



A two-center assessment of histopathologic diagnostic performance for fungal organism identification

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Abstract

Background:

Accurate detection and identification of invasive fungal pathogens relies on concordance of several complementary laboratory techniques, including fungal culture, serology, and histopathologic identification. Histopathologic stains such as the Gomori methenamine silver stain (GMS) are used to highlight fungal cell wall in tissue specimens. We sought to determine the diagnostic performance of histopathology fungal stains as compared to fungal culture for diagnosis of invasive fungal tissue infection at two tertiary medical centers with dissimilar patient populations.

Methods:

We performed a retrospective review of all surgical pathology specimens with reported GMS results and concurrent fungal culture at Keck Medical Center (Keck) and Los Angeles County + USC Medical Center (LAC) from July 2015 through December 2018. Ratios of GMS diagnostic performance were compared using chi squared analyses, with fungal culture as the gold standard for detection.

Results:

Of 1347 LAC surgical pathology specimens stained with GMS to evaluate for fungal infection, 229 (17.0%) had concurrent tissue specimens submitted for fungal culture. Of 1546 Keck GMS-stained surgical pathology specimens, 358 (23.2%) had concurrent tissue submitted for fungal culture. GMS stain performance at LAC showed a sensitivity of 53.7% (95% CI: 37.4-69.3%) and specificity of 90.4% (95% CI: 85.2-94.2%). At Keck, GMS showed a sensitivity of 64.1% (95% CI: 52.4-74.7%), specificity of 88.9% (95% CI: 84.7-92.4%), without significant difference in performance between sites. (Table 1) Among filamentous fungi, GMS false negative frequency at LAC was 5.3% (10/190) and 4.0% (11/277) at Keck, without significant difference ($p=0.51$). A subset of pathology reports suggested the fungus genus based on histologic morphology. Of 10 LAC pathology specimens with fungal genus specified, 2 (20.0%) reports gave the incorrect genus and 8/18 (44.4%) reports at Keck gave incorrect genus as per concurrent culture isolate result. (Table 2)

Conclusions:

GMS stain had low-to-moderate sensitivity when compared to fungal tissue culture. Increased submission of concurrent tissue for fungal culture is therefore likely to improve detection. When genus level identification was attempted, fungal forms were incorrectly identified in about one-third of histopathology specimens.

Results

Figure 1. Utilization of GMS stain on surgical pathology specimens by tissue type at LAC and Keck Medical Centers from July 2015 through December 2018.

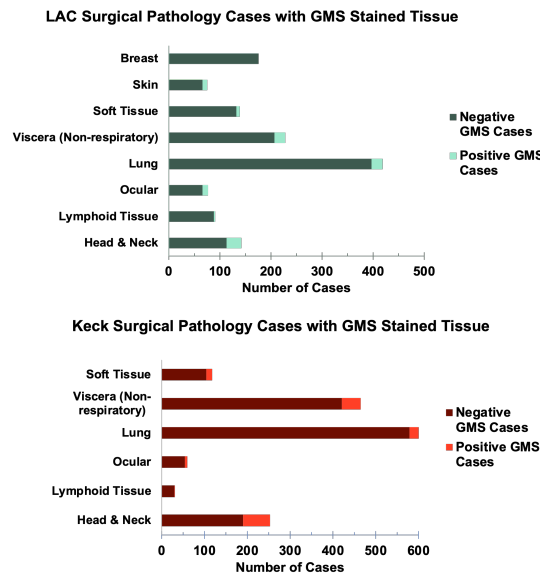


Table 2. Pathology reports with incorrect filamentous mold genus specification by GMS stain compared to tissue fungal culture results at LAC and Keck Medical Centers from July 2015 through December 2018.

Site	Tissue Type	GMS Interpretation	Fungal Tissue Culture Result
LAC	Head & Neck	Mucormycosis	<i>Aspergillus fumigatus</i>
	Lung	Aspergillus	<i>Rhizopus</i>
	Head & Neck	Mucormycosis	<i>Aspergillus flavus</i>
Keck	Head & Neck	Aspergillus	<i>Candida albicans</i>
	Head & Neck	Aspergillus	<i>Dematiaceous fungus</i>
	Head & Neck	Aspergillus	<i>Penicillium</i>
	Head & Neck	Aspergillus	<i>Curvularia</i>
	Lung	Aspergillus	<i>Scedosporium apiospermum</i>
	Lung	Aspergillus	<i>Candida albicans</i>
	Soft Tissue	Aspergillus	<i>Rhizopus</i>

Table 1. Diagnostic performance of GMS histopathology stain on surgical pathology specimens compared to tissue fungal culture at LAC and Keck Medical Centers from July 2015 through December 2018.

	LAC (95% CI)	Keck (95% CI)
Sensitivity	53.7 (37.4 - 69.3)	64.1 (52.4 - 74.7)
Specificity	90.4 (85.2 - 94.2)	88.9 (84.7 - 92.4)
Positive Predictive Value	55.0 (38.5 - 70.7)	61.7 (50.3 - 72.3)
Negative Predictive Value	89.9 (84.7 - 93.8)	89.9 (85.7 - 93.2)

Conclusions

- GMS stain had low-to-moderate sensitivity when compared to fungal tissue culture
- Frequency of false negative GMS stain for filamentous mold identification was similar between sites
- Genus level specification of filamentous molds was rare on pathology reports, and incorrectly identified in ~1/3 of cases
- Increased submission of concurrent tissue for fungal culture is likely to improve detection of invasive fungal disease

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