Acute Deep Infections of the Upper Extremity: The Utility of Obtaining Atypical Cultures and Factors Associated with Culture Positivity

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Introduction

Deep infections of the hand, wrist, and elbow are an important clinical entity[1-13] that may result in patient morbidity and loss of productivity. Treatment with surgical irrigation and debridement is the gold standard. These infections are typically caused by bacterial rather than atypical pathogens (fungus or acid-fast bacillus [AFB])[6], and the utility of ordering aerobic and anaerobic cultures has been established[1]. Although atypical pathogens may also be causative—especially in the immunocompromised population—there is no evidence to guide the decision whether or not to obtain atypical cultures during surgical debridement of deep infections of the hand or wrist[10].

The primary purpose of this study was to determine the incidence of positive fungal and AFB cultures in a patient cohort undergoing surgical debridement of acute deep infections of the hand, wrist, and elbow and to determine the rate at which the treatment plan was altered by atypical culture results. Secondarily, we aimed to identify patient and disease factors that affected the positivity of atypical cultures.

Methods

This retrospective cohort study (IRB-approved) reviewed 203 consecutive patients undergoing surgical debridement for acute deep space infections of the hand, wrist, and elbow by three hand fellowship-trained orthopaedic surgeons at an urban academic medical center between October 2013 and December 2015. Patients with diagnoses of superficial infections of skin or nail structures and necrotizing infections were excluded.

Adult patients ($\geq$ 18 years of age) with acute onset of symptoms were considered for inclusion. Sub-acute and chronic infections with symptoms >30 days were excluded. Documentation of intraoperative microbiological cultures, including bacterial (aerobic and/or aerobic) plus at least one atypical culture (fungal and/or AFB) was required. 100 patients meeting all criteria were identified for further analysis.

For each included patient, clinical, operative, and microbiological documentation were reviewed. Infections were classified as subjectively purulent if the operative note included one of five possible descriptors: "pus," "purulence," "purulent," "seropurulent," or "cloudy." When applicable, charts were further reviewed regarding the interpretation of positive atypical cultures, and a determination was made whether atypical culture results altered clinical management (infectious disease consultation, change in antibiotic regimen).

Descriptive statistics were used to summarize patient demographic and disease-specific data. The reported culture data were obtained from operating room cultures only. To evaluate risk factors associated with atypical culture positivity, cohorts with positive and negative atypical cultures were compared with bivariate analysis for all collected variables (continuous variables—Student t-test or Mann-Whitney; categorical variables—Fisher exact test). A significance level of $\alpha = 0.05$ was used.

Results

One hundred patients were included in the final analysis. Mean age was 47.8 years (range: 20 to 85 years; median: 48 years), and preoperative infectious symptoms were present for a median of 5 days (range: 1 to 30 days) prior to surgical treatment (Table 1). Preoperative antibiotics had been given in 87% of cases, and 46% of all patients had one or more immunocompromising comorbidities. Infection diagnoses included soft tissue abscess (46%), suppurative flexor tenosynovitis (22%), septic arthritis (21%), osteomyelitis (9%), and septic bursitis (2%). Aerobic bacterial, anaerobic bacterial, fungal, and AFB cultures were sent in 100%, 99%, 94%, and 82% of patients for each culture type, respectively. Corresponding rates of culture positivity were 74% (74/100), 34.3% (34/99), 5.3% (5/94), and 2.4% (2/82), respectively (Table 2). Median postoperative follow up duration for all patients was 22 days (range 0-472 d). Patients with positive atypical cultures had a median follow up of 40 days (range 4-318 d).

Atypical cultures were positive for 7% of all patients (7 of 100) and 2.9% (7 of 238) of all atypical tests (cultures, stains) sent (Table 2). Of the patients with positive AFB cultures, one

Table 1. Baseline patient characteristics, including patient- and disease-specific factors.

Patient Factors		Disease Factors	
Mean age (years)	47.8	Mean pre-op symptom duration (days)	7.8
Sex		> 3 days (%)	69.0
Male (%)	37.0	> 7 days (%)	32.0
Female (%)	63.0	Recent hand procedure (%)	23.0
Mean BMI (kg/m^2)	28.8	Initial I&D in emergency room (%)	25.0
Obesity (%)	34.0	Subjective purulence in ER (%)	16.0
Morbid obesity(%)	7.0	Received pre-operative antibiotics (%)	87.0
Smoker (%)	32.0	IV (%)	61.0
Immunocompromising condition (%)	46.0	PO(%)	26.0
Diabetes (%)	22.0	Mean number of OR events	1.2
Cardiac disease (%)	14.0	Subjective purulence in OR(%)	69.0
IV Drug Use (%)	9.0	Mean post-op antibiotic duration (weeks)	3.4
Immunocompromising medication (%)	6.0	Mean post-op follow-up (weeks)	
Rheumatic disease or on DMARD (%)	5.0	Orthopaedic	6.5
End stage renal disease	3.0	Infectiousdisease	4.3
Active malignancy (%)	3.0	Infectious disease consulted (%)	43.0
HIV positive (%)	2.0	For bacterial infection (%)	40.0
Organ transplant (%)	1.0	For atypical infection(%)	3.0

patient with flexor tenosynovitis and underlying systemic lupus erythematosus on multiple immunosuppressants grew *Mycobacterium avium*. The positive fungal culture patients grew *Candida* species most frequently (3 of 5).

Patients with positive atypical cultures had an average duration of 12.0 days of symptoms compared to 7.5 days for negative atypical culture patients ($p = 0.11$; refer to Table 3). Of the 69 patients that exhibited subjective purulence during the index procedure, six patients had atypical positive cultures (representing 86% of all atypical culture positive patients). Of the six patients with positive atypical cultures and subjective purulence, four (67%) had bacterial cultures that were also positive.

Of all variables tested (Table 3), bivariate analysis demonstrated an association with atypical culture positivity and only one studied factor, symptom duration > 7 days (OR 6.0, CI 1.2-44.8, $p < 0.05$).

Discussion

At the time of irrigation and debridement, it is common to obtain intraoperative cultures to guide postoperative infection pharmacologic treatment. Nonetheless, several studies have reported the difficulty in diagnosing and treating patients with atypical infections in the upper extremity[2,11,12]. Although the utility of atypical cultures has been studied in other fields of orthopaedic surgery, this has not been previously established in the setting of deep space infections of the upper extremity[14,15].

Atypical cultures were positive in 7% of all patients in our retrospective series. Interestingly, 86% of patients with positive atypical cultures demonstrated intraoperative purulence, which in the majority of cases was explained by concomitant bacterial infection. Therefore, although atypical culture results are uncommonly positive in the setting of surgically-treated acute deep infections of the upper extremity, infections that are purulent may still harbor atypical organisms. Our results are consistent with other orthopaedic literature reporting similarly low incidences of positive fungal cultures (1.7%) and AFB cultures (0.5%) in arthroplasty patients[15].

When evaluating the effect of atypical cultures on patient management, we observed that infectious diseases referrals were made for 43% (3 of 7) of patients and the antibiotic regimen altered in only 14% (1 of 7) of patients with positive

Table 2. Summary of culture results and infection diagnoses.

	Patients (%)	Aerobic / Anaerobic			Fungal			AFB		
			Number per			Number per			Number per	
Diagnosis		Sent (%)	Patient	Positive (%)	Sent (%)	Patient	Positive (%)	Sent (%)	Patient	Positive (%)
Abscess	46 (46.0%)	46 (46.0%)	2.50	39 (50.6%)	43 (45.7%)	1.24	2 (40.0%)	36 (43.9%)	0.96	1 (50.0%)
Flexor Teno.	22(22.0%)	22 (22.0%)	3.41	14 (18 .2%)	20 (21.3%)	1.45	0 (0.0%)	20 (24.4%)	1.59	1 (50.0%)
Septic Joint	21(21.0%)	21 (21.0%)	2.71	15 (19 .5%)	21 (22.3%)	1.33	2(40 .0%)	16 (19.5%)	1.05	0 (0.0%)
Osteomyelitis	9 (9.0%)	9 (9.0%)	2.44	9 (11.7%)	8 (8.5%)	1.11	1 (20.0%)	8 (9.8%)	1.11	0 (0.0%)
Septic Bursitis	2 (2.0%)	2 (2.0%)	2.00	0 (0.0%)	2 (2.1%)	1.00	0 (0.0%)	2 (2.4%)	1.00	0 (0.0%)
TOTAL:	100 (100%)	100 (100%)	2.73	77 (77.0%)	94 (94.0%)	1.29	5 (5.0%)	82 (82.0%)	1.13	2 (2.0%)

Table 3. Bivariate analysis to determine risk factors for atypical culture positivity.

	Difference	95% Confidence Interval		*p* value
Risk Factor (continuous)				
Mean age (years)	−9.8[a]	−21.8	2.2	0.11
Mean BMI (kg/m^2)	−3.1[a]	−8.7	2.5	0.19[b]
Mean pre-operative symptom duration (days)	4.5[a]	−1.1	10.1	0.11
	Odds Ratio	**95% Confidence Interval[c]**		**pvalue**
Risk Factor (categorical)				
Pre-operative symptoms > 7 days	6.0	1.2	44.8	0.03
Rheumatologic disease or on DMARD	3.6	0.1	33.8	0.31
Immunocompromising medication	2.9	0.1	27.9	0.36
Subjective purulence	2.8	0.4	66.8	0.43
Pre-operative symptoms > 3 days	1.1	0.2	8.5	1.00
Smoker	0.8	0.1	4.3	1.00
Obese (BMI ≥ 30 kg/m^2)	0.8	0.1	53.9	1.00
Diabetes	0.6	0.0	4.3	1.00
Immunocompromsing condition	0.5	0.1	2.3	0.45
Cardiac disease	0.0	0.0	3.7	0.59
Intravenous drug use	0.0	0.0	6.9	1.00
Morbidly obese (BMI ≥ 40 kg/m^2)	0.0	0.0	10.1	1.00
Active malignancy	0.0	0.0	24.7	1.00
ESRD	0.0	0.0	24.7	1.00
HIV positive	0.0	0.0	48.6	1.00
Organ transplant	0.0	0.0	252.4	1.00

a. M eanatypical positive valueminus atypical negativevalue
b. Mann-Whitney performed due to non-normally distrib uted data
c. Calculated usingBlaker method

atypical cultures. Therefore, atypical cultures infrequently altered treatment (3% of patients)—even when positive—without evidence of adverse clinical consequence. Infectious disease referral may not be necessary for every patient with a positive atypical culture result, and a combination of clinical concern and surgeon discretion should guide this decision.

Interestingly, despite previous reports, (13, 16) we did not identify a statistically significant association between use of an immunosuppressant medication and atypical culture positivity. We did, however, observe that symptom duration > 7 days was positively associated with atypical culture positivity. This finding reinforces the notion that atypical infections may present in a more indolent fashion compared to typical bacterial infections.

This study has several limitations. We recognize the limitations of a retrospective chart review, including risk for selection bias. Moreover, the atypical culture yield of 7% observed in this study likely overestimates the true incidence of positive atypical cultures, given that only patients that had both bacterial as well as AFB and/or fungal cultures sent for analysis were included. Finally, the secondary objective of this study—to identify risk factors associated with atypical culture positivity—was limited by the relatively small number of patients with positive atypical cultures (n = 7) identified in this series, which may predispose to type-2 error.

Conclusions

We report a low incidence of positive atypical cultures in patients with acute deep space hand infections in our series. Symptom duration > 7 days was associated with positive atypical cultures, and management decisions were infrequently altered by positive atypical culture results. We recommend that physicians consider patient risk factors and the low incidence of atypical positivity before routinely sending atypical cultures in patients with acute deep space hand infections.

References

1. Trionfo A, Thoder JJ, Tosti R. The Effects of Early Antibiotic Administration on Bacterial Culture Growth From Hand Abscesses. *Hand* (N Y). 2016;11(2):216-20.

2. Milby AH, Pappas ND, O'Donnell J, Bozentka DJ. Sporotrichosis of the upper extremity. *Orthopedics.* 2010;33(4).

3. Abzug JM, Cappel MA. Benign acquired superficial skin lesions of the hand. *The Journal of Hand Surgery.* 2012;37(2):378-93; quiz 93.

4. Al-Qattan MM, Al-Namla A, Al-Thunayan A, Al-Omawi M. Tuberculosis of the hand. *The Journal of Hand Surgery.* 2011;36(8):1413-21; quiz 22.

5. Al-Qattan MM, Helmi AA. Chronic hand infections. *The Journal of Hand Surgery.* 2014;39(8):1636-45.

6. Houshian S, Seyedipour S, Wedderkopp N. Epidemiology of bacterial hand infections. *Int J Infect Dis.* 2006;10(4):315-9.

7. McDonald LS, Bavaro MF, Hofmeister EP, Kroonen LT. Hand infections. *The Journal of Hand Surgery.* 2011;36(8):1403-12.

8. Ong YS, Levin LS. Hand infections. *Plast Reconstr Surg.* 2009;124(4):225e-33e.

9. Osterman M, Draeger R, Stern P. Acute hand infections. *The Journal of Hand Surgery.* 2014;39(8):1628-35; quiz 35.

10. Elhassan BT WS, Gonzales MH. Infections of the hand in the immunocompromised host. *The Journal of Hand Surgery.* 2004;4(2):121-7.

11. Noguchi M, Taniwaki Y, Tani T. Atypical Mycobacterium infections of the upper extremity. *Arch Orthop Trauma Surg.* 2005;125(7):475-8.

12. Kozin SH, Bishop AT. Atypical Mycobacterium infections of the upper extremity. *The Journal of Hand Surgery.* 1994;19(3):480-7.

13. Klein MB, Chang J. Management of hand and upper-extremity infections in heart transplant recipients. *Plast Reconstr Surg.* 2000;106(3):598-601.

14. Wadey VM, Huddleston JI, Goodman SB, Schurman DJ, Maloney WJ, Baron EJ. Use and cost-effectiveness of intraoperative acid-fast bacilli and fungal cultures in assessing infection of joint arthroplasties. *J Arthroplasty.* 2010;25(8):1231-4.

15. Tokarski AT, O'Neil J, Deirmengian CA, Ferguson J, Deirmengian GK. The routine use of atypical cultures in presumed aseptic revisions is unnecessary. *Clin Orthop Relat Res.* 2013;471(10):3171-7.

16. Eo S JN. Fungal infections of the hand and upper extremity. *Journal of the American Society for Surgery of the Hand.* 2004;4(4):250-5.