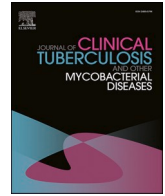


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Case Report

SARS-CoV-2 and *Mycobacterium tuberculosis* coinfection: A case of unusual bronchoesophageal fistula

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ABSTRACT

Tuberculosis is a treatable and curable bacterial disease caused by *Mycobacterium tuberculosis* that most often affects the lung. Since 2018, it has become the leading cause of death from infectious diseases. Tuberculosis is a public health problem in French Guiana. The majority of reported cases are diagnosed among people coming from neighboring Latin American countries. Since March 2020, French Guiana has been affected, like the rest of the world, by the new infectious disease COVID19 linked to the SARS-CoV-2 coronavirus. We here report a case of COVID19 and pulmonary tuberculosis coinfection. COVID19 pneumonia was the mode of discovery of the tuberculosis. In the present case, the tuberculosis appeared as parenchymal and endobronchial pseudotumoral lesion, which has been complicated by a bronchoesophageal fistula. The evolution of the parenchymal, endobronchial lesion and bronchoesophageal fistula was favorable after two months of anti-tuberculosis treatment.

1. Introduction

Tuberculosis is an infectious bacterial disease caused by *Mycobacterium tuberculosis* (Mtb), which may infect up to one quarter of the world's population [1]. The global incidence ranges from 5 to 500 new cases per 100 000 inhabitants/year, with a global average of 130 new cases per 100 000 inhabitants/year [1]. Since 2015, tuberculosis has become the leading cause of death from infectious diseases, with 1.5 million deaths recorded in 2018 [1]. Diabetes, human immunodeficiency virus (HIV) infection, smoking, overconsumption of alcohol and undernutrition are the main risk factors associated with the new cases of tuberculosis. Tuberculosis mainly affects vulnerable populations, making precariousness, promiscuity and migration the major risk factors in many regions [1–3]. Nevertheless, tuberculosis remains a curable and preventable infectious disease. The fight against tuberculosis worldwide since the 2000s has saved 58 million people [1].

France is a country with a low incidence of pulmonary tuberculosis. However, there are marked differences between the different French departments. Ile-de-France, French Guiana and Mayotte have the highest incidence rates [2,3]. The tuberculosis incidence rate in French Guiana in 2018 is 25.7/100 000 inhabitants [3], which is higher than the rate in metropolitan France (16.1/100 000 in Ile-de-France), and

Mayotte (11.5/100 000) [3]. It mainly affects the city of Cayenne and its surroundings. Most cases involve migrants from Haiti, the country with the highest rate of tuberculosis in the Americas, with 139 cases per 100 000 inhabitants in 2017 [4].

Since March 2020, French Guiana has been affected like the rest of the world by the coronavirus disease 2019 (COVID19) pandemic related to SARS-CoV-2 coronavirus. COVID19 is responsible for 78 deaths in French Guiana among the 16,200 cases confirmed up to early February 2021.

We report here a case of pulmonary SARS-CoV-2 and *Mycobacterium tuberculosis* coinfection, in which COVID19 pneumonia was the mode of discovery of the tubercular lesion.

2. Case report

A 30-year-old man of Haitian origin living in French Guiana since 2016 attended the emergency unit of our hospital in June 2020 for altered general condition and a fever of 38.9 C. The patient also suffered from a cough for three weeks, night sweats, dyspnea and lost 10 kg in one month. His weight on presentation was 51 kg.

The polymerase chain reaction (RT-PCR) test of SARS-CoV-2 performed on admission was positive. Blood analysis showed an

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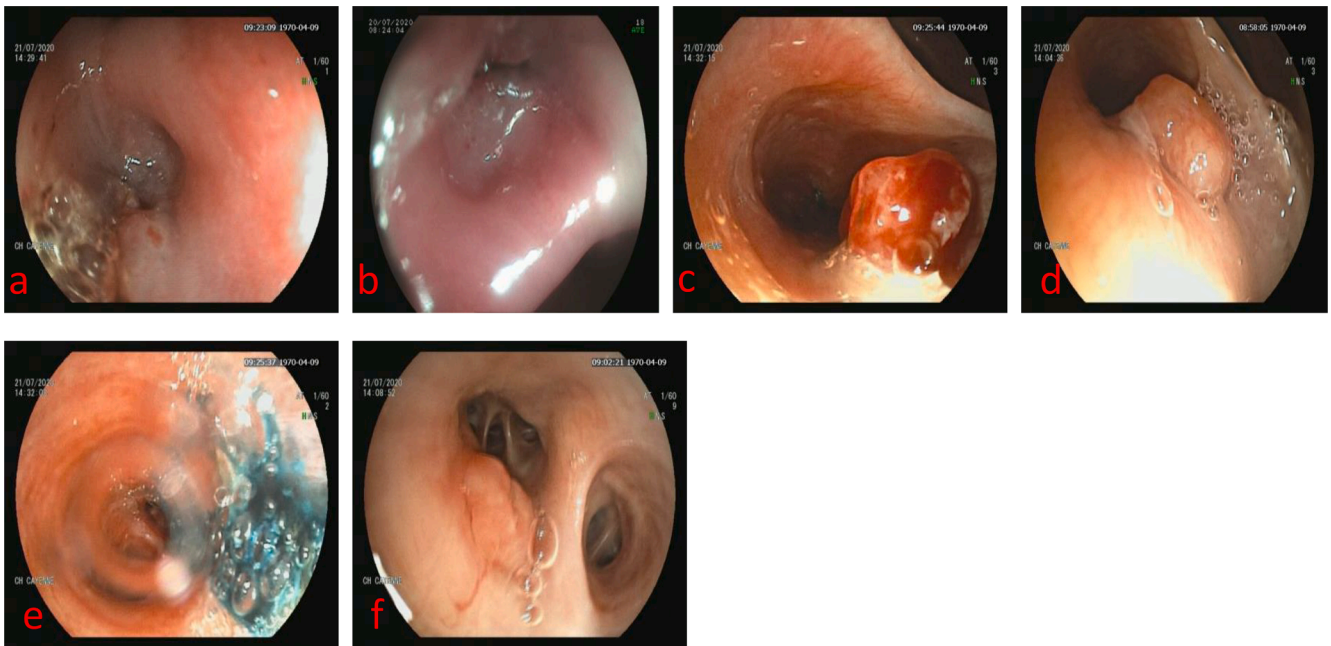


Fig. 1. Endoscopy images of the bronchoesophageal fistula and the pseudotumoral tuberculosis lesions. **Fig. 1a** and **b** show the orifice of the bronchoesophageal fistula in the upper third of the esophagus. **Fig. 1c** and **d** show the first endobronchial tuberculosis lesion of pseudotumoral appearance located at the entrance of the left main bronchus, red-pink in color, bleeding on contact, without visualization of the fistula. **Fig. 1e** Blue methylene test: we can see the blue fluid at the site of the first endobronchial pseudotumoral lesion after instillation of methylene blue at the esophageal fistula orifice. **Fig. 1f** shows the second smaller tuberculosis lesion at the entrance of the left lower lobe. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

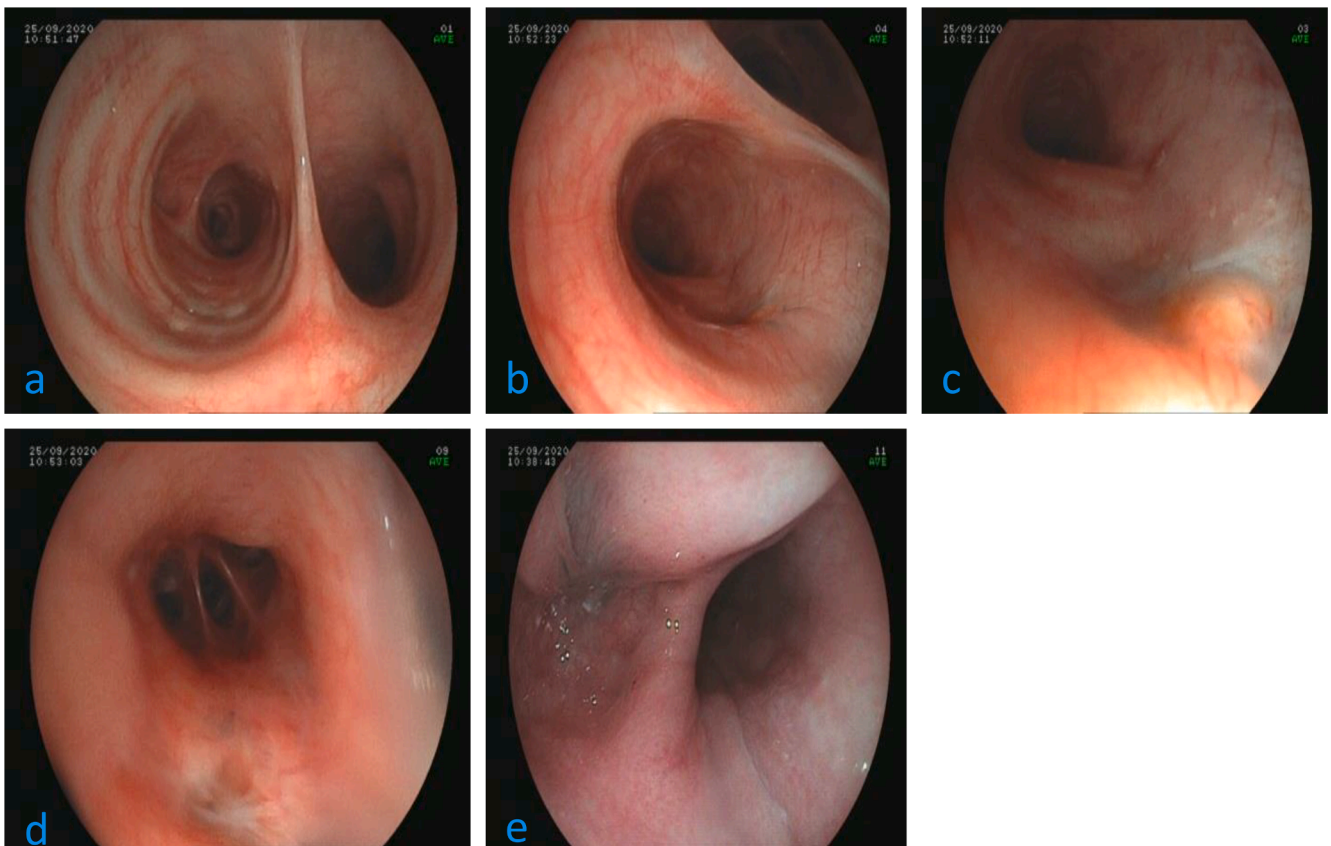


Fig. 2. Endoscopy images after two months of tuberculosis treatment. **Fig. 2a–c** show the complete disappearance of the two pseudotumoral tuberculosis lesions at the entrance of the left main bronchus, and at the entrance to the left lower lobe (**Fig. 2d**). **Fig. 2e** shows the complete healing of the esophageal fistula.



Fig. 3. Chest CT scan. **Fig. 3a** shows the appearance of centrilobular micro-nodules (Tree-in-bud sign) in the lingula and left lower lobe. **Fig. 2b** shows the pulmonary consolidation of the right middle lobe. **Fig. 3c** reveals the marked improvement in lung lesions after two months of tuberculosis treatment.

inflammatory syndrome with C reactive protein (CRP) at 141 mg/L. The HIV serology was negative. The blood gas monitoring showed a partial pressure of oxygen (PaO₂) 68 mmHg in room air.

The chest computed tomography scan (CT scan) showed lung consolidation in the right middle lobe and interstitial alveolar involvement with nodules in the left lower lobe and lingula. Due to this atypical appearance of the COVID19 pneumonia on the chest CT scan [5], the patient was put on oxygen therapy at 1 L/min, and treated with antibiotics (ceftriaxone and doxycycline). Sputum microscopy was negative for acid fast bacilli, but culture was in progress, so no corticosteroid therapy was administered. The evolution was favorable with rapid oxygen withdrawal, so the patient returned home after ten days of hospitalization.

The patient attended the emergency unit again in July 2020 for severe abdominal pain that appeared in the evening. A digestive endoscopy was performed and showed an ulcerated lesion in the middle third of the esophagus suggesting a fistula (**Fig. 1a** and **b**). The chest CT scan performed with ingestion of gastrografin product detected a bronchoesophageal fistula.

The bronchial endoscopy revealed a budding endobronchial lesion with a pseudotumoral appearance of red color, which bled on contact, located at the entrance of the left main bronchus, without visualization of fistula (**Fig. 1c** and **d**). Another smaller lesion was also noted at the entrance of the left lower lobe (**Fig. 1f**). Multiple biopsies of these lesions were performed.

The instillation of methylene blue through the esophageal fistula orifice showed its exteriorization at the level of the first lesion of the left main bronchus (**Fig. 1e**).

The patient was put on a strict fasting diet, and a percutaneous endoscopic gastrostomy (PEG) with exclusive enteral feeding was then performed.

The bronchial biopsy found epithelioid and gigantocellular granuloma without necrosis, associated with a few micro-abscesses. In the presence of granuloma and despite the absence of caseous necrosis, tuberculosis diagnosis was histologically suspected. This diagnosis was later confirmed by a positive MbT culture on a sputum sample taken when the patient was first hospitalized for COVID19 pneumonia, confirming the coexistence of the two infections at the same time.

Then, the patient was placed in air isolation, and quadruple anti-tuberculosis treatment was started, administered through PEG. To avoid the risk of inhalation, the patient was fed by PEG and remained nil by mouth while the fistula healed.

After two months of antituberculosis treatment with PEG, the follow-up chest CT scan with ingestion of gastrografin showed a complete collapse of the fistula confirmed by the absence of passage of contrast agent in the bronchi (**Figs. 2** and **3**). We also noted an almost complete regression of parenchymal pulmonary lesions (**Fig. 3c**). The patient's general condition has also improved and he weighed 57 kg after two

months of treatment.

Bronchial and oesophageogastric fibroscopy showed complete healing of the fistula orifice at the esophageal level, disappearance of endobronchial pseudotumoral lesion, leaving only a small scar without bronchial stenosis.

The PEG was withdrawn, and the patient was allowed to resume oral feeding. Treatment for tuberculosis was prescribed for an additional four months (six months in total).

3. Discussion

Tuberculosis is a public health problem in French Guiana. Most of the reported cases are diagnosed among migrants from the neighboring Latin American countries where the prevalence rate of tuberculosis is higher. The SARS CoV-2 infection in this patient was responsible for a transient desaturation that resolved rapidly, leading to the discovery of pulmonary tuberculosis. Radiologically, the lung damage with centrilobular micro-nodules connected to multiple branching linear structures (Tree-in-bud sign) in the lingula and left lower lobe is consistent with pulmonary tuberculosis [6]. The pulmonary consolidation of the middle lobe may be in favor of COVID19 pneumonia, because the desaturation and the respiratory discomfort described at the time of initial management can only be explained by COVID19 pneumonia (**Fig. 3a** and **b**).

In our case, the pulmonary tuberculosis was both parenchymal (located in the lingula and left lower lobe) and endobronchial with a pseudotumoral appearance, fistulized in the left main bronchus, but not in the left lower lobe.

This form of pseudotumoral endobronchial tuberculosis is rare [8–10,11]. It may lead to the suspicion of a malignant lesion, since the association between tuberculosis and lung cancer has already been described [9]. Other forms of endobronchial tuberculosis have been described including inflammatory, bronchial edema, whitish granulation and bronchial stenosis forms [7,8].

The bronchoesophageal fistula is most of the time a complication due to necrotic granulomatous infection, malignant tumor, trauma or endotracheal intubation. In addition, bronchoesophageal fistula caused by tuberculosis is a rare complication, occurring as a result of a break in a peribronchial lymph node with caseous necrosis [12]. In this case, we report a rare fistulized form of tuberculosis with pseudotumoral appearance. The fistula is located in the middle third of the esophagus opposite the carina, originating from the necrotic pseudotumoral tuberculosis lesion of the left bronchus, due to an endobronchial perforation towards the esophagus, without radiological aspect of necrotic lymph node. There was no tuberculosis involvement of the esophageal mucosa and as far as the origin of this fistula is concerned, there was no necrotic lymphadenopathy or mediastinal involvement found.

The treatment is usually based on standard anti-tuberculosis quadruple therapy. In our case, the fistula is completely healed with almost complete endobronchial (Fig. 2a–e) and pulmonary regression (Fig. 3c) after two months of anti-tuberculosis treatment.

4. Conclusion

We have described a case of COVID19 and pulmonary tuberculosis coinfection that were clinically confirmed. The modes of discovery of this form of parenchymal and endobronchial tuberculosis complicated by bronchoesophageal fistula is exceptional. Anti-tuberculosis treatment has proven to be effective for both endobronchial tuberculosis and for the fistula, which is completely healed after two months of treatment.

In high-prevalence countries, tuberculosis must remain among the diagnoses to be evoked in the face of all pulmonary pathologies, because of its clinical, radiological and endoscopic polymorphism.

Ethical statement

All the patients of our institute are informed that their biological samples and associated data may be used for scientific purposes, and have the right to object. The CHC welcome booklet is intended for hospitalized patients, and contains information on sample donation written in several languages. An information leaflet is also given to the patient, in whom the information is reminded, the rights of donors including the procedure for withdrawing consent is described.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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