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Forensic Challenges in Diagnosing Meningococcal Sepsis Postmortem

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Abstract

Neisseria meningitidis septicemia remains a critical cause of sudden death, yet postmortem diagnosis is frequently obscured by nonspecific autopsy findings and postmortem bacterial overgrowth. In a retrospective case control forensic analysis of 25 suspected meningococcal sepsis cases, conventional cultures yielded confirmatory results in only 9 (36%) instances, primarily when postmortem interval (PMI) was under 72 hours. In contrast, PCR on vitreous humor detected meningococcal DNA in 21 cases (84%), while immunohistochemical (IHC) staining of formalin-fixed tissues confirmed meningococcal antigens in 18 of these. Vitreous humor PCR exhibited the highest sensitivity. PMIs beyond 96 hours correlated with decreased culture positivity but did not affect molecular diagnostics. E-selectin IHC in pulmonary endothelium was present in 10/12 evaluated cases, supporting a septic process. These findings underscore the necessity of integrating molecular and immunohistochemical tools in forensic practice, especially when decomposition obscures classical microbiology, and promote structured sampling protocols to enable accurate determination of meningococcal sepsis as the cause of death.

Keywords: meningococcal sepsis; postmortem diagnosis; forensic microbiology.

Introduction

Sudden unexpected deaths caused by meningococcal sepsis pose a significant public health and forensic challenge, in part due to rapid disease progression and the nonspecificity of gross autopsy findings (2023). Waterhouse–Friderichsen syndrome, characterized by bilateral adrenal hemorrhage and purpura fulminans, may raise suspicion, yet can be masked by decomposition or misattributed in forensic evaluations.1-3

Traditional postmortem microbiological culture is frequently confounded by postmortem microbial translocation and autolytic changes, particularly when the PMI exceeds 72 hours (2021). Reports highlight that culture positivity may drop to as low as 20–30% in decomposed bodies, complicating forensic decision-making .4-6 Thus, forensic pathologists are compelled to adopt more reliable methods for pathogen detection in suspected septic deaths.

Molecular diagnostics, particularly polymerase chain reaction (PCR) assays on vitreous humor and formalin-fixed tissues, have emerged as sensitive and specific modalities for identifying Neisseria meningitidis postmortem.7-8 Vitreous humor provides a relatively protected niche with delayed autolytic degradation, enabling bacterial DNA detection even in advanced decomposition (2022) . Similarly, immunohistochemical (IHC) staining on fixed tissues permits visualization of meningococcal antigens within vascular endothelium and inflammatory cells, offering additional confirmation .9-10

Despite promise, molecular and IHC techniques face limitations. Antigen preservation is tissue-specific and declines with PMI and environmental factors such as temperature—especially within visceral organs—requiring careful tissue selection and optimized protocols (2023) . Moreover, PMIs longer than 96 hours may produce false negatives in cultures but less so in PCR and IHC assays.

Additional histological markers, such as endothelial E-selectin expression, have been proposed to support a septic process. E-selectin expression in pulmonary and cerebral vessels correlates with systemic inflammatory activation and may serve as a complementary IHC marker when specific bacterial assays are inconclusive. However, its forensic application remains investigational.

Methodology

A retrospective case control study was conducted at Allama Iqbal Medical College, Lahore . Inclusion criteria comprised (1) sudden death with clinical or scene indications of sepsis/purpura; (2) autopsy performed; and (3) available postmortem samples: blood, CSF, vitreous humor, and tissue blocks. Cases with traumatic cause or confirmed alternative etiology were excluded. PMIs ranged from 24 to 192 hours.

Conventional microbiology cultures were performed on heart blood and CSF at autopsy. Vitreous humor, blood, and tissue specimens—lung, spleen, adrenal gland, and skin—were processed for real-time PCR targeting N. meningitidis capsular genes. IHC staining included anti–N. meningitidis polyclonal and serogroup-specific antibodies, as well as E-selectin detection in pulmonary and cerebral endothelium.

Antigen preservation was evaluated through pan–cytokeratin and vimentin in parallel tissue sections. Staining intensity and distribution were graded semi-quantitatively. Results were correlated with PMI, decomposition grade, and gross findings.

Diagnostic yield by modality was calculated. Sensitivity was defined as proportion of PCR-positive cases confirmed by culture or IHC. Associations between PMI and test performance were analyzed using Fisher's exact test. p-values <0.05 were considered significant.

Results

Table 1. Diagnostic yield by method and postmortem interval

PMI (hours)	n	Culture +ve (%)	Vitreous PCR +ve (%)	Tissue IHC +ve (%)
<72	12	5 (42%)	11 (92%)	10 (83%)
72–96	7	2 (29%)	6 (86%)	5 (71%)
>96	6	2 (33%)	4 (67%)	3 (50%)

Table 2. E-selectin expression in endothelial tissues (n=12)

Tissue	E-selectin +ve (%)
Lung vessels	10 (83%)
Brain vessels	8 (67%)

Table 3. Antigen preservation by tissue type vs PMI

Tissue	PMI <96 h +ve (%)	PMI >96 h +ve (%)
Skin	12/12 (100%)	6/6 (100%)

Tissue	PMI <96 h +ve (%)	PMI >96 h +ve (%)
Adrenal gland	10/12 (83%)	1/6 (17%)
Kidney	11/12 (92%)	2/6 (33%)

Brief explanation: Vitreous PCR demonstrated highest sensitivity across PMIs, outperforming culture and IHC. Antigen detection in skin was robust regardless of PMI, whereas results in viscera declined significantly after 96 hours (p=0.003).

Discussion

These findings emphasize the superior sensitivity of molecular detection in vitreous humor compared to culture and tissue IHC, particularly when decomposition has progressed. Vitreous PCR yielded positive results in up to 92% of early (<72 h) and 67% of late (>96 h) PMI cases, aligning with earlier reports that vitreous humor is a preferred matrix for postmortem pathogen detection . Culture remained unreliable with positive results in only 36% of cases, underscoring its limitations for forensic confirmation.11-13

Tissue IHC confirmed antigen in 72% of cases overall; however, antigen preservation in adrenal and visceral organs diminished significantly when PMI exceeded 96 hours, likely due to autolysis—consistent with prior studies on antigen decay in IHC. Conversely, skin tissue maintained antigen integrity even after long PMIs, confirming its utility for immunohistochemical sampling.14-16

E-selectin expression, detected in vascular endothelium of lung and brain in 83% and 67% respectively, provides supportive evidence of a systemic inflammatory process consistent with sepsis in cases lacking direct bacterial markers. This aligns with recent investigations highlighting endothelial activation markers as adjunctive forensic indicators of sepsis, based on these observations, a postmortem sampling protocol is proposed: collection of vitreous humor for PCR in all suspected cases; skin tissue for IHC regardless of PMI; visceral tissues if PMI is less than 96 hours; and E-selectin IHC as ancillary evidence. Rapid and accurate diagnosis facilitates timely public health interventions such as contact prophylaxis.17-20

Limitations include retrospective design, small sample size, and case selection bias toward suspected meningococcal deaths. Further prospective validation with standardized protocols is warranted.

Conclusion

Integration of vitreous humor PCR and immunohistochemistry—particularly on skin—significantly enhances postmortem diagnosis of meningococcal sepsis, especially when traditional cultures fail. E-selectin vascular staining offers valuable corroborative evidence. Adoption of standardized sampling aligned with PMI considerations can improve forensic accuracy and public health responsiveness.

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