# Title: Not Your Typical Host: Disseminated Staphylococcus aureus Infection Following Initiation of IL-6 Inhibitor

**Authors:** Collins Onwuka, Matthew Lempel, David Podell
Yale Waterbury Internal Medicine Residency Program, Waterbury, Connecticut

## Introduction

Tocilizumab is an interleukin 6 (IL-6) inhibitor utilized to treat patients with rheumatoid arthritis (RA) who have had suboptimal response to disease-modifying antirheumatic drugs (DMARDS).

The use of Tocilizumab is associated with immunosuppression. Thus, individuals receiving it must be fastidiously evaluated as they can exhibit mild symptoms despite having severe disseminated infections.

## Case Description

**History:** A 63 year old woman with seropositive RA and total hip replacement recently started on tocilizumab several weeks prior presented to her rheumatologist due to new onset left sided neck pain. She was initially started on a prednisone taper with no relief and subsequently presented to the emergency department for further evaluation. At that point she was found to be afebrile, with tachycardia and leukocytosis to 17 thousand/mm3. After a lumbar puncture was performed and her cerebrospinal fluid was found to be benign, she was discharged with recommended close outpatient follow up. However, due to worsening neck pain now associated with progressive lethargy and confusion she was brought back to the hospital six days later for reevaluation where she was noted to be lethargic with bilateral knee effusions.

**Physical examination**: Vitals: T: 99.4 ° F (Oral) HR: 118 RR: 18 BP: 134/90 SpO2: 94% (RA).

General: She was drowsy but easily arousable.

HEENT: Atraumatic, normocephalic; pupils equal and reactive, EOM intact, sclera clear; negative JVD or tracheal deviation. No neck rigidity. Tenderness to L trapezius.

CARDIOVASCULAR: Normal S1-S2, no m/g/r.

RESPIRATORY: Lungs CTA.

GASTROINTESTINAL: soft, non tender.

MUSCULOSKELETAL: no active synovitis of the small joints of the hands, wrists, elbows, or shoulders; L knee fullness; NEUROLOGICAL: Oriented x4; no focal neurological deficit observed; motor strength equal and normal bilaterally; speech normal.

**Laboratory Analysis**

**CBC**: WBC 19.8 thous/mm3 (Bands 11%), RBC 4.49 mill/mm3, Hgb 15.0 g/dL, HCT 42.7 %, MCV 95.0 fL,
MCH 33.4 pg., MCHC 35.2 g/dL, RDW 12.8 %, Plat elets 249 thousand/mm3, MPV 7.1 fL.

**Sed. rate:** 23 mmHg.; **CRP:** 37 mg/L.

**Blood culture:** Positive for methicillin sensitive Staphylococcus aureus (MSSA).

ANA: negative; RF 111.6 IU/mL; C3 111 mg/dL; C4 20 mg/dL; Cryoglobulin: negative.

**CT head:** Left posterior frontal subarachnoid hemorrhage laterally, without mass effect.

**CT neck with IV contrast: (Images1a and 1b)** Extensive retropharyngeal edema with likely superimposed abscesses extending from the skull base to at least the level of C3-C4 on the right, crossing the midline to the left at the level of the left carotid artery bifurcation and apparently contiguous with a large collection/abscess in the deep tissues of the left posterior lateral neck.

**MR cervical spine with and without IV contrast**: (Image 2) Extensive retropharyngeal soft tissue swelling and inflammation. More extensive inflammatory disease involves the posterior paraspinal musculature bilaterally, greater on the left than on the right, with multiple loculated abscesses in the left posterior paraspinal musculature.

**Left Knee XR: (Image 3)** Moderate-sized joint effusion.

**Left knee arthrocentesis and synovial fluid Gram staining and culture:** Positive for MSSA.

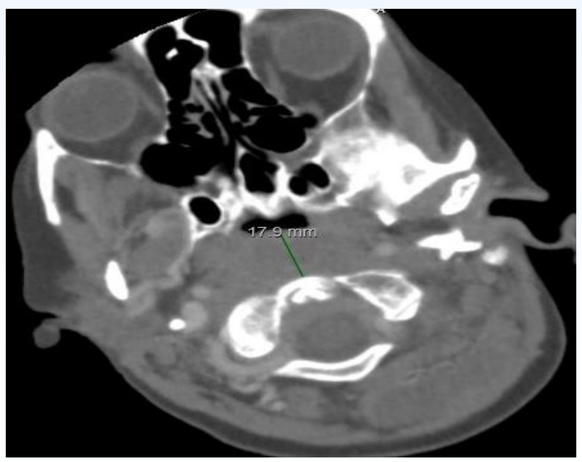


Image 1a

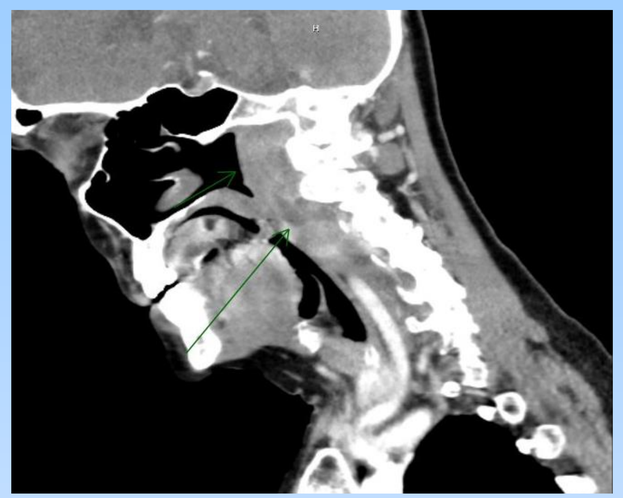

Image 1b

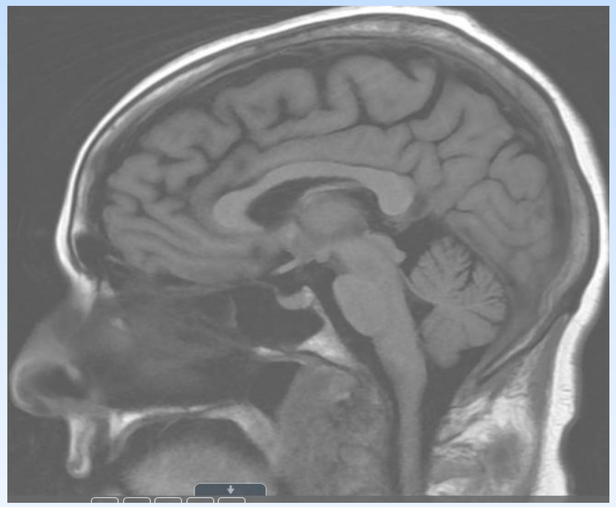

Image 2

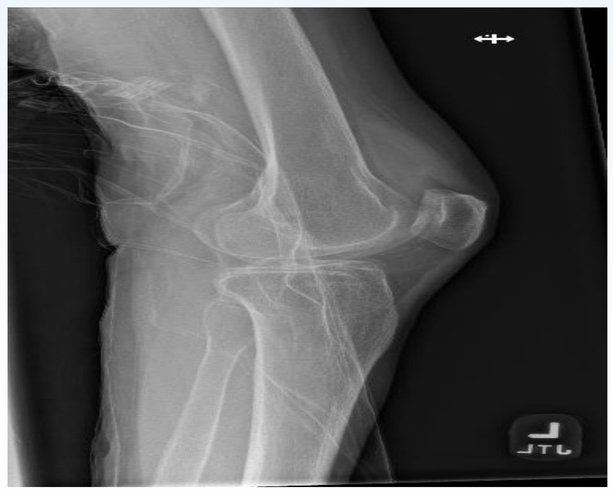

Image 3

**Management**
Patient was taken to the operating room for incision and drainage of the deep neck abscesses and, as knee arthrocentesis was consistent with septic arthritis, she underwent arthroscopic bilateral knee washouts. However, despite improvement in her clinical status and theoretical control of the source of infection, her blood cultures remained persistently positive for MSSA, prompting a transthoracic echocardiogram to be performed which demonstrated a 0.6cm vegetation on the mitral valve with a micro perforation and perivalvular abscess.

Per recommendations of Cardiothoracic surgical service she was discharged on intravenous oxacillin with plan for subsequent mitral valve replacement at least four weeks following intracerebral hemorrhage.

At the time of this writing our patient is doing well at a subacute rehabilitation facility on intravenous antibiotics and is anticipating cardiothoracic surgery later this month.

## Discussion

Tocilizumab inhibits the production of C-reactive protein. This inflammatory marker may be low despite underlying infection or inflammation and can be falsely reassuring. Furthermore, because tocilizumab is administered by injection once a month, it may not be included on the patient's active medication list. Interestingly, as was the case in our patient, the risk of severe infection has been found to be higher for patients with prosthetic joints. While a patient's story and symptoms are always key to uncovering the primary diagnosis, appreciation of a hosts underlying immunodeficiency is vital.

## Conclusions

Physicians must maintain a high index of suspicion for disseminated infection in patients treated with tocilizumab or other biologic agents because they are severely immunosuppressed and may only show mild initial symptoms.