presentation, our patient has been discharged from hospital, and is stable from a haematological perspective (Hb 107 g/dL) with a Miami J collar still in place. The factors that likely contributed to her survival so far include: firstly, she suffered an Anderson and D'Alonzo type III odontoid peg fracture, which has a higher survival rate than the more unstable type II fractures. Secondly, she was transfused early when her anaemia was discovered. Thirdly, treatment with rituximab was initiated within the first week and, finally, the haemopneumothorax developed slowly, allowing time for diagnosis and treatment. ■

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Clinical Medicine 2020 Vol 20, No 4: 435–7 **LESSONS OF THE MONTH**

Lessons of the month 2: Chronic eosinophilic pneumonia (CEP): A rare manifestation of infliximab therapy

Authors: Iftikhar Nadeem,[A] Usman Khatana,[B] Masood Ur Rasool,[C] Asma Wasil[D] and Mohammed Azher[E]

ABSTRACT

We present a rare and unusual case of 22-year-old man who was on infliximab therapy for his uncontrolled ulcerative colitis. Infliximab was stopped as he didn't get any benefit from it and he ended up having subtotal colectomy and ileostomy. He presented with shortness of breath and eosinophilia and underwent a number of investigations and finally a diagnosis of chronic eosinophilia secondary to infliximab was made.

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KEYWORDS: Chronic eosinophilic pneumonia, infliximab therapy, infliximab antibodies, pharmacology

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Introduction

Biologic agents are increasingly used for many autoimmune and inflammatory conditions, as they are both steroid sparing and can potentially induce and maintain remission. Notably tumour necrosis factor (TNF)-alpha antagonists are particularly useful in inflammatory bowel diseases (IBD) such as Crohn's and ulcerative colitis (UC).

Infliximab is a chimeric monoclonal antibody that targets TNF-alpha (a cytokine involved in modulation of inflammatory

responses) and neutralises its effects. As infliximab is a generic TNF-alpha inhibitor and thus non-specific in its actions, it has the potential to cause immune-mediated side effects.[1] The adverse pulmonary effects have been reported following infliximab infusion, including latent tuberculosis reactivation, invasive aspergillosis, interstitial pneumonitis, pulmonary oedema and alveolar haemorrhage.[2–4]

Case presentation

We present a case of 22-year-old man, who had never smoked, with background history of severe and difficult to control UC for which he was put on infliximab in December 2018 and received it until January 2019. He was not on any other medications. Since his UC flare ups were not controlled even with infliximab, he had subtotal colectomy and ileostomy in February 2019. He made an uneventful recovery and was discharged home.

He then presented to the emergency department with a 1-day history of shortness of breath and wheeze in May 2019. Vitals on presentations were blood pressure of 130/71 mmHg, pulse rate of 103 beats/minute, oxygen saturation of 89% on room air (RA), respiratory rate of 21 breaths/minute and afebrile. His UC was well controlled even without infliximab. He didn't have any courses of steroids since his surgery.

Bloods on admission showed microcytic anaemia (haemoglobin of 113 g/L; mean corpuscular volume of 67.9 fL), a raised D-dimer (1.53 mg/L) and a raised eosinophil count of 0.6×10^9/L (normal range 0.04–0.4), which had been normal previously. Rest of the routine bloods including urea, creatinine, electrolytes, C-reactive protein and liver function tests were all normal.

Arterial blood gases on RA were pH 7.46, partial pressure of carbon dioxide of 4.11 kPa, partial pressure of oxygen of 7.7 kPa, bicarbonate of 24 mEq/L, oxygen saturation of 87% and lactate of 1.1 mmol/L.

Chest X-ray on admission showed patchy interstitial shadowing in both lower lobes. Computed tomography pulmonary angiography (CTPA) showed no pulmonary embolism but patchy ground glass opacification at both lung bases. He was discharged with oral co-amoxiclav and clarithromycin.

He presented again to our hospital a month later with same symptoms. Haemoglobin was normal at 144 g/L but it showed raised eosinophils of 2.0×10^9/L. Rest of the bloods were unremarkable. He had a repeat CT of the chest, which showed new upper lobe and peripheral ground glass changes suggestive of disease progression. A respiratory opinion was sought at that time. Bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsies were carried out.

BAL showed 55% eosinophils, 30% mononuclear cells, 12% lymphocytes and 3% neutrophils. The airways appeared normal, with minimal secretions. Gram stain; bacterial, fungal and viral cultures; and special stains for *Cytomegalovirus*, *Pneumocystis* and acid-fast bacilli were negative. Transbronchial biopsy showed interstitial and intra-alveolar eosinophilic infiltrates.

There was no evidence of granulomas, vasculitis, fibrosis or interstitial lung disease. The case was discussed at multidisciplinary team meeting and the diagnosis of chronic eosinophilic pneumonia (CEP) was made. The patient was started on high-dose steroids and showed significant improvement clinically as well as radiologically (Fig 1). The patient was discharged home and is being followed up regularly in the respiratory clinic.

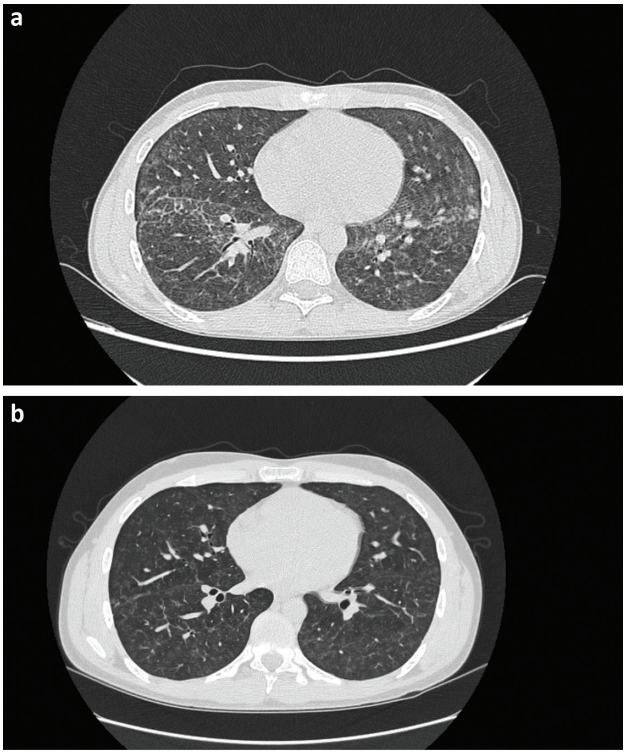

Fig 1. Computed tomography of the lung bases. a) Reticular nodular shadowing noted in lower zones. b) Almost complete resolution of reticular nodular shadowing in lower zones.

Discussion

This is a complex case of eosinophilic pneumonia in a patient who was on infliximab therapy. Our patient was thoroughly investigated for different causes of pulmonary eosinophilia including:

- eosinophilic granulomatosis with polyangiitis: ruled out by negative anti-neutrophil cytoplasm antibodies (ANCA), no rash, no polyneuritis, no history of asthma and no vasculitis on biopsy
- vasculitis: ruled out by negative anti-nuclear antibodies, ANCA, extractable nuclear antigen and no vasculitis on biopsy
- atypical pneumonia: ruled out by negative screen
- allergic bronchopulmonary aspergillosis: ruled out by normal *Aspergillus* specific immunoglobulin E (IgE), normal *Aspergillus* precipitins, IgE level of 215 IU/mL
- infectious aetiologies: ruled out by negative stool studies for helminths and negative blood and bronchoalveolar lavage cultures for bacteria and fungi
- *Pneumocystis jirovecii* pneumonia serology and serological testing for *Strongyloides*, *Wuchereria* and *Schistosoma* were negative; HIV and hepatitis serology were negative; avian antibodies were negative.

CT of the sinuses was normal. Lung function testing (Table 1) showed restrictive lung disease with reduced carbon monoxide transfer coefficient (69%) and transfer capacity of the lung for the uptake of carbon monoxide (45%) which improved tremendously after treatment (87% and 77%, respectively).

It was suspected that the cause of his eosinophilic pneumonia was infliximab. Infliximab antibodies were checked which were

Table 1. Pulmonary function test results

Pulmonary function tests	Pre-treatment	Post-treatment
Forced expiratory volume 1 / forced vital capacity	77.65	82.12
Forced expiratory volume 1, L	1.95 (46%)	2.98 (70.6%)
Forced vital capacity, L	2.51 (50%)	3.98 (80%)
Total lung capacity, L	4.19 (62%)	5.2 (77%)
Residual volume, L	1.33 (84%)	1.40 (88%)
Carbon monoxide transfer coefficient (KCO)	1.18 (67%)	1.50 (87%)
Transfer capacity of the lung for the uptake of carbon monoxide (TLCO)	5.25 (45%)	8.91 (77%)

significantly raised at more than 200 IU/mL (normal range <20) even 6 months after stopping infliximab.

Conclusion

CEP is extremely rare and should be considered in patients receiving infliximab who develop eosinophilia, and pulmonary infiltrates with dyspnoea. Infliximab antibodies should always be checked before commencing infliximab therapy. To our knowledge there are only three reported cases of pulmonary eosinophilia with infliximab therapy, but all those patients developed eosinophilia acutely.[5,6] Our patient developed symptoms 3 months after discontinuation of infliximab therapy. This makes it the first reported case of delayed reaction to infliximab leading to CEP. ■

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Clinical Medicine 2020 Vol 20, No 4: 437–9 LESSONS OF THE MONTH

Lessons of the month 3: ST-elevation myocardial infarction and left ventricular thrombus formation: an arterial thrombotic complication of severe COVID-19 infection

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ABSTRACT

We describe a case of an 82-year-old man who developed an anterior ST-elevation myocardial infarction (STEMI) and left ventricular thrombus while an inpatient following a diagnosis of severe COVID-19 infection (SARS-CoV-2). His D-dimer was significantly elevated at 12,525 ng/mL (normal range <243). He unfortunately died despite management with thrombolysis, warfarin and non-invasive ventilation. This case provides an example of a likely arterial thrombotic complication of severe COVID-19 infection. Clinicians should be aware of this possibility in such patients, with a severely prothrombotic state as a possible underlying aetiology. Further research is required to establish any causative link, pathophysiological mechanisms and whether modification to existing venous thromboembolism prophylaxis strategies may also reduce arterial thrombotic complications of severe COVID-19 infection.

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KEYWORDS: COVID-19, myocardial infarction, ventricular thrombus, arterial thrombosis, D-dimer

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