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Case Reports and Series

A microbiological analysis of 210 cases of hand osteomyelitis

Dallan Dargan [a,b,*], Matthew Wyman [a,b], Dominic Ronan [a], Mark Heads [c], Dave Partridge [d,e], Jennifer Caddick [a], Victoria Giblin [a,b]

[a] Sheffield Hand Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK
[b] Academic Medical Unit, The University of Sheffield, Beech Hill Road, Broomhall, Sheffield S10 2RX, UK
[c] Sheffield Medical School, University of Sheffield, Beech Hill Road, Sheffield S10 2RX, UK
[d] Department of Microbiology, Sheffield Teaching Hospitals NHS Foundation Trust, UK
[e] Florey Institute for Host-Pathogen Interactions, University of Sheffield, Sheffield, UK

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ABSTRACT

Objective: Osteomyelitis of the hand in adults often requires debridement of necrotic tissue and antibiotics targeted at organisms isolated from bone samples. This study aims to review organisms associated with hand osteomyelitis to inform clinical decision making.
Methods: A retrospective review of the organisms isolated from 210 patients with osteomyelitis of the phalanges and metacarpals of the hand in a major trauma centre was performed over twelve years.
Results: Microbiological cultures were performed for 195 patients including 122 with positive bone cultures. *Staphylococcus aureus* was identified in 104 patients (50%), with coagulase negative staphylococci in 57 (27%) and Enterobacterales in 53 (25%). Eighty-eight were polymicrobial infections (42%). Arterial calcification was associated with polymicrobial infections, Enterobacterales and enterococci. Multi-drug resistant organisms occurred in 13 patients and were more frequently Enterobacterales than staphylococci or enterococci.
Conclusions: The high incidence of polymicrobial infections and coagulase negative staphylococci in this series suggests that for suspected cases, early microbiological and histopathological confirmation, ideally via bone biopsy, is optimal for osteomyelitis of the hand.
Level of evidence: IV.

Introduction

The organisms implicated in osteomyelitis of the phalanges and metacarpals of the hand are thought to follow patterns for osteomyelitis at other sites. The oral versus intravenous antibiotics (OVIVA) trial in adult osteomyelitis confirmed non-inferiority of oral antibiotics (McMeekin et al., 2019; Li et al., 2019). Oral antibiotics are adequate for the treatment of osteomyelitis of the hand in children (Kargel et al., 2020). Outcomes for septic arthritis of the hand showed non-inferiority of a two-week course of oral antibiotics when compared with a four-week course (Gjika et al., 2019). These recent studies renew the focus on appropriate empirical and early targeted antibiotics for adult hand osteomyelitis.

The guidelines of the Infectious Diseases Society of America on diabetic foot infections make a series of recommendations for osteomyelitis. These include the use of the probe to bone test, MRI as the imaging of choice where diagnosis remains uncertain after plain radiographs, bone biopsy for culture and histology even if debridement is not performed. In patients with radical resection (leaving no infected tissue) a short course of antibiotics is sufficient (2–5 days). If persistent infection is present then a longer course of $\geq$4 weeks is appropriate (Lipsky et al., 2012).

Hand osteomyelitis is often contiguous-focus, according to the Waldwogel classification (Waldvogel et al., 1970), which refers to an inoculation of bacteria from an adjacent soft tissue infection or wound. Common causes include an overlying abscess, traumatic wound, open fracture or chronic ulcer and occasionally indwelling metalwork. Antibiotic therapy in the absence of positive cultures in hand osteomyelitis focuses on *Staphylococcus aureus*. Empirical antibiotics are tailored according to aetiology, such as human or animal bites, medication allergy status and host colonisation with resistant organisms. The link between host status and osteomyelitis in long bones by Cierny et al. (2003) remains pertinent today. Antibiotic recommendations vary for specific groups such as intravenous drug users, haemodialysis patients or

* Corresponding author at: c/o Plastic Surgery Secretaries, Sheffield Hand Centre, Northern General Hospital, Sheffield S5 7AU, UK.
E-mail address: dallan.dargan@nhs.net (D. Dargan).

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Table 1
Demographics, aetiology and types of positive microbiological cultures for each case.

Demographics	Number of patients (total 210)
Age at diagnosis (mean ± SD) years	57.8 ± 17.2
Male / female; n (%)	141 (67) / 69 (33)
Type 1 / type 2 diabetes; n (%)	15 (7) / 51 (24)
CKD stage 5; n (%)	22 (10)
eGFR (mean ± SD)	67.8 ± 28.3
Digital artery calcification; n (%)	29 (14)
History of tobacco smoking; n (%)	88 (42)
History of intravenous drug use; n (%)	10 (5)
Microbiology sample method	
Bone biopsy; n (%)	125 (60)
Wound swab; n (%)	54 (26)
Soft tissue biopsy; n (%)	10 (5)
Removed metalwork; n (%)	4 (2)
Blood culture; n (%)	2 (1)
No sample; n (%)	15 (7)

*Includes five spontaneous, with no other aetiology documented, two with associated osteoarthritis only, and one with incomplete documentation of aetiology.
**Includes two septic emboli from infective endocarditis, one pyelonephritis, one disseminated tuberculosis, and one related to intravenous drug abuse.

individuals with sickle cell disease, immunocompromise or tuberculosis (Public Health England, 2015). The Romano (Romano et al., 2011) osteomyelitis classification system includes the organism involved.

The presence of vascular insufficiency in a limb with contiguous-focus osteomyelitis is associated with a different microbiological profile, and is frequently polymicrobial (Public Health England, 2015). *Staphylococcus aureus* remains the most common pathogen. Gram-negative bacilli such as *Escherichia coli, Klebsiella pneumoniae,* and *Proteus* species are common. Low virulence colonizers such as coagulase negative staphylococci and *Corynebacterium* species occur and obligate anaerobes are cultured relatively infrequently (Lipsky et al., 2012).

However, the microbiology of chronic osteomyelitis in the United Kingdom has demonstrably changed even across the last decade. A comparison of 2001–2004 with 2013–2017 demonstrated two-thirds lower rates of methicillin resistant *Staphylococcus aureus* (MRSA) in line with national trends as outlined by Dudareva et al. (2019). To facilitate comparison, this article has been structured similarly to that of Dudareva et al. (2019) and the STROBE guidelines (von Elm et al., 2014).

The aim of this study was to present the microbiological organisms cultured from cases of osteomyelitis of the metacarpals and phalanges of the hand. Secondary aims were to identify organisms associated with arterial calcification on plain x-ray and compare with findings in cases with diabetes mellitus/ end stage renal failure and all other patients. Tertiary aims were to correlate aetiologies and comorbidities with patterns of polymicrobial infections and types of organisms and review empirical therapy.

Methods

A retrospective cohort of patients with osteomyelitis of the hand was identified over a twelve-year period from 2008 to 2019 inclusive in a tertiary referral major trauma centre. The study was approved by our Institutional Review Board (STH 21024). Cases were identified from radiological, clinical and operative records and the detailed selection process outlined in another article (Wyman et al., 2021). A subgroup of patients with secondary Raynaud's phenomenon was presented separately (Haque et al., 2020). Anonymised data underwent observational microbiological analysis of identified cases. In cases in which multiple

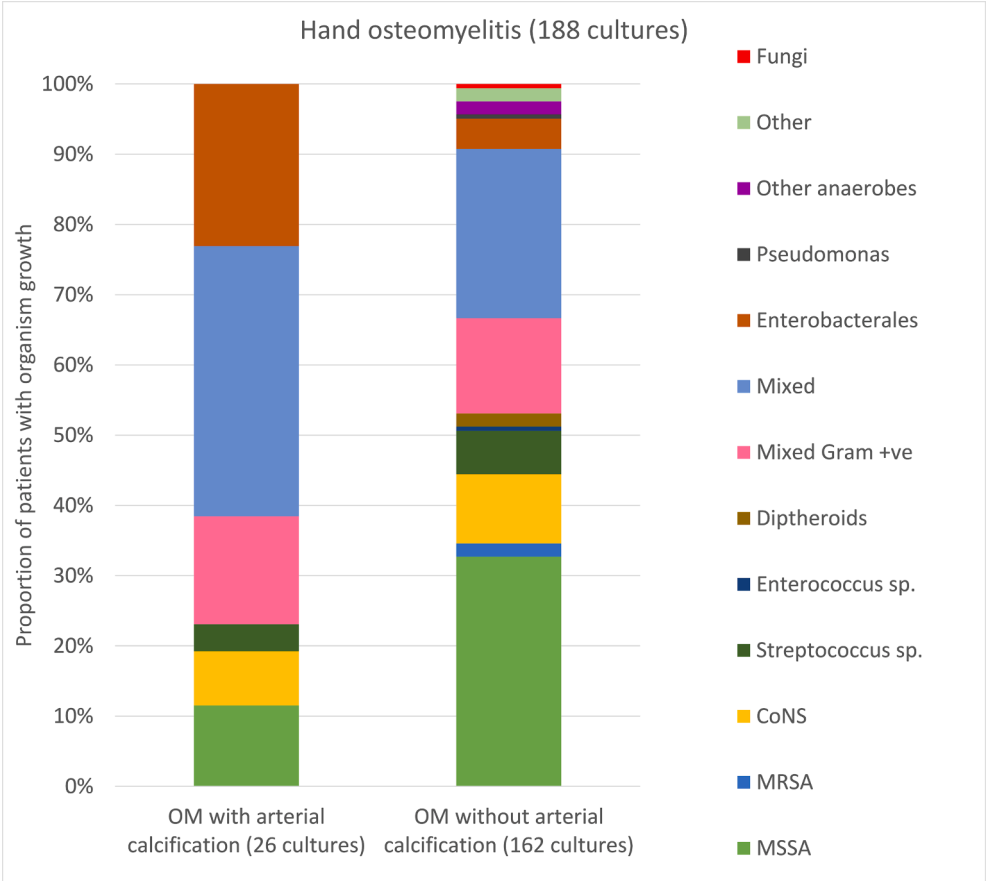

Fig. 1. Organisms cultured from a series of 210 cases of hand osteomyelitis, in which 195 cases had samples and 188 cases had organisms identified. The higher rate of 'mixed' cultures in those with arterial calcification, 10/26 (38%) versus those without, 39/162 (24%), was not significant ($p = 0.12$, chi squared). Abbreviations: MSSA- meticillin sensitive Staphylococcus aureus; MRSA- meticillin resistant Staphylococcus aureus; CoNS- coagulase negative staphylococci; OM- osteomyelitis; sp.- species; +ve – positive; -ve – negative.

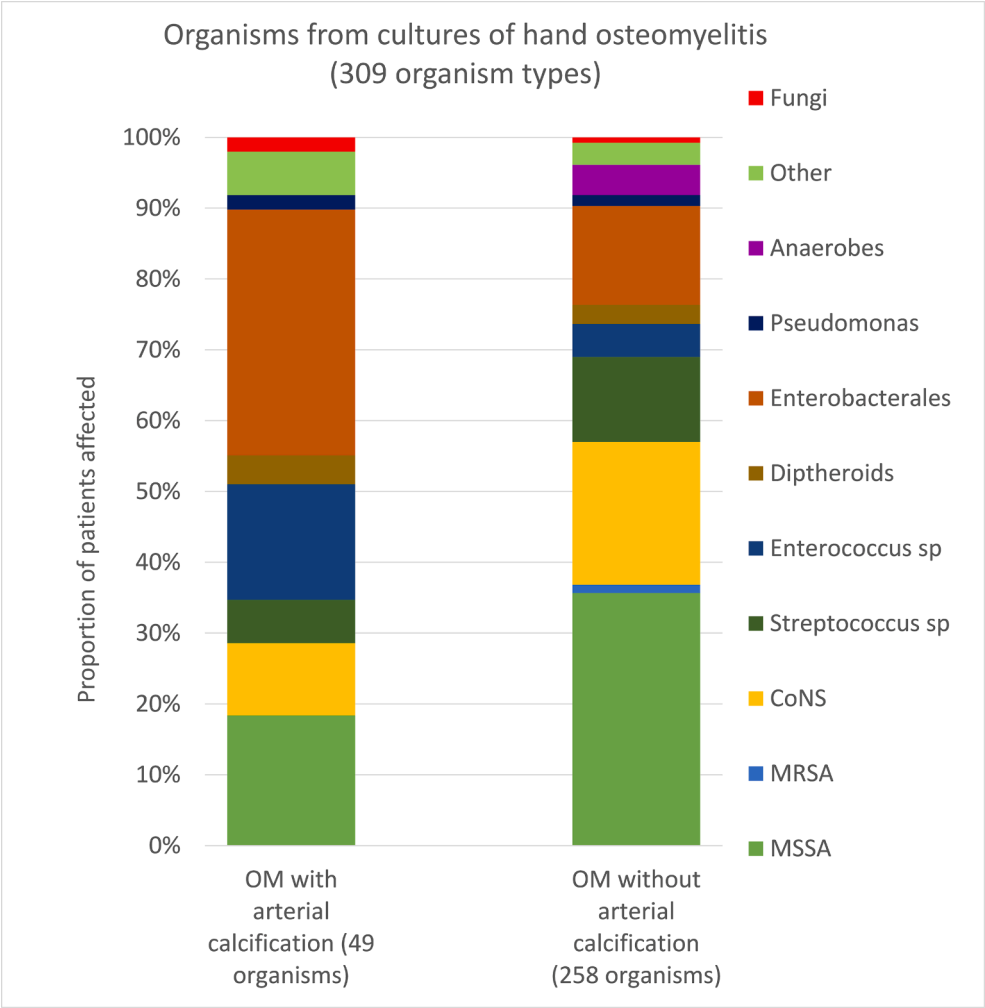

Fig. 2. Organisms cultured in hand osteomyelitis, presented according to total number of patients affected by each organism type. Some cultures had multiple similar organisms, which were counted once per patient. Abbreviations: MSSA- meticillin sensitive Staphylococcus aureus; MRSA- meticillin resistant Staphylococcus aureus; CoNS- coagulase negative staphylococci; OM- osteomyelitis; sp.- species; +ve – positive; -ve – negative.

microbiological samples were obtained, the first bone biopsy result was deemed representative. In cases without bone biopsy, the first microbiological cultures obtained after the onset of symptoms were used.

Diagnosis of osteomyelitis of the hand

A diagnosis of osteomyelitis was made based on radiological evidence of bone changes consistent with osteomyelitis, plus either a positive microbiological bone culture, or clinical or intra-operative findings (discharging sinus over bone, exposed bone with overlying soft tissue infection, abscess with bone erosion, purulence within bone). Cases with an alternative clinical diagnosis were excluded. Microbiology samples were processed to the current UK Standards for Microbiological Investigation (Public Health England, 2015) in the on-site accredited microbiology laboratory. Organism identification was achieved by biochemical means prior to 2009 and by matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry subsequently. Susceptibility testing was performed by disc diffusion or by multipoint breakpoint minimum inhibitory concentration inoculation (Pease et al., 1988).

Clinical information

Clinical records were reviewed for aetiology of osteomyelitis and selected comorbidities. Microbiological culture results were evaluated according to sample type and organisms cultured. A result was considered polymicrobial if more than one organism was isolated from the sample. Histopathological analysis of specimens, where available, was analysed for comparison. Organisms were categorised by genus and species, grouped according to the aetiology of the osteomyelitis, presence of comorbidities and mono- or polymicrobial infections.

The date of onset of symptoms, first presentation for medical treatment and first assessment by the hand surgery team were recorded, as well as the date that osteomyelitis became clinically apparent. A threshold for chronic osteomyelitis of more than four weeks from symptom onset was set for the purpose of the study.

Statistical analysis

Descriptive frequency analysis was undertaken for continuous variables. Parametric data was displayed as mean and standard deviation (SD). Binomial variables were compared using Pearson's chi squared test, or Fisher's exact test for values <5. Statistical significance was set at $p < 0.05$.

Results

A total of 210 patients were identified with osteomyelitis of the hand during 2008–2019. The demographics of the cohort and the microbiological sampling methods (bone biopsy or other method) are listed in

Table 2
Organisms cultured for 210 patients with hand osteomyelitis.

Organisms grown[†]		210 patients	Organisms grown (continued)		210 patients (continued)
Staph. aureus	**MSSA**	101 (48%)	**Enterococcus**	**(Any enterococcus sp.)**	20 (10%)
	MRSA	3	**Anaerobes**	**(Any anaerobes)**	12 (6%)
CoNS	**(Any *CoNS* species)**	57 (27%)		*Pseudomonas*[*]	5
	S. lugdunensis[††]	3		*Clostridium perfringens*	2
Streptococcus	**(Any *streptococcus* species)**	34 (16%)		*Clostridium sporogenes*	1
	Milleri group streptococci[*]	15		*Peptostreptococcus anaerobius*	1
	Viridans group streptococci[*]	4		*Cutibacterium acnes*	1
	Group A streptococci[*]	3		Cutibacterium[*]	1
	Group B streptococci[*]	8		Bacteroides[*]	1
	Group C streptococci[*]	3	**Other**	Other Gram + ve	17
	Group G streptococci[*]	5		Other Gram -ve	2
Enterobacterales	**(Any Enterobacterales species)**	53 (25%)		Other anaerobes [**]	5
	Escherichia coli	15		*Pasteurella multocida*	1
	Escherichia hermannii	1		*Haemophilus parainfluenzae*	2
	Klebsiella oxytoca	11		*Aeromonas hydrophilia*	1
	Klebsiella pneumoniae	5	**Fungi**	*Candida albicans*	1
	Proteus mirabilis	7		*Candida parapsilosis*	2
	Proteus hauseri	1	**No organisms**	No growth	7
	Proteus vulgaris	1		No culture	15
	Serratia marcescens	4			
	Serratia liquefaciens	2			
	Enterobacter cloacae	10			
	Enterobacter ludwigii	1			
	Other Enterobacterales[*]	6			
	Providencia rettgeri	1			
	Kluyvera ascorbate	1			
	Morganella morganii	6			
	Citrobacter freundii	4			
	Citrobacter koseri	3			

Abbreviations: IV- intravenous; MSSA- meticillin sensitive Staphylococcus aureus; CoNS- coagulase-negative staphylococcus species; sp- species.

[†] Category totals represent total number of cases with any organism of this category. Multiple organisms from the same category in the same culture were counted once per patient.

[††] Staphylococcus lugdunensis was analysed separately from other CoNS as it is recognised as being more virulent, however, many CoNS were not identified to species level.

[*] Not identified to species level (Milleri group streptococci include S. anginosus, S. intermedius and S. constellatus).

[**] Not identified further than morphology.

Table 3
Comparison of organisms isolated in acute and chronic hand osteomyelitis (similar organisms in same patient excluded).

Organism types	Acute, symptoms <4 weeks (%)	Chronic, symptoms >4 weeks (%)	Fisher's exact test, p-value
MSSA	60 (48%)	37 (48%)	0.56
MRSA	1 (1%)	2 (3%)	0.34
CoNS	33 (27%)	20 (26%)	0.67
Streptococcus sp.	21 (17%)	13 (17%)	0.80
Enterobacterales	31 (25%)	20 (26%)	0.87
Enterococcus sp.	3 (2%)	8 (6%)	**0.02**
Diptheroids	3 (2%)	6 (8%)	0.10
Pseudomonas	2 (2%)	2 (3%)	0.69
Anaerobes	5 (4%)	5 (6%)	0.51
Other	7 (6%)	4 (5%)	0.79
Fungi	1 (1%)	2 (3%)	0.35
No growth	9 (7%)	11 (14%)	0.15

Abbreviations: MSSA- meticillin sensitive staphylococcus aureus; MRSA- meticillin resistant staphylococcus aureus; CoNS - coagulase negative staphylococci; sp. – species.

Table 1, with a high rate of bone biopsy sampling overall (60% of cases). Among 210 patients, 371 bones were involved across 246 rays. The number of cases with a single organism identified (monomicrobial) was 100 (48%) and with more than one (polymicrobial) was 88 (42%).

Included cases without microbiological organism confirmation

Twenty-two cases in the series had no microbiological organism identified including fifteen (7%) with no microbiological sampling recorded. Two had histological confirmation of the diagnosis. One with associated gout had histological confirmation of chronic osteomyelitis and another with septic arthritis and osteolysis had similar histological confirmation. One had a positive microbiological culture but organisms were unavailable having been cultured in another centre and reported as 'mixed organisms'. The remaining nineteen cases were diagnosed on clinical and radiological evidence alone.

Organisms identified

A total of 349 organism isolates were identified among 188 positive cultures (Fig. 1). Excluding similar organisms in the same patient, this number was 309 organisms (Fig. 2). The most common organism identified overall was *Staphylococcus aureus* identified in 104 cases (54% of cultures, including three meticillin resistant). Coagulase negative staphylococci (CoNS, 57 cases, 27%, excluding 3 with *Staph. lugdunensis* which is recognised as being more virulent than most coagulase negative staphylococcal species), Enterobacterales (53 cases, 25%) and enterococci featured prominently (20 cases, 10%, Table 2). In 39 of 57 (75%) cases with coagulase negative staphylococci, a mix of organisms were isolated, increasing the likelihood that these typically low virulence organisms were contaminants. A pure growth of coagulase negative staphylococci was present in the remaining 18/57 (32%) of cases and 2 (11%) of these were infections related to prosthetic material, with the remaining aetiologies being trauma in 9 (50%), abscess in 4 (22%) and burn, ischaemia and spontaneous in one case each (6% each).

Resistant bacterial strains

Three instances of MRSA infection (1.5%) were identified, two

Table 4
Microbiology sample types and culture results for cohort A (29 patients with hand osteomyelitis and arterial calcification).

Study ID no.	Microbiology confirmation sample type	Organisms cultured, including from repeat biopsies
1	Bone	*Milleri strep., Staph. aureus, Coliforms, Proteus mirabilis, Enterococcus* sp., *Klebsiella, Serratia marcescens, Viridans strep., group C strep.*
2	Bone	*Staph. aureus*
3	Bone	*Staph. aureus, other Gram positive cocci*
4	Bone	*Staph. aureus, Aeromonas hydrophilia, E. coli, Enterococcus* sp.
5	Swab	*Klebsiella pneumonia*
6	Bone	*Proteus mirabilis, E. coli, Enterobacteria cloacae*
7	Bone	*Morganella morganii, Candida parapsilosis, Enterococcus faecium*
8	Swab	*Nil*[*]
9	Bone	*Staph. aureus, E. coli, Enterococcus, Coliform bacillus, Enterobacter cloacae*
10	None	*Nil*[**]
11	Bone	*Serratia marcescens, Enterococcus* sp.
12	Bone	*Coagulase negative staph., Staph. aureus*
13	Bone	*Staph. aureus*
14	Bone	*E. coli, Proteus vulgaris, Serratia marcescens, Morganella morganii, coagulase negative staph.*
15	Bone	*Staph. aureus, Klebsiella oxytoca, Enterococcus faecium, Proteus mirabilis, Milleri strep.*
16	Bone	*Staph. aureus, Haemophilus parainfluenzae, Corynebacterium*
17	Swab	*Morganella morganii, Klebsiella pneumoniae*
18	Bone	*Proteus mirabilis, group B strep., Staph. aureus*
19	Swab	*E. coli, Enterobacter cloacae*
20	Bone	*Morganella morganii, E. coli*
21	Swab	*E. coli, Corynebacterium*
22	Bone	*Viridans strep.*
23	None	*Nil*[†]
24	Bone	*Klebsiella oxytoca, Proteus hauseri, Enterococcus faecalis*
25	Bone	*Morganella morganii, coagulase negative staph.*
26	Bone	*Milleri strep., coagulase negative staph.*
27	Bone	*Coagulase negative staph.*
28	Bone	*Pseudomonas aeruginosa, Enterococcus* sp.
29	Bone	*Staph. aureus*
Total	Bone = 22 Swab = 5 None = 2	*Staph. aureus = 11* *Enterococcus* sp. = *9* *Escherichia coli = 7* *Proteus* sp. = *6* *Klebsiella* sp. = *5* *Morganella morganii = 5* *Coagulase negative staph. = 5* *Enterobacter cloacae = 3* Other = 22

Abbreviations: ID no. = identification number; sp. = species; Staph. = Staphylococcus; Strep. = Streptococcus; E. coli = Escherichia coli.

[*] Patient 8 did not have a bone biopsy, and wound swabs were negative. Diagnosis was based upon radiological evidence of osteolysis, and the presence of purulent bone on surgical exploration.

[**] Patient 10 did not have a bone biopsy or wound swabs. Diagnosis was based upon radiological evidence of osteolysis underlying a necrotic lesion at the tip of the affected finger. No procedures were performed due to advanced age and co-morbidities.

[†] Patient 23 did not have a bone biopsy or wound swabs. Diagnosis was based upon radiological evidence of osteomyelitis underlying a necrotic lesion on the affected finger. The patient died from unknown causes before further investigations could take place.

vancomycin resistant enterococcus (VRE) strains, seven AmpC beta-lactamase producing Enterobacterales, and one extended spectrum beta-lactamase (ESBL) producing strain. No carbapenemase-producing Enterobacterales (CPE) were identified.

Chronicity of infections and delayed presentations

Date of onset of symptoms and first assessment by a health professional were available for 195 patients. The median duration from symptom onset to first assessment was 4 days (interquartile range 0–11, range 0–118) and from symptom onset to clinically apparent osteomyelitis was 16 days (interquartile range 6–46, range 0–265).

The number of 'acute' and 'chronic' cases, with symptoms less or more than 4 weeks prior to diagnosis, was 119 acute, 80 chronic and 11 were unknown. In 29 patients with digital artery calcification, these were 11 acute, 14 chronic and 4 were unknown, which was a similar proportion of chronic cases to the rest of the series (p = 0.08, chi-squared). Organism types were similar in acute and chronic cases except that enterococci were more prevalent in chronic cases (Table 3). Histological analysis of bone specimens was available in 23 cases (32 tissue histology samples in total). The histological evaluation of whether osteomyelitis was acute or chronic based on the histological appearances was compared with the clinical 4-week categorisation. A correlation between bone histology and 4-week time interval was present in 12 cases (52%). Only five of 210 patients had symptoms for over 6 months prior to diagnosis.

Table 5
Comparison of microbiology of osteomyelitis in patients with arterial calcification, diabetes mellitus or end stage renal failure and all others.

Organisms grown[*]	Total (210 pts)	Cohort A Arterial calcification (29 pts)	Cohort B DM and/or end stage renal failure without calcification (43 pts)	Cohort C All others (138 pts)	p-Value Chi-squared test
Staph. aureus (includes MRSA)	*104 (50%)*	*9 (31%)*	*20 (47%)*	*75 (54%)*	$p = 0.15$
CoNS (includes *Staph. lugdunensis*)	*57 (27%)*	*5 (17%)*	*10 (23%)*	*42 (30%)*	$p = 0.28$
Streptococci	*34 (16%)*	*3 (10%)*	*12 (28%)*	*19 (14%)*	$p = 0.06$
Enterobacterales (includes AmpC and ESBL)	*53 (25%)*	***17 (59%)***	*10 (23%)*	*26 (19%)*	***p < 0.01***
Enterococci (includes VRE)	*20 (10%)*	***8 (28%)***	*3 (7%)*	*9 (7%)*	***p < 0.01***
Others	*39 (19%)*	*7 (24%)*	*8 (19%)*	*24 (17%)*	*N/A*

Abbreviations: MRSA- meticillin resistant staphylococcus aureus; AmpC- AmpC beta-lactamase; ESBL- extended spectrum beta lactamase; VRE- vancomycin resistant enterococci; pts- patients; Staph. - Staphylococcus; CoNS - coagulase negative staphylococci; DM- diabetes mellitus.

[*] Some cultures had organisms from more than one category, and some had no growth.

Host status

Diabetes mellitus was present in 66 patients and end stage renal failure in 22. Ten patients had a history of intravenous drug use. One patient had disseminated tuberculosis. No patients in the series had sickle cell anaemia or human immunodeficiency virus infection.

Arterial calcification, diabetes mellitus (DM) and end stage renal failure (ESRF)

The presence of digital artery calcification on plain x-ray was used as a surrogate for vascular insufficiency (cohort A, 29/210, 14%) including 25 with DM, 20 with a history of end stage renal failure and 17 with both. Most arterial calcification patients (cohort A) had polymicrobial cultures (20/29 patients, 69%, Table 4). By comparison, cohort B, those with DM or ESRF but no calcification (43/210, 20%) had lower rates of polymicrobial cultures (19/210, 44%, p = 0.038). Those with neither ESRF nor DM were termed cohort C (138/210, 66%). Cohort C had lower

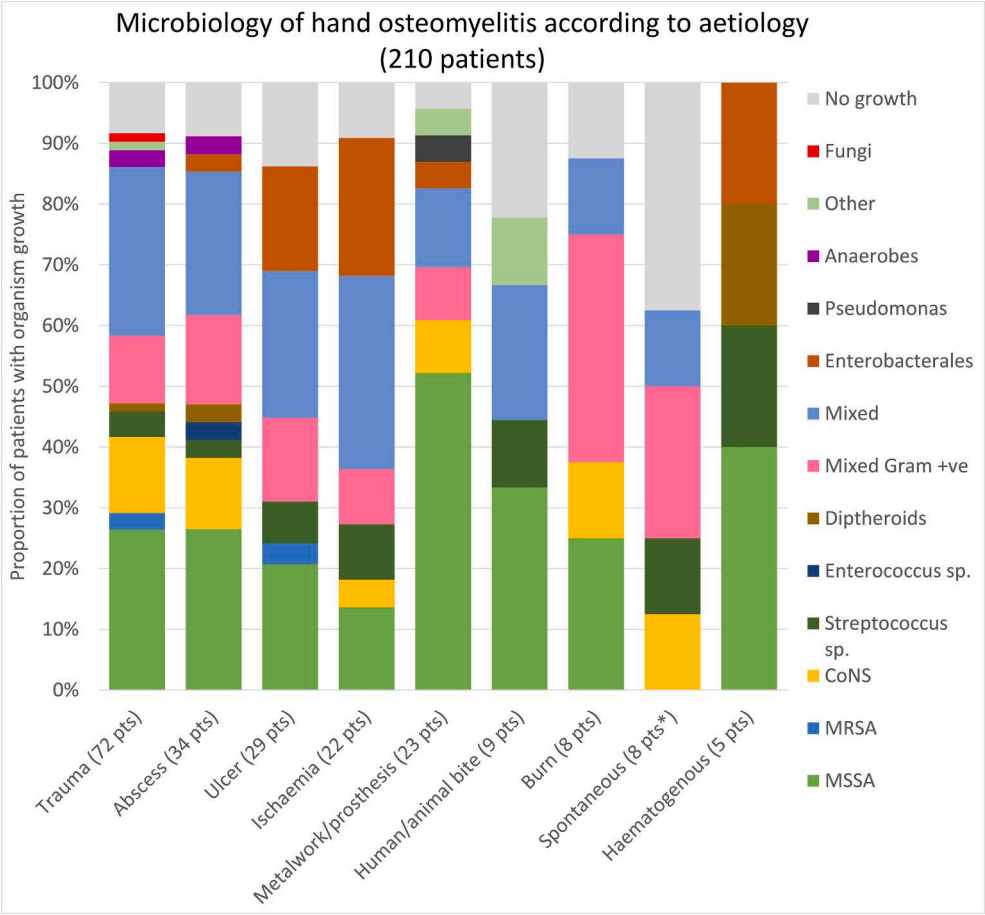

Fig. 3. Organisms cultured in osteomyelitis presented according to aetiology of infection. Abbreviations: MSSA- meticillin sensitive Staphylococcus aureus; MRSA- meticillin resistant Staphylococcus aureus; +ve – positive; -ve – negative, pts- patients; sp.- species. * Includes five spontaneous, with no other aetiology documented, two with associated osteoarthritis only, and one with incomplete documentation of aetiology.

rates of polymicrobial cultures (46, 33%) than cohort B, but this was not significant ($p = 0.20$). A comparison of organisms from cohorts A, B and C are presented in Table 5. Those in cohort B had significantly higher levels of streptococci when compared with the rest of the patients ($p = 0.02$, χ^2), but not when evaluating DM versus non-DM patients ($p = 0.08$, χ^2). Figures 1 and 2 further outline the comparison in organism types between hand osteomyelitis in digits with and without arterial calcification.

Infected metalwork or prosthesis and post-operative infections

Twenty-three cases (11%) had previous evidence of metalwork or prosthesis insertion, including K-wire fixation of open and closed fractures, plate and screw fixation, static and dynamic external fixators. Two cases developed after elective arthrodesis and one after elective metacarpophalangeal joint arthroplasty. None of these cases had MRSA or arterial calcification.

Contiguous abscesses

The group with a contiguous abscess (34/210, 16%) included 18 paronychiae, 13 pulp space abscesses (including one with both), one flexor sheath infection, one other soft tissue abscess and one abscess at an intravenous drug user injection site. Eighteen (47%) had monomicrobial cultures and 16 (42%) had MSSA. Abscesses were occasionally secondary to trauma or burns with some overlap between these categories. No patient with a contiguous abscess had evidence of arterial calcification on x-rays.

Ulcers

The group with an overlying ulcer (29/210, 14%) included nine cases with arterial calcification and therefore collinearity was observed with vascular insufficiency and ischaemia. The microbiology according to aetiology of hand osteomyelitis is presented in Fig. 3.

Discussion

The low rate of MRSA infection (three patients, 1.5%) compares favourably with MRSA rates in other recent series of osteomyelitis in the UK of 11.4% (Dudareva et al., 2019). Higher rates published in other countries include 62% in non-hand osteomyelitis in the USA (Johnson et al., 2019), 50% in hand infections in Queensland, Australia (Matthews et al., 2018) and 21% for other hand infections parts of the USA (Sharma et al., 2020). A recent review of hand bone and joint infections did not report MRSA incidence (Sendi et al., 2020) and the oral versus intravenous antibiotic therapy trial (OVIVA) also did not specify the rate of MRSA in the 378/1003 instances of *Staphylococcus aureus* osteomyelitis although these may have been excluded as part of the protocol (Li et al., 2019). In one series of hand osteomyelitis (Henry and Lundy, 2021) MRSA was identified in 22% of 69 patients, with 18% *Staphylococcus epidermidis*, 13% meticillin sensitive *Staphylococcus aureus* (MSSA), 10% streptococcus species and 6% other staphylococci among others. Reilly et al. (1997) found that among 46 patients, four had no growth of organisms (7%). The most common organisms were Gram-positive (35%), although 35% of cultures were mixed, 15% were Gram-negative, 12% were fungal infections and 3% were mycobacterial.

Table 6
Guidelines for management of hand osteomyleitis.

Suspect osteomyelitis if:

- Radiological evidence of osteolysis or periosteal reaction
- Discharging sinus over bone
- At surgical removal of infected metalwork
- Clinical soft tissue infection with exposed bone
- Open fracture with soft tissue infection

Initial management

- **Bloods:** FBC, U&E, CRP. Add Uric Acid, Glucose/HbA1C if indicated
- **X-ray**
- **Swab** for microbiology
- **List** for urgent debridement, washout & bone biopsy (within 72 hours)

Initial antibiotics

- Assess for red flag signs of **sepsis** that require admission and IV antibiotics – discuss individual cases with microbiology
- Unless the patient is clinically unwell:
  - Do **not** start antibiotics until patient has had a bone biopsy.
  - If patient already on antibiotics, **withhold** for 72 hours prior to biopsy
  - If chronic osteomyelitis, withhold for 2 weeks prior to biopsy.

Surgical management

- **Bone biopsy** for microbiology (ideally 2 or more samples) & histology
- Separate instruments and pots for each sample
- Thorough washout & debridement of all non-viable tissue
- Commence **antibiotics** once biopsies have been taken (see below)
- Post-op **x-ray** before discharge if significant debridement of bone

Post-surgical antibiotics

- Total of **6 weeks antibiotics** usually required
- Discuss **all** cases with microbiology
- Uncomplicated cases/well patients, pending definitive cultures, start with:
  - 1st line: **Flucloxacillin**
  - Penicillin allergic: **Doxycycline**
  - Human or animal bite: **Co-amoxiclav**

Follow up

- **Hand surgery** review **3-5 days** (ward attender or consultant clinic) to:
  - Assess for clinical improvement - escalate to senior if not improving.
  - Check culture results and adjust antibiotics accordingly – discuss with microbiologist and document clearly in clinical record.
  - This can be at a dressing clinic but patient **must** see a doctor.
- **Consultant review** (operating consultant if available) at:
  - Week 2 – chase enrichment **cultures**, repeat **FBC** & **CRP**
  - Week 6 – review off antibiotics, **x-ray** on arrival

Implementation of the non-inferiority of oral antibiotics after surgery for osteomyelitis has potential cost benefits of up to £17 million annually for the United Kingdom National Health service alone (McMeekin et al., 2019). The Cochrane systematic review of antibiotic therapy in chronic osteomyelitis included 8 trials and overall found that provided the bone was debrided and the cultured bacteria were susceptible to the antibiotic, the route of antibiotic delivery had no effect on recurrence at 12 months (Conterno and Turchi, 2013).

Coagulase negative staphylococci (CoNS) were present in 27% of cases, which may represent transferred organisms from acute injuries. CoNS were often implicated in cases with metalwork or a prosthesis, or abscess, in keeping with high rates with infections of other indwelling prostheses, including prosthetic joint infection (Flurin et al., 2019) and in paronychiae and abscesses (Natsis and Cohen, 2018). While CoNS are often contaminants or commensals, CoNS are recognised pathogens in the context of diabetic foot infection (Aragon-Sanchez et al., 2010) and it is difficult to rule out their significance in the absence of a more likely pathogen or in the presence of foreign body or vascular insufficiency.

In the group with digital arterial calcification, there is a tension between the need to cover the relevant pathogens and the expected comorbidities of the patient leading to an increased susceptibility to adverse effects of antibiotics, especially the risk of severe musculoskeletal and neurological side effects associated with the fluoroquinolones. For this reason, we would recommend that mild infections are managed with an initial focus on Gram-positive pathogens using flucloxacillin or doxycycline. Failure to respond or more severe disease at the outset could be managed with piperacillin-tazobactam and a glycopeptide intravenously or ciprofloxacin and amoxicillin orally. Piperacillin-tazobactam and a glycopeptide intravenously would have been expected to have adequate activity against all the organisms cultured in 67% of cases and oral ciprofloxacin and amoxicillin would have activity against 83% of cases for which susceptibilities were available. Expected reduced activity against the combination of piperacillin-tazobactam and teicoplanin was due to the presence of organisms with an inducible AmpC beta-lactamase in all but one case and initial activity of the combination in this context would usually be expected, allowing the opportunity to convert to alternative agents on receipt of biopsy results. Other centres with different spectra of resistance in aetiological pathogens may need to modify this approach. In the population of hand osteomyelitis patients, frequent healthcare attendance is common and a desire to avoid the unnecessary selection of antimicrobial resistance is even more important. Our local guidelines for management of suspected hand osteomyelitis are shown in Table 6.

Sampling methods for chronic osteomyelitis are outlined in the UK guidance (Public Health England, 2015) suggesting 4–5 bone samples per patient, with separate instruments and specimen pots. In chronic osteomyelitis, 2 weeks without antibiotics prior to sampling is advised (Public Health England, 2015), however, hand osteomyelitis in our series was often acute and a 72 h window has been selected unless emergency surgery is required.

Organisms in our series were isolated from bone samples, prostheses, deep soft tissue samples, or wound swabs. Wound swabs have been shown consistently to lack correlation with deep tissue samples in osteomyelitis (Vemu et al., 2018). The threshold for identifying an organism in this series was based on presence in a single sample, rather than at least two samples as suggested in the fracture related infections consensus guidelines (Metsemakers et al., 2018). These sampling issues may skew our results, however we feel the size of the study population helps compensate for this.

Staphylococcus aureus is the most common organism as expected, but only occurs in around half of patients and coagulase negative staphylococci are common. A low rate of resistant organisms, particularly Amp-C beta-lactamase producing Enterobacterales, extended spectrum beta-lactamase (ESBL), MRSA and VRE was noted. A high rate of polymicrobial cultures in hand osteomyelitis, particularly among those with DM, ESRF, or peripheral vascular disease was observed. An aetiology-specific and organism sensitivity targeted therapy should be sought where possible.

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Ethical approval declaration

The analysis was performed of anonymised data from a study protocol approved by the Institutional Review Board, study number STH20214.

CRediT authorship contribution statement

Dallan Dargan: Conceptualization, Methodology, Formal analysis, Writing – original draft, Visualization, Supervision. **Matthew Wyman:** Conceptualization, Writing – original draft, Formal analysis, Data curation, Investigation, Visualization. **Dominic Ronan:** Data curation, Investigation, Writing – review & editing. **Mark Heads:** Visualization, Formal analysis, Writing – review & editing. **Dave Partridge:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Jennifer Caddick:** Conceptualization, Supervision, Writing – review & editing. **Victoria Giblin:** Conceptualization, Supervision, Project administration, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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