Clinical Case Report

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A case report of ocular tuberculosis in a patient with membranous nephropathy

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Abstract

Rationale: Membranous nephropathy (MN), a chronic kidney disease (CKD), due to hypoproteinemia, malnutrition, anemia, long-term intake of immunosuppressive agents, changes in cellular immune state, and decrease in antimicrobial peptides, is a high risk for Mycobacterium tuberculosis (MTB) infection, which can cause tuberculosis (TB). TB manifests by various clinical symptoms. Ocular symptoms is a rare presentation of TB. Here, we describe a case of ocular tuberculosis in a patient with MN.

Patient concerns: A 63-year-old man with membranous nephropathy (MN) history presented with ocular symptoms.

Diagnoses: According to the pathological manifestations of ocular tissue biopsy and a positive polymerase chain reaction (PCR) on samples from sputum and bronchoalveolar lavage fluid (BALF), we elicited a diagnosis of disseminated tuberculosis.

Intervention: The patient received antituberculous therapy and immunosuppressive therapy.

Outcomes: The clinical manifestations significantly improved.

Lessons: Clinicians should be aware of the possibility of TB in cases of immunocompromised patients and perform an appropriate diagnostic work-up for TB.

Abbreviations: γ-IFN = γ-interferon, ADA = adenosine deaminase, BALF = bronchoalveolar lavage fluid, CKD = chronic kidney disease, CT = computed tomography, MN = membranous nephropathy, MTB = Mycobacterium tuberculosis, PCR = polymerase chain reaction, TB = tuberculosis.

Keywords: membranous nephropathy, ocular tuberculosis, pulmonary tuberculosis, tuberculous pleuritis

1. Introduction

Mycobacterium tuberculosis (MTB) can invade many organs and cause infectious diseases called tuberculosis (TB). TB remains one of the leading causes of death among adults worldwide and a global epidemic that poses a threat to human life and health.[1–2] The World Health Organization reported that there were about 10 million new TB cases worldwide in 2015, in association with multidrug resistant TB, HIV, and global migration.[3] Ocular TB is either primary in which MTB directly infects ocular tissue, or secondary to pulmonary TB, cerebral TB, lymph node TB, and so on. Ocular TB, with nonspecific symptoms, is relatively rare and often overlooked in clinical practice.[4–5]

Due to hypoproteinemia, malnutrition, anemia, long-term intake of immunosuppressive agents, changes in cellular immune state and decreases in antimicrobial peptides, membranous nephropathy (MN) is a high risk of MTB infection.[6] Clinicians should suspect the possibility of TB in those immunocompromised patients, such as MN. We herein describe the case of a 63-year-old man with MN history, who initially presented with ocular symptoms and was misdiagnosed as conjunctivitis. Further examinations demonstrate ocular TB and pulmonary TB as well as tuberculous pleuritis.

2. Case report

A 63-year-old man was admitted to hospital for suppuration of his right eye in January 2017. He had MN history and had already been treated with glucocorticoids, tacrolimus, and tripterygium glycosides for 3 years. He stopped the drugs above following renal physicians' advice in August 2016. Ocular symptoms developed 2 months before admission and was diagnosed as conjunctivitis in an ophthalmology clinic. In spite of treatment with Levofloxacin eye drops, ocular symptoms became serious. Then an ulcer on the surface of the right sclera was found and biopsy was performed. The pathological diagnosis was granulomatous inflammation and inflammatory granulation tissue, with positive acid fast stain (Fig. 1), suggesting ocular TB.

Physical examination at presentation showed conjunctival congestion of the right eye, with an ulcer approximately 0.5×0.5 cm on the surface of the right sclera, which was confirmed by B-scan ultrasonography. He had normal blood pressure of 134/89 mmHg, with 97% saturation. Lymphadenopathy was absent. Pulmonary examination revealed left-sided low breath sound

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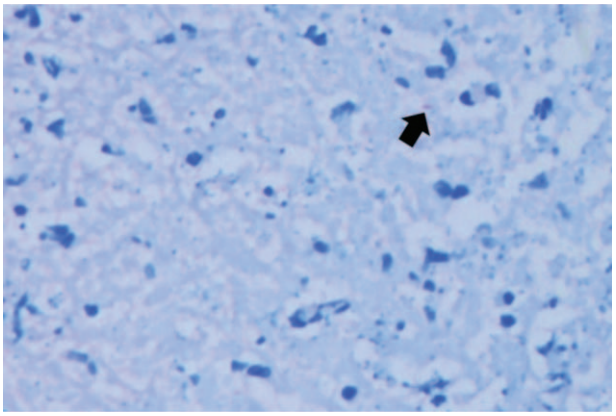

Figure 1. The acid fast staining (×400) of the pathological examination of the patient's right sclera ulcer showing positive acid fast stain (marked with black arrow).

without rales. Pitting edema of both lower limbs was present. Computed tomography (CT) of the chest showed multiple tiny nodules distributed throughout both lungs and pleural fluid in the left pleural cavity (Fig. 2A and B). Laboratory examination showed erythrocyte sedimentation rate 104 mm/h (reference range, 0–15 mm/h) and C-reactive protein 30.68 mg/L (reference range <10 mg/L). 24-hour urinary protein excretion was 9016 mg (reference range, 0–150 mg). Blood chemistry revealed albumin 20 g/L (reference range, 35–55 g/L), with a mildly elevated creatinine and urea nitrogen. Although 3 separate smears of sputum for acid fast bacillus were negative, the polymerase chain reaction (PCR) detection of sputum for MTB was positive. Closed drainage of left pleural cavity was performed, draining cloudy and deep yellow liquid with total protein 21.2 g/L, adenosine deaminase (ADA) 60 U/L (reference range, 4–22 U/L), and γ-interferon (γ-IFN) >800 ng/L (reference range, 0–40 ng/L), suggesting tuberculous pleuritis. Bronchoscopy showed the dorsal segment of the left lower lobe was slightly narrow and bronchoalveolar lavage (BALF) was PCR positive for MTB. MTB cultures on samples from sputum, pleural effusion and BALF were all negative.

Antituberculous chemotherapy was begun with daily administrations of isoniazid (300 mg), ethambutol (750 mg), rifampin (450 mg), and pyrazinamide (1000 mg). After 2 weeks, the chest ultrasound and chest CT showed left pleural effusion had significantly reduced (Fig. 2C and D) and the left drainage tube was removed. However, the right pleural effusion emerged and closed drainage of the right pleural cavity was performed, draining cloudy and light yellow liquid, with total protein 10.9 g/L, ADA 32 U/L, and γ-IFN >800 ng/L, suggesting tuberculous pleuritis with transudate. Antituberculous chemotherapy and closed drainage of the right pleural cavity were continued for another 10 days. However, the drainage volume of the right pleural cavity was not correspondingly reduced, about 200 to 400 mL every day. He refused the treatment with human albumin and prednison, and requested hospital discharge for poverty.

One month later, the patient came back. Blood chemistry showed albumin decreased to 13.9 g/L, while creatinine and urea nitrogen further elevated. 24-hour urinary protein excretion was elevated to 12,221 mg. He received administrations with tripterygium glycosides (60 mg/d), prednisone (30 mg/d), human albumin (10 g every other day), diuretics, and continuous antituberculous chemotherapy for 2 weeks. The patient's symptoms gradually improved. 24-hour urinary protein excretion decreased to 1844 mg. Chest ultrasound showed little encapsulated pleural effusion in the left pleural cavity while no pleural effusion on the right side. Three months after antituberculous chemotherapy, the right conjunctival congestion obviously relieved, and the ulcer of the right sclera decreased in size (about 0.3 × 0.3 cm) as well. The patient has been doing well so far.

3. Discussion

The epidemic situation of TB is becoming increasingly severe worldwide. According to data published by the World Health Organization, in 2015, there were about 10 million new TB cases worldwide, 4,800,000 new cases of multidrug-resistant TB were added, and 1.4 million cases died from TB.[3] However, extrapulmonary TB such as ocular TB, cerebral TB, lymph node TB, pleural TB, and so on, accounting for 80% of TB, is not easily identifiable for nonspecific symptoms.

Ocular tissue except crystalline lens can be infected by MTB, which is called ocular TB. Ocular TB is either primary in which MTB directly infects ocular tissue, or secondary to pulmonary TB, cerebral TB, lymph node TB, and so on. The secondary type is in the majority. Ocular TB is relatively rare in clinical practice and easily overlooked by clinicians. Furthermore, the early symptoms and signs of ocular TB have no obvious specificity, and most patients with ocular involvement have no history of pulmonary TB or other systemic manifestations, resulting in underdiagnosis or misdiagnosis. The diagnosis of ocular TB can be confirmed by acid fast stain, MTB culture, or PCR detection of ocular fluid, which varies on criteria in published literatures and most of the time the diagnosis of ocular TB is only presumptive.[4–5] In this case, the patient was initially misdiagnosed as conjunctivitis and there was no improvement after treatment. Then the sclera ulcer was found for biopsy and the pathological examination showed granulomatous inflammation and inflammatory granulation tissue with positive acid fast stain. Following antituberculous chemotherapy, symptoms and signs of the right eye significantly improved, and the patient suffered no complications as a result of ocular TB. It was a pity that cultures of the eye excretion were not taken.

The gold standard for the definitive diagnosis of pulmonary TB remains the finding of the MTB in the sputum or BALF. However, the finding of the MTB is always difficult. In recent years, real-time PCR with better sensitivity and specificity, has provided great convenience for the screening and differential diagnosis of TB, and can be a rapid, simple, and objective alternative to smear and culture.[7] From the monistic view, the diagnosis of pulmonary TB in this case was based on the MN history, long-term intake of immunosuppressive drugs, positive acid-fast staining, typical pathology manifestation in ocular tissue, and positive PCR on samples from sputum and BALF.

The definite diagnosis of tuberculous pleuritis depends on pleura biopsy or pleural fluid culture of MTB. Due to the invasiveness of pleural biopsy and low sensitivity of pleural fluid culture, pleural fluid ADA, and γ-IFN measurements with pivotal role are recommended for differential diagnosis of tuberculous pleuritis.[8] In this case, according to pleural fluid ADA (>45 U/L) and γ-IFN values (>800 ng/L), the clinical diagnosis of tuberculous pleuritis was confirmed. After 2-week antituberculous chemotherapy, the left pleural fluid disappeared, but the right pleural fluid appeared and was difficult to control. The possible reasons were as follows. Firstly, herxheimer-liked reaction was possible for amounts of MTB were killed in short time which made a hypersensitive individual develop a greater allergic

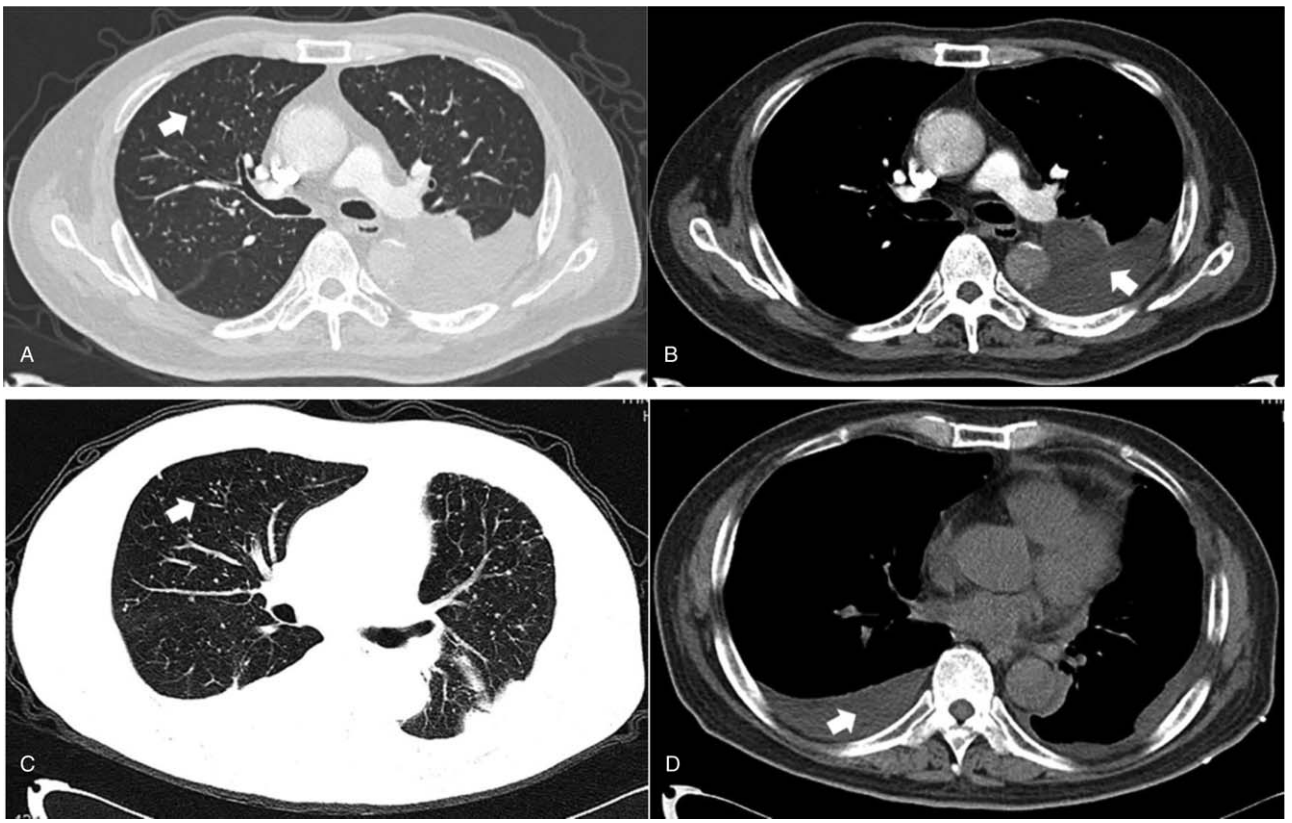

Figure 2. (A–B) Chest CT examination on admission showing multiple tiny nodules distributed throughout both lungs and pleural fluid in the left pleural cavity (marked with white arrow); A is the lung window, B is the mediastinal window. (C–D) Chest CT examination after 2 weeks' treatment showing significant reduction of left pleural fluid and the appearance of right pleural fluid (marked with white arrow); C is the lung window, D is the mediastinal window. CT = computed tomography.

reaction. The phenomenon above was called Pseudo deterioration. Secondly, uncontrolled TB such as drug-resistant TB was also possible, but there was no evidence of drug resistance. Thirdly, the active nephrotic syndrome resulted in severe hypoproteinemia, low plasma colloid osmotic pressure, and transudate formation. According to the test results of right pleural effusion, we assumed that the property of the right pleura effusion was TB exudate combined with transudate. It was several factors that involved in the formation of the right pleural effusion, which disappeared after treatment of sustained antituberculous drugs, immune inhibition, blood albumin input, and diuretic drugs.

MN as a chronic kidney disease (CKD), due to hypoproteinemia, malnutrition, anemia, long-term intake of immunosuppressive agents and other factors, changes in cellular immune state and decreases in antimicrobial peptides, leading to high risk of MTB infection, easy progress into active TB, and more extrapulmonary TB patients than TB patients.[6] TB can also cause diseases such as urinary TB, chronic interstitial nephritis, renal amyloidosis, glomerulonephritis, and so on.[9] In this case, after suffering from TB, large amount of proteinuria and severe hypoproteinemia appeared and serum creatinine level elevated, presenting even a progressive aggravation trend. We supposed that TB as an infection inducer resulted in the activity of nephrotic syndrome. Secondly, both of TB and antituberculous drugs may lead to secondary interstitial lesion of kidney. However, there was a lack of renal biopsy to confirm this conjecture. After antituberculous chemotherapy and low-dose prednisone therapy, 24-hour urinary protein significantly decreased and serum creatinine also decreased, suggesting obvious treatment effect and indirect confirmation of the conjecture mentioned above.

In this case, the immunocompromised state of the patient with MN history probably contributed to the multiple infection of MTB. We concluded the following points. Firstly, MN patients are at risk of TB for immune insufficiency. The detailed TB history, TB contact history, and antituberculous treatment history should be taken. Furthermore, regular physical examination including the eyes, lungs, kidneys, and other organs is necessary, as well as regular chest film check. Secondly, ocular TB is relatively rare in clinical practice. Due to lack of specific symptoms, the diagnosis of ocular TB is often delayed, suggesting that the clinicians should be aware of this disease when encountering immunocompromised patients with eye symptoms. Early detection, early diagnosis, and early antituberculous treatment can prevent serious ocular complications such as ophthalmectomy. Thirdly, close coorperation between nephrologists and TB specialists is recommended. Lastly, for TB and CKD interact with each other and form vicious cycle, TB patients should start antituberculous chemotherapy as soon as possible and CKD patients should be screened for the presence of latent MTB infection. However, the evidence of when to screen and how to screen is still limited, pending further study.

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