Review Article

Open Access

Pulmonary Tuberculosis Co-infection and COVID-19 in Senegal

Agbogbenkou Tevi Déla-dem Lawson^{1,3*}, Fulgence Abdou Faye^{2,3}, Adama Berthe^{2,3}, Aminata Dia Gueye^{2,3}, Madocky Maguette DIOP^{2,3} and Sylvie Audrey Diop Nyafouna^{1,3}

¹Thies Infectious Diseases Service / UFR health sciences

²Internal Medicine Department of the Thiès Regional Hospital Centre

³Epidemic Treatment Centre (CTE) in the Thies Region

SUMMARY

New Coronavirus Disease (SARS-CoV-2) is responsible for the severe acute respiratory syndrome. Appeared in Wuhan, China, in December 2019, it affects more than 188 countries around the world to date. Africa is not spared by this pandemic (COVID-19), which is on the rise. Tuberculosis (TB), a disease endemic in Africa with a fatality of 1.5 million people per year, like COVID-19, is transmitted mainly by the respiratory route and affects the lungs [1,2]. In the literature, few studies have demonstrated the association and interactions between these two pathologies. However, the fragmented data reveal that tuberculosis with pulmonary localization must be considered as a potential risk factor for aggravation or complication of the disease. COVID-19, especially since the lung damage is significant, therefore In the fight against the COVID-19 pandemic, we must not forget to suspect and appropriately manage tuberculosis [2]. We report here the case of 3 patients who presented with COVID-19-Tuberculosis co-infection, treated at the level of the Epidemic Treatment Center (CTE) of the Thiès regional hospital in Senegal and whose evolution is favorable under early and adequate treatment.

*Corresponding author

Lawson AT Dela-dem, Thies Infectious Diseases Service / UFR health sciences, Sénégal. Tel: + 221774466617; Email: lawsalomon@yahoo.fr

Received: September 05 2020; **Accepted:** October 05, 2020; **Published:** October 10, 2020

Keywords: Pulmonary Tuberculosis, Covid-19, Co-Infection, Cte, Thies-Senegal

Introduction

Covid-19 infection caused by SARS Cov-2 is responsible for acute and severe respiratory distress syndrome that affects much of the world [1]. This pandemic presents, to date,.... confirmed cases according to the WHO. In Senegal, people are infected with SARS Cov-2 with death [2]. This infection causes a transient immune deficiency that can reactivate diseases such as latent tuberculosis, which is also correlated with genetic susceptibility [3,4]. Tuberculosis is an endemic infection in developing countries, including Senegal. About 10 million people worldwide and 13663 people in Senegal contracted it [5,6] in 2018. The problem will mainly reside in the differential diagnosis between the two pathologies or the subtlety of their association in a pandemic context [2,4,7,8]. The association between COVID-19 and tuberculosis active is still little reported [7-9]. However, their coexistence arouses scientific interest in possible interaction [7,8,9,11].

We are not yet aware of any work on such particularity in Senegal.

Observations

We report here 3 cases of active TB -COVID-19 co-infection observed in a COVID-19 CTE in Senegal. They are two men aged 29 and 33 and a 23-year-old woman, all with no medical-surgical history, no comorbidity, no notion of TB, or COVID-19 contact. They were hospitalized at the COVID-19 Epidemics Centre in the

Central Regional Hospital in Thies, Senegal. Symptoms occurred in a subacute setting (10 days) clinically marked by insomnia, dry then productive cough with mucous or yellowish sputum observed in all patients. A case of low abundance hemoptysis associated with clots without hemodynamic disturbance was observed. This picture is associated with basithoracic pain exacerbated by coughing fits in all three patients. Stage III dyspnea, like superficial polypnea and influenza-like illness (odynophagia, arthralgia, and myalgia) were observed in one patient. There was no notion of headache, anosmia, or ageusia.

The clinical symptoms occurred in the context of vespero-nocturnal fever, without chills with profuse sweating, physical asthenia, non-selective anorexia, and unstated weight loss, especially in the two patients. On physical examination, pulmonary condensation syndrome was found in all patients. The patient presented acute breathable distress syndrome with superficial polypnea, flapping of the wings on the nose, intercostal draw, and oxygen saturation (SatO₂) to ambient air at 80%. In the face of the COVID-19 pandemic, and in view of the clinical symptomatology, RT-PCR on nasopharyngeal and oropharyngeal smear to search for SARS-Cov 2 performed came back positive in all patients. The patients were admitted to the COVID-19 CTE at the Thiès Regional Hospital.

Due to the subacute course and the peculiarities of the symptomatology, a paraclinical assessment was performed. Thus the complete blood count showed microcytic hypochromic anemia and moderate lymphopenia. The C-reactive protein was positive in 2/3 cases. The thoracic scan performed in the patient had shown a

bilateral micronodular infiltrates that showed a bud tree appearance in the upper lobes consistent with bronchiolitis associated with mediastinal adenopathies located in the aortopulmonary window. This scenographic aspect was consistent with bilateral lung disease of TB origin very likely. In this patient, a cytobacteriological examination of sputum in search of acid-alcoholic-resistant bacillus returned negative. GeneXpert TB could not be realized. The diagnosis of pulmonary tuberculosis with negative bacilloscopy was accepted on clinical, biological, and radiological arguments. In the other two patients, the bacteriological diagnosis of TB was positive.

The extension workup in all patients found no secondary focus. HIV serology was negative in all patients. The diagnosis of active pulmonary tuberculosis and COVID-19 co-infection was therefore retained in our three patients.

As part of the treatment of tuberculosis, national recommendations have been applied. Fixed-dose quadruple therapy of rifampicin,

isoniazid, pyrazinamide, and ethambutol was prescribed for two months, followed by dual treatment with a fixed-dose combination of rifampicin and isoniazid for four months. The protocol of hydroxychloroquine at a dose of 600 mg per day divided into three doses for ten days combined with azithromycin at a dose of 500 mg per day for three days was administered to all patients as part of the dose burden of COVID-19. Adjuvant treatment was initiated, in particular, 1 g of vitamin C for 15 days, anticoagulation at a preventive dose with enoxaparin 0.4 ml for nine days. No patient was admitted to intensive care or mechanically ventilated. The course of the disease in all patients is marked by an improvement in the clinical condition with regression of cough and dyspnea and fever resolution. Two COVID-19 monitoring RT-PCR tests at 48-hour intervals came back negative, confirming the patient's recovery from the COVID-19 infection. Tuberculosis follow-up was planned according to the guidelines of the national tuberculosis control program in Senegal.

Data summary table

Variables		Patient 1	Patient 2	Patient 3
Kind	Man	+	+	
	Wife			+
Age		Age 29	Age 33	Age 23
Clinical signs	Productive cough	+	+	+
	Hemoptysis	-	+	-
	Dyspnea	-	-	+
	Chest pain	+	+	+
	Influenza syndrome	-	-	+
	Aguesie	-	-	-
	Anosmia	-	-	-
	SDRA	-	-	+
	Pulmonary condensation syndrome	+	+	+
	SRIS	+	+	+
	Anémis syndrome that	-	+	+
	AEG	+	+	+
Biology	Blood formula count	Normal	Microcytic hypochromic anemia	Microcytic hypochromic anemia Moderate lymphopenia
	CRP	48 mg/l	48 mg/l	Negative
	Bacilloscopie	Positive at 2X	Positive at 3X	Negative
	Genexpert	Not done	No Fact	Not done
Evolution	Length of hospitalization	11 days	10 days	10 days

Discussion

In Senegal, despite the advent of the global strategy, "Ending TUBERCULOSIS is or End TB," which has seen improved screening and management conditions, TB remains a priority health problem [6]. According to the WHO, the estimated incidence is 140 cases of tuberculosis of all forms per 100,000 inhabitants (approximately 21,000 cases) with a detection rate of 63% (44-98). Mortality from this disease was estimated at more than 3,000, representing a mortality rate of 0.25%. Analysis of TB's epidemiological data shows that the proportion of TB cases among young people aged 15 to 34 is continuously increasing. This suggests an intense transmission of this disease in the Senegalese population. [5,6]. In addition to TB endemic disease, the infection

with SARS-Cov-2, which has spread globally since its appearance in December 2019 in China, counts to date de confirmed cases and affects more than 188 countries. Africa is not spared from this pandemic, even though it is one of the least affected continents with about 1,321,738 confirmed cases, including 31,902 deaths [1, 2]. In Senegal, the first case of COVID 19 was recorded on March 2, 2020. Since then, the disease has continued to spread. A response plan has been put in place to deal with COVID 19 while ensuring continuity of care, surveillance, and management of other endemic diseases, including tuberculosis. Few studies have been carried out globally on the association TB-COVID-19; therefore, the overall prevalence of the association of these two diseases, which share the same respiratory transmission route and mainly affect the lungs, is

unknown. day. In the first multicenter study conducted by Tadolini et al., 81.6% of patients associating Covid-19 and tuberculosis infection were predominantly male. The median age was 48 years, Stochino et al. found male predominance in 60% of cases and a median age of 39 years [7,8]. In our observation, 2/3 of the patients were men, but they were younger than in the cohort of Tadolini and Stochino et al. No comorbidities were found in our patients. Risk factors such as advanced age and certain comorbidities, such as diabetes and chronic respiratory diseases, are significantly associated with the lethality for tuberculosis and COVID-19 [7, 9]. However, only limited information on COVID-19 co-infection and active tuberculosis has been reported to date [7-9]. Concerns persist that COVID-19 could have a negative impact on the clinical course of tuberculosis and the survival of patients [7-10]. In the long term, it is also accepted that COVID-19 may be the cause of reactivation of latent tuberculosis or exacerbation of primary tuberculosis infection [9,10].

Clinically, tuberculosis presents a subacute to chronic pictures compared to SARS-Cov-2 infection, which presents with acute symptomatology. The latter is manifested mainly by respiratory signs, including dry cough, dyspnea, chest pain, rhinitis.

Extra-respiratory signs are often anosmia, ageusia, diarrhea, nausea-vomiting, headache, myalgia, asthenia, and sometimes cervical lymphadenopathy. The general signs in this infection are most often fever, tachycardia, and superficial polypnea [1,2, 5,7, 8].

In pulmonary tuberculosis, the symptomatology is a productive cough with sometimes hemoptysis, dyspnea, deterioration of the general condition with significant weight loss, asthenia, and anorexia [5,6].

These different clinical manifestations when they coexist in a patient can lead to confusion and lead to misdiagnosis. If in the literature, cases of secondary bacterial infections have been described in the field of COVID-19, it seems necessary to us in endemic areas to eliminate tuberculosis when signs of impregnation are present.

In our study, these signs of TB impregnation were present in all patients and predominantly in men. The radiographic lesions of active Koch's bacillus infection are multiple. The involvement is often bilateral and extensive, according to Kombila et al. The preferred site of pulmonary tuberculosis is the posterior segment of one of the upper lobes or the apical segment of the lower lobe [11]. Other signs may be found: infiltrates, caverns, alveolar or bronchial syndrome, sometimes associated with mediastinal lymphadenopathy, pleurisy, and pneumothorax. The chest scanner can detect complex lesions, especially if the bacilloscopy is negative in front of a strong clinical presumption. The lesions encountered are bronchiolar micronodules, alveolar filling, bronchial syndrome, retraction or atelectasis, necrotic lymphadenopathy, bronchogenic or hematogenous miliaria [11]. In fact, in one of our patients, the clinic suggested pulmonary tuberculosis despite AFB sputum's negativity. The appearance of her chest CT scan was consistent with a very probable bilateral pneumonitis of tuberculous origin. This result made it possible to diagnose smear-negative pulmonary tuberculosis, but the GeneXpert could not be performed. In SARS-Cov-2 infection, the chest x-ray is unspecific. The thoracic scanner has better sensitivity, especially in the early detection of rather peripheral and posterior multifocal frosted glass images [12]. The other most reported presentations are mosaic appearance (crazy paving),

bilateral alveolar condensation, linear opacities, and airborne bronchograms [12]. There is also a correlation between the severity of the clinical picture and the extent of CT opacities [7, 8, 12].

The scan alone did not show lesions related to SARS-Cov-2 infection. Microscopy, GeneXpert, or histology make the diagnosis of tuberculosis. For Covid-19 infection, confirmation is provided by RT-PCR. The diagnosis of the latter was fortuitous in 2/3 of the patients. Indeed, it was in the context of the pandemic that nasopharyngeal and oropharyngeal swabs were taken. This is the reason why the diagnosis was made simultaneously for both infections. However, in the study by Tadolini et al., 53% of patients in their cohort were known to have tuberculosis before diagnosing COVID-19 infection and only 18.3% in the same week at most [7]. The prognosis of tuberculosis is linked to the existence of risk factors. The latter are advanced age, cachexia, alcoholism, active smoking, HIV infection, progressive general disease (cancer, cirrhosis, blood disease, diabetes, chronic renal failure on dialysis) or chronic respiratory disease [4]. These factors are also detrimental to the progression of SARS-Cov-2 infection [9,10]. Other comorbidities are described, particularly high blood pressure, morbid obesity, organ transplants, sickle cell anemia-splenectomy, and pregnancy in the 3rd trimester [3]. Pulmonary tuberculosis itself is considered to be a potential risk factor for aggravation or complication due to these genetic peculiarities leading to transient immunosuppression especially as the pulmonary lesions are important [3,9,10].

In our study, only the woman had significant cachexia as a risk factor, but the other two had a good prognosis. In Senegal, the treatment of COVID-19 infection is based on a protocol that combines hydroxychloroquine and azithromycin, with vitamin C and Zinc as adjuvant treatment. This protocol is approved and used in clinical trials, taking the precaution of performing electrocardiographic monitoring to detect a possible rhythm disturbance before, during, and after treatment [9]. In the Stochino cohort, patients received hydroxychloroquine 400 mg/day, which was well tolerated. However, it should be noted that the combination of hydroxychloroquine and rifampicin may present drug interactions, so its use must be done with caution [5,7,9]. We did not find any side effects in the drug in our patients—Association of the two protocols. The outcome under treatment was favorable with the progressive disappearance of clinical symptoms and the negation of two negative SARS Cov-2 RT-PCR tests after ten days of hospitalization on average. This hospital stay is shorter than that described in the study by Stochino, where the SARS Cov-2 RT-PCRs are negative 14 days after the first nasal sample in 63% of cases, 28 days in 21% of cases and respectively. 35 days in 10% of cases and on day 42 in 6% of cases. However, it should be noted that in the Stochino study, 33% of patients had comorbidity, 60% extensive pulmonary lesions, and 12% extra-pulmonary forms with a case fatality rate of 5%. This lethality is 11.6% in the study by Motta et al. [8].

Conclusion

The TB-COVID-19 association is not systematically researched in our daily practices in areas of high tuberculosis endemicity. This snapshot of 3 patients who present an active pulmonary COVID-19-TB association does not analyze the interactions between these two diseases. Our descriptive presentation in which certain elements on tuberculosis were incomplete and specific diagnostic confirmatory examinations unavailable, however, motivate further studies to understand better the determinants of this association in the short, medium, and long term.

Ethical aspects: The authors do not declare any conflict of interest.

References

1. Plaçais I, Richier Q (2020) COVID-19: Clinical, biological, and radiological characteristics of adult, pregnant woman, and child. A focus at the heart of the pandemic. *J RevMed* 41: 308-318.
2. Lederlin M, Revel MP (2020) Epidemic COVID-19: Literature Review. CERF-SFR 2020 watch bulletin; 1 <https://ebulletin.radiologie.fr/actualites-covid-19/bulletin-veille-cerf-sfr-ndeg1-2020-edition-speciale-covid-19>.
3. Jalaledin Ghanavi, Poopak Farnia, Parissa Farnia1, Ali Akbar Velayati (2020) Human Genetic Background in Susceptibility to Tuberculosis. *International Journal of Mycobacteriology* September 16.
4. Zumla A, Marais BJ, McHugh TD (2020) The increasing threat of respiratory tract infections to global health security—COVID-19 and tuberculosis. *Int J Tuberc Lung Dis*.
5. WHO (2019) World Tuberculosis Report: Guidance Summary 2019. https://www.who.int/tb/publications/global_report/fr/.
6. PNT. Annuel 2018 du PNT report. <https://pntsenegal.com/wp-content/uploads/2019/08/RAPPORT-ANNUEL-PNT-2018.pdf>.
7. Tadolini M, Codecasa LR, Garcia-Garcia JM (2020) Active tuberculosis, sequelae and COVID-19 co-infection: First cohort of 49 cases. *Eur Respir J* 56.
8. Stochino C, Villa S, Zucchi P (2020) Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital. *Eur Respir J* 56.
9. High Health Authority (2020) Quick responses under COVID-19: Continuity of follow-up of TB patients.
10. Motta I, Centis R, D'Ambrosio L (2020) Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology*.
11. Kombila UD, Kane YD, Mbaye FB (2018) Radiological features of pulmonary tuberculosis with positive microscopy at the Pneumology department of the FANN National University Hospital Center, Dakar. *Pan Afr Med J* 30.
12. Guan C S, Lv Z B, Yan S (2020) Imaging features of coronavirus disease 2019 (COVID-19): Evaluation on Thin-Section CT. *Acad Radiol* 27 : 609-613.

Copyright: ©2020 Lawson AT Dela-dem, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.