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Case report

Marked deterioration in rheumatoid arthritis associated bronchiectasis following treatment with Rituximab

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A B S T R A C T

We report a 67 year old lady with Rheumatoid Arthritis (RA) and mild bronchiectasis (BE) whose treatment was escalated to Rituximab. Nine months after commencing Rituximab her lung sepsis worsened dramatically with repeated hospitalization, new sputum isolation of *Stenotrophomonas maltophilia* and *Pseudomonas aeruginosa* and marked radiological deterioration in BE. She was found to have a low serum IgG and IgM levels almost certainly as a complication of Rituximab. Immunoglobulin replacement therapy was instituted and her clinical status has slowly improved.

1. Introduction

RA has long been recognised as a cause of BE with a clinical prevalence of about 3% in RA cohorts [1]This is very challenging to manage as the treatment for extra-pulmonary disease often requires intense immunosuppression which in turn can predispose to increased airway sepsis and a vicious cycle of worsening BE.

2. Case report

A 67 year old female with a 33 year history of seropositive RA, serum anti-citrullinated peptide (CCP) antibodies measuring at > 340 U/ml and Rheumatoid factor (RhF) antibodies measuring 46 IU/ml, was diagnosed with mild basal secondary BE in 2011 (Fig. 1).

She was tutored in sputum clearance and commenced on prophylactic macrolides. Her BE remained stable but flaring joint disease limiting her quality of life necessitated commencement of Rituximab in January 2016 with a 2nd dose in January 2017. From February 2017 to February 2018 she was admitted on 4 occasions totaling 101 days with severe recurrent lung sepsis. Bronchoalveolar lavage and sputum samples grew a sensitive *Stenotrophomonas maltophilia* on 3 occasions in 2017 and 5 sputum cultures in 2018 (last early September 2018) grew a highly resistant *Pseudomonas aeruginosa*.

The last dose of Rituximab was administered in January 2017. Serum immunoglobulins in March 2017 revealed a normal serum IgG of 6.98 g/L (normal 6.80 to 15.3) and were repeated in December 2017 revealing a reduced serum IgG of 3.84g/L. Serum IgM was mildly low in 2013 at 0.28 g/L (normal 0.38 to 1.88) and was < 0.18 g/L on repeat in March and December 2017. Repeat HRCT thorax in February in 2018 revealed marked progression of BE now present in all lobes with severe bronchiolitis (Fig. 2).

Immunoglobulin replacement therapy was commenced in February 2018. She was admitted twice more with acute respiratory sepsis in May and August 2018 for a total of 21 days. Serum IgG normalized at 8.21g/l by mid July 2018. Spirometry in October 2018 now revealed severe obstruction with an FEV1 of 50% predicted compared to non-obstructed spirometry in July 2016 with a FEV1 of 81% predicted.

The patient hasn't required admission for 3 months, has completed an 8 week pulmonary rehabilitation program and may shortly be able to discontinue long-term oxygen therapy.

3. Discussion

RA is a well recognised cause of BE both as a primary airway disorder or as a traction phenomenon in patients with rheumatoid arthritis associated interstitial lung disease [2] BE can precede the diagnosis of RA, sometimes by many years [3], raising the possibility, that, in some patients, chronic bronchial sepsis may be causal in RA. Interestingly, BE is often sub-clinical in RA and up to 35% of patients have radiological BE on high-resolution CT imaging with risk factors including older age, disease duration and male gender [4]. One study found a higher prevalence of anti-CCP antibodies, but not RhF antibodies, in a BE population compared to healthy controls [5]. A further study also detected higher levels of anti-CCP and RhF in patients with RA and BE compared to RA alone [6].

Rheumatoid arthritis associated BE is also probably unique, apart from obliterative bronchiolitis associated BE in lung transplant recipients, in its combination of BE and the requirement for intense immunosuppression. It has been shown in 2 multi-centre studies that RA patients with BE have an increased mortality with an odds ratio of 1.78

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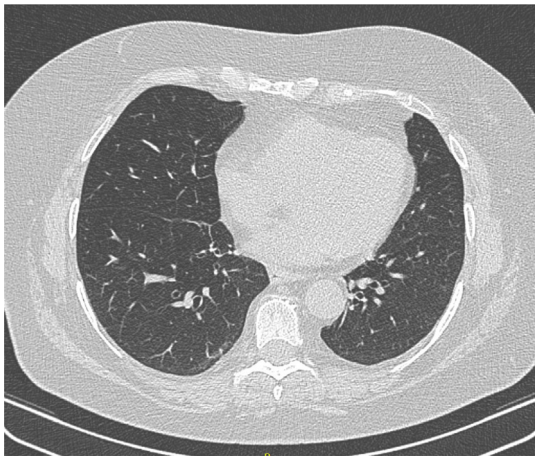

Fig. 1. Mild basal bronchiectasis.

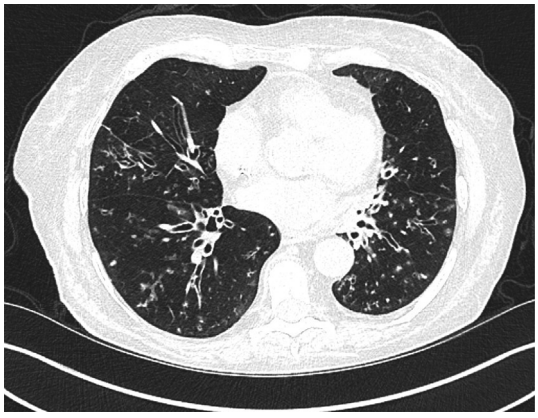

Fig. 2. Extensive bronchiectasis with some bronchiolitis.

and 2 compared to a control group of idiopathic BE and BE patients without RA respectively [7,8].

Clearly disease modifying anti-rheumatic drugs (DMARDs) increase the risk of sepsis. Rituximab is now commonly used in refractory RA and, as in our patient's case, can cause significant hypogammaglobulinaemia. Interestingly, our patient's RA has significantly improved on Rituximab, reducing her acute flares frequency, improving her functional ability, reducing her anti-CCP to 64 U/ml (from > 340 U/ml) and normalising her RhF. This supports our theory of her BE being exacerbated by secondary hypogammaglobulinaemia leading to recurrent airway injury rather than poorly controlled RA causing related lung disease. Whether Rituximab is more airway immunosuppressive than other DMARDs is unknown but, one common sense approach to using this drug in patients with RA and clinical BE could include shared care, frequent review, 2–3 monthly antibody checks [9] pre/post sputum surveillance and repeat high-resolution imaging at 6–12 months after drug institution.

Conflicts of interest

The authors have no conflict of interest to declare.

Patient's consent was provided by verbal and written consent to use the case for publication.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.rmcr.2019.100904.

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