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Case report

Clinical spectrum of *Cutibacterium acnes* infections: The SAPHO syndrome

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ABSTRACT

Cutibacterium acnes, previously known as Proprionobacterium, is a commensal Grampositive bacterium of the skin commonly implicated in prosthetic joint infections. However, it has been documented to play a role in other conditions, including SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis), a rare autoinflammatory disorder. Diagnosing SAPHO syndrome is cumbersome, as the clinical manifestations are variable and overlap with many inflammatory joint disorders. Herein, we describe a 56-year-old female patient with a presumed diagnosis of longstanding seronegative rheumatoid arthritis and history of C. acnes prosthetic joint infection following revision arthroplasty of the right shoulder. She presented to our clinic with a rash over the upper extremities and trunk and joint symptoms involving the right shoulder. Treatment was initiated with ceftriaxone followed by doxycycline suppressive therapy, with clinical improvement of joint and skin involvement. Symptoms recurred upon brief cessation of antibiotic therapy due to adverse gastrointestinal effects; however, symptoms abated once again upon re-initiation of treatment. Given the patient's cutaneous lesions and longstanding history of arthritis that improved with antimicrobial therapy against C. acnes, the diagnosis of SAPHO syndrome was entertained. The present case demonstrates the clinical challenges of diagnosing SAPHO syndrome and the importance of its consideration on the differential for a patient with osteoarticular and cutaneous features. Additional literature is needed to improve diagnostic criteria and treatment guidelines.

Introduction

Cutibacterium acnes (C. Acnes), formerly *Propionibacterium acnes*, is an anaerobic, slow growing, non-motile, non-spore-forming, pleomorphic gram-positive rod. This bacterium is a commensal organism of the skin and tends to colonize the skin around the shoulders more frequently than that surrounding the hips and the knees. Notably, men tend to have higher bacterial colonization with this commensal than women.

As an opportunistic pathogen, *C. acnes* is a low virulence organism. It can, however, produce biofilms, leading to smoldering subacute to chronic infections of prosthetic devices. Consequently, *C. acnes* is known to cause surgical infections, prosthetic joint infections, and infections of implanted devices (cerebrospinal fluid shunts, deep-brain stimulators, spine hardware, prosthetic heart valves, and pacemakers) [1–3] (Table 1). *Cutibacterium acnes* infections often produce a paucity of clinical symptoms of inflammation. However, previous literature has reported delayed-onset clinical manifestations, such as implant-related pain and stiffness, in the setting of *C. acnes* infection of prosthetic material [4].

Additionally, *C. acnes* may cause the autoinflammatory manifestations of SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) [1,2]. *C. acnes* infection is also associated with other autoinflammatory disorders, including chronic recurrent multifocal osteomyelitis (CRMO), and there is increasing report of an association with sarcoidosis [3,5]. SAPHO syndrome is often diagnosed late due to its overlapping manifestations with inflammatory diseases such as seronegative rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis [6–8].

Herein, we report a patient who was initially diagnosed with seronegative rheumatoid arthritis. After demonstrating lack of a response to disease-modifying antirheumatic drugs (DMARDs) and biologic therapies for RA, this patient was found to meet the clinical criteria for

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Table 1
Clinical Manifestations of *Cutibacterium acnes* Infection.

Implanted devices (Biofilm-related)	*Central nervous system:*
	-Cerebrospinal fluid shunts
	-Intracranial reservoirs
	-Drains
	Endovascular implanted devices:
	-Prosthetic heart valves
	Intracardiac devices (pacemaker, or Automated Implantable Cardiac Defibrillator (AICD))
	Other sites:
	-Breast implants
Orthopedic	*Prosthetic joints:*
	-Shoulder
	-Hip/knee (less common)
	Other:
	-Spine hardware
Suppurative	Acne vulgaris
	Vertebral osteomyelitis
	Septic arthritis
	Brain abscess
	Subdural empyema
	Peritonitis
	Liver abscess
Surgical wound	Post-craniotomy, craniectomy or cranioplasty
Autoinflammation	SAPHO syndrome[a]
	Chronic Recurrent Multifocal Osteomyelitis (CRMO)
	Sarcoidosis
	Granulomatous mastitis[b]

[a] SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis)
[b] It has been postulated that granulomatous mastitis results from dysbiosis of the skin flora surrounding the nipple and areola in women. *Cutibacterium spp* and *Corynebacterium spp* are often implicated in this pathogenic process

SAPHO syndrome and subsequently experienced substantial clinical improvement with the antimicrobial therapy doxycycline. The hallmark manifestations of SAPHO syndrome are bone and joint disorders that may occur even without the presence of active dermatologic findings.

Case description

A 56-year-old female with a presumed diagnosis of longstanding seronegative rheumatoid arthritis (RA) non-responsive to DMARDs presented as a referral to an infectious disease clinic. For almost two decades, her rheumatological condition had progressed without any signs of improvement, despite the institution of multiple regimens of DMARDs and biologics. She required three different cervical spine surgeries over a span of 10 years due to spinal instability and spondyloarthritis, as well as right shoulder arthroplasty. At the time of her referral, the patient had recently undergone a revision of her right shoulder prosthesis, which had been placed eight years prior. Cultures obtained during the revision of her right shoulder prosthesis demonstrated the presence of *Cutibacterium acnes*, and consequently, her orthopedic surgery team requested an infectious disease consultation. Following her evaluation in clinic, the patient underwent a course of ceftriaxone for 6 weeks followed by doxycycline long-term suppressive therapy. With the initiation and continuation of antimicrobial therapy, she reported not only improvement of her right shoulder stiffness and pain, but also substantial improvement of skin lesions, increased joint mobility, and reduced areas of hyperostosis. Due to gastrointestinal intolerance, she discontinued doxycycline for a short period, resulting in the recurrence of some symptoms, such as limited mobility of her large joints. Once she restarted doxycycline, she regained joint mobility and experienced overall improvement in her quality of life and ability to perform daily activities. On further examination, our patient had diffuse skeletal hyperostosis, particularly of the anterior chest wall, with deformity and hyperostosis of the sternocostal and sternoclavicular joints. She also presented with multiple nodular and ulcerative cutaneous lesions, predominantly in the arms and chest wall. Given our patient's longstanding history of large joint and spinal arthritis, joint deformities, hyperostosis

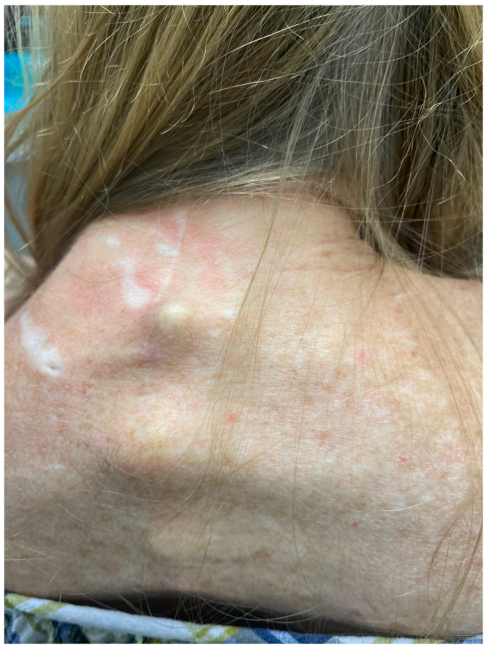

Fig. 1. Joint disfiguration and spinal arthritis in SAPHO syndrome.

(Fig. 1), and cutaneous lesions (Fig. 2) that consistently improved with the institution of antimicrobial therapy against *C. acnes* infection, we entertained the diagnosis of SAPHO syndrome.

Discussion

Cutibacterium acnes is an organism frequently identified in the clinical setting. The identification of *C. acnes* often poses a diagnostic challenge requiring clinical correlation to rule out the possibility of contamination, given the ubiquity of this organism as a commensal in human skin. However, infections caused by *C. acnes* are increasingly recognized for a multitude of reasons. First, cultures obtained from device-related infections are maintained for up to 14 days. Secondly, sonification of infected hardware improves the yield of cultures and

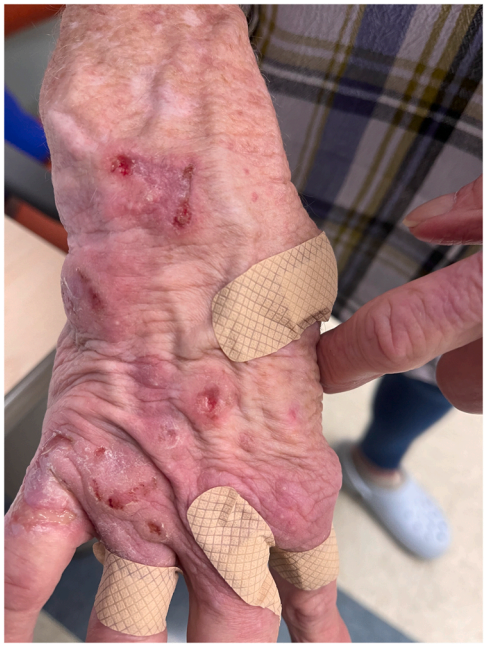

Fig. 2. Cutaneous lesions on the hand and wrist in SAPHO syndrome.

there is increasing availability of molecular diagnostic methods, such as 16S rRNA nucleic amplification to detect *C. acnes*. As our case demonstrates, surgical treatment of patients can yield evidence of C. acnes in cultures obtained at the time of removal of hardware.

Diagnosing SAPHO syndrome can be a cumbersome process since clinical criteria thus far have not been adequately validated [6,9]. The diagnosis of SAPHO syndrome is a clinical diagnosis that is important to consider among patients presenting with bone and joint symptoms consistent with focal or multifocal inflammatory arthritis, especially affecting the anterior chest wall, and concomitant dermatoses should be assessed for SAPHO syndrome [6–8]. As it occurred in our patient, a study of twenty-five patients with SAPHO syndrome who received antimicrobial therapy for 16 weeks caused significant improvement in their bone, joint, and cutaneous manifestations [9]. Relapse of symptoms following discontinuation of antimicrobial therapy occurred in all cases, suggesting that *C. acnes* plays a role in the pathogenesis of this condition [6–8,10]. Therefore, evidence of clinical improvement in osteoarticular or cutaneous manifestations beyond the site of infection after the institution of effective antimicrobial therapy against *C. acnes* should raise clinical suspicion of SAPHO syndrome in patients with underlying osteoarticular disorders.

The pathogenesis of SAPHO syndrome, CRMO, and sarcoidosis is a dysregulated innate immune response to *C. acnes* or other commensals [3,5]. In addition to potential impaired autophagy caused by lipoteichoic acid of the *C. acnes* cell membrane in tissue macrophages, *C. acnes*-derived circulating immune complexes may play an important role [3,10–11]. In summary, it is important for clinicians to be aware of not only the well-known clinical presentations of *C. acnes* infections, but also of its role in osteoarticular autoinflammatory disorders and its potential association cardiac and cutaneous manifestations of sarcoidosis.

Financial disclosure

None.

Ethical approval

The patient provided written approval for the publication.

Consent

Written and verbal consent was obtained from the patient. Patient acknowledges and consents to work presented.

CRediT authorship contribution statement

Michaele Francesco Corbisiero: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing. **Hannah Kyllo**: Writing – Original Draft, Writing – Review & Editing. **Nisha Batta**: Writing – Original Draft, Writing – Review & Editing. **Anthony Smyth**: Writing – Original Draft, Writing – Review & Editing. **Lorna Allen**: Writing – Original Draft. **Carlos Franco Paredes**: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing, Visualization, Project Administration.

Conflict of Interest

All authors none to declare.

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