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BRIEF REPORT

Predicting the pathogen of diabetic toe osteomyelitis by two consecutive ulcer cultures with bone contact

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Abstract In this study, we investigate the accuracy of two consecutive ulcer cultures with bone contact compared to bone biopsy for the diagnosis of diabetic toe osteomyelitis. The same nurse and orthopaedic surgeon obtained all samples: sample A-1: bone contact swabbing through the ulcer; sample A-2: a second culture swabbing from the bone surface within 24 h; sample B: surgical bone biopsy in the operating theatre. The kappa statistic measure between samples A-1 and A-2 (bone contact swabs) indicated 82.35% agreement. The sensitivity, specificity, positive and negative predictive values of the two samples A compared to B were 96%, 79%, 92% and 88%, respectively, for the causative pathogen. These results were similar with prior antibiotic treatment, discordant bone surface swabs or with monomicrobial infections. As a conclusion, two consecutive diabetic toe cultures with bone contact accurately predict the pathogen of diabetic toe osteomyelitis in 90% of cases.

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Pathogen identification and antibiotic susceptibility testing are important to provide appropriate antibiotic therapy for chronic infectious osteomyelitis [1]. Bone cultures (with histological confirmation) represent the gold standard for its diagnosis [1, 2], but usually require a surgical biopsy, which is resource-consuming, anaesthesia-demanding and associated with a non-negligible potential for adverse events [1–3].

Diabetic toe osteomyelitis is a different clinical entity. In contrast to chronic osteomyelitis of long bones [1, 4], infected toes are difficult to sample. Orthopaedic surgeons often are reluctant to perform a toe biopsy in an immune-suppressed patient, compromised by arterial insufficiency, ulcers and neuropathic osteopathy.

Superficial wound swabbing has been proven inadequate for predicting the infecting microorganisms [1, 2]. However, several studies investigated the accuracy of consecutive deep sinus tract cultures compared to bone biopsy [3–9]. In cases of monomicrobial osteomyelitis with sinus tract, concordant tract cultures with bone contact accurately predicted the pathogen of bone cultures [3, 6–8], which, however, was not unanimously confirmed [4, 5, 9]. Many of these studies did not include patients with diabetic toe osteomyelitis [4, 9], nor did they stratify patients between long bone and diabetic foot infection [3].

We performed a prospective study at the Orthopaedic Surgery Service of the Geneva University Hospitals to assess the accuracy of two deep consecutive ulcer cultures with bone contact in the identification of the pathogen of underlying osteomyelitis [3]. During a three-year-period, all adult patients with diabetic toe osteomyelitis with bone contact were enrolled in a non-randomised protocol. Osteomyelitis was confirmed by histological, radiological (magnetic resonance imaging [MRI] or standard X-rays) and/or microbiological specimens from a surgical bone

biopsy. Exclusion criteria were implant-related infections, absence of surgery for cure or patient refusal. Approval from the Ethical Committee was waived, since it was an internal quality assessment project.

The same nurse and orthopaedic surgeon obtained all samples: sample A-1: bone contact swabbing through the ulcer; sample A-2: a second culture swabbing from the bone surface at the same localisation as A-1; sample B: surgical bone biopsy in the operating theatre through a clinically uninfected area outside of the ulcer, from a distance of 2 to 4 cm. For samples A-1 and A-2, sterile cotton swabs were inserted until contact with the bone that was swabbed. The time interval between samples A and B was 24 h at the most. The microbiological specimens were transported to the laboratory within 30 min and quantitatively cultured with standard aerobic and anaerobic methods [10] over 5 days. According to the study definitions, the dominant pathogen required at least a three times higher growth in bone cultures than other microorganisms.

A total of 68 patients with diabetic toe osteomyelitis participated in the study (median age 70 years). All infections were secondary to a pre-existing ulcer. In 39 episodes (57%), the patients were already on antibiotic therapy for a median of 9 days (range 1 to 30 days). Sample B specimens yielded 22 polymicrobial infections (32%, range 1–3 pathogens). The dominant pathogens were: *Staphylococcus aureus* (n=18; three methicillin-resistant), *Streptococcus* sp. (n=8), *Enterobacteriaceae* (n=10), *Pseudomonas aeruginosa* (n=6), other non-fermenting Gram-negative rods (n=5), other aerobic (n=9) and anaerobic bacteria (n=1). In 20 episodes (29%), there was no growth, of which 17 cases were due to preceding antibiotic treatment. The non-dominant pathogens were mostly coagulase-negative staphylococci, Corynebacteria or *Stenotrophomonas maltophilia*.

Sample B (bone biopsy) was the gold standard. The unweighted kappa statistic measure between samples A-1 and A-2 (bone contact swabs) indicated 82.35% agreement. The sensitivity, specificity, positive and negative predictive values of the two samples A compared to B were 96%, 79%, 92% and 88% for the dominant pathogen (Table 1). These results were similar for the patient strata with prior antibiotic treatment, discordant bone swabs on the bone surface or with monomicrobial infections (Table 1). In seven cases (10%), samples A yielded additional pathogens that were not confirmed in sample B. Regarding the exact number and identification of all pathogens (independently of dominant or non-dominant microorganisms), the sensitivity, specificity, positive and negative predictive values were 90%, 58%, 78% and 79%, respectively.

We conclude that two consecutive diabetic toe cultures with bone contact accurately predict the dominant pathogen in greater than 90% of cases, independently of discordant bone swabs samples or prior antibiotic treatment. The sensitivity is always better than the specificity. Our findings are congruent with prior results regarding chronic osteomyelitis non-related to diabetic foot infection (91% sensitivity and 86% specificity of samples A compared to B) [3] or with the recent literature of this topic [11]. However, there is also conflicting results reported by Senneville et al. revealing a poor reliability in identifying bone bacteria through ulcer swab cultures, with concordance between bone biopsy specimens and superficial ulcer swabs oscillating between 22.5 and 42.8% depending upon the pathogen investigated [12]. However, their prospective trial showed some differences from ours that might explain the differences. We performed two consecutive samples from the bone surface, whereas in Senneville et al.'s study, one single sample was performed from the ulcer. Their protocol did not grant a bone contact per se. We sampled toe osteomyelitis (phalanx), while in Senneville et al.'s study, at least 40% of all specimens were sampled from the metatarsal bone. Bone samples were taken in the operating theatre in our study compared to sampling on the ward in Senneville et al.'s study. Moreover, their bone

Table 1 Comparison of two consecutive bone contact swabbings through an ulcer in the predilection of the pathogen of diabetic toe osteomyelitis (gold standard: bone biopsy)

Sample	No. of samples	Sensitivity	Specificity	Positive predictive value	Negative predictive value
All A-1 and A-2 samples	68	96%	79%	92%	88%
A-1 and A-2 concordant	56	95%	100%	100%	88%
A-1 and A-2 with prior antibiotic treatment	39	95%	82%	88%	93%
A-1 and A-2 in monomicrobial infections	46	96%	79%	94%	87%

Sample A-1: deep ulcer culture with bone contact

Sample A-2: second deep ulcer tract culture at a different time but at the same localisation as A-1

Sample B: surgical bone biopsy through a clinically uninfected area

Concordant: same microbiological result of samples A-1 and A-2

biopsies yielded a significant higher proportion (25.6%) of coagulase-negative staphylococci as the only pathogen [12], whereas in our study with quantitative cultures, coagulase-negative staphylococci were considered as commensals, since their quantification was inferior to other concomitant and more classical pathogens of osteomyelitis, such as *S. aureus* or *P. aeruginosa*.

Our good results concern the prediction of pathogens that dominate the bone cultures and constitute the classic bacteria of osteomyelitis [1]. The described method is less useful when it comes to the identification of non-dominant pathogens usually interpreted as commensals of superficial swabs. In our opinion, our alternative diagnostic method might be sufficient in situations where bone biopsy is difficult or amputation is refused [1]. In reality, this situation would likely concern only a minority of cases. In no way should deep ulcer specimens from the bone surface should replace bone cultures in situations where biopsy can be readily obtained, because bone cultures together with histology remain the gold standard for the diagnosis of osteomyelitis [1–9, 11]. Further trials are needed to confirm our findings.

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