Review Article

Cytologic Detection and Clinical Significance of Candida Species in Sputum: A Comprehensive Review

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Abstract

Candida species are common commensals of the oro-pharyngeal mucosa, yet their presence in sputum cytology continues to generate diagnostic uncertainty. This narrative review synthesises cytomorphologic hallmarks, diagnostic adjuncts, and evolving clinical evidence to guide cytopathologists and clinicians in differentiating colonisation from true infection. Characteristic sputum findings include 3–4 µm budding yeasts with elongated pseudohyphae penetrating desquamated squamous cells amid acute inflammation. Conventional culture remains standard but is slow and less sensitive; fluorescent real-time PCR, β-d-glucan, and mannan/ anti-mannan assays provide faster, more sensitive detection, although interpretation still hinges on clinicoradiologic correlation. Recent series show that while invasive Candida pneumonia is exceedingly rare (<1 %), persistent lower-respiratory colonisation is associated with higher mortality in hospital-acquired pneumonia, more frequent exacerbations in COPD, and impaired lung function in bronchiectasis. Judicious reporting e.g., “Candida spp. present; may represent colonisation versus infection in the appropriate clinical context”together with adherence to IDSA antifungal guidelines, optimises patient management.

Key words

Candida, Sputum cytology, Pseudohyphae, PCR, β-d-glucan, Colonisation, Pneumonia.

Introduction

Candida species account for roughly 90 % of human fungal isolates, with C. albicans still predominating despite the global rise of non-albicans variants. Their regular isolation from respiratory secretions complicates interpretation: is the finding mere colonisation, a marker of host debility, or an underestimated pathogen [1, 2]. Classic autopsy-based teaching relegated Candida pneumonia to a medical curiosity, yet recent molecular studies and large clinical datasets have reopened the debate. This review summarises current evidence with a focus on sputum cytology the most readily available yet often under-appreciated diagnostic modality.We searched PubMed, Scopus, and Google Scholar to April 2025 using "Candida," "sputum," "cytology," "pneumonia," "bronchiectasis," "PCR," and "β-d-glucan." Priority was given to peer-reviewed original studies, systematic reviews, and guidelines. Reference lists of retrieved articles were screened for additional citations.

Importance of Sputum cytology in Pulmonary candidiasis

Oral or Pulmonary candidiasis is usually a disease of immunocompromised patients. The patients with pulmonary candidiasis present with fever, cough, dyspnoea and pulmonary infiltrates on chest radiography whereas the ones with oral candidias is usually have an oral thrush. As candida species can be a colonizer of the respiratory tract normally in absence of a disease, the diagnosis of pulmonary candidiasis is a difficult task. The identification of these candidal species in sputum and/or in bronchoalveolar lavage will prompt the further confirmation with the help of biopsy showing evidence of direct lung parenchymal invasion by these organisms or by transthoracic FNA in which these can be directly viewed and confirmed through culture studies. Pulmonary candidiasis is thought to be occurring in patients with an immunocompromised status or ongoing diseases. However, Hellstein JW, et al. found that it is not limited to age extremes, malnourishment, metabolic disease, concurrent infections, antibacterial therapy, immunocompromising conditions, radiotherapy, transplant patients, salivary gland hypofunction, or long-term steroid therapy [1].

The vast majority of these microorganisms exist as commensal colonization rather than a pathologic process. Hence is it crucial to know whether these fungal elements are a part of microbiome or are pathogenic. When host immunity diminish, the dimorphic property of Candida albicans permits the organism to transform to biofilms that are extremely resistant to relatively high doses of antifungal medications [3, 4]. The embedded organisms on host surfaces break out and permeate the systemic circulation, provoking life-threatening candidemia from simple oral or mucosal candidiasis. Few studies have suggested that the existence of germ tubes is strongly indicative of Candida albicans as the source species and not a simply commensal [5].

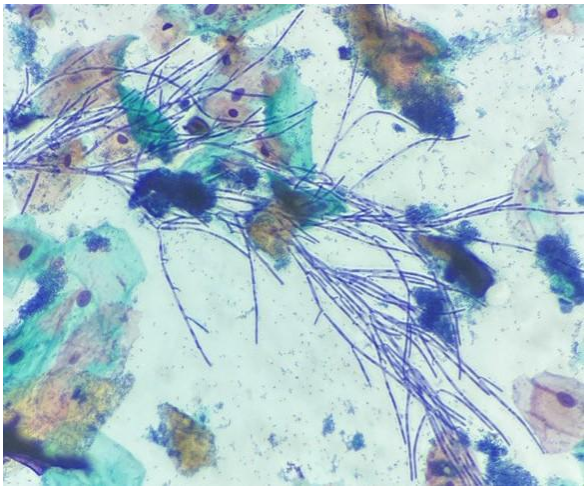
Cytomorphology of Candida in Sputum

Cytologic feature	Description	Significance
Budding yeasts	Round-to-oval 3–4 μm cells; narrow-based budding	Indicates active replication
Pseudohyphae	Elongated chains with constrictions at septa	Suggests tissue invasion potential
Penetration of squamous cells	Hyphae traverse cell membranes	Correlates with pathogenicity
Background	Neutrophils, necrotic debris	Reflects host response

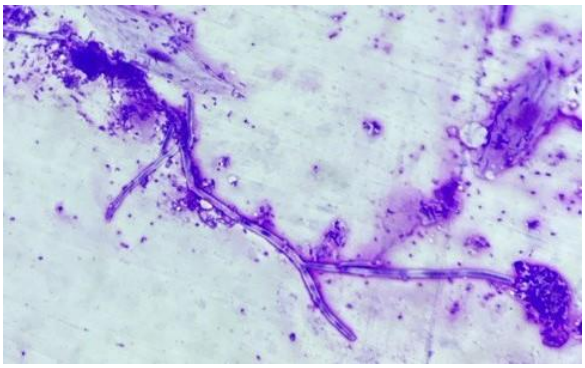
On Papanicolaou or Diff-Quik smears, simultaneous observation of budding yeasts and pseudohyphae especially when they pierce epithelial clusters strongly suggests lower-airway colonisation/ infection rather than oropharyngeal carry-over [2, 3]. (**Photograph - 1, 2**) Special stains (PAS, GMS) highlight fungal cell walls,

whereas Calcofluor white provides rapid fluorescence-based confirmation [3].

Photograph – 1: showed budding yeasts and pseudohyphae in sputum cytology (Pap stain, 10X).



Photograph – 2: showed budding yeasts and pseudohyphae (PAS stain, 40X).



Other Diagnostic Modalities Beyond Light Microscopy

Sabouraud dextrose agar yields results in 24–48 hours, with reported positivity of approximately 50 % in prospective sputum series [7, 8]. However, culture cannot distinguish colonisation from infection and under-detects mixed biofilms. Fluorescent real-time PCR detects Candida DNA in approximately 3 hours and improved positivity to 65–70 % in a 300-sample comparison ($P < 0.001$) [9, 10]. Multiplex ITS-based PCR panels further distinguish C. albicans from azole-resistant species, facilitating targeted therapy [11, 12]. β-d-Glucan (BDG) assays, though validated for serum, demonstrate high negative predictive value in broncho-alveolar lavage (BAL) and tracheal aspirate, particularly when BDG > 80 pg/mL [13, 14].

Mannan/ anti-mannan ELISAs detect circulating antigen-antibody complexes; combined testing achieved 84–87 % specificity for candidemia and showed promising results in tracheal aspirate-positive cohorts [15].

Conclusion

Detection of Candida in sputum cytology is common but seldom equates to pneumonia. A composite assessment including cytomorphology, rapid PCR/antigen tests, and host factors best stratifies patients for observation versus antifungal therapy. Clear, contextualised reporting by cytopathologists prevents unnecessary treatment while ensuring true infections are not overlooked.

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