



## Case Report

# Ceftobiprole: A New Indication for the Treatment of Hidradenitis Suppurativa: A Case Report

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## Abstract

We report the case of a 44-year-old man diagnosed with hidradenitis suppurativa affecting the axillae and groins. Very good postsurgical outcome in axillae, where the patient received ceftobiprole. Therefore, the drug is proposed as an interesting option for targeted antibiotic therapy of polymicrobial skin infections in patients with this disease.

**Keywords:** Acne; Ceftobiprole; Hidradenitis; Inversa; Suppurativa

## Introduction

Ceftobiprole is a fifth-generation cephalosporin that was introduced in Spain in late 2018. It was approved for treatment of community-acquired pneumonia and non-ventilator associated hospital-acquired pneumonia [1,2]. Ceftobiprole has a broad spectrum of activity against both gram-positive and gram-negative bacteria, including *Enterobacteriales* and *Pseudomonas aeruginosa*; therefore, it covers the bacteria that most frequently cause skin infections [3]. In this context, it has been hypothesized that the drug could prove useful for the treatment of complicated skin and soft tissue infections, whether empirically in areas with a high prevalence of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) or as targeted treatment in extensive and severe polymicrobial infections in elderly patients and patients with significant comorbidity [4].

Treatment of Hidradenitis Suppurativa (HS) with ceftobiprole has not been addressed in the literature. This chronic inflammatory disease is characterized by skin disorders that range from nodules and abscesses to fistulous tracts and scars [5]. The disease is classified according to its severity using the Hurley classification, which divides patients into 3 stages [6]. Treatment is based on anti-inflammatory treatment, antibiotics, and surgery, which is reserved for severe cases (Hurley III) that do not respond

to the other 2 strategies and present with severe irreversible skin disorders such as fistulas, scars, and contractures [7]. We report the first case of HS treated using debridement, immunosuppressive therapy, and adjuvant antibiotic therapy with ceftobiprole.

## Case Description

The patient was a 44-year-old man diagnosed with HS (Hurley III) involving the axillae, suprapubic area, and groins in 2015. He was obese (BMI, 32 kg/m<sup>2</sup>) and a smoker. Once diagnosed, he started treatment with isotretinoin. Since the response was unfavorable and the adverse effects poorly tolerated (cheilitis and dry facial skin), treatment was switched to adalimumab 40 mg/wk (January 2016-April 2017), infliximab (April 2017-January 2018), and ustekinumab (February 2018-April 2018). He followed concomitant topical and systemic antibiotic therapy (mupirocin, clindamycin, co-trimoxazole [combined or not with rifampicin, linezolid, quinolones, cephalosporins]) because of polymicrobial skin infections, with positive culture results for MRSA, *Streptococcus anginosus*, *Enterococcus faecalis*, *Corynebacterium striatum*, *Citrobacter koseri*, *Escherichia coli*, *P. aeruginosa*, and *Prevotella* spp. These treatments led to a partial and temporary improvement.

In May 2018, while receiving ustekinumab, the patient underwent surgery for treatment of the inguinal and suprapubic HS (radical excision in both areas). An abdominoplasty-type closure was used in the suprapubic region, and the wounds were left open

in the inguinal area for subsequent closure with autologous split-thickness skin grafts. Empirical treatment was prescribed with intravenous amoxicillin/clavulanic acid 1000/200 mg/8 h, which was stepped up to intravenous piperacillin/tazobactam 4 g/8 h because of *P. aeruginosa*, *E. coli*, and *Prevotella* spp in the surgical cultures. The surgical wound was superinfected by MRSA, which was managed with oral linezolid 600 mg/12 h. The second surgical procedure was performed after 46 days of local wound care and targeted antibiotic treatment. The suprapubic area was debrided and left open for second-intention healing, and the groins were covered with autologous split-thickness skin grafts taken from the thigh. Epithelialization was complete 1 month later. The patient was followed up at the outpatient clinic after discharge. In October 2018, the patient started adalimumab 40 mg/wk until July 2019, when the dose was increased to 80 mg/wk. During this period, he experienced recurrences in the groins (fissures and skin lesions that required occasional drainage) and axillae (multiple abscesses). Therefore, based on the results of culture of the pus drained from the lesions, several antibiotic and antifungal regimens were prescribed.

In January 2020, surgery of the axillary lesions was planned in 2 procedures separated by 2 weeks (Figure 1a). Before surgery, the patient underwent skin MRSA decolonization. The first procedure involved complete excision of the foci of HS without closure of the skin defects, which were treated topically (Figure 1b). Empirical treatment was started with meropenem 2 g/8 h and fluconazole 400 mg/24 h. The cultures taken during surgery were positive for MRSA, *Corynebacterium striatum*, *Enterococcus avium*, *Cutibacterium acnes*, *P. aeruginosa*, *Citrobacter youngae*, *Citrobacter freundii*, *Fusobacterium* spp., and *Prevotella* spp. Therefore, on day 5 after surgery, antibiotic treatment was switched to intravenous ceftobiprole 500 mg/8 h combined with oral metronidazole 500 mg/8 h. Clinical progress was acceptable and, after 9 days of treatment (14 after debridement), the second procedure was performed. The skin defect in the left axilla was covered using 2 VY advancement flaps. The defect in the right axilla, which was larger, was treated using a parascapular pedicled flap (upper half) and a VY advancement flap (lower half) (Figure 1c). A drain was placed on each side; this was removed during the first few days after surgery owing to a low flow rate. The surgical samples from the second procedure were negative; therefore, antibiotic treatment was suspended on the fourth day and the patient was discharged. One month after surgery, adalimumab 80 mg/wk was restarted. Today, 6 months after surgery, the patient is asymptomatic with the surgical wounds closed and no signs of infection (Figure 1d).



**Figure 1:** (A) Hurley III affecting the left and right axillae. (B) Left and right side after first surgical axillary excision. (C) Left and right axillae after surgical coverage with local flaps. (D) Left and right axillae 6 months after surgery.

## Discussion

HS is an inflammatory skin disease characterized by chronic or recurrent painful and suppurative lesions affecting the pilosebaceous unit [4,7]. The most common locations are the axillae, groins, buttocks, and perineum [4,7]. Management of HS remains challenging, and surgery is reserved for severe, treatment-refractory cases (Hurley III) [7]. Etiology is multifactorial and includes genetic factors (positive family history in approximately 30% of cases) and environmental factors (obesity and smoking) [4]. These factors lead to an immune reaction around the hair follicles in intertriginous areas mediated by proinflammatory cytokines that lead to chronic inflammation, and, consequently, massive pus collections and irreversible tissue destruction with scarring [7].

Chronic HS lesions are often characterized by polymicrobial colonization. The most commonly identified pathogens are gram-positive cocci (*S. aureus*, often MRSA, coagulase-negative staphylococci, and anginosus group *Streptococcus*) and anaerobes (*Prevotella* and *Porphyromonas* spp.) [8]. These data agree with the culture results for the present case, which were positive for MRSA, *Fusobacterium* spp., *Prevotella* spp., and *C. acnes*, although we also identified gram-negative bacteria, including *P. aeruginosa*, *E. coli*, and *Citrobacter* spp. While some gram-negative bacteria are less common in HS, they can be explained in the present case by the long disease course, long-term immunosuppressive treatment,

and multiple antibiotic regimens administered. The same surgical strategy was used for both the axillae and the groins (broad resection of the affected tissue and closure in 2 procedures), although the postsurgical course was very different (indolent in the groins and acceptable in the axillae). The only 2 differences to which we can attribute these differences in outcome are the immunosuppressive and antibiotic treatments prescribed.

The immunosuppressive treatment in the first procedure was ustekinumab, a monoclonal antibody that has proven useful in moderate-severe HS [9]. While adalimumab is the only biologic approved for treatment of HS, ustekinumab has similar efficacy in reducing the modified Sartorius score. As explained above, the patient received adalimumab 40 mg/wk, although this was switched to 80 mg/wk owing to poor symptom control. The increased dose of adalimumab and the fact that all antibiotic treatments administered since June 2019 were indicated based on microbiology results would probably explain the end of recurrences in the groins; however, they did not control the outcome in the axillae, thus necessitating surgery. In the axillae, ceftobiprole made it possible to optimize treatment using a beta-lactam with broad-spectrum activity against MRSA and *P. aeruginosa* and with activity against most of the pathogens isolated in the cultures. Adding metronidazole enabled us to complete coverage against some of the anaerobes identified.

Ceftobiprole is a new broad-spectrum cephalosporin that is equivalent to the combination of a third-generation cephalosporin with vancomycin. It is very active against all staphylococci (including MRSA), *S. pneumoniae*, *E. faecalis*, *P. aeruginosa*, non-extended-spectrum betalactamase-producing Enterobacterales, carbapenemases, and AmpC hyperproducers [10]. It is also active against anaerobes such as *C. acnes*, *Clostridium difficile*, and *Peptococcus* spp. and gram-negative bacteria such as *Fusobacterium nucleatum*, although not against others, such as *Bacteroides* [11,12]. Ceftobiprole is characterized by its very low protein binding, which facilitates tissue penetration, with good levels being achieved in soft tissues and the lungs [11]. It is not approved for the treatment of skin infections, although preliminary results are promising. Ceftobiprole has broad-spectrum bactericidal activity against the most common pathogens in HS, including MRSA, as well as pathogens that are isolated less frequently but were found in the present case (eg, *P. aeruginosa*) [8,10,12]. Our findings indicate that ceftobiprole is an attractive candidate for targeted antibiotic treatment in complicated skin infections involving *P. aeruginosa* and MRSA.

## Conclusions

Ceftobiprole could be an interesting antibiotic for the treatment of HS involving polymicrobial flora such as MRSA and drug-sensitive gram-negative bacteria. Our results should be confirmed in studies with larger numbers of patients.

## Conflict of Interest

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest (such as personal or professional relationship, affiliations, knowledge or beliefs) in the subject matter. Or materials discussed in this manuscript.

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