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Case report

Intestinal tuberculosis in a patient with Cushing's syndrome

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ABSTRACT

A 39-year-old woman presented with cushingoid features was worked up and diagnosed to have ACTH-independent Cushing's syndrome. Computed tomography of the whole abdomen revealed a left adrenal mass. She was scheduled for elective laparoscopic left adrenalectomy, however, a few days prior to the surgery, the patient had hematochezia. Colonoscopy revealed multiple ulcers on the terminal ileum, to which biopsy revealed *Mycobacterium tuberculosis* infection. The patient underwent laparoscopic left adrenalectomy on the same admission, which revealed adrenal adenoma on histopathology.

Introduction

Unilateral masses or tumors of the adrenal gland are prevalent. They are commonly discovered incidentally when the diameter is 3.0–3.5 cm as most of the patients are asymptomatic. Adrenocortical tumors can be categorized as benign or malignant, and non-functioning or functioning. Examples of the former include hormone-secreting adenomas that may cause Cushing's syndrome or primary aldosteronism [4].

Tuberculosis is endemic in the Philippines. Approximately 1 million Filipinos have active tuberculosis, and around 70 die daily from this curable disease [1]. The pathogen *Mycobacterium tuberculosis primarily* causes pulmonary tuberculosis (PTB); however, it is also capable of causing disease in extrapulmonary organs, posing a significant threat to health.

The most common form of transmission of *M. tuberculosis* is via inhalation of droplet nuclei from a person who has active pulmonary TB. The bacteria can be aerosolized by sneezing, coughing, or speaking. They can remain in the air for several hours and when inhaled, may reach the alveoli and multiply [2]. Aside from the lungs, one of the organs that could be rarely affected by TB is the gastrointestinal tract. Gastrointestinal tuberculosis (GI TB) can be transmitted by swallowing infected sputum with direct seeding, hematogenous spread, or through contaminated food particularly ingestion of milk from cows with bovine TB. Its symptoms include weight loss, either diarrhea or constipation, nausea, and vomiting [3].

In this case report, we present a 39-year-old female with ACTH-independent Cushing's syndrome from adrenal adenoma who presented with hematochezia from intestinal tuberculosis.

Case presentation

A 39-year-old hypertensive, non-diabetic female presented with one year history of moon facies, proximal myopathy, buffalo hump, abdominal striae, easy fatigability and hirsutism. The following laboratories were done and revealed a normal ACTH of 8.5 pg/mL [Reference range: 5–46 pg/mL] and elevated 1 mg Dexamethasone suppression test of 17.96 ug/dl [Reference range: < 1.8 ug/dL]. Whole abdominal CT scan revealed a $3.6 \times 2.9 \times 2.9$ cm well-defined heterogeneously enhancing solid mass on her left adrenal. Patient was then diagnosed with Cushing's syndrome secondary to a cortisol-producing adrenal adenoma and was scheduled for elective laparoscopic adrenalectomy. However, a few days prior to the scheduled operation, the patient suddenly had eight episodes of hematochezia with an estimated cumulative blood loss of 800cc. It was not accompanied with abdominal pain, diarrhea, constipation, vomiting, fever, night sweats, weight loss, or cough. She was then admitted for colonoscopy. On physical examination upon admission, the patient was coherent, not in respiratory distress, with an estimated body mass index of 27 kg/m^2. She had pale palpebral conjunctiva, normal blood pressure of 120/80, tachycardic at 105 beats per minute, and afebrile. Abdominal exam revealed normoactive bowel sounds, presence of violaceous striae, and no organomegaly, while rectal examination showed good sphincter tone and fresh blood per examining finger.

Colonoscopy showed a semi-circumferential white based ulcer on the terminal ileum (Fig. 1). Biopsies were taken and submitted for histopathology revealing acute on chronic inflammation with suspicious focus of granuloma with no intact ileal mucosa appreciated (Fig. 2).

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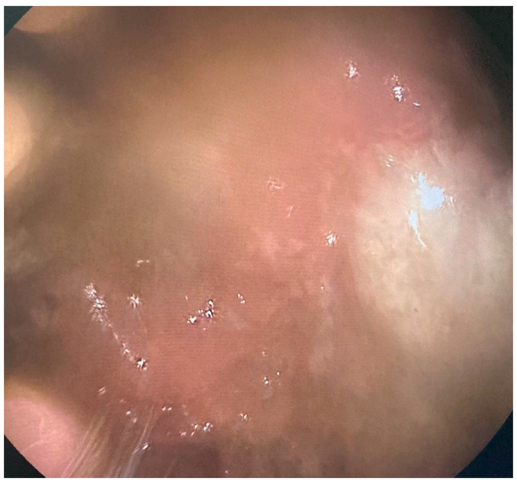

Fig. 1. Colonoscopy revealed multiple white based ulcers on the terminal ileum.

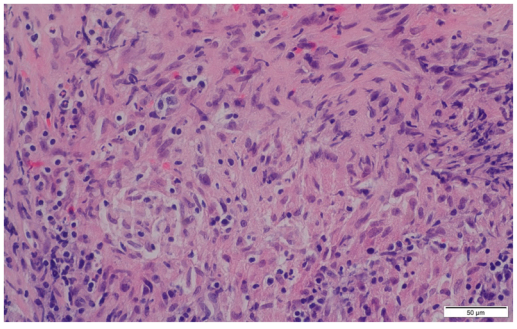

Fig. 2. Terminal ileum biopsy showing acute on chronic inflammation with suspicious focus of granuloma.

Tissue Gene Xpert revealed positive results for *M. tuberculosis* with no rifampicin resistance. Patient was then started on isoniazid, rifampicin, pyrazinamide, and ethambutol.

On the same admission, laparoscopic adrenalectomy (Fig. 3) of the left adrenal gland was performed showing adrenal cortical adenoma, consisting of a fairly pyramidal, brown to orange, doughy tissue, measuring 4.5 × 3.0 × 2.5 cm and weighing 50.0 g (Fig. 4) Microscopic sections showed features of adrenal cortical adenoma characterized by a well- encapsulated benign tumor composed of sheets of cells in an organoid pattern. The individual cells show relatively monomorphic, centrally located, round, bland nuclei and clear, vacuolated cytoplasm with well-defined borders. No features of malignancy such as atypical

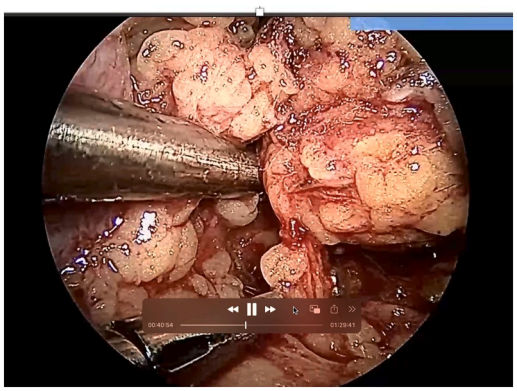

Fig. 3. Intraoperative laparoscopic adrenalectomy.

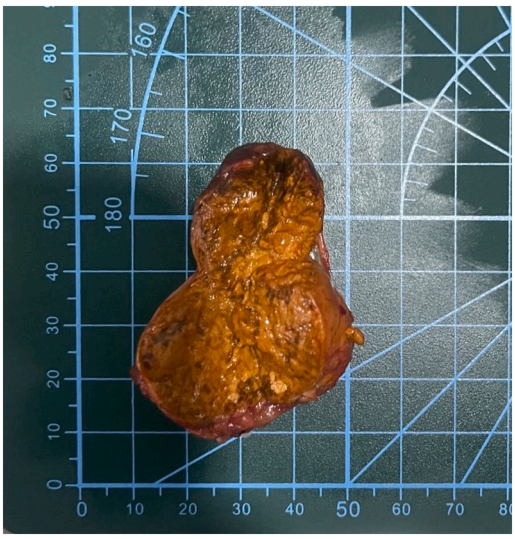

Fig. 4. Adrenal gland left.

mitotic figures, venous invasion, or necrosis were noted (Fig. 5). The final pathologic report was adrenal adenoma.

Discussion

This report presents a 39-year-old female diagnosed with Cushing's syndrome secondary to a cortisol-producing adenoma who had lower gastrointestinal bleeding due to intestinal tuberculosis.

Cushing's syndrome is a metabolic disorder which results from chronic exposure to excessive circulating levels of glucocorticoids. It can be divided into two categories based on its etiology: ACTH-dependent and ACTH-independent. ACTH-dependent forms are due to excessive ACTH production of the pituitary gland stimulating all three layers of adrenal cortex to produce aldosterone, cortisol, and sex hormones. ACTH-independent forms have low levels of ACTH because the excess glucocorticoids trigger the adrenals to send negative feedback to the pituitary. The excess steroids can either be from the adrenals oversecreting glucocorticoids or due to exogenous administration [5]. Cushing's syndrome predisposes patient to infections because of decreased number of NK cells and CD4 cells, and inhibited synthesis of cytokines, all brought about by excessive glucocorticoids [6].

Gastrointestinal (GI) tuberculosis (TB) is rare and is present only in

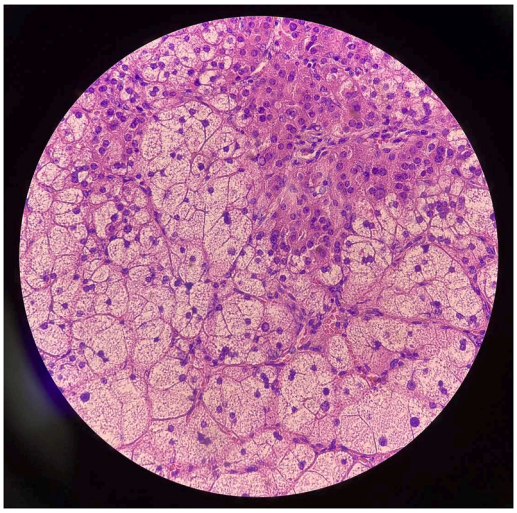

Fig. 5. Histopathology of adrenal cortical adenoma.

about 1% of all TB cases worldwide [7]. It commonly occurs in the setting of active pulmonary TB but can sometimes present as a primary infection even without pulmonary affectation. The ileocecal region is the most common site of intestinal TB but it can cause disease on any part of the GI tract [8]. The propensity of the said segments for GI TB is a combination of factors such as having a narrow lumen, low digestive activity, increased physiologic stasis, and the presence of lymphatic tissue`s M cells which take up the tubercle bacilli [9].

Well-established risk factors in the development of active TB infection include malnutrition, human immunodeficiency virus infection, and young age. There are also emerging variables identified such as diabetes, indoor air pollution, smoking, and alcohol [10]. Another well-known risk factor for developing active TB infection is immunosuppression. Prolonged glucocorticoid therapy increases the risk of tuberculosis. These individuals include solid organ recipients, hematopoietic stem cell transplant recipients, patients on biologic therapies, and patients undergoing chronic corticotherapy [11]. According to American Thoracic Society and Centers for Disease Control and Prevention (CDC), a prednisone of >15 mg/day (or its equivalent) administered for at least 1 month increases the risk for tuberculosis [12]. In one case-control study, it is noted that the odds ratio for TB was 2.8 (95% CI: 1.0–7.9) for prednisone doses lower than 15 mg/day. It was lower compared to the odds ratio of 7.7 (95% CI: 2.8–21.4) for prednisone doses greater than 15 mg/day [11].

According to research at Leiden University Netherlands by Xie et al. involving larval zebrafish models for tuberculosis to study the effect of glucocorticoids, they have concluded that steroids inhibit the macrophages` phagocytic activity, thereby increasing severity of bacterial infections such as tuberculosis [13].

In a case report by Bakker R.C. et. al, they found out that there is a higher frequency of opportunistic infections and increased mortality as the serum cortisol increases. The same study noted an increased risk of *Pneumocystis carinii* infection when plasma cortisol concentration reaches 2500 nmol/L [14].

Treatment of GI TB is similar to the treatment of pulmonary TB, with 2 months of intensive phase with four medications (rifampicin (H), isoniazid (R), pyrazinamide (Z), and ethambutol (E)), followed by maintenance phase with HR for an additional 4 months [15].

There are only a few reports of tuberculosis in patients with Cushing's syndrome, let alone a GI TB without pulmonary involvement. The patient has no other established or emerging risk factors such as HIV infection, diabetes, malnutrition, heavy smoking or alcohol intake. In this study, we found out that the excess cortisol due to Cushing's syndrome put our patient at risk for developing GI TB that caused the bleeding ulcer from her terminal ileum. We then recommend testing for serum cortisol level in patients who have Cushing's syndrome.

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Ethical approval

No ethics approval sought for the conduct of this study.

Consent

We did not close any names in the report of this case. No consent secured.

CRediT authorship contribution statement

Johanne Myrrh E. Soriano: writing of the paper, review of literature. **Rene A. Amadore Jr.:** writing of the paper. **Roy Raoul H. Felipe:** consultant, writing of final draft, **Lovell B. Gatchalian:** consultant, editing of final paper.

Conflict of interest

There are no conflict of interests with any of the authors.

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