

Streptococcal lung abscesses from a dental focus following tocilizumab: a case report

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ABSTRACT

Patients suffering from dental infections and concurrently using immunosuppressive medication are at increased risk of developing systemic streptococcal infections. Tocilizumab is a novel therapeutic agent targeting interleukin-6. We describe a case of streptococcal lung abscesses from a dental focus after use of tocilizumab for treatment of Takayasu arteritis.

Introduction

Tocilizumab is a recently introduced monoclonal antibody against interleukin-6. In most countries, the drug is currently registered to treat rheumatic diseases unresponsive to anti-TNF treatment (1). Tocilizumab is associated with an approximately doubled risk of infections in comparison to treatment without biologicals (2). This risk is similar for both anti-TNF and tocilizumab treatment (3-4).

Lung abscesses are a serious complication of immunosuppression (5). Lung abscesses are frequently caused by streptococcal infections, which often originate from a dental focus. In oncology patients, dental screening is routinely performed before start of immunosuppression (6, 7). In contrast, dental screening is seldomly considered before start of rheumatologic immunosuppressive regimens.

Case report

A 63-year-old woman using tocilizumab for treatment of Takayasu arteritis presented with complaints of increasing shortness of breath and dry cough for one week. In addition, she suffered from chills, night sweats and left thoracic pain. A chest x-ray, taken for routine purposes 8 months before the start of symptoms, was normal. At a routine visit to the dentist at 6 months before presentation, no abnormalities were noticed except for calculus formation, which was removed. The patient maintained a good level of oral hygiene.

The patient was diagnosed with Takayasu arteritis 3 years and 5 months before presentation. Treatment was started with prednisolone, and methotrexate was added 5 months later during a relapse, but was replaced by azathioprine

due to gastro-intestinal complaints. Infliximab was started two years after diagnosis, but was not sufficiently effective. Therapy was switched to a monthly infusion of tocilizumab 8 mg/kg at 6 months before presentation, in combination with azathioprine 50 mg twice daily and prednisone 3.75 mg once daily.

At presentation, the patient had suffered for one week from toothache while she was awaiting an appointment with the dentist. Clinical examination revealed a painful swelling of the right jaw. Her body temperature was normal. Inspiration was limited by local left thoracic pain. Laboratory tests revealed normal CRP levels and blood counts. Electrolytes, liver and renal function were normal. A chest x-ray showed bilateral lung consolidations. Chest CT revealed two sharply confined consolidations with central necrosis surrounded by ground glass area in the right upper lobe, one consolidation anterior in the left upper lobe and one enlarged lymph node in the aortopulmonary window (Fig. A). All lesions were positive at positron emission tomography (PET) scanning. In addition, the PET scan showed regression of the Takayasu arteritis (Fig. B).

The patient was admitted to the hospital for further analysis. The differential diagnosis included pulmonary abscess, malignancy or Takayasu associated nodules. The latter diagnosis was considered unlikely because the PET scan had shown that other Takayasu lesions were in regression. Bronchoscopy was performed and the results were normal. Broncho-alveolar lavage fluid stained negative for tuberculosis and contained no pathogenic bacteria or malignant cells. Transbronchial biopsy showed non-specific interstitial inflammatory changes with no signs of granuloma formation, vasculitis or malignancy.

The dentist diagnosed a dental abscess and root canal treatment was performed. The abscess was treated by amoxicillin/clavulanic acid for five days. A culture was not taken from the abscess. The patient improved temporarily and was discharged; however she was re-admitted to the hospital with similar symptoms three weeks after presentation. The CRP levels and leukocyte counts were increased (169 mg/

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1 and 14×10^9 /l, respectively). A culture obtained by CT guided puncture of the right lung lesions showed growth of *Streptococcus intermedius*, a member of the *Streptococcus anginosus/milleri* group. As such, a diagnosis of *S. intermedius* lung abscess was established. However, the bacteria were susceptible to penicillin. The patient was treated by 6 weeks of intravenous penicillin (6 million units/day) and made a full recovery.

Discussion

This report shows a case of streptococcal lung abscesses following tocilizumab treatment, originating from a dental focus.

Potential risk factors for infection in patients using tocilizumab were investigated in two studies: one study found previous anti-TNF treatment, high disease activity and concomitant use of prednisolone and/or leflunomide (8), whereas another study identified presence of respiratory disease, use of prednisolone ≥ 5 mg/day and age ≥ 65 years (9). Our case had used previous anti-TNF treatment and was using prednisolone. Of note, the prednisolone dose used by the patient was 3.5 mg daily, which is a relatively low dose. The patient also used azathioprine. This drug is associated with a less increased risk of infections in comparison to prednisolone (2). Nevertheless, both drugs may have contributed to some extent to the total immunosuppressive effect of tocilizumab, as well as the previous use of infliximab.

Bacterial lung abscesses have not been described in previous studies including a large post-marketing surveillance study and other cohorts in patients treated with tocilizumab (3, 8, 9). The lung abscess in our patient showed growth of *S. intermedius*, a usually commensal bacterium in the oral cavity, associated with periodontitis and subsequent systemic (pulmonary) infections (10).

In cancer patients receiving chemotherapy, pre-treatment dental clearance is often advised to prevent infectious complications, according to recommendations by the National Institute of Health (6). The rationale is based upon case reports of systemic streptococcal

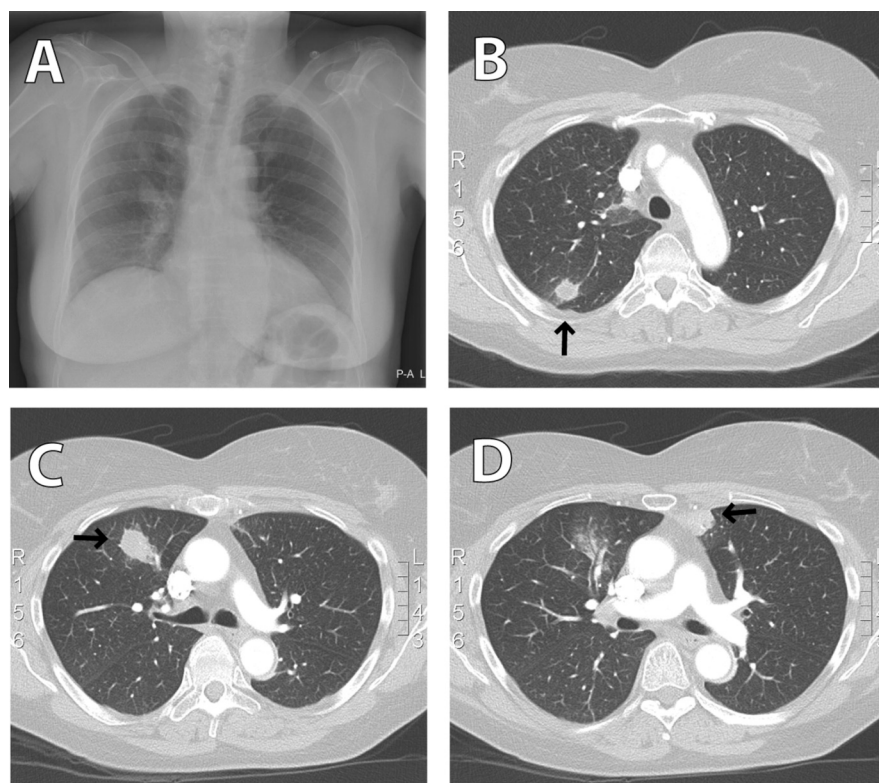


Fig. 1. Lung abscesses. X-thorax at presentation (A) and CT scan showing two lesions in the right upper lobe (B and C) and one lesion located anterior in the left upper lobe (D).

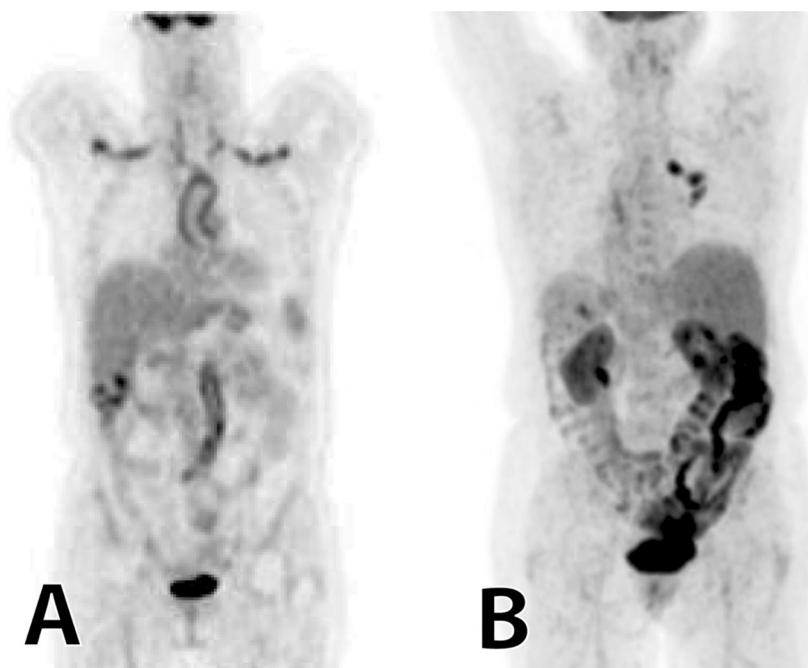


Fig. 2. PET-scan. Scan showing large vessel arteritis three years before presentation (A) and follow-up scan showing regression of vessel lesions but new pulmonary consolidations (B).

infections; unfortunately, no systematic clinical trials were performed to show efficacy of dental clearance guidelines (7). In rheumatic disease, the prevalence of periodontitis is increased two-

fold in comparison to the general population (11). The current case report may contribute to a discussion about dental clearance prior to start of biological agents.

In conclusion, our report demonstrates systemic spread of dental infection in a patient immunocompromised by use of tocilizumab. In case of dental complaints, dental consultation may be considered before start of tocilizumab, especially when risk factors for infection are present.

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