

Fungal Contribution in Chondroradionecrosis of the Larynx



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INTRODUCTION

- Chondroradionecrosis of the larynx is a potential complication of radiation therapy to the neck.
- Primary treatment of laryngeal malignancies has trended toward organ preservation modalities.
- Due in part to these changing practice patterns, the prevalence of chondroradionecrosis could reasonably be expected to rise.
- A total laryngectomy is often indicated for recurrent or persistent laryngeal or hypopharyngeal malignancies; it is also employed when severe chondroradionecrosis causes the larynx to become nonfunctional.
- If fungal organisms are implicated in the development of chondroradionecrosis, empiric treatment with antifungal medication may reduce the progression to cartilage destruction in the compromised larynx.
- This study seeks to establish whether a correlation exists between the diagnosis of nonfunctional larynx and the presents of fungal invasion on histopathological analysis of these larynges after total laryngectomy.*

METHODS

Patients included those who underwent total laryngectomy at University of Louisville Hospital from January 1999 to December 2014 (n=180) and at an affiliated teaching hospital from January 2003 to December 2014 (n=70). Demographic data was collected. Pathology reports were reviewed for each of the laryngectomy specimens, and key terms including "chondroradionecrosis," "necrosis," "post-radiation changes," "hyalinization," "fibrosis," and "ulceration" were used to identify specimens that could be further examined for evidence of chondroradionecrosis. Special designation was given to specimens that showed evidence of chondroradionecrosis but did not harbor recurrent or persistent malignancy. These pathology specimens were independently reviewed by two academic pathologists. Gomori Methenamine (GMS) and Periodic acid Schiff (PAS) stains were employed to detect the presence of fungal elements.

RESULTS

Of the 250 medical records reviewed for patients who underwent total laryngectomy during the study period, 91 did not meet inclusion criteria. Sample demographic and disease characteristics are presented in Table 1. Of the 159 patients in the sample, **12 (7.5%) laryngectomy specimens were found to have evidence of chondroradionecrosis** in the absence of recurrent or persistent malignant disease. **Three (25%) of these specimens showed microscopic evidence of fungal invasion.** Incidentally, **Actinomyces species were also noted in two (16%) of these specimens.**

There was no statistical difference in demographic or treatment-related variables between patients who had persistent or recurrent malignancy and patients who underwent total laryngectomy without evidence of residual or recurrent malignant disease. No significant difference was observed when comparing time to laryngectomy between patients who were found to have recurrent malignancy versus those who only had evidence of chondroradionecrosis. there was no survival difference noted between the persistent or recurrent malignancy and the nonfunctional larynx cohorts.

Patients with evidence of ulceration or necrosis in the laryngectomy specimen had reduced overall survival, irrespective of the presence of persistent malignancy (HR=2.923, 95% CI=1.023-8.352, p=.045).

CONCLUSION

Fungal infection may play a critical role in the progression of chondroradionecrosis. The contribution of fungal elements to chondroradionecrosis has likely been underestimated, both pathologically and clinically. Close monitoring and **proactive antifungal treatment for patients at risk for chondroradionecrosis may decrease the progression of the disease process and ultimately reduce the necessity for laryngectomy in a non-neoplastic larynx. Shorter overall survival was seen when "ulceration" or "necrosis" was documented on pathology reports compared to those with no evidence of ulceration or necrosis.** No significant survival impact was seen in those with evidence of only "post radiation changes." This survival data is preliminary and further research is warranted.

REFERENCES

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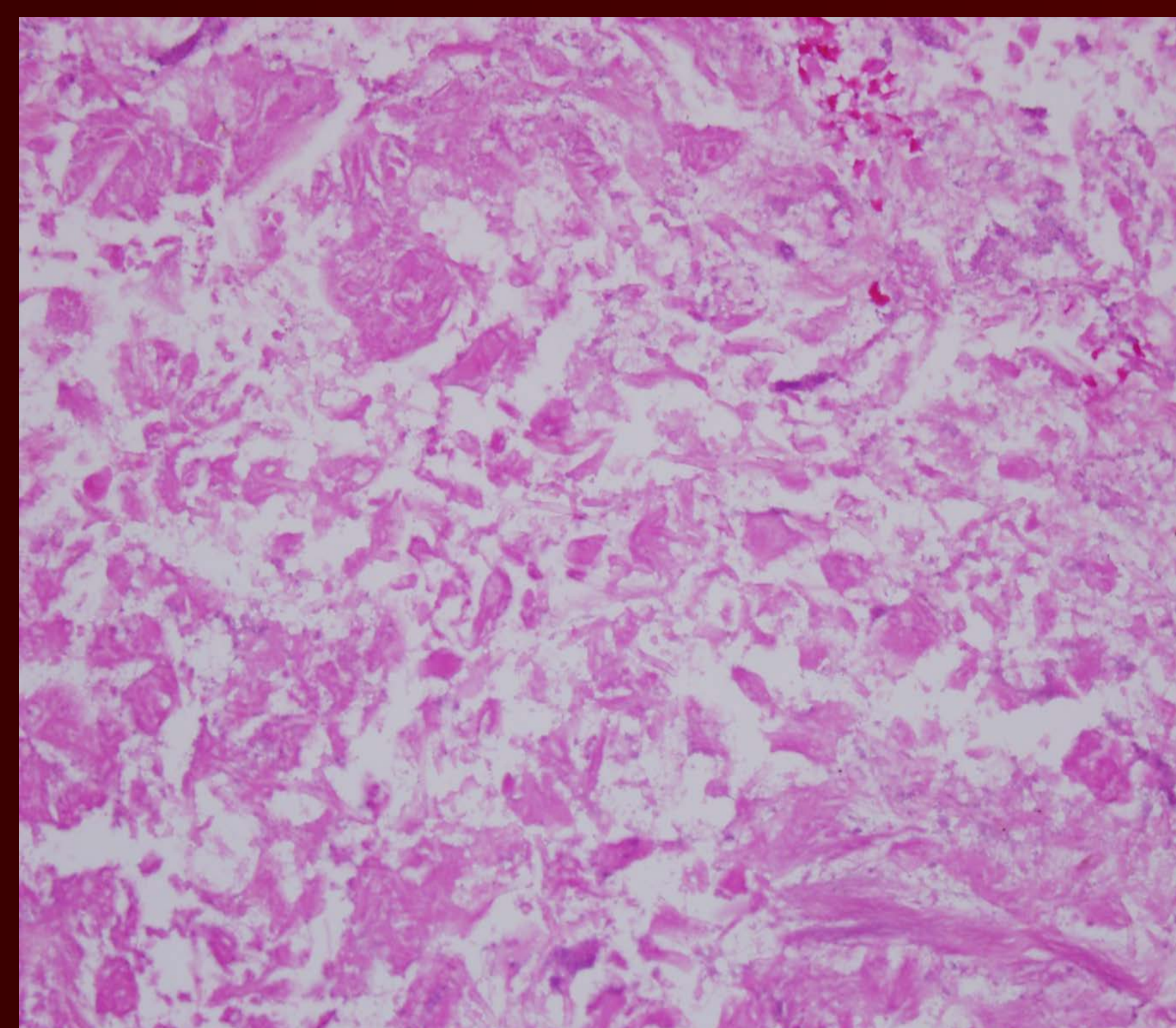


Image 1 H&E stain shows fungal hypha.

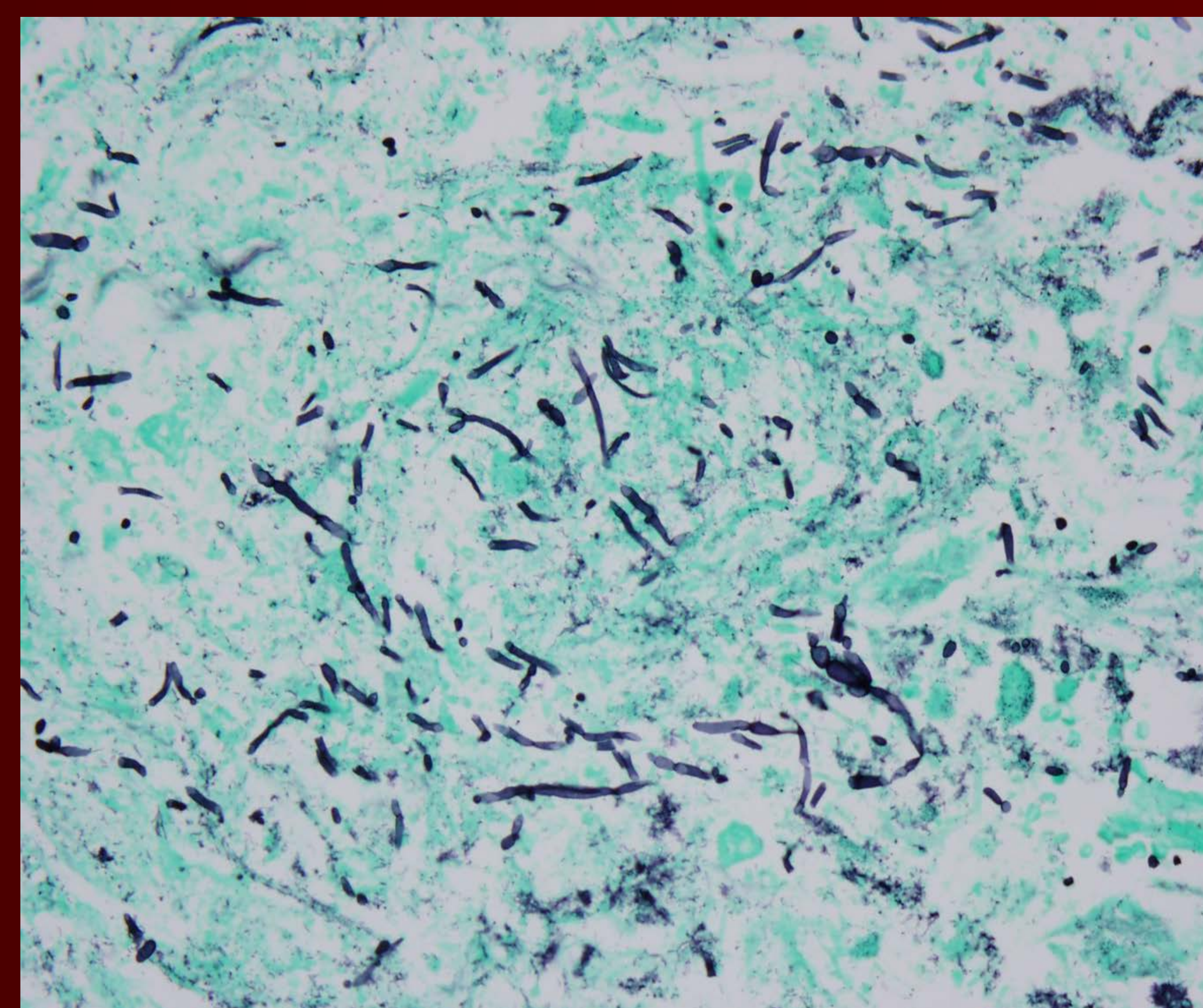


Image 2. GMS stain highlights the fungal organisms.

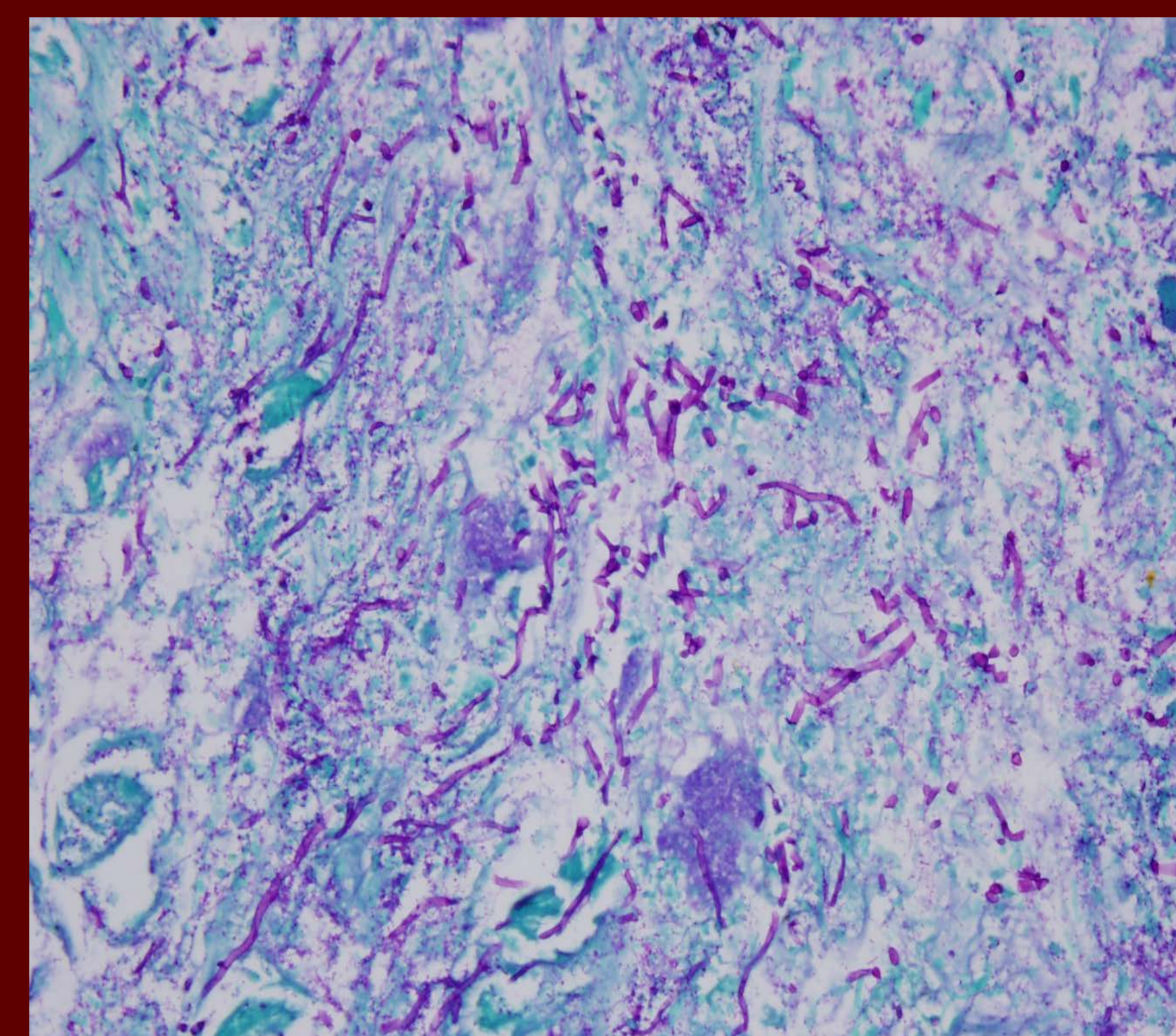


Image 3. PAS stain highlights the fungal organisms.

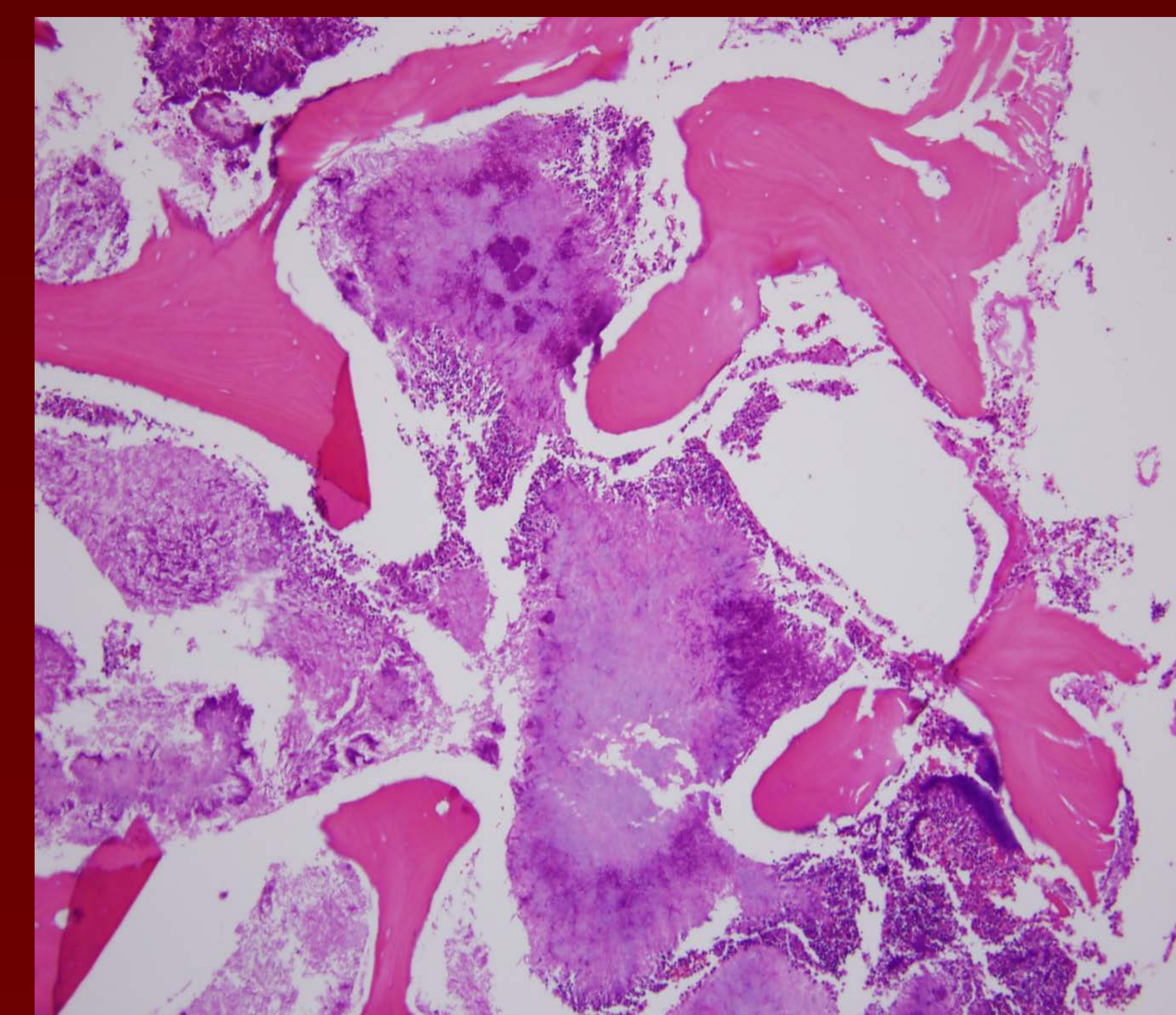


Image 4. Actinomyces species seen on H&E.

Table 1. Sample demographic and clinical characteristics (N=159). Significance level (p-value) is presented for group comparisons made using independent samples t-tests, Chi-square, or Cox proportional hazard models.

	Residual Tumor (N=147)				Chondroradionecrosis (N=12)				p-value
	M	SD	N	%	M	SD	N	%	
Age, years	59.10	10.34			53.08	9.72			.054
Ethnicity									.999
White			121	82.3%			10	83.3%	
African American			25	17.0%			2	16.7%	
Hispanic			1	0.7%			0	0%	
Pack Years	45.17	24.54			45.13	31.34			.996
Comorbidities									
Cardiac			24	16.3%			5	41.7%	.999
DM			24	16.3%			0	0%	.006
Thyroid Disease			12	8.2%			5	41.7%	.496
Site of Disease									.460
Supraglottic			86	58.5%			9	75%	
Glottic			58	39.4%			3	25.0%	
Subglottic			1	0.7%			0	0%	
Stage*									
T1-T2			52	35.3%			5	41.7%	
T3-T4			82	55.7%			7	58.3%	
TL to XRT, months	22.72	30.79			17.16	14.70			.543
TL to expiration, months	23.59	29.81			34.75	32.03			.238

*Complete staging data unavailable for 13 patients.

