CASE REPORT

Endogenous endophthalmitis and osteomyelitis associated with interleukin 17 inhibitor treatment for psoriasis in a patient with diabetes

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SUMMARY

A 64-year-old man with type 2 diabetes mellitus and plaque psoriasis presented to the emergency room with 3 days of progressive right eye pain and decreased vision. After extensive workup and multidisciplinary team effort, the patient was diagnosed with and treated for unilateral endogenous methicillin-sensitive *Staphylococcus aureus* endophthalmitis, bacteraemia and osteomyelitis of the foot. The patient had been started on the interleukin 17 (IL-17) inhibitor secukinumab for his treatment-resistant plaque psoriasis 4 weeks prior to presentation. After treatment, his final vision was light perception and the foot infection resolved without sequelae. To our knowledge, this is the first reported case of both endogenous endophthalmitis and osteomyelitis associated with an IL-17 inhibitor.

system. The US Food and Drug Administration (FDA) approved secukinumab, an interleukin 17A (IL-17A) inhibitor, for treatment of moderate-to-severe plaque psoriasis in January 2015 and the medication received European approval in November 2015. IL-17 is a pro-inflammatory cytokine that plays a major role in mucocutaneous immunity and also in the altered immune response against self-antigens, such as occurs in psoriasis.^{8,9} Secukinumab is a fully human monoclonal antibody that selectively inhibits IL-17A and its safety profile has previously been felt to be similar to other biologics.^{9,10} To our knowledge, there have been no prior reports of serious ocular or bone infections associated with secukinumab.

CASE PRESENTATION

A 64-year-old Caucasian man presented to the emergency department with chief complaint of 3 days of right eye pain and decreased vision. He had no history of ocular surgery or trauma. His medical history was significant for type 2 insulin-requiring diabetes mellitus with bilateral peripheral neuropathy (haemoglobin A1c 7.3%) and plaque psoriasis. His psoriasis had been resistant to treatment with multiple medications including fluticasone cream, betamethasone cream, ustekinumab, adalimumab and etanercept. Six weeks prior to presentation, he was treated with a 10-day course of ciprofloxacin for a puncture wound of his left foot after stepping on a screw. Four weeks prior to presentation, he was seen by his dermatologist and started on subcutaneous secukinumab for treatment of his resistant-plaque psoriasis. The patient denied any active infection at that time. He was initially prescribed 300 mg weekly, and on the fourth week of treatment noticed vision loss and pain in his right eye.

On initial presentation in the emergency department, the vision in his right eye was hand motion. Eye exam was notable for reactive ptosis, conjunctival injection, chemosis, fine keratic precipitates and dense fibrinous anterior chamber reaction with 1.5 mm hypopyon (figure 1). There was no view to the fundus, and B-scan ultrasound demonstrated large amount of vitreous debris (figure 2). The left eye exam was unremarkable. He was afebrile and his vital signs were normal. Complete physical examination revealed significant cellulitis of his left mid-foot and forefoot without any open wounds

BACKGROUND

Endogenous endophthalmitis is a serious intraocular infection due to haematogenous dissemination of bacterial organisms. Endogenous bacterial endophthalmitis is rare.¹ Most cases are associated with diabetes, malignancy, intravenous drug abuse, immunocompromise or immunosuppression.^{2,3} Gram-positive infections predominate in Europe and the USA. Among Gram-positive isolates, *Staphylococcus aureus* is the leading cause of endogenous endophthalmitis.³ In the acute setting, empirical intravitreal antibiotics targeting both Gram-positive and Gram-negative organisms are the mainstay of treatment.^{4,5} Visual outcomes are typically devastating and nearly one quarter of eyes eventually require enucleation or evisceration.³

Osteomyelitis is a serious bone infection due to contiguous spread of bacterial organisms from adjacent tissues and joints, haematogenous dissemination or trauma with direct inoculation of bacteria into the bone. The foot is the most frequent location for development of osteomyelitis and diabetes is known to be an important risk factor.⁶ Worldwide *S. aureus* is the most common causative bacterial pathogen.⁶ In patients who fail medical and conservative surgical treatment, amputation is often required.⁷

Immunosuppressive medications are indicated for the treatment of many medical conditions including organ transplantation and autoimmune disease. Such medications carry the risk of serious infections due to suppression of the immune

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Figure 1 Photo of the right eye the day after presentation to the emergency department with conjunctival injection, chemosis and hazy iris details due to significant anterior chamber inflammation.

(figure 3). He denied foot pain, but sensation to both feet was notably diminished.

INVESTIGATIONS

The patient was diagnosed with endogenous endophthalmitis and left foot cellulitis. He underwent emergent anterior chamber tap and injection of intravitreal vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL). He was admitted to the hospital for further workup and treatment of his infections. His white blood cell count (WBC) was elevated at $16.4 \times 10^9/L$ (normal $4.5\text{--}11.0 \times 10^9/L$). Blood and aqueous cultures were both positive for methicillin sensitive *Staphylococcus aureus* (MSSA). Transesophageal echocardiogram was negative for vegetation. X-ray and MRI of his left foot were equivocal for the diagnosis of osteomyelitis, and subsequent Indium-111 WBC scan demonstrated acute osteomyelitis of his first metatarsophalangeal joint of his left foot (figure 4).

TREATMENT

Intravenous piperacillin/tazobactam and vancomycin were started at first and switched to penicillin G 12 million units every

Figure 2 Ultrasound (B-Scan) of the right eye in the emergency department demonstrating vitreous debris.

Figure 3 Photo of the patient's feet on initial presentation with notable cellulitis of his left foot.

12 hours once the blood and aqueous cultures returned positive for MSSA. On hospital day 4, the intraocular inflammation worsened despite the initial intravitreal treatment of the eye, and the patient underwent anterior chamber washout and limited vitrectomy with injection of intravitreal clindamycin (1 mg/0.1 mL), vancomycin (1 mg/0.1 mL) and dexamethasone (0.4 mg/0.1 mL).

Due to concern for osteomyelitis based on the WBC scan he underwent surgical washout and debridement of the first metatarsophalangeal joint on hospital day 13. His intraoperative bone biopsy was consistent with osteomyelitis and his intraoperative cultures were negative. He was treated with a 6-week course of intravenous penicillin.

OUTCOME AND FOLLOW-UP

The patient was discharged on day 14 of hospitalisation. Three weeks later, he underwent lensectomy due to a white cataract (figure 5) and was left aphakic because of a small amount of persistent anterior chamber inflammation. Postoperatively his vitreous was notable for diffuse membranous debris and B-scan demonstrated possible funnel retinal detachment. His final visual acuity 2 months after initial presentation was light perception in his right eye. Due to lack of utility, further ocular surgical intervention was not recommended. Following completion of antibiotic therapy, repeat left foot MRI demonstrated resolution of his osteomyelitis.

DISCUSSION

Our patient was both diabetic and immunocompromised secondary to treatment with secukinumab. Diabetes is known to be a major predisposing condition underlying the development of both endogenous endophthalmitis and osteomyelitis.^{2,3,7} With regard to endophthalmitis, diabetes is thought to change the vascular architecture in a manner that compromises the blood-retinal barrier.¹ Peripheral neuropathy is a major predisposing factor in the development of osteomyelitis and other diabetic foot infections.⁷

Unilateral endogenous endophthalmitis has previously been reported in association with vertebral osteomyelitis.¹¹ Bilateral

Figure 4 Indium-111 white blood cell scan of the left foot demonstrating acute osteomyelitis of the first metatarsophalangeal joint.

MSSA endogenous endophthalmitis has been reported secondary to tenosynovitis in a poorly controlled diabetic.¹² Other reported infectious aetiologies of endogenous endophthalmitis include endocarditis, cellulitis, urinary tract infection and abscesses in various locations.⁴

In pooled data from 10 phase II and III randomised controlled trials for the treatment of moderate to severe plaque psoriasis, secukinumab was associated with an increased risk of non-serious infection requiring antimicrobial treatment compared with placebo. The most common infections within the first 12 weeks of treatment were nasopharyngitis (11.8% of patients) and upper respiratory tract infection (3.3% of patients).^{13 14} The incidence of serious infection or infestation within the first 12 weeks of treatment with any dose was not significantly different from placebo: 0.21% in the secukinumab group (6/2877 patients) and 0.3% in the placebo group

Figure 5 Photo of the right eye 1 week after initial presentation with improved chemosis and anterior chamber inflammation, small fibrous hypopyon (arrow) and dense white cataract with associated fibrous membrane on the anterior capsule.

Patient's perspective

The experience of being totally blind in my right eye (dominant eye) has been both humbling and quite negative at this time. All my work, hobbies and interests require good depth perception and the ability of using both eyes. The current situation can be frustrating to say the least. I've been an individual who has always worked hard for what I have, what I need and what I believe in. I am dedicated to my family. At this time, I cannot complete my job function as a technical manager. Work is what I know, what I enjoy and a way to prevent the collapse of my family unit. I must work!

Besides the work-related issues, there's my wife and I need to be taking care of her, the house and finances. I feel practically worthless not being able to assist her with chores. The humbling part is that I definitely have much more appreciation for those who have no sight at all. Going through life is always a learning experience and I'm learning something new; even if it is a negative experience on my part. As is typical throughout my life, I attempt to keep a positive outlook and not dwell on the negative aspects, but this time, knowing what is involved and what is at stake it does become more difficult. Time will tell.

I'm just thankful that this full-body blood infection still left me with one good eye, so as bad as it is, I can still get a few basic things accomplished around the home and for my job providing I take my time and allow for decent preparation beforehand.

Learning points

- ▶ Diabetes mellitus is a major predisposing factor in the development of endogenous endophthalmitis and osteomyelitis.
- ▶ Ensure that patients are educated on the possibility of rare but serious infections that may occur due to treatment with immunomodulatory agents.
- ▶ Inquire about current or recent infections and injuries before starting a patient on immunomodulatory therapy.
- ▶ Consider examining the feet of patients with diabetes prior to starting them on immunomodulatory therapy.
- ▶ Consider waiting longer than 2 weeks after cessation of active infection before starting a patient on secukinumab.

(2/793).^{13 14} The longer term data showed that at 52 weeks, the exposure-adjusted infection incidence rates were comparable between the secukinumab 150 mg group (85.29/100 subject-years), secukinumab 300 mg group (91.06/100 subject-years) and etanercept group (93.68/100 subject-years).¹³ Regarding susceptibility to specific organisms, secukinumab was associated with a higher incidence of mild to moderate mucocutaneous *Candida* infections (0.66%) than the placebo (0.3%) or etanercept groups (0.3%).^{13 14}

Our patient was started on secukinumab 2 weeks after a traumatic puncture wound of his foot, in line with the studies described above that excluded patients with active infection within 2 weeks prior to initiation of treatment. Despite completing antibiotic therapy for the injury and having no symptoms of infection, the IL-17 inhibitor and underlying diabetes likely contributed to the development of osteomyelitis. To our knowledge, this is the first reported case of both

endophthalmitis and osteomyelitis associated with secukinumab.

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