

CASE REPORT

Multifocal tuberculosis on certolizumab pegol in a patient followed for rheumatoid arthritis

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Abstract

Tuberculosis must be considered in front of deterioration in general condition in patient with rheumatic disease under biological therapy. Rheumatologists may pay attention and screen infections before and after prescribing biological therapy.

KEYWORDS

certolizumab pegol, rheumatoid arthritis, TNF inhibitor, tuberculosis

1 | INTRODUCTION

Immunocompromised patients by chronic inflammatory diseases or by immunosuppressive therapy are susceptible to tuberculosis. Disseminated and severe forms have been described under anti-TNF. We reported a case of multifocal tuberculosis, especially the involvement of hematopoietic organs in a patient followed for rheumatoid arthritis who has been on certolizumab pegol.

Tuberculosis (TB) is a public health problem worldwide and in Tunisia. Patients immunocompromised by a chronic inflammatory disease such as rheumatoid arthritis (RA) or by immunosuppressive therapy are susceptible to this infection. Some studies estimate that the risk of TB is 3 times higher in patients with RA under conventional treatments and 17 times higher in those under biotherapy. We report a case of complicated multifocal tuberculosis in a patient followed for RA who has been on certolizumab pegol for 6 months. We have not found any case of multifocal tuberculosis reported in the literature and in particular under certolizumab pegol, and this improves the originality of our case report.

2 | CASE REPORT

Mrs B.H, 67 years old, diabetic on Metformin, is followed in our service for a deforming RA evolving for 30 years. She was initially put on methotrexate orally then into injected form; the injections were stopped for digestive intolerance. Given the persistence of an active disease, the decision was to put the patient on biotherapy. According to Tunisian recommendations, screening for latent TB has been done. The search for Koch's Bacilli (BK) in sputum was negative. The intradermal reaction to tuberculin (IDR) was negative, and the chest X-ray did not show any suspicious lesions. In front of the normality of all the prebiotherapy assessment, the patient was put on certolizumab pegol with a good evolution. Six months later, the patient presented with a progressive deterioration in general condition with asthenia, weight loss, and night sweats evolving in a febrile context. She was hospitalized in the infectious disease department. She had lymphopenia at $1140/\text{mm}^3$ controlled at $760/\text{mm}^3$; thrombocytopenia at $98\,000/\text{mm}^3$; and anemia at 10.4 g/dL . Face to this case of pancytopenia, an osteomedullary biopsy was made. It has

I, Emna Hannech, hereby certify that all authors have seen and approved the final version of the manuscript being submitted. I on behalf of all authors warrant that the article is the authors' original work, has not received prior publication, and is not under consideration for publication elsewhere.

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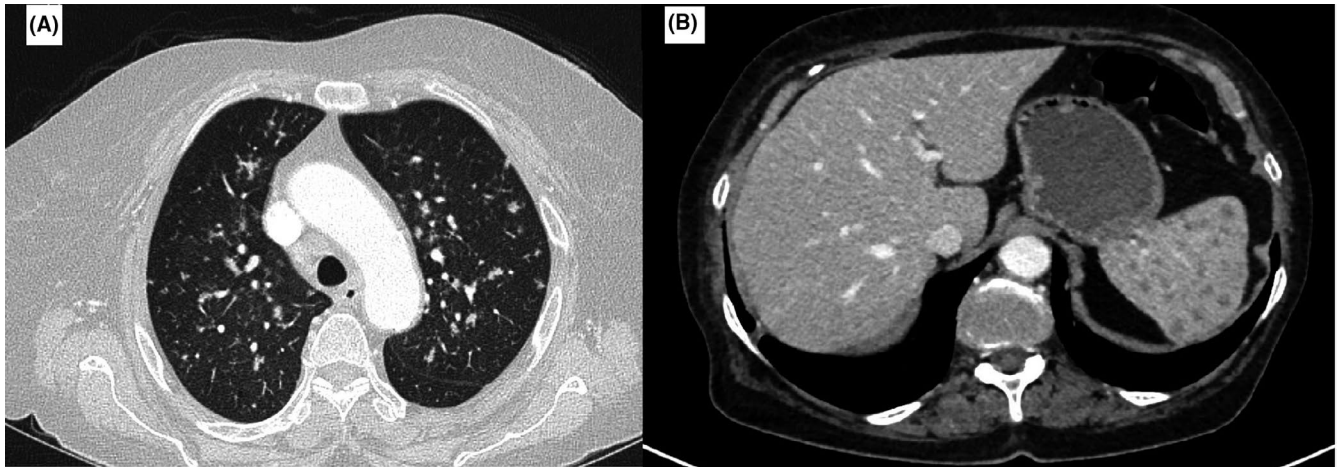


FIGURE 1 CT scan of the patient. A, pulmonary parenchymal window, showing diffuse involvement of the two pulmonary fields, made of micronodules in places achieving the appearance of rosette nodules. B, abdominal CT scan in parenchymal window, showing a multinodular aspect of the spleen

shown the existence of epithelioid and gigantocellular granulomas without associated necrosis. As part of the etiological assessment, a thoraco-abdomino-pelvic scanner showed the presence of micronodular lesions of the lungs and the spleen (Figure 1) suggesting disseminated tuberculosis with dual localization: pulmonary and hematopoietic organs (lymph nodes and spleen). The patient was initially put on quadruple anti-tuberculosis antibiotic therapy (HRZE). Regarding her RA, she is currently (4 months after starting anti-TB treatment) receiving symptomatic treatment and corticosteroid therapy.

3 | DISCUSSION

One of the main risks for patients on anti-TNF therapy is TB. A meta-analysis by Zheng et al¹ have shown that the risk of TB in patients followed for chronic inflammatory rheumatism is increased and even doubled with anti-TNF. A study showed that in regions where the incidence of TB is higher (Asian countries), the risk of infection is 26 times higher in people on anti-TNF α .² Among them, infliximab and adalimumab are the most providers of TB with an incidence of around 259/100 000 and 113/100 000 patient-years, respectively.³ There are insufficient data in the literature for certolizumab pegol. It can either be a reactivation of latent tuberculosis or a primary infection. According to the studies, the average duration of onset varies between three months and one year. It occurred early for infliximab (10-12 weeks), later for etanercept (3-5 times longer).⁴ These data were not found for certolizumab. In our case, the TB appeared 6 months after the start of the treatment and it was multifocal. Studies showed that the infection can be pulmonary (39%) or extra-pulmonary (61%). Disseminated forms (25%) and

severe forms, sometimes lethal, have been described under anti-TNF.⁵ The particularity of our case is the involvement of the hematopoietic organs discovered with a bone marrow biopsy following a pancytopenia. Similar cases have not been found in the literature. To modulate this risk, a comprehensive infectious investigation and careful screening for TB should be done in prebiotherapy. Several screening recommendations have been developed by several societies. With the application of these recommendations, the risk of reactivation of TB is divided by four.⁶ It is for this reason that it was not made for our patient. Studies describe a specificity rate for IDR test varying between 92% and 97% depending on the BCG vaccination status with a sensitivity rate of around 46%.⁷ The use of the QuantiFERON-TB and the IDR test at the same time could improve screening performance despite the discrepancies that have been noted.⁸

4 | CONCLUSION

The use of biotherapy for rheumatic disease may increase the infectious risk. For that reason, we highlight the importance of infectious investigation and complying with the recommendations.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

EH: is the corresponding author and contributed to the conception, design, and manuscript preparation. SB: contributed

to the manuscript redaction and discussion. SR, SJ, and HA: contributed to data analysis. EC and HS: contributed to the bibliographic research. ME: approved final version the manuscript.

ETHICAL APPROVAL

This manuscript was approved by the ethical committee.

CONSENT TO PARTICIPATE

The patient consented to participate in this article.

CONSENT FOR PUBLICATION

The patient consented to the publication of this article.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. Zhang Z, Fan W, Yang G, et al. Risk of tuberculosis in patients treated with TNF- α antagonists: a systematic review and meta-analysis of randomised controlled trials. *BMJ Open*. 2017;7(3):e012567.
2. Wang X, Wong SH, Wang XS, Tang W, Liu CQ, Niamul G, et al. Risk of tuberculosis in patients with immune-mediated diseases on biological therapies: a population-based study in a tuberculosis endemic region. *Rheumatology*. 2019;58(5):803-810.
3. Atzeni F, Sarzi-Puttini P, Botsios C, et al. Long-term anti-TNF therapy and the risk of serious infections in a cohort of patients with rheumatoid arthritis: comparison of adalimumab, etanercept and infliximab in the GISEA registry. *Autoimmun Rev*. 2012;12(2):225-229.
4. Godfrey MS, Friedman LN. Tuberculosis and biologic therapies: Anti-tumor necrosis factor- α and beyond. *Clin Chest Med*. 2019;40(4):721-739.
5. Xie X, Li F, Chen JW, Wang J. Risk of tuberculosis infection in anti-TNF- α biological therapy: from bench to bedside. *J Microbiol Immunol Infect*. 2014;47(4):268-274.
6. Keane J, Gershon S, Wise RP, Levens ME, Kasznica J, Schwietzman WD, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. *N Engl J Med*. 2001;345(15):1098-1104.
7. Lioté H. Tuberculose, agents anti-TNF et autres immunosuppresseurs. *Rev Mal Respir*. 2008;25(CRLF):62-64.
8. Doan TN, Eisen DP, Rose MT, Slack A, Stearnes G, McBryde ES. Interferongamma release assay for the diagnosis of latent tuberculosis infection: a latent-class analysis. *PLoS One*. 2017;12(11):e0188631.

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