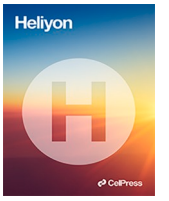
Heliyon 10 (2024) e28469

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Case report

Thyroid tuberculosis and cold abscess after infection with COVID-19: A case report

Xinru Xiao [1], Qi Cao [1], Yujia Shi [*]

Department of Respiratory and Critical Care Medicine, The Affiliated Changzhou No.2 People's Hospital of Nanjing Medical University, Changzhou, 213003, China

ARTICLE INFO

Keywords:
Thyroid tuberculosis
Tuberculosis
Cold abscess
COVID-19
Immune dysregulation

ABSTRACT

There is mounting evidence that coronavirus disease 2019 (COVID-19) can cause immune dysregulation. The consequence of this immune dysregulation may contribute to susceptibility to tuberculosis (TB). Thyroid gland involvement by TB is extremely uncommon and typically the result of disseminated infection. It can be hard to diagnose because there are no identifiable symptoms. We present the case of a Chinese patient who had a fever again after COVID-19 infection that was finally diagnosed as thyroid tuberculosis with a cold abscess. Clinicians should maintain a high index of suspicion for high-risk patients from endemic regions with medical comorbidities, such as immunocompromised disease and malnutrition.

1. Introduction

Tuberculosis (TB) was the world's second leading cause of death from a single infectious agent in 2022, after coronavirus disease 2019 (COVID-19). An estimated 10.6 million people fell ill with TB worldwide in 2022. The TB incidence rate is estimated to have increased by 3.9% between 2020 and 2022, with COVID-related service disruptions leading to nearly half a million TB deaths in these three years [1].

TB typically begins in the lungs, but it can also manifest in other organs, including the thyroid gland. Thyroid tuberculosis has been reported in very few instances, even in countries with a high prevalence of TB. It is frequently misdiagnosed or delayed due to its nonspecific signs and symptoms, which include fever, night sweats, fatigue, single or multiple nodules, goiter with caseation, chronic fibrosing nodules, and cold or acute abscesses [2,3]. Here, we report a case of tuberculosis of thyroid gland with cold abscess and review the literature. The patient has given written consent for publication of this manuscript and any identifying images or data.

1.1. Clinical case

The patient was a 76-year-old elderly man from China who worked as a farmer. He had no history of smoking. Four weeks prior to his visit, he presented to a local doctor with the principal complaint of fever. A lung infection is indicated by computed tomography (CT), and the polymerase chain reaction (PCR) test for COVID-19 was positive. Following approximately two weeks of treatment with piperacillin and levofloxacin, the patient's temperature returned to normal and he was discharged. However, ten days after discharge,

* Corresponding author.
E-mail address: shiyujia1986@163.com (Y. Shi).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e28469
Received 28 October 2023; Received in revised form 19 March 2024; Accepted 19 March 2024
Available online 22 March 2024

the patient developed a painful neck swelling, with a temperature of up to 39 °C. There was no history of weight loss, anorexia or asthenia. His parents, brothers and children had no history of tuberculosis. CT scan revealed diffuse miliary nodules, patchy shadow in both lungs, and punctate calcification in left upper lobe. The patient was subsequently referred to our hospital's department of respiratory and critical care medicine. White blood cell counts and erythrocyte sedimentation rate were normal, but the hemoglobin was 113.0 g/L and C-reactive protein (CRP) level was 10.3 mg/L. The percentage of neutrophils was increased (87.7%), the percentage of lymphocytes was decreased (7.9%), and the percentage of monocytes was normal. Serum ferritin was 703.9 ng/mL. And the patient was positive for TB-infected T cells. T cell subset detection showed that the percentage of $CD3^+$ $CD4^+$ helper T cell was decreased. Thyroid function was normal (thyroid-stimulating hormone, 1.61 μIU/mL, free T3, 3.21 pmol/L, free T4, 13.24 pmol/L). Antithyroid peroxidase antibody (TPOAb) and antithyroid stimulating hormone receptor antibody (TRAb) were negative. However, thyroglobulin levels were above 500 ng/mL and reverse t3 levels were 0.25 ng/mL. After admission, the patient continued to have fever, and the fever peak did not decrease. Therefore, tigecycline was given for empirical anti-infection treatment, but the temperature did not decrease significantly. To further determine the source of the fever, we performed a bone marrow aspiration and abdominal CT. None of the results, however, explained the origin of the fever. Then Positron Emission Tomography-Computed Tomography (PET-CT) was performed. Since PET-CT showed enlargement of the right lobe of the thyroid gland and cervical lymph node with abnormal increase in glucose metabolism (Fig. 1). Therefore, an ultrasound (Fig. 2) and ultrasound-guided puncture were conducted on the thyroid. The thyroid puncture drew out a mud-like fluid and puncture fluid smears showed inflammatory necrosis without malignant tumor cells (Fig. 3), which suggested an abscess. In view of the possibility of an infectious etiology, more stains were performed, evidencing acid fast bacilli using the Ziehl-Neelsen technique. The results showed that the patient was positive for acid fast bacilli. Based on the above findings, thyroid tuberculosis was diagnosed. The patient was then transferred to the infectious diseases department where

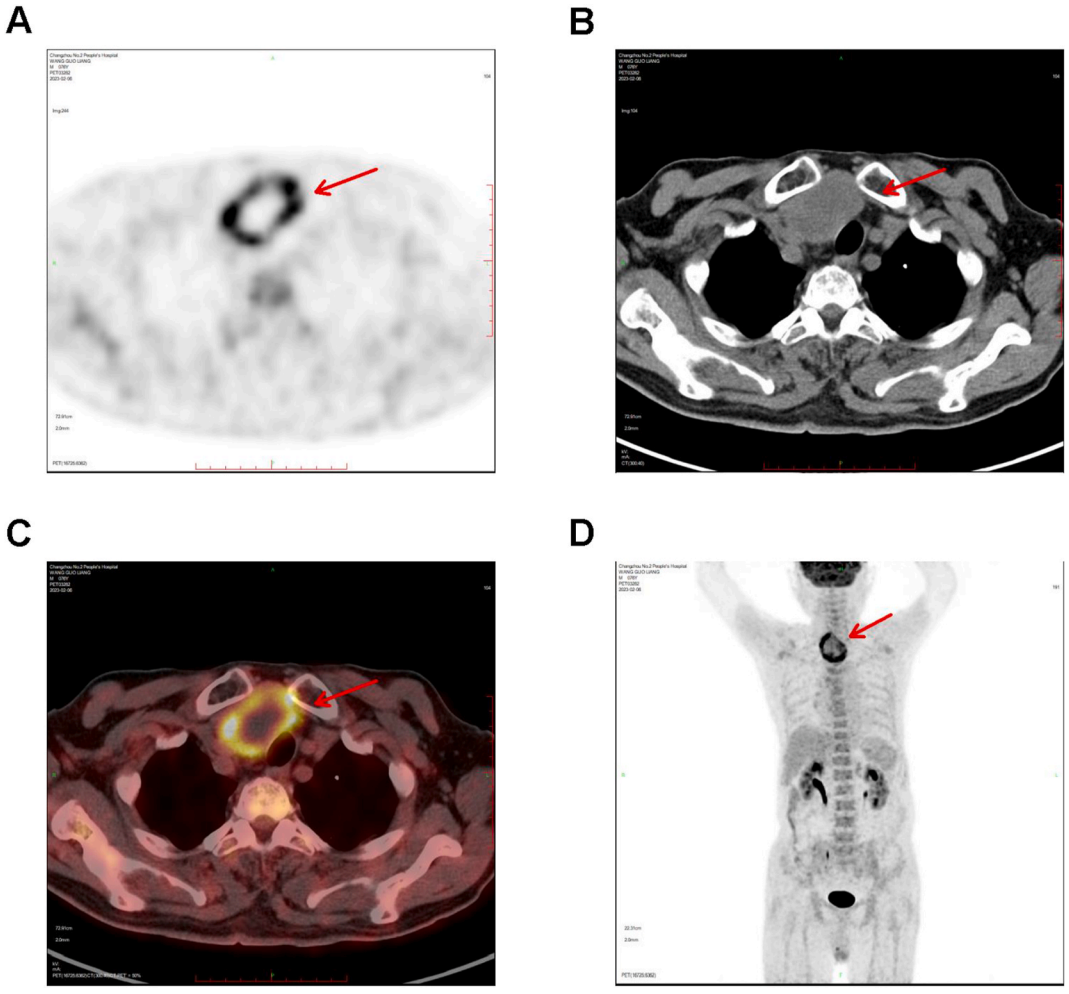


Fig. 1. PET/CT: FDG accumulation was observed in the thyroid gland. (A) Axial FDG PET image showing hypermetabolic thyroid gland (red arrow). (B) Axial CT images showing goiter with hypodense foci (red arrow). (C) Axial PET/CT image showing high FDG uptake in the thyroid gland (red arrow). (D) High FDG uptake in thyroid gland on maximum-intensity-projection PET image (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article).

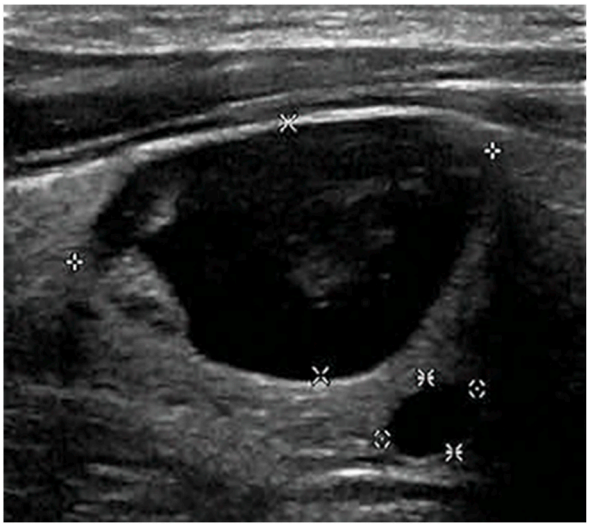


Fig. 2. The right lobe of the thyroid gland was anechoic with a punctate echo within it.

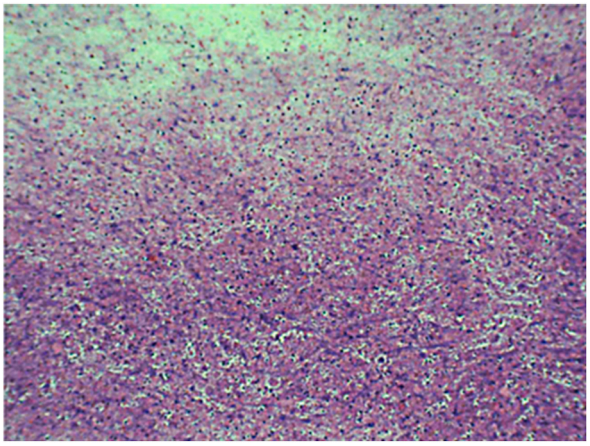


Fig. 3. Thyroid puncture fluid smears showed inflammatory necrosis without malignant tumor cells.

complementary tests were performed excluding affectation at other levels. In addition, XPERT test, a polymerase chain reaction (PCR) technique, was performed on the patient's thyroid aspirate, which confirmed the presence of TB bacteria. Subsequently, the patient was treated with puncture and aspiration of the thyroid abscess. Also, quadruple antituberculosis therapy with isoniazid, rifampin, pyrazinamide, and ethambutol was started. After 6 months of systemic anti-tuberculosis treatment, the patient had a good response, with normal liver and renal function. The patients were followed up for 3 and 6 months, respectively. and no tuberculosis recurrence and hypothyroidism were found.

2. Discussion

Thyroid tuberculosis is a rare clinical tuberculosis, with an incidence of only 0.4%–0.76% in China [4]. This may be due to the antimicrobial properties of colloids within thyroid follicles and the high vascular density of the thyroid gland, making the thyroid gland highly resistant to infection [3]. Only when the invading mycobacterium tuberculosis (MTB) is more numerous and virulent, accompanied by the decrease of the body's immune function, the disease will occur. There are no distinctive clinical manifestations of thyroid tuberculosis. Patients exhibit a variety of symptoms, including fever of unclear cause, discomfort in the neck, and dysphagia, and there are not many particular laboratory discoveries [3,5]. Sometimes patients present with acute infectious thyroiditis or subacute granulomatous thyroiditis or chronic nonsuppurative thyroiditis, which may be accompanied by thyrotoxicosis, hypothyroidism, and thyroid abscess [6–9]. In most cases, however, the patient is euthyroid, which was the case in our patient.

The clinical and radiological features of thyroid tuberculosis are nonspecific, and ultrasound can show single nodules, multiple nodules, diffuse goiter, or rare abscess formation resembling cancer, mostly showing heterogeneous hypoechoic masses. CT may show

a goiter, and enhanced CT may show a necrotic center that is hypodense with peripheral marginal enhancement associated with caseous lesions [10]. PET-CT for thyroid tuberculosis is rarely described, and in the present case FDG-PET-CT showed FDG accumulation in the right thyroid and cervical lymph nodes.

The diagnosis rate is reported to be 55.9% in thyroid tuberculosis [11]. Fine-needle ultrasonography-guided aspiration It was determined that a biopsy is an essential diagnostic procedure for cytology and acid-fast bacteria culture [2,3,12]. The diagnosis of tuberculosis was confirmed if tuberculous granulomas or caseous necrosis were present. In addition, Ziehl-Neelsen staining showing acid-fast bacilli in the glands, or a positive tuberculin culture of the biopsy tissue also confirm the diagnosis. In cases of suspected granulomas and negative cultures, PCR can be performed for thyroid tissue tuberculosis and positive result would support the diagnosis. In our case, the diagnosis was confirmed by Ziehl-Neelsen staining and PCR of the puncture fluid. This diagnostic step helps to avoid unnecessary surgery. But we were unable to obtain pathological specimens of thyroid gland tissue to further determine the type of inflammation.

Once thyroid tuberculosis is diagnosed, antituberculosis drugs can be given first. Although anti-tuberculous is still the cornerstone of therapy, surgery is frequently used to promote abscess extraction and avoid total thyroid tissue degradation [2,3,12]. About 1% of cases fail to respond to anti-tuberculous drugs and relapse because of resistance to multiple drugs [3]. Although extremely uncommon, atypical manifestations of extrapulmonary tuberculosis in the thyroid necessitate a comprehensive history and examination. Clinicians should be highly suspicious of high-risk individuals who have medical comorbidities, such as immunocompromised diseases, from endemic regions.

There is mounting evidence that COVID-19 can lead to an immune dysregulation [13]. Multiple mechanisms may be involved, such as cytokine-mediated inflammation (such as interleukin 6), direct viral invasion of cardiomyocytes resulting in unopposed effects of angiotensin II, increased metabolic demand, immune activation, or microvascular dysfunction [14–16]. While COVID-19 infection can have long-term effects on the body [17], it is unclear whether this patient's thyroid tuberculosis is due to a weakened immune system following COVID-19 infection. A recent study reported a case in which COVID-19 promoted the development of active tuberculosis in a patient with latent tuberculosis infection [18]. In our case, tuberculosis also developed after COVID-19 infection. This patient had an increased percentage of neutrophils and a decreased percentage of lymphocytes. T cell subset detection showed depletion of $CD3^+$ $CD4^+$ helper T cells. This case appears to confirm concerns that COVID-19-related T-cell dysfunction may facilitate the progression of latent infection to active tuberculosis disease like HIV does. The underlying mechanisms of the association between viruses and autoimmunity remain inadequately understood. Historically, cross-reactive T-cell recognition, also known as molecular mimicry, and bystander T-cell activation, culminating in epitope dissemination, were the most prevalent mechanisms by which an infection can induce a T-cell-mediated autoimmune response. However, other hypotheses, such as virus-induced immune system decoy, should also be discussed in terms of their potential to initiate autoimmunity [19,20].

There are many similarities between the pathogenesis and clinical outcomes of COVID-19 and TB. Lung is the main site of severe acute respiratory syndrome coronavirus (SARS-CoV) and MTB infection. However, both pathogens are capable of invading cells in numerous organs. SARS-CoV-2 spreads and multiplies within ciliated mucus-secreting cells of bronchial epithelium, type-II alveolar/pneumocyte cells, and macrophages in the lungs, similar to MTB. Both pathogens elicit pro-inflammatory cytokines upon entry into host cells and, once unregulated, result in a cytokine storm. In turn, elevated levels of pro-inflammatory cytokines result in neutrophil infiltration at the site of infection, causing acute lung tissue injury [21]. The unrestrained production of pro-inflammatory cytokines leads in a seriously weakened immune response, which creates opportunities for co-infections, such as MTB. Virus-triggered T helper 1 (Th1) response results in the infiltration of immune cells into the airways and accelerates inflammation. In certain instances, the resulting dysfunctional immune response can result in severe pulmonary and systemic lesions, such as severe COVID-19 [22]. Unrestricted infiltration of inflammatory monocytes results in excessive production of reactive oxygen species and protease secretion, which eventually leads to lung tissue destruction. In addition to lung cells, SARS-CoV-2 is able to attack immune cells, similar to MTB, resulting in abnormal generation of cytokines and a switch to the M2 transcriptional program, which triggers immune paralysis and further promotes the development of COVID-19 [23]. In response, both pathogens possess sophisticated mechanisms to suppress host responses and evade subsequent immunity, including antagonizing interferon reactions, modulating cytokine signaling, hindering the presentation of antigens and regulating death of cells [24,25].

Furthermore, severe COVID-19 can cause lung injury and subsequent susceptibility to tuberculosis [26]. Care for patients with severe COVID-19 remains difficult due to the limited treatment options available. Immunosuppressive medications, such as corticosteroids, have demonstrated promise in the treatment of severe cases of COVID-19 [27]. However, immunosuppressive therapy carries a higher probability of opportunistic infections, such as viral infections. Immunosuppression regimens against SARS-CoV-2 may result in recurrence of inactive MTB, which may be harmful in TB endemic regions.

One of the advantages of this study is the availability of PET-CT images of thyroid tuberculosis, which are very rare in other cases of thyroid tuberculosis. In addition, we performed a T-cell subset analysis in this patient and found a decrease in the percentage of $CD3^+CD4^+$ helper T cells, although it is not clear whether this is due to the sequelae of COVID-19 infection or the effect of TB, but there is no doubt that this patient had an immune abnormality. We speculate that COVID-19-related T-cell dysfunction may promote the progression of latent infection to active tuberculosis.

3. Conclusion

On retrospective analysis of this case, there were several findings suggestive of TB. Elevated CRP and fever in blood tests, enlargement and tenderness in thyroid lesions, and immunocompromised after COVID-19 infection. In conclusion, thyroid tuberculosis is a rare disease with highly variable clinical presentation and complex diagnosis when it is not suspected. Therefore, it is

necessary to consider the differential diagnosis of thyroid tuberculosis in immunocompromised patients.

Statement of ethics

This study was submitted to the Ethics Committee of Changzhou NO.2 People's Hospital as case report and was approved. This patient provided his written informed consent to participate in this study.

Funding

This study was supported by grants from the Sci & Tech Project for Young Talents of Changzhou Health Commission (WZ202010 to Yujia Shi), Changzhou Healthy Seedling Talent Training Project (CZQM2020077 to Yujia Shi), Postdoctoral fund of Changzhou NO.2 People's Hospital (BSH202305 to Yujia Shi) and Changzhou Sci & Tech Program (CJ20235091 to Yujia Shi).

Data availability

The datasets generated for this study are available upon request to the corresponding author.

CRediT authorship contribution statement

Xinru Xiao: Writing – original draft, Visualization. **Qi Cao:** Visualization. **Yujia Shi:** Writing – review & editing, Conceptualization.

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.

References

[1] World Health Organization, Global Tuberculosos Report 2023, World Health Organization, 2023.
[2] A. Maa, B. Mna, A. Ahk et al.Metastatic tuberculous abscess: a rare manifestation of cutaneous tuberculosis[J]. IDCases,26:e01257.
[3] E. Bulbuloglu, H. Ciralik, E. Okur, et al., Tuberculosis of the thyroid gland: review of the literature[J], World J. Surg. 30 (2) (2006) 149–155.
[4] L.-L. Sun, S. Dong, J.-L. Xu, et al., Clinical diagnosis and treatment of primary thyroid tuberculosis: a retrospective study[J], Sao Paulo Med. J. 140 (2022) 547–552.
[5] B.M. Laitman, S. Samankan, S. Hwang, et al., Primary thyroid tuberculosis: an uncommon presentation of a thyroid mass[J], Ear Nose Throat J. (9) (2020), 014556132094948.
[6] A. Ghosh, S. Saha, B. Bhattacharya, et al., Primary tuberculosis of thyroid gland: a rare case report[J], Am. J. Otolaryngol. 28 (4) (2007) 267–270.
[7] D. Das, C. Pant, K. Chachra, et al., Fine needle aspiration cytology diagnosis of tuberculous thyroiditis. A report of eight cases[J], Acta Cytol. 36 (4) (1992) 517–522.
[8] P. Barnes, R. Weatherstone, Tuberculosis of the thyroid: two case reports[J], Br. J. Dis. Chest 73 (1979) 187–191.
[9] A. Johnson, M. Phillips, R. Thomas, Acute tuberculous abscess of the thyroid gland[J], Br. J. Surg. 60 (8) (1973) 668–669.
[10] K. Madhusudhan, A. Seith, R. Khadgawat, et al., Tuberculosis of the thyroid gland: magnetic resonance imaging appearances[J], Singap. Med. J. 50 (7) (2009) e235–e238.
[11] N. Gupta, K. Sharma, A. Barwad, et al., Thyroid tuberculosis–role of PCR in diagnosis of a rare entity[J], Cytopathology 22 (6) (2011) 392–396.
[12] S.P. Kataria, P. Tanwar, S. Singh, et al., Primary tuberculosis of the thyroid gland: a case report[J], Asian Pac. J. Trop. Biomed. (10) (2012) 2.
[13] A.E. Gracia-Ramos, E. Martin-Nares, G. Hernández-Molina, New onset of autoimmune diseases following COVID-19 diagnosis[J], Cells 10 (12) (2021) 3592.
[14] E. J. Rubin, D. L. Longo, L. R. Baden.Interleukin-6 receptor inhibition in Covid-19 - cooling the inflammatory soup[J].N. Engl. J. Med.,384(16): 1564-1565.
[15] P.P. Liu, A. Blet, D. Smyth, et al., The science underlying COVID-19: implications for the cardiovascular system[J], Circulation 142 (1) (2020) 68–78.
[16] C.M. Campbell, K. Rami, Will complement inhibition Be the new target in treating COVID-19-related systemic thrombosis?[J], Circulation 141 (22) (2020) 1739–1741.
[17] V. Higgins, D. Sohaei, E.P. Diamandis, et al., COVID-19: from3 an acute to chronic disease? Potential long-term health consequences[J], Crit. Rev. Clin. Lab Sci. (8) (2020) 1–23.
[18] M. Khayat, H. Fan, Y. Vali, COVID-19 promoting the development of active tuberculosis in a patient with latent tuberculosis infection: a case report[J], Respiratory Medicine Case Reports 32 (2021) 101344.
[19] D.R. Getts, E.M. Chastain, R.L. Terry, et al., Virus infection, antiviral immunity, and autoimmunity[J], Immunol. Rev. 255 (1) (2013) 197–209.
[20] C. Münz, J.D. Lünemann, M.T. Getts, et al., Antiviral immune responses: triggers of or triggered by autoimmunity?[J], Nat. Rev. Immunol. 9 (4) (2009) 246–258.
[21] D. Ragab, H. Salah Eldin, M. Taeimah, et al., The COVID-19 cytokine storm; what we know so far[J], Front. Immunol. 11 (2020) 1446.
[22] C.G. Ziegler, V.N. Miao, A.H. Owings, et al., Impaired local intrinsic immunity to SARS-CoV-2 infection in severe COVID-19[J], Cell 184 (18) (2021) 4713–4733. e4722.
[23] A. Boumaza, L. Gay, S. Mezouar, et al., Monocytes and macrophages, targets of severe acute respiratory syndrome coronavirus 2: the clue for coronavirus disease 2019 immunoparalysis[J], J. Infect. Dis. 224 (3) (2021) 395–406.
[24] W. Zhai, F. Wu, Y. Zhang, et al., The immune escape mechanisms of Mycobacterium tuberculosis[J], Int. J. Mol. Sci. 20 (2) (2019) 340.
[25] E. Callaway, Fast-spreading COVID variant can elude immune responses[J], Nature 589 (7843) (2021) 500–501.
[26] G.T. Mousquer, A. Peres, M. Fiegenbaum, Pathology of TB/COVID-19 co-infection: the phantom menace[J], Tuberculosis 126 (2021) 102020.
[27] J.A. Sterne, S. Murthy, J.V. Diaz, et al., Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis[J], JAMA 324 (13) (2020) 1330–1341.