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Original Research

Diagnostic concordance of clinical diagnosis, tissue culture, and histopathology testing for skin and soft tissue infections: A single-center retrospective study

Christina M. Herbosa BA [a], Trisha S. Bhat BA [a,*], Yevgeniy R. Semenov MD [b,c], Ilana S. Rosman MD [a,d], Amy C. Musiek MD [a]

[a] Division of Dermatology, Washington University School of Medicine, St. Louis, MO, United States
[b] Department of Dermatology, Massachusetts General Hospital, Boston, MA, United States
[c] Department of Biomedical Informatics, Harvard Medical School, Boston, MA, United States
[d] Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, United States

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ABSTRACT

Background: Tissue culture and histopathology are the conventional diagnostic modalities for skin and soft tissue infections (SSTIs), but few studies have investigated their concordance.
Objective: Determine concordance between histopathology and tissue culture in the diagnosis of suspected SSTIs.
Methods: Single-center retrospective study of 355 cases with suspected SSTIs identified from the dermatology inpatient consultation log January 2014-July 2017.
Results: Overall concordance between histopathology testing and tissue culture results was high (76.1%). Concordance was high for cases defined as no evidence of infection, fungal infection and mycobacterial infection by histopathology (77.8%, 74.2%, and 80.0%) and tissue culture (92.1%, 67.7%, and 83.3%). Concordance was lower for suspected SSTIs with bacterial infection by histopathology (61.9%) and tissue culture (28.4%). Concordance rates were not significantly affected by age, sex, race, antimicrobial agent use, immunologic status, or biopsy size.
Limitations: Retrospective and single-institution nature of the study.
Conclusion: This study demonstrated a high concordance between histopathology and tissue culture in SSTIs with no clinical evidence of infection and suspected fungal and mycobacterial SSTIs, though concordance was lower for suspected SSTIs with evidence of bacterial infection. Clinicians should not be deterred from relying on initial histopathological results based on patients' immunosuppressed status, antimicrobial agent use, age, or biopsy tissue size.

Introduction

Skin and soft tissue infections (SSTIs) affect approximately 7% to 10% of hospitalized patients and account for 6.3 million physician office visits per year (Ki and Rotstein, 2008; Stevens et al., 2014). Although SSTIs often remain mild, superficial SSTIs may progress to systemic and even fatal infections over days, particularly in immunosuppressed patients (Gonzalez Santiago et al., 2014; Ki and Rotstein, 2008). Therefore, a timely diagnosis and pathogen classification is essential for early and targeted treatment (Esposito et al., 2016).

The variable clinical presentations of SSTIs pose a challenge to clinical diagnosis, often resulting in a reliance on microbiological studies. A histopathologic examination and tissue culture are the conventional diagnostic techniques for SSTIs (Stevens et al., 2014). Histopathology testing provides rapid identification of the pathogen but requires trained personnel. Tissue culture provides more specific characterization of the pathogen and its sensitivities to medications but its use is limited by the prolonged turnaround time and its inability to cultivate some pathogens (Drinka et al., 2012; Guarner and Brandt, 2011). Tissue culture testing is considered the gold standard for SSTIs (Fan et al., 2017). As a result, tissue cultures are often run concurrently with histopathological examinations in clinical practice (Woods and Walker, 1996).

* Corresponding author.
E-mail address: trishabhat@wustl.edu (T.S. Bhat).

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Although past studies have focused on the utility of the individual diagnostic tests, a limited number of studies have questioned their concordance and, in turn, the necessity of performing both diagnostic tests in the setting of suspected SSTIs. In an effort to reduce patient morbidity and costs from unnecessary procedures, we evaluated the concordance of histopathology testing and tissue culture results of suspected SSTIs.

Methods

Approval was obtained from the institutional review board at Washington University in St. Louis, Missouri. Cases of suspected SSTIs were identified from the log of inpatient consultations seen by the dermatology service between January 2014 and July 2017 at Barnes Jewish Hospital in St. Louis, Missouri. Cases with tissue culture and a concurrent histopathological examination were included. Viral infections and cases with insufficient documentation were excluded.

Demographic, microbiological, and clinical variables were collected retrospectively from clinical records. Biopsy tissue size was categorized as $\leq$4 mm and $\geq$5 mm. Antimicrobial use at the time of biopsy testing was documented. Cases were considered immunosuppressed if a patient had a history of transplant (solid and bone marrow transplants), lymphoma or leukemia, primary malignancies, systemic lupus erythematous, human immunodeficiency virus/acquired immunodeficiency syndrome, lymphoproliferative disorders (e.g., myelodysplastic syndrome), leukopenia, neutropenia, or pancytopenia.

The primary outcome measure was the concordance rate between histopathology testing and tissue culture results in the diagnosis of SSTIs. Concordance was defined as the rate of agreement between the diagnostic modalities on the presence and type of infection, subclassified into bacterial, fungal, and mycobacterial, calculated based on the number of concordant cases divided by the total number of cases (concordant + discordant). Tissue cultures were defined as positive if they grew at least one identifiable organism and negative if they had no growth, growth of skin flora, or contamination. Histopathology test results were classified as positive if the pathologist reported a definitive diagnosis or high likelihood of infection and negative if the pathologist reported a low likelihood or no concern for infection. Histopathology results positive for infection without specification of type or positive for >1 type of infection were considered concordant with positive tissue cultures. To account for chance, Cohen's kappa was also reported.

The secondary outcome measures were the concordance rates of final clinical diagnosis with tissue culture and histopathology test results. A final clinical diagnosis was considered concordant with histopathology and tissue culture results if the final clinical diagnosis agreed with the tissue culture or histopathology results. Final clinical diagnoses and type of infection were determined from dermatology, infectious disease, and discharge summary notes. If the final diagnosis was not clearly stated in the electronic medical record before patient discharge or death, the dermatology attending physician retrospectively reviewed the patient chart and determined the final diagnosis.

Baseline demographic and medical history factors were characterized as frequency distributions and percent of total for nominal variables, mean and standard deviation for ordinal variables, and median and interquartile ranges for continuous variables. Baseline comparisons stratified by concordance status were tested using χ^2 for categorical variables and Mann-Whitney for continuous variables.

Results

Demographic, medical, and diagnostic variables

Details of the demographic, health, and diagnostic variables and the subclassification of the histopathology results and tissue culture are presented in Table 1. Of a total of 355 patients, 252 were immunosuppressed (70.99%) and 303 were on antimicrobial treatments (85.35%; Table 1). The median age was 58 years (interquartile range, 26).

Concordance

The overall concordance between histopathology and tissue culture results was high for suspected SSTIs (agreement: 76.1%; Cohen's kappa: 0.4476 [standard error: 0.352; $p < .001$]). Notably, concordance rates were not significantly affected by age ($p = .852$), sex ($p = .874$), race ($p = .307$), antimicrobial use ($p = .212$), immunosuppressed status ($p = .235$), or tissue biopsy size ($p = .779$; Table 1). Concordance between tissue culture and histopathology differed by the type of infection. There was a high concordance between tissue culture and histopathology for cases with no evidence of infection, fungal infection, and mycobacterial infection by histopathology (77.82%, 74.19%, and 80.00%, respectively) and by tissue culture (92.08%, 67.65%, and 83.33%, respectively; Table 1). Concordance was lower for cases defined as bacterial infection by histopathology (61.90%) and tissue culture (28.38%; Table 1). Of the 53 cases with positive bacterial cultures and discordant histopathology results, the organisms most commonly identified were *Staphylococcus aureus* (64.15%; 34 of 53 cases) and *Pseudomonas aeruginosa* (9.43%; 5 of 53 cases). Final clinical diagnosis had a high concordance with tissue culture (83.66%) and histopathology (80.00%; Fig. 1).

Discussion

In an effort to reduce patient morbidity and unnecessary cost, we investigated the necessity of performing both tissue culture and histopathology testing for suspected SSTIs by examining their concordance. Our study revealed a 76.1% concordance between tissue culture and histopathological examination of suspected SSTIs, similar to previously reported data for deep cutaneous fungal infections and suspected SSTIs in primarily outpatient settings (Fan et al., 2017; Gonzalez Santiago et al., 2014).

Our findings revealed a high concordance between tissue culture and histopathology testing for suspected SSTIs with no evidence of infection as well as fungal and mycobacterial infection, indicating a high reliability of microbiological testing for these types of infections. Therefore, there should be a low threshold to initiate or change therapy in patients with fungal or mycobacterial infections based on the results of histopathological testing, enabling clinicians to take advantage of the rapidity of a histopathological diagnosis for early initiation and modification of treatment plans.

However, we found that concordance between tissue culture and histopathology differed by infection type, with a lower concordance for suspected SSTIs with evidence for bacterial infection. The higher rates of discordance for bacterial infections may reflect an increased difficulty in identifying bacterial organisms through histopathological examination. This may be explained by the low sensitivity of gram staining for common bacterial SSTIs, particularly after damage to the cell walls of gram-positive organisms by antimicrobial agents or during tissue processing (Wilson and Winn, 2008; Woods and Walker, 1996). Alternatively, tissue cultures may have grown bacterial organisms that were not clinically

Table 1
Baseline characteristics and concordance of histopathology and tissue culture results.

Characteristic			All cases (n = 355)	Tissue culture and histopathology concordance		
				Discordant (n = 85)	Concordant (n = 270)	*p* value
Age, median (interquartile range)			58 (41–67)	60 (44–68)	57 (41–67)	.279
Sex, n (%)						
	Male		202 (56.90)	49 (57.65)	153 (56.67)	.874
	Female		153 (43.10)	36 (42.35)	117 (43.33)	
Race, n (%)						
	Non-Hispanic white		286 (80.56)	64 (75.29)	222 (82.22)	.307
	Non-Hispanic black		60 (16.90)	19 (22.35)	41 (15.19)	
	Other		9 (2.54)	2 (2.35)	7 (2.59)	
Antimicrobial medications[†], n (%)			303 (85.35)	69 (81.18)	234 (86.67)	.212
Immunosuppressed[‡], n (%)			252 (70.99)	56 (65.88)	196 (72.59)	.235
Tissue biopsy size (mm), mean (standard deviation)			4.69 (1.08)	4.76 (1.22)	4.72 (1.04)	.779
Biopsy tissue size, mm						
	≤4		192 (54.1)	46 (54.12)	146 (54.07)	.994
	≥5		163 (45.9)	39 (45.88)	124 (45.93)	
Histopathology results, n (%)[*]						
	No infection		284 (80.00)	63 (22.18)	221 (77.82)	
	Infection		71 (20.00)	22 (30.99)	49 (69.01)	
		Bacterial infection	21 (5.92)	8 (38.10)	13 (61.90)	
		Fungal infection	31 (8.73)	8 (25.81)	23 (74.19)	–
		Mycobacterial infection	5 (1.41)	1 (20.00)	4 (80.00)	
		Multiple infections[c]	2 (0.56)	1 (50.00)	1 (50.00)	
		Infection, not otherwise specified[§]	12 (3.38)	4 (33.33)	8 (66.67)	
Tissue culture results, n (%)[*]						
	Negative culture		240 (67.61)	19 (7.92)	221 (92.08)	
	Positive culture		115 (32.39)	66 (57.39)	49 (42.61)	
		Bacterial culture	74 (20.85)	53 (71.62)	21 (28.38)	
		Fungal culture	34 (9.58)	11 (32.35)	23 (67.65)	–
		Mycobacterial culture	6 (1.69)	1 (16.67)	5 (83.33)	
		Multiple infections[‖]Multiple infections[‖]	1 (0.28)	1 (100.00)	0 (0.00)	

[*] Frequency of concordant and discordant histopathology and tissue culture results are reported as rows rather than columns.
[†] Some patients (n = 197) were on >1 type of antimicrobial treatment.
[‡] Immunosuppressed was defined as a history of transplant (solid and bone marrow transplants), lymphoma, leukemia, primary malignancies, systemic lupus erythematous disorder, human immunodeficiency virus/acquired immunodeficiency syndrome, lymphoproliferative disorders (e.g., myelodysplastic syndrome), leukopenia, neutropenia or pancytopenia.
[§] Positive histopathology results without the specification of type of infection were classified as infection, not otherwise specified.
[‖] Cases with histopathology or tissue culture reports with >1 type of infection were classified as multiple infections.

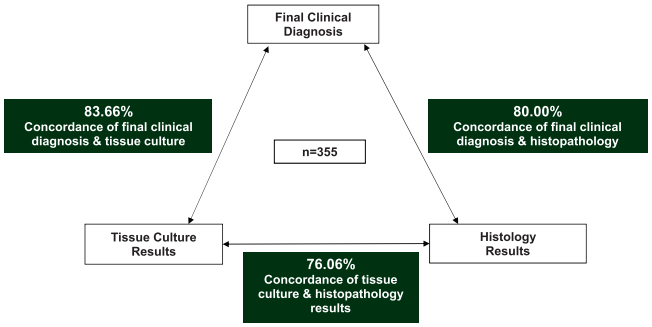

Fig. 1. Overall concordance of tissue culture results, histopathology results, and final clinical diagnosis on the presence and type of infection of cutaneous lesions.

significant; however, only cultures containing normal skin flora or containments were considered negative cultures to minimize this possibility. Overall, the low concordance rates of tissue culture and histopathology testing for bacterial infections emphasizes the importance of clinical context in determining the significance of diagnostic testing for SSTIs in patients with these infections.

Previous studies suggest that tissue cultures in immunosuppressed patients and patients on antimicrobial treatments have limited diagnostic utility owing to a low yield of true positive cultures (Woods and Walker 1996). In contrast to these studies, we found that the rates of positive tissue cultures and concordance rates of tissue culture with histopathology testing did not differ significantly based on immunosuppressed status or antimicrobial use. Concordance rates were also not affected by biopsy size or patient age. Our findings suggest that in most clinical situations, clinicians should not be deterred from diagnostic and therapeutic decision-making based on initial histopathological results due to a patient's immunosuppressed status, antimicrobial use, age, or biopsy size, because the concordance of histopathology results with tissue culture results does not differ based on these parameters.

Our study is limited because of its retrospective and single-institution nature. Retrospective evaluations of a clinical diagnosis in the absence of a clinical diagnosis in the electronic medical record is a potential source of misclassification bias. Patients were identified from the dermatology inpatient consultation log, subjecting our study to a selection bias. Antimicrobial therapy may have affected the ability to detect infection for both histopathology testing and tissue culture.

Conclusion

Our study reveals a high concordance between tissue culture and histopathology in cases of suspected SSTI. Clinicians should

not be deterred from relying on initial histopathological test results based on patients' immunosuppressed status, antimicrobial use, age, or biopsy size. Our findings suggest that in most clinical situations, an initial histopathological diagnosis is sufficient for early initiation and modification of therapy. Future studies should investigate additional sources of discordance, particularly in suspected SSTIs with evidence of bacterial infection.

Conflicts of Interest

None.

Funding

None.

Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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