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CASE REPORT

Swollen Necrotic Lymphadenitis Infected with *Mycobacterium Paracondontium* in an AIDS Patient: a Case Report and Literature Review

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Background: *Non-tuberculous mycobacteria* (NTM) are a group of mycobacteria that are commonly found in the environment and can cause disease in humans. The symptoms of NTM infection can be similar to those of tuberculosis, making diagnosis challenging. The morbidity associated with NTM is increasing, and clinical management can be challenging.

Case Description: This report details the case of a 32-year-old male who was found to have multiple enlarged and partially necrotic lymph nodes in the neck, axilla, mediastinum, and retroperitoneum. The causative agent was rapidly identified as *Mycobacterium paracondontium* through pathogen-targeted sequencing (tNGS). After two weeks of treatment with azithromycin, moxifloxacin, rifabutin, and amikacin, the patient's uncomfortable symptoms had resolved, and he is currently undergoing further review.

Conclusion: It is imperative that clinicians remain vigilant for the presence of NTM, particularly those that are rare, given their pervasiveness in the environment. Prompt diagnosis is of paramount importance, and molecular identification techniques represent a crucial tool in this regard. In vitro drug sensitivity testing should be conducted whenever feasible to guarantee the administration of an efficacious treatment regimen.

Keywords: *non-tuberculous mycobacteria*, *Mycobacterium paracondontium*, lymph nodes, case report

Introduction

NTM are mycobacteria that are distinct from *Mycobacterium tuberculosis complex* (MTC) and *Mycobacterium leprae* (MLE). They are widespread in nature, partially pathogenic but of low virulence, and most commonly cause pulmonary disease,[1] often in immunocompromised populations or those with a history of pulmonary disease, and more than 200 species of NTM have been identified.[2] NTM are categorized into fast-growing and slow-growing mycobacteria based on genome typing. Fast-growing NTMs include *Mycobacterium abscessus complex* (MABC), *Mycobacterium fortuitum* (MFO), and *Mycobacterium chelonae* (MCH), while slow-growing NTMs include *Mycobacterium avium complex* (MAC), *Mycobacterium kansasii* (MKA), and *Mycobacterium xenopi* (MXE).[3]

Clinical symptoms caused by NTM are similar to those of tuberculosis, both in terms of local damage and systemic toxicity. As a result, they are often misdiagnosed as tuberculosis. The incidence of NTM-associated morbidity has gradually increased with the development and improvement of medical testing technology.[4] However, clinical diagnosis and treatment remain difficult due to the irrational use and abuse of clinical drugs, leading to an increase in the drug resistance rate of NTM, as well as the long treatment cycle, drug side effects, and a wide range of causative organisms.[5,6] This makes it one of the global public health problems.

Here, we report a case of multiple swollen and necrotic lymph nodes caused by *Mycobacterium paracondontium*. Early diagnosis and appropriate treatment are crucial to improve the patient's prognosis. We also reviewed the available literature on *Mycobacterium paracondontium* infections to raise awareness among physicians.

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Case Presentation

The patient is a 32-year-old male who presented with a fever two months ago. The highest recorded temperature was 38.6 °C. He also reported coughing and producing sputum, but did not experience chest tightness or shortness of breath. Despite these symptoms, he did not seek medical attention until one week prior to hospitalization. Blood tests conducted at a local hospital revealed WBC of 4.45×10^9 / L, Hb of 115g / L, PLT of 193×10^9 / L, hs-CRP of 90.12mg/L, and negative Mycoplasma pneumoniae IgM. The CT scan of the Chest revealed multiple patchy low-density shadows under the pleura of the upper lobes of both lungs, clumped high-density shadows in the upper mediastinum measuring about 48mm x 29mm, and solid nodules in the extra-basal segment of the left lower lobe of the lungs (SE203, IM171,200) with a larger size of about 5mm x 4mm. The patient was treated with Levofloxacin 0.5g/dose for a total of 4 days, resulting in a peak temperature decrease and improvement of the cough. The patient presented to our hospital on 2024.3.29 with intermittent low-grade fever and mild cough with sputum.

The patient has a 10-year history of AIDS and was taking lamivudine, zidovudine, and lopinavir ritonavir for anti-retroviral therapy (ART) for 6 years. However, the patient stopped taking the medication without authorization 4 years ago and has not been retested until 2023.4.12 when he was tested for HIV-

Upon admission, the patient underwent physical, laboratory (Table 1), and radiological examinations. The physical examination revealed a body temperature of 36.5°C, a heart rate of 124 beats/min, a respiratory rate of 17 beats/min, and a blood pressure of 142/97mmHg. Multiple swollen superficial lymph nodes were palpable in the neck and left axilla, with the largest measuring approximately 2.5cm x 1.0cm. The borders were clear, and there was no compression pain, redness, swelling, or ulceration of the skin. There was no pharyngeal congestion or whiteness in the oral cavity. The respiratory sounds of both lungs were slightly coarse, with no obvious dry or wet rhonchi detected. The abdomen was soft and non-tender.

Table 1 Laboratory Examinations at Admission

	At admission (2024.3.29)	**Reference**
White blood count, (10^9/L)	3.89	3.5–9.5
Neutrophil ratio, (%)	77.1	40.0–75.0
Red blood cell, (10^12/L)	4.15	4.30–5.8
Hemoglobin, (g/L)	117	130–175
Platelets, (10^9/L)	255	125–350
C-reactive protein, (mg/L)	14.35	0–6.0
Serum amyloid A, (mg/L)	209.19	0–10.0
Procalcitonin, (ng/mL)	0.048	0–0.5
Lactic acid, (mmol/L)	1.62	0.7–2.1
Serum creatinine, (μmol/L)	52	57–111
ALT, (U/L)	37	9–50
AST, (U/L)	28	15–40
CD4+ T-lymphocytes, (cells/μL)	16	432–1341
CD4+/CD8+, (%)	0.06	0.71–2.78
HIV-RNA, (IU/mL)	4.24	<100
Xpert MTB/RIF assay (neck lymph node tissue)	-	-
T-SPOT.TB assay	+	-
Sputum smear for antacid bacilli	-	-
Fungal (1-3)-β-D glucan	-	-
Cryptococcal capsular antigen	-	-
Aspergillus galactomannan	-	-
Mycobacterium tuberculosis IgG/IgM antibody	-/-	-

Notes: +, positive; -, negative.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; Xpert MTB/RIF assay, detection of rpoB gene and mutations in Mycobacterium tuberculosis.

The patient underwent an enhanced chest CT in 2024.3.30, based upon the results of her previous outpatient chest CT. The imaging revealed a mass of inhomogeneous soft tissue density shadow measuring approximately 56mm x 42mm x 46mm at the right edge of the upper mediastinum. The solid part showed obvious continuous enhancement after enhancement, and a patchy unenhanced area was seen within it (Figure 1A). The lesion was poorly demarcated from the right subclavian artery, vein and trachea. Scattered, few, streaky shadows with clear margins were observed in both lungs, along with a few fine nodules. The larger nodule, measuring approximately 4mm x 3mm, was located in the outer basal segment of the lower lobe of the left lung (Se4 (IM144)) and appeared solid. Furthermore, additional examinations were conducted. A posterior peritoneal CT scan with enhancement revealed enlarged lymph nodes on the right side of the retroperitoneal abdominal aorta, one of which had central necrosis (Figure 1B). Ultrasound scans of the neck, axillary, and inguinal lymph nodes showed multiple hypoechoic nodules in the left axilla, with regular shapes. The largest nodule measured 1.5cm x 0.5 cm. No abnormally enlarged lymph nodes were detected in the right axilla. No abnormal enlarged lymph nodes were found in the bilateral inguinal region. Multiple hypoechoic nodules with clear borders and regular shapes were detected in the bilateral neck. The larger nodule, measuring approximately 2.7cm x 1.1cm (Figure 2), was located on the right side and showed some blood flow signal in the periphery and interior of the neck on CDFI.

To obtain a pathogenetic basis for the patient's multiple swollen and necrotic lymph nodes, we performed an ultrasound-guided aspiration biopsy of the right supraclavicular lymph node on 2024.4.1. A total of three lymph node tissues were obtained, and they tested negative for Mycobacterium tuberculosis and rifampicin resistance. In light of this, on 2024.4.1, we conducted tNGS on the lymph node tissues we obtained. Fortunately, we were successful in detecting *Mycobacterium paracondontium*, with a sequence number of 29 and a relative abundance of 0.31%. Based on the results mentioned above, we identified *Mycobacterium paracondontium* as the causative agent. With the patient's consent, we prescribed a combination of azithromycin (0.5 g once daily), moxifloxacin (0.4 g once daily), rifabutin (0.3 g once daily), and amikacin injection (0.4 g once daily) as the anti-infective treatment on the same day. The pathological findings of the lymph node tissue (Figure 3) further confirmed our diagnosis with the following pathological diagnosis: (right clavicular lymph node puncture) thickening of the fibrous envelope, the structure of the lymph node underneath it was poorly defined, and a fuzzy granuloma without caseous necrosis was seen (combined with antacid staining (+), which was consistent with granulomatous lymphadenitis- Tuberculosis). Immunohistochemistry: CD20 (-), CD3 (T-cells +), CD68 (histiocytes +), CMV (-), EBV (-), PAS (-), antacid (+), hexosamine silver stain (-). In the meantime, the patient

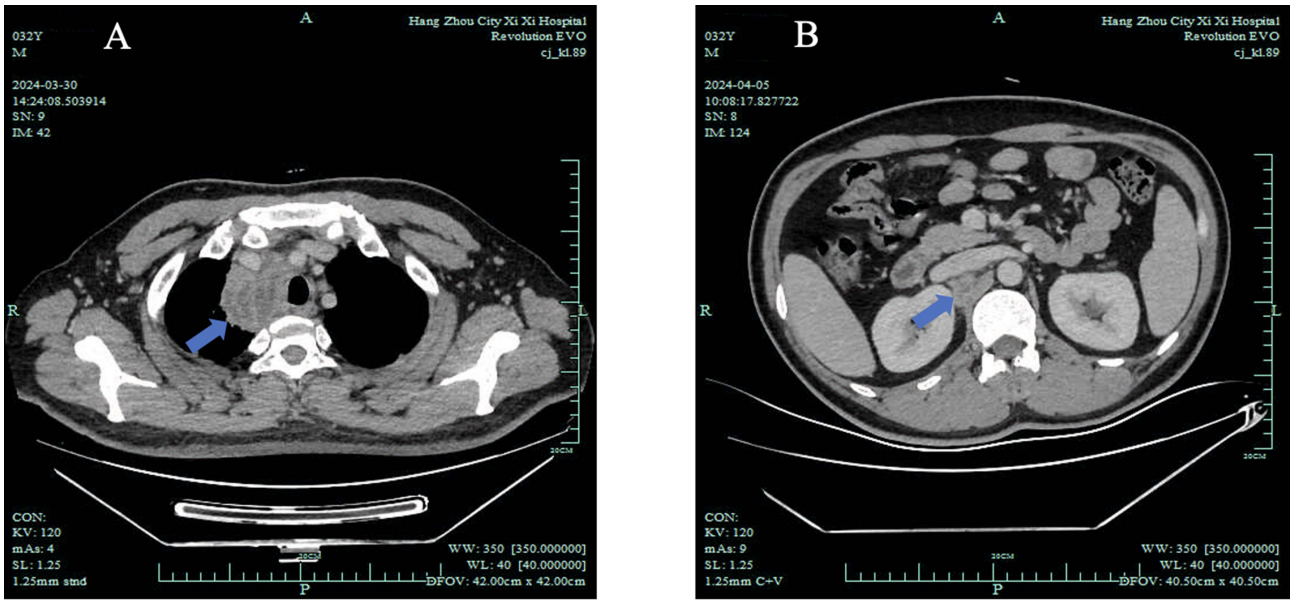

Figure 1 The radiographic examination. (**A**) uneven enhancement of the upper mediastinal paratracheal area with blue arrows indicating localized necrosis within the lesion, approximately 5.51 cm × 4.33 cm in size;(**B**) The blue arrow indicates that the necrotic lymph node in the center of the retroperitoneal right pararenal area, approximately 2.45 cm × 1.33 cm in size.

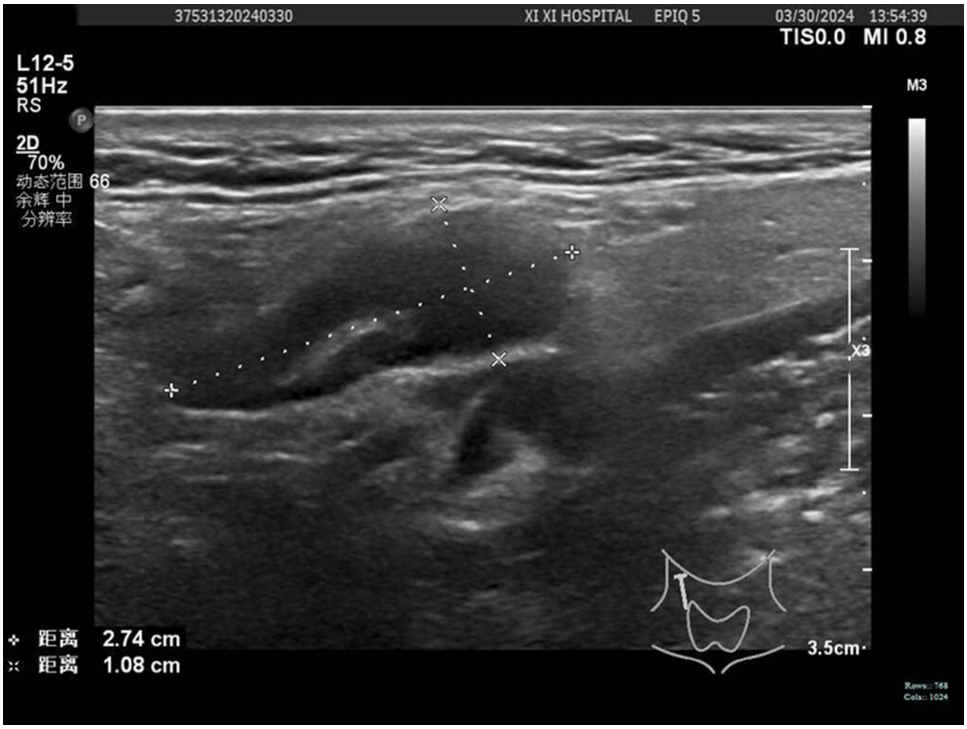

Figure 2 Boundaries are clear, morphology is regular, similar to lymph node echogenicity, and internal echogenic corticomedullary-like demarcation is clear, with larger nodules measuring approximately 2.7 cm × 1.1 cm.

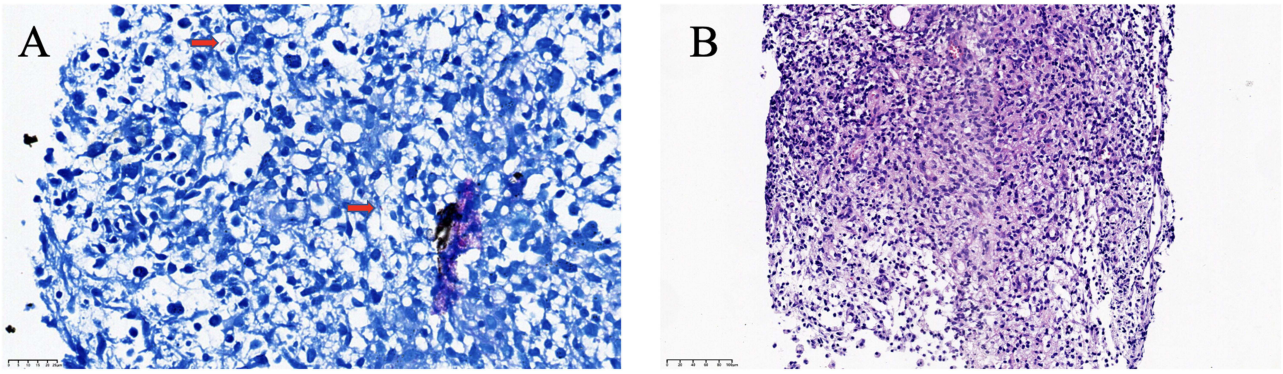

Figure 3 The histopathological examination. (**A**) Antacid staining magnified 400 times shows antacid bacilli, the red arrows indicate antacid bacilli;(**B**) HE staining magnified 200 times. Few lymph nodes are organized, lymph node structure is unclear, and histiocytes, lymphocytes, and epithelioid cells are seen constituting a non-caseous necrotic granulomatous nodule.

underwent HIV-1 resistance genotyping, suggesting no detectable resistance, ART (tenofovir + lamivudine dolutegravir) was given, to be restarted on 2024.4.5.

Discussion

Phylogenetic analysis based on 16S rRNA sequences revealed that *Mycobacterium paracondontium*, like *mycobacterium gordonae*, belongs to the slow-growing NTM type, with a 99.0% similarity between the two. It was first isolated from the sputum of a patient with lung disease in Korea in 2014.[7] Since then, only a few sporadic cases of infections caused by *Mycobacterium paracondontium* have been reported. We conducted a literature review on infections caused by *Mycobacterium paracondontium* (Table 2). Our findings indicate that a total of 12 patients were reported to have been infected. The sites of infection were diverse, including the lungs,[8,9] pericardium,[10] lumbar vertebrae,[11] and peritoneum.[12] The lungs were predominantly the site of infection (9/12). Clinical symptoms differ depending on the site of infection. Lung infections are characterized by coughing up sputum and

Table 2 Demographics, Underlying Conditions, Clinical Features, Drug Sensitivity, Treatment, and Outcomes of Patients with M. Thermoresistibile Infection

Author (Year)	No.of cases	Age	Sex	District	Underlying conditions	Presenting Symptoms	How Was Diagnosis Made?	Drug sensitivity	Site	Treatment (Duration)	Outcome
Chi Yuen Cheung (2017)[12]	1	55	M	Hong Kong	Diabetic nephropathy, end-stage kidney disease, peritoneal dialysis	Cloudy peritoneal dialysate effluent, abdominal pain	Peritoneal dialysate culture	Sensitive to CLA, Am, ETH, Rfb, resistant to RMP and CIP	Peritonitis	Am, AZM, ETH	Improve
Tan yz (2021)[11]	1	53	M	Hunan Province, China	NR	Fever, low back pain	Pus culture, metagenomic next-generation sequencing	NR	Lumbar	RMP, ETH, AZM, MOX	improve
Li yuanchun (2022)[8]	8	42.38± 9.92	3M/5F	Shenzhen, China	2hepatitis B,1diabetes mellitus,1pulmonary maculopathy,1gout	All cough,sputum, 2 blood-stained sputum,1 chest pain	5 bronchoalveolar lavage fluid and 3 sputum gene sequencing and culture	Sensitive to CLA, Rfb, Am, LZD, MOX, SMZ, DOX. Resistant to RMP	lung	3INH, RMP, PZA, ETH,2Other antibiotics,3Untreated	2remained stable /6NR
Masahiro Uchiyama (2023)[9]	1	55	F	Japan	BMI 21.1	Lung horseshoe opacity	Culture of the purulent liquid	NR	lung	Tracheoscopic drainage of pus	improve
Rehman Jinah (2023)[10]	1	60	F	Canada	Hypothyroidism, short course of steroids	Chest pain, hypoxia	Pericardial fluid Mycobacterial culture	NR	pericardium	ETH, CIP, DOX (12months)	NR

Abbreviations: Am, Amikacin; AZM, azithromycin; CLA, Clarithromycin; CIP, Ciprofloxacin; SMZ, cotrimoxazole; DOX, doxycycline; ETH, ethambutol; INH, isoniazid; MOX, Moxifloxacin; PAS, para-amino-salicylic acid; RMP, rifampicin; STR, streptomycin; Rfb, rifabutin; PZA, pyrazinamide; LZD, linezolid; ptNGS, Pathogen-targeted next-generation sequencing; NR, not report.

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patchy or striated shadows on CT images. Infections in other parts of the body typically cause fever and pain at the site of infection. It is important to note that some infections may not cause any discomfort, which can only be detected through imaging.[9] In general, it is more likely to occur in middle-aged women with a low BMI.[8] It typically manifests as localized purulent changes without specific clinical symptoms.

Mycobacterium paracondontium is a rare opportunistic pathogen that is generally considered non-pathogenic to humans. It is widespread in environments such as soil and water and is commonly found in hospital environments, including tap water, aerators/rectifiers in faucets, and disinfection devices. The growth temperature and optimal temperature for *Mycobacterium paracondontium* are still a matter of debate. Kim et al[7] stated that the bacterium grows well between 25–30°C but fails to grow at 37°C In his initial report. However, Li[8] demonstrated that it can be grown between 25–37°C, with an optimal temperature of 37°C. Azadi[13] found that the optimal temperature for culturing *Mycobacterium paracondontium* is 35°C. Taken together, *Mycobacterium paracondontium* has a low temperature growth requirement and can thrive in conditions that are pathogenic to humans.

To the best of our knowledge, this may be the first case of swollen and necrotic lymph nodes caused by *Mycobacterium paracondontium* infection, the mode of infection is unknown as this pathogen is widespread and severe immunosuppression (CD4+ T lymphocytes <200/μL) may be a factor in the infection. Diagnosis of NTM infection is typically based on traditional culture methods, which can take weeks due to the slow-growing nature of the bacteria. However, it may be easily missed by traditional bacterial culture protocols with short incubation periods. Additionally, traditional culture methods are unable to perform strain identification. The isolation rate of *Mycobacterium paracondontium* in NTM infections is only 0.46%,[8] leaving those with rapidly changing medical conditions underserved. tNGS has become increasingly important due to its ability to detect dozens to hundreds of known pathogenic microorganisms, as well as their virulence and/or resistance genes in tested samples. Compared to mNGS, tNGS offers the advantages of a well-defined pathogen spectrum and lower sequencing costs. In this case, a positive result was obtained the day after the lesion tissue was sent for testing. This result was consistent with the delayed pathologic result and provided valuable time for the patient's treatment.

The reviewed literature had limited drug sensitivity data. LI et al[8] demonstrated the sensitivity of eight strains of *Mycobacterium paracondontium* to clarithromycin, rifabutin, amikacin, linezolid, moxifloxacin, cotrimoxazole, and ciprofloxacin, and only two strains of *Mycobacterium paracondontium* were resistant to rifampicin. Cheung, C.Y.et al[12] demonstrated that *Mycobacterium paracondontium* grown in peritoneal dialysis exudate was susceptible to clarithromycin, amikacin, ethambutol, and rifabutin, but not to rifampicin and ciprofloxacin In their study. In this case, the patient presented with prolonged fever and cough, along with radiological indications of multiple swollen and necrotic lymph nodes. Immediate treatment was deemed necessary. Unfortunately, in vitro drug sensitivity testing was not performed, and since all current guideline-based[14,15] treatment strategies for NTM require multidrug combinations and there is a lack of standardized treatment regimens and protocols for *Mycobacterium paracondontium*, we chose the four potentially susceptible drugs in order to achieve as much of the desired therapeutic effect as possible. It is encouraging that fever and cough disappeared after 1 week of treatment, and lymph node examination has not yet been performed due to the short course of treatment, and longer follow-up is needed to assess overall efficacy.

Conclusion

Unexplained persistent fever or lymph node swelling can have a wide range of causes, including NTM infection. It is important to consider NTM as a potential pathogen in these cases. Given the prevalence of NTM in the environment, clinicians must remain vigilant for its presence, particularly rare strains. Treatment success rates for immunocompromised and comorbid chronic disease patients are less than 50%,[16,17] making early diagnosis crucial. tNGS is a valuable diagnostic method, and in vitro drug susceptibility tests should be optimized to provide appropriate treatment options whenever possible, potentially saving patients' lives and improving their prognosis.

Ethics Approval and Informed Consent

The authors certify that the patient consent form has been obtained. Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. All procedures performed in the study

involving human participants were in accordance with the ethical standards of the Ethics Committee of the Hangzhou Xixi Hospital. The ethics committee approved the waiver in this case report, based on the ethical standards to publish the case details.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors report no conflicts of interest in this work.

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