Letter

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Post-mortem diagnosis of sepsis: when it's too late

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Abstract

Post-mortem diagnosis of sepsis is often very difficult to make, especially in the elderly affected by multiple comorbidities. However, clinical evaluation following histology, immunohistochemistry, microbiological tests, immunoassays and proteomics can improve reliability of this post-mortem diagnosis. ***Clin Ter 2021; 172 (1):e60-62. doi: 10.7417/CT.2021.2284***

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Sepsis is a global health problem which is expected to increasingly affect health care systems, especially in the wake of the Sars-CoV-2 pandemic (1). In the last decade, sepsis has been increasingly found on Internal Medicine wards (2), due to ageing population and multiple-morbidity (3).

Sepsis diagnosis requires a conscious clinical eye, early recognition and treatment to reduce morbidity and mortality. However, identifying a septic patient may not be straightforward, due to an absence of signs and symptoms, especially in elderly patients with various comorbidities and sometimes the diagnosis is too late.

Coroners may request autopsies be performed on people who died from suspected sepsis, or during their hospital stay, in order to assess whether there has been any medical malpractice or other failures of care (4,5).

Post-mortem diagnosis of sepsis presents several difficulties which are often linked to the lack of complete and adequate health records that could suggest or demonstrate the process of the patient deteriorating into a septic state. Moreover, in sepsis, pathological findings are often nonspecific, and can often be compatible with different clinical pictures. Mortality is also closely related to the presence of organ dysfunction (consequence of the syndrome and its severity marker).

There are no specific macroscopic anatomic-pathological characteristics of "sepsis"; even the so-called "septic spleen" has no objective value, and "shock lung" or "acute tubular necrosis" are difficult to identify because of the transformative phenomena undergone by the corpse.

Even the histological picture does not provide a conclusive diagnosis of sepsis or sepsis-related death. The cardiac finding most often detected in patients who died from sepsis is sepsis-related myocardial dysfunction, which is generally called hibernating myocardium. In the hibernating myocardium, cardiomyocytes show a reversible depressed contractility and ultrastructural and biochemical changes (6). Septic myocardial calcification represents another nonspecific finding (7). However, in the brain, micro and macroscopic features do not change or, at least, are not a direct expression of sepsis or septic shock.

Certainly, the most characteristic findings are observable in the lungs: a microscopic picture of diffuse alveolar damage (DAD), alveolar collapse with haemorrhage and oedema, intra-alveolar neutrophils and erythrocytes. Clearly, these findings support a diagnosis of lung infection, but not of sepsis.

In the last few years, several studies focused attention on the importance of immunohistochemistry to prove the expression of different inflammatory markers on organs involved by sepsis.

Numerous studies demonstrate that leukocyte cells markers, especially of the myelomonocyte line, such as CD15, LF, LZ, CX3CR1, CCR2, and VLA-4 are involved. Other studies, imply that molecules expressed by vascular endothelium, such as ICAM-1, E-selectin, VE-cadherin, and ACE are present. Furthermore, specific mediators and targeting molecules such as TNFα, PCT, VEGF, and s-TREM-1 have been studied (8, 9 ,10).

Moreover, immunohistochemistry could allow us to identify pathogens on tissue samples collected during the autopsy by demonstrating the presence of bacterial or viral membrane antigens (11).

Post-mortem PCR, a microbiological diagnostic, could also be an important aid in the post-mortem diagnosis of

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sepsis (12, 13). The PCR could be used for testing various organic samples, liquid or solid (i.e. liquor, blood, pericardial effusion…) with acceptable sensitivity and specificity.

Naturally, the validation of the result needs appropriate technical precautions during the draw to minimise the risk of sample contamination.

Indeed, during the interpretation of the microbiological post-mortem samples there are a lot of variables which must be taken into account. Particular attention should be paid for the examination of gastrointestinal, respiratory and urinary tracts, which are rich of bacterial flora (14).

Every time a microorganism is isolated in a bacterial culture, the examiner should distinguish if it is a real pathogen or an ordinary commensal. Additionally, is important to evaluate if the isolated bacterium comes from other sites of the body, since such event is possible throughagonal diffusion of the microorganism viapre-existing breaches in the mucosa or through ruptures induced by attempts of resuscitation. Furthermore, it is important to rule out the possibility of a samplescontamination during the autopsy.

Also, immunology and proteomics could provide the forensic pathologist with further information to make diagnosis of sepsis-related death.

The immunological quantification of specific biomarkers in biological fluids (i.e. PTC, PCR, TNF and IL-10) is a useful tool in the identification of biomolecular responses against infectious insults, thus explaining sepsis-related organ alterations and death (15, 16).

Proteomics is the study of the set of proteins expressed in tissue, cell or in organism at a given time. Hinkelbein et al (17) found particular changes in theexpression of 40 serum proteins in rats affected by sepsis.

In view of the above, it seems clear that post-mortem diagnosis of sepsis results extremely difficult. Thus, pathologists should take in consideration not only clinical and pathological data, but also lab results and immunohistochemical and microbiological findings.

Only considering all of this information together it is possible to reachthe difficult post-mortem diagnosis of sepsis with a reasonable degree of certainty.

In conclusion, the forensic pathologist to arrive at a correct diagnosis of sepsis must follow a multidisciplinary approach (18, 19, 20, 21).

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Ethical approval

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