

PRIMARY SUPRARENAL GLANDULAR TUBERCULOSIS MIMICKING A MALIGNANT TUMOR

¹Hikmat Satria, ¹Kurnia Penta Seputra, ¹Basuki Bambang Purnomo.

¹Department of Urology, Faculty of Medicine/University of Brawijaya, Saiful Anwar General Hospital, Malang

ABSTRACT

Objective: Our case demonstrates effective tuberculosis-related Addison's disease care with laparoscopic adrenalectomy and anti-tuberculosis medication. **Case(s) Presentation:** A 43-year-old patient complained of left flank pain for two months before admission, unexplained weight loss, general weakness, decreased appetite, and without long-term cough. The physical examination resulted in hyperpigmentation on the fingers of both hands. MRI revealed an enlarged left adrenal gland and the blood test showed elevated cortisol to 1668 mmol/L. Three-port left laparoscopic transperitoneal adrenalectomy was used. Histopathology results showed epithelioid histiocytes that formed granulomas with caseous necrosis and Dutta Langerhans cells referring to tuberculosis; no malignancy was found from the same sample. **Discussion:** Addison's illness is the primary cause of tuberculosis. Due to the widespread use of anti-TB medications, the incidence of adrenal tuberculosis has been on the decline recently; nonetheless, in developing nations, tuberculosis is still the predominant cause of Addison's disease. **Conclusion:** Surgery and standard treatment for extrapulmonary tuberculosis were adequate to diagnose and alleviate the symptoms of cortisol disturbance caused by Addison's disease.

Keywords: Endocrine glands, adrenalectomy, tuberculosis endocrine.

ABSTRAK

Tujuan: Kasus ini menunjukkan perawatan penyakit Addison terkait tuberculosis yang efektif dengan adrenelektomi laparoskopi dan obat anti-tuberkulosis. **Presentasi kasus:** Seorang pasien berusia 43 tahun mengeluhkan nyeri pinggang kiri selama dua bulan sebelum masuk rumah sakit, penurunan berat badan yang tidak dapat dijelaskan, kelemahan umum, penurunan nafsu makan, dan tanpa batuk jangka panjang. Pemeriksaan fisik menghasilkan hiperpigmentasi pada jari kedua tangan. MRI mengungkapkan pembesaran kelenjar adrenal kiri dan tes darah menunjukkan peningkatan kortisol menjadi 1668 mmol/L. Adrenalectomi transperitoneal laparoskopi tiga port kiri digunakan. Hasil histopatologi menunjukkan histiosit epiteloid yang membentuk granuloma dengan nekrosis kaseosa dan sel Dutta Langerhans mengacu pada tuberculosis; tidak ada keganasan yang ditemukan dari sampel yang sama. **Diskusi:** Penyakit Addison adalah penyebab utama tuberculosis. Karena meluasnya penggunaan obat anti-TB, kejadian tuberculosis adrenal telah menurun akhir-akhir ini; meskipun demikian, di negara berkembang, tuberculosis masih menjadi penyebab utama penyakit Addison. **Simpulan:** Ketik Pembedahan dan pengobatan standar untuk tuberculosis ekstrapulmoner cukup memadai untuk mendiagnosis dan meringankan gejala gangguan kortisol yang disebabkan oleh penyakit Addison simpulan case report.

Kata kunci: Kelenjar endokrin, adrenalectomi, tuberculosis endokrin.

Correspondence: Kurnia Penta Seputra; c/o: Department of Urology, Faculty of Medicine/University of Brawijaya, Saiful Anwar General Hospital, Jl. Jaksa Agung Suprpto No.2, Klojen, Kec. Klojen, Kota Malang, Jawa Timur 65112, Indonesia. Email: uropnt.fk@ub.ac.id

INTRODUCTION

Globally, tuberculosis is a leading cause of infectious diseases that lead to death. The World Health Organization forecasts that tuberculosis will continue to rise, estimated 12 million cases per year occurring globally. Endocrine glands can contract tuberculosis, as can all organ systems.¹ Asymptomatic infection is not uncommon with the Mycobacterium

tuberculosis complex, which spreads to the adrenal glands through the blood and can take years to manifest. In a series of autopsies, 6% of active tuberculosis patients had adrenal involvement. Before the symptoms of insufficiency appear, more than 90% of the gland must have been damaged. According to numerous studies, people with pulmonary tuberculosis may have an enlargement of the adrenal glands without the glands being actively involved.²

Inflammation and stress could develop into contributing factors. Studies on hypothalamic-pituitary-adrenal (HPA) activity are widely available. The variability of results may be due to the absence of a common definition of "normal cortisol response" following stimulation of ACTH. Numerous studies have linked increased basal cortisol levels to reduced ACTH responsiveness, although the therapeutic relevance of these findings is unclear.³⁻⁵

Although they do not offer a conclusive diagnosis, radiographic imaging, such as computed tomography-scan (CT-scan), magnetic resonance imaging (MRI), and positron emission tomography (PET), are helpful non-invasive adjuncts to diagnosis. The imaging selection depending on the disease stage and is typically bilateral in adrenal involvement. The most frequent CT findings during the first two years are lucent appearance with non-calcified enlarged adrenal glands, reflecting caseous necrosis; it may manifest as peripherals necrosis.⁶



Figure 1. Clinical and radiological appearance. A) One physical sign of Addison's disease is generalized cutaneous hyperpigmentation. B) T2-weighted MRI of adrenal glands showed a 6 x 3 x 1.5 cm³ left suprarenal gland (3 times larger than normal volume of left adrenal gland, 19.4 ± 3.8 mm). C) Follow up after two weeks of post-operative improvement, generalized skin hyperpigmentation as a physical characteristic of Addison's disease has almost disappeared.

CASE(S) PRESENTATION

A 43-year-old man came with a chief complaint of left flank pain for about a year that had been worsening during the last two months before hospital admission. The patient also complained of sudden weight loss without lethargy, anorexia, and any other reason. The patient has never been diagnosed with tuberculosis and has no history of previous medical treatment. In addition, similar history and chronic cough in the family were also denied.

On the physical examinations, the patient's vital signs were within normal limits, but both sides of his fingers has been found hyperpigmentation (Figure 1A). The examination of the lungs did not show abnormal findings and enlarged lymph nodes were also not found.

Following the physical examinations, the patient underwent a chest X-ray in the AP position, which showed no abnormalities. The patient then had an MRI examination of the kidney, and the results showed an enlarged left suprarenal gland (Figure 1B). The patient then underwent blood laboratory examination, and the results showed an increase of

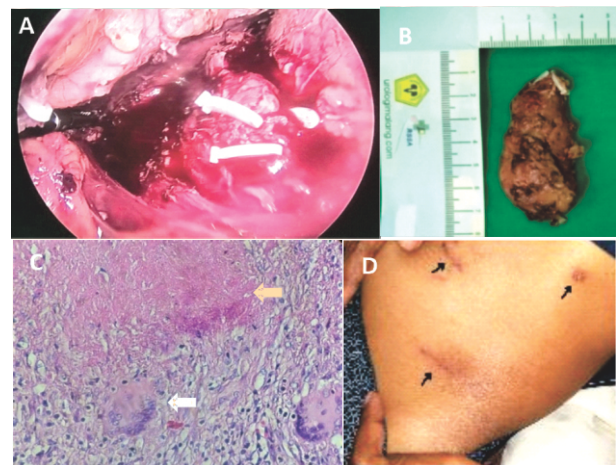


Figure 2. During and after adrenalectomy. A) Three-port left laparoscopic transperitoneal adrenalectomy. B) Left adrenal gland after left laparoscopic adrenalectomy. C) Histopathology of the left suprarenal gland using HE staining at 400x magnification shows caseous necrosis (orange arrow) and Dutta Langhans (blue arrow). D) Two-week post-surgical abdominal scar.

cortisol level up to 1.668 mmol/L. The patient was diagnosed with a left adrenal tumor and underwent a left trans-peritoneal laparoscopic adrenalectomy (Figure 2A) using 11 mm optic and 2 working elements 5 mm. After the procedure was completed, histopathological examination from the adrenal gland (Figure 2B) and results showed tuberculosis infection without any evidence of malignancy (Figure 2C)

This patient was finally diagnosed with Addison's disease due to mycobacterium tuberculosis infection. After five days of hospitalization, the patient's condition improved, the cortisol level decreased to a near-normal limit (595.50 mmol/L), and skin hyperpigmentation on the fingers disappeared (Figure 1C). Therefore, the standard regimen of extrapulmonary tuberculosis drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) was administered for nine months after the procedure.

DISCUSSION

In 1855, the main cause of adrenal insufficiency was initially identified by Thomas Addison as bilateral adrenal failure caused by Mycobacterium tuberculosis infection. According to Guttman's research from 1930, Addison's illness is the primary cause of tuberculosis. Due to the widespread use of anti-tuberculosis medications, the adrenal tuberculosis incidence has declined recently; nonetheless, In developing countries, tuberculosis is still the leading cause of Addison's disease.

Nomura et al. (1994)⁷ noted that although these patients did not have conventional tuberculosis, 93% of patients with adrenal tuberculosis had a prior history, typically from the lung and pleura. Examinations of the lungs and pleura revealed no evidence of tuberculosis.^{3,7} One in 100.000 persons has the rare condition Addison's disease. Only 7-20% are caused by tuberculosis, despite the fact that autoimmune disease causes 70%-90% of the underlying diseases. The average time between TB and the beginning of Addison's disease is 32±15 years, and tuberculosis typically makes Addison's disease worse.^{4,8,9}

One outward sign of Addison's illness is generalized cutaneous hyperpigmentation. Although generalized hyperpigmentation could be visible on sun-exposed skin and pressure points like the elbows and knees, it is uncommon to witness freckles darkening or even developing new ones.^{8,10} Hyperpigmentation is the other physical finding

characteristic, while chronic malaise, weariness, weakness, anorexia, and weight loss are common clinical symptoms. The usual, homogenous, brown hyperpigmentation is seen in sun-exposed areas, such as the face, neck, and backs of the hands, as well as areas subjected to persistent pressure or friction, is associated to ACTH melanogenesis.¹¹

For diagnosing adrenal insufficiency, blood cortisol, serum ACTH, and rapid ACTH stimulation tests are essential. Hyponatremia, hyperkalemia, azotemia, hypoglycemia, and hypercalcemia are frequent laboratory results. The diagnosis was established based on the symptoms and the low blood cortisol, low urine cortisol concentration, and its metabolites as a result of the high plasma ACTH, and supported by a poor cortisol response to synthetic ACTH.¹² In this case, elevated cortisol serum was found, even though it might be caused by the period of acute disease. Both the fast ACTH stimulation test and the serum ACTH concentration were skipped in this instance.

MRI often shows a bilateral enlargement of the adrenals in active tuberculosis and atrophy with calcification in remote infection. Definitive diagnosis is made by biopsy of the adrenal gland, showing caseating granuloma. It is common to find caseous necrosis or classic granulomatous inflammation with Langhans large cells.¹²⁻¹³ MRI showed an enlargement of unilateral sides, which was the left side of suprarenal glands, and histopathology showed caseating granuloma. Unilateral laparoscopic adrenalectomy was carried out to obtain the etiology of the disease, as was done by Soedarso et al.¹⁴ Since one of the etiologies of Addison's disease is tuberculosis, it is necessary to consider appropriate diagnostic and treatment strategies; best treatment option is laparoscopic adrenalectomy in combination with anti-tuberculosis drugs.

CONCLUSION

Our case showed a unique case of Addison disease that caused by tuberculosis infection. Difficulty on diagnosis was encountered, thus the diagnosis can be made only after the surgery and histology examination was performed. Our evidence shows that surgery and standard treatment for extrapulmonary tuberculosis was adequate to diagnose and alleviating the symptoms of cortisol disturbance caused by Addison disease.

REFERENCES

1. Sarin B, Sibia K, Kukreja S. Study of adrenal function in patients with tuberculosis. *Indian J Tuberc.* 2018; 65(3): 241-5.
2. Vinnard C, Blumberg E. Endocrine and metabolic aspects of tuberculosis. *Tuberculosis and Nontuberculous Mycobacterial Infections.* 2021; 5(1): 436-47.
3. Upadhyay J, Sudhindra P, Abraham G, Al E. Tuberculosis of the adrenal gland: a case report and review of the literature of infections of the adrenal gland. *International Journal of Endocrinology.* 2014.
4. Sarkar S, Sarkar S, Ghosh S, Al. E. Addison's disease. *Contemporary clinical dentistry.* 2012; 3(4): 484.
5. Kim W, Lee J. Adrenal Tuberculosis Mimicking a Malignant Tumor with Primary Adrenal Insufficiency. *Soonchunhyang Med Sci.* 2017; 23(1): 49-51.
6. Maller V, Afzal M, Shankar S. Primary adrenal tuberculosis causing adrenal insufficiency. *Hong Kong J Radiol.* 2016; 19: e6-9.
7. Nomura K, Demura H, Saruta T. Addison's disease in Japan: characteristics and changes revealed in a nationwide survey. *Intern Med.* 1994; 33(10): 602-6.
8. Barnett A, Espiner E, Donald R. Patients presenting with Addison's disease need not be pigmented. *Postgrad Med J.* 1982; 58(685): 690-2.
9. Nagler M, Müller B, Briner V, Al E. Severe hyperkalemia and bilateral adrenal metastasis. *J Oncol.* 2009; 2009.
10. Lanza A, Heulfe I, Perillo L, Al E. Oral pigmentation as a sign of Addison's disease: a brief reappraisal. *Open Dermatol J.* 2009; 3(1).
11. Namikawa H, Takemoto Y, Kainuma S, Al E. Addison's Disease Caused by Tuberculosis with Atypical Hyperpigmentation and Active Pulmonary Tuberculosis. *Intern Med.* 2017; 56(14): 1843-7.
12. Dabrowska A, Tarach J, Prystupa A, Al E. Addison's disease due to tuberculosis of the adrenal glands. *J Pre-Clinical Clin Res.* 2012; 6(2): 88-92.
13. Rajesh B, Mahendran M, Kumar P. Primary Adrenal Tuberculosis Presenting as Addison's Disease. *Journal Indian Academy of Clinical Medicine.* 2018; 19(3): 233-234.
14. Soedarso M, Nugroho K, Dewi K. A case report: Addison disease caused by adrenal tuberculosis. *Urol case reports.* 2018; 20: 12-4.