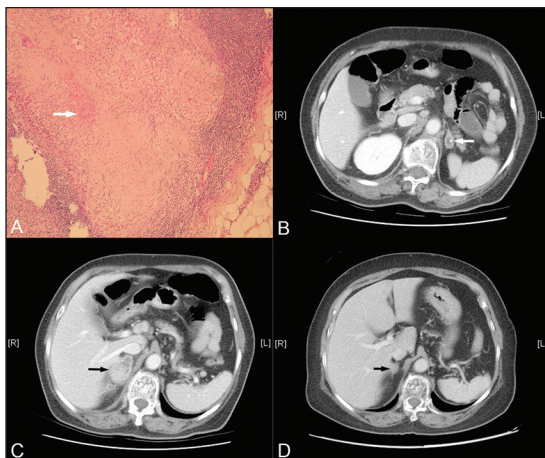


Figure 2: (a) Right neck lymph node biopsy specimen showing caseous granuloma with Langhans giant cells (arrow), (b) (before treatment) Soft tissue measuring 1.59 cm × 0.76 cm, with dense calcification in the left suprarenal space, (c) (before treatment) Abdominal computed tomography scan showing a heterogeneous tumor measuring 3.66 cm × 2.26 cm, with preserved contour and peripheral enhancement in the right adrenal gland, (d) Much regression of the right adrenal mass after 18 months of anti-tuberculosis treatment

DISCUSSION

In a few large studies, the incidence of extrapulmonary TB has approached 5% of active TB cases; however, it exceeded that in an autopsy series.¹ In a large retrospective analysis of autopsies, the adrenal gland was the fifth most common site of extrapulmonary TB. Primary adrenal insufficiency occurred in only 15% of patients with adrenal TB.² The clinical features of adrenal insufficiency are not noted until over 90% of the adrenal glands have been destroyed.³ The clinical symptoms of primary adrenal insufficiency are mostly nonspecific. Therefore, it is often overlooked and eventually leads to a delayed diagnosis, even when unique hyperpigmentation is present.

Percutaneous adrenal biopsy has been proven to be of great value, with 90% accuracy in determining the final diagnosis of adrenal masses in patients with a history of malignancy; however, in other pathologic conditions, such as adenomas, infectious disease, primary malignant tumors, or adrenal hemorrhage, its application is much more limited.⁴ Fine-needle aspiration is also not helpful in diagnosing adrenal TB. In nononcologic patients, a more conservative diagnostic approach is suggested.⁵ As such we did not go ahead with percutaneous adrenal biopsy in this patient and performed right neck lymph node biopsy instead, to study the possible link with adrenal tumor. The pathology of cervical lymph node biopsy revealed a surprising result: Caseous granuloma.

The radiological pattern may be crucial to supporting the diagnosis of adrenal TB infection without a histological process. Contrast-enhanced CT could provide evidence of a series of specific characteristics, including bilateral involvement, contour preservation, peripheral enhancement, and calcification to discriminate adrenal TB from primary tumors.⁶ Another study suggested that the difference in the CT attenuation value of the tuberculous lesion was less in the central area than in the peripheral area between the unenhanced and contrast-enhanced scan.⁷ We were able to find all the above-mentioned imaging characteristics in the CT images of our patient. These findings strongly supported the presumptive diagnosis of adrenal TB. The diagnosis was solidified by the remarkable regression of the right adrenal tumor and the disappearance of paraaortic and iliac lymph nodes in serial abdominal CT scans after complete anti-TB treatment.

The proportion of residual viable adrenal tissue at the time of diagnosis and the adequacy of anti-TB treatment determine the resumption of adrenal function. Despite the fact that the adrenal gland cortex has considerable capacity for regeneration, and effective anti-TB therapy may lead to some recovery of hormonal, adrenal function, patients usually have to remain on hormone replacement therapy.³ In addition,

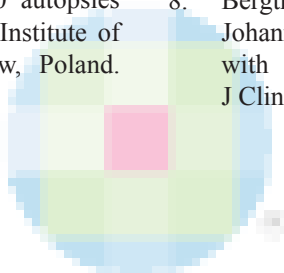
a large population-based study⁸ found increased mortality in patients with primary adrenal insufficiency. Thus, we emphasize the importance of a timely diagnosis of primary adrenal insufficiency to prevent further complications.

CONCLUSION

CT images of adrenal tumors associated with the pathology of accessible superficial lesions may provide powerful hints to the diagnosis of adrenal TB. Prompt anti-TB treatment and hormone replacement should be given to minimizing the patient's morbidity. It is imperative that health professionals should bear in mind the typical clinical presentation of primary adrenal insufficiency to make an early diagnosis and improve the patient's quality of life.

REFERENCES

1. Rowinska-Zakrzewska E, Szopinski J, Remiszewski P, Szymanska D, Miller M, Pawlicka L, *et al.* Tuberculosis in the autopsy material: Analysis of 1500 autopsies performed between 1972 and 1991 in the Institute of Tuberculosis and Chest Diseases, Warsaw, Poland. *Tuber Lung Dis* 1995;76:349-54.
2. Lam KY, Lo CY. A critical examination of adrenal tuberculosis and a 28-year autopsy experience of active tuberculosis. *Clin Endocrinol (Oxf)* 2001;54:633-9.
3. Bhatia E, Jain SK, Gupta RK, Pandey R. Tuberculous Addison's disease: Lack of normalization of adrenocortical function after anti-tuberculous chemotherapy. *Clin Endocrinol (Oxf)* 1998;48:355-9.
4. Welch TJ, Sheedy PF nd, Stephens DH, Johnson CM, Swensen SJ. Percutaneous adrenal biopsy: Review of a 10-year experience. *Radiology* 1994;193:341-4.
5. Penne D, Oyen R, Demedts M, Baert AL. Tuberculosis of the adrenal glands: Diagnosis by CT-guided fine needle biopsy. *J Belge Radiol* 1993;76:324-5.
6. Yang ZG, Guo YK, Li Y, Min PQ, Yu JQ, Ma ES. Differentiation between tuberculosis and primary tumors in the adrenal gland: Evaluation with contrast-enhanced CT. *Eur Radiol* 2006;16:2031-6.
7. Ma ES, Yang ZG, Li Y, Guo YK, Deng YP, Zhang XC. Tuberculous Addison's disease: Morphological and quantitative evaluation with multidetector-row CT. *Eur J Radiol* 2007;62:352-8.
8. Bergthorsdottir R, Leonsson-Zachrisson M, Odén A, Johannsson G. Premature mortality in patients with Addison's disease: A population-based study. *J Clin Endocrinol Metab* 2006;91:4849-53.



Author Help: Reference checking facility

The manuscript system (www.journalonweb.com) allows the authors to check and verify the accuracy and style of references. The tool checks the references with PubMed as per a predefined style. Authors are encouraged to use this facility, before submitting articles to the journal.

- The style as well as bibliographic elements should be 100% accurate, to help get the references verified from the system. Even a single spelling error or addition of issue number/month of publication will lead to an error when verifying the reference.
- Example of a correct style
Sheahan P, O'leary G, Lee G, Fitzgibbon J. Cystic cervical metastases: Incidence and diagnosis using fine needle aspiration biopsy. *Otolaryngol Head Neck Surg* 2002;127:294-8.
- Only the references from journals indexed in PubMed will be checked.
- Enter each reference in new line, without a serial number.
- Add up to a maximum of 15 references at a time.
- If the reference is correct for its bibliographic elements and punctuations, it will be shown as CORRECT and a link to the correct article in PubMed will be given.
- If any of the bibliographic elements are missing, incorrect or extra (such as issue number), it will be shown as INCORRECT and link to possible articles in PubMed will be given.