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Original Research Article

Significance of detailed and careful morphological evaluation of organs in sepsis related deaths

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ARTICLE INFO

Article history:
Received 23-04-2021
Accepted 29-04-2021
Available online 29-05-2021

Keywords:
Sepsis
Histopathology
Autopsy
death

ABSTRACT

Background: In this retrospective study we studied macroscopic changes and histology of various organs in sepsis related deaths in correlation with relevant clinical, laboratory and microbiology data.
Materials and Methods: Medical records and autopsy records of all patients were reviewed where final cause of death after complete macroscopic and histological examination of organs following autopsy was given as sepsis/septic shock. Sepsis related death in diabetics, hypertensives, and pregnancy related death and unnatural deaths were excluded from this study.
Results: Sixty five cases were selected for this study involving detailed morphological examination of different organs. Most common system involved was respiratory system (33.84%). Lungs were chief primary site of infection mainly pneumonia (35.4%) and tuberculosis (7.7% cases) followed by liver abscess (18%), renal abscess/ pyelonephritis (16.4%) and, peritonitis (16.4%). Most frequent non- specific organ changes presented grossly as diffluent/soft mushy spleen with red pulp congestion (83.08%) followed by mild to moderate cerebral oedema(41.5%) and pulmonary oedema(35. 4%). Most frequent findings that contributed to death was intrapulmonary haemorrhage (33.8%), acute tubular necrosis (11, 17%), disseminated intravascular coagulation/ micro thrombi (8, 12.3%) and, acute respiratory distress syndrome (3, 4. 61%). In this study population, the commonest organism obtained on culture was Pseudomonas (24.07%) followed by E. coli and Klebsiella (20.37% each).
Conclusion: Careful and detailed morphological evaluation of various organs at autopsy is significant for both pathologist and clinicians to understand the course of events occurred and to reach an accurate diagnosis of sepsis related death.

1. Introduction

Sepsis is a life-threatening entity caused by a dysregulated host response to infection.[1] In many sepsis-related deaths the clinical information is scarcely available at autopsy, mostly due to the short duration of hospital's stay. Autopsy pathologist, not infrequently, has to verify and uncover an uncontrolled focus of sepsis and to search for the underlying disease process that had contributed to the death. This observational study was conducted to record the frequent morphological changes in various organs in sepsis-related deaths that assist in post-mortem tissue diagnosis of sepsis.

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2. Materials and Methods

A retrospective study was carried out over 4 years 6 months, evaluating of medical and autopsy records at a tertiary care hospital.

All the cases included in study, had the final cause of death reported as sepsis/septic shock, after a thorough macroscopic and histological examination provided by an autopsy. Sepsis-related death in patients with diabetes mellitus, hypertension, and pregnancy and those whose death was considered unnatural were excluded from this study.

Medical and autopsy records were reviewed for (i)age, (ii)gender, (iii)duration of hospital's stay, (iv)

https://doi.org/10.18231/j.achr.2021.019

vital parameters[1] including blood pressure (<90mmHg systolic or <60mm Hg diastolic),pulse (> 90/min.), temperature(>38°C or <36°C), Altered mental status, respiratory rate (>30 breaths/minute). The laboratory indicators for sepsis studied were[2,3] (i) White blood cell count (>12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms), (ii) Hyperglycemia (plasma glucose >110 mg/dL or 7.7mmol/ L) in the absence of diabetes, (iii) Thrombocytopenia (platelet count <100,000/μL), (iv) Hyperbilirubinemia (plasma total bilirubin >4 mg/ dL or 70 mmol/ L), (v) Creatinine increase ≥0.5mg/dL, (vi) Hyperlactatemia (>3 mmol /L), and (vii) C-reactive protein(C-RP).

Supporting microbiology data showing positive cultures from various samples like blood, sputum, urine, ascitic fluid, pleural fluid, pus, skin scrapings were also documented.

The clinical impression, as given by the treating clinicians was recorded in all cases.

Thorough macroscopic examination of organs, including the brain, lungs, liver, heart, spleen, kidney, intestine, and pancreas was done to identify grossly visible septic foci. After fixation in 10% neutral buffered formalin for 24-48 hours, the slides were stained with Hematoxylin & Eosin and special stains like PAS, GMS, and Gram stain (to look for fungus and bacteria). Slides were studied for histopathological features of sepsis as documented in the literature.[4–9]

All the relevant ante-mortem details and post-mortem findings of each organ system were documented.

2.1. Statistical analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences version 20 (SPSS v20, IBM). Categorical variables between the two groups were compared using the Chi-square test and Fisher's exact test. A p-value of <0.05 was considered significant.

3. Observations and Results

During the study period, 1657 autopsies were performed, out of which 109 were sepsis-related deaths. Sixty-five cases (49 males, 16 females) were selected for this study after excluding cases of diabetes (22), hypertension (19), and maternal mortality (13). Most of the cases were hospitalized in a general ward. The maximum and minimum duration of hospital stay was 17 days and ≤24 hrs (30.8%), respectively. The most common age group was between 41-60 years amongst males (25 cases) and 61-80 years amongst females (6 cases).

Most of the cases presented with fever (56.92%), followed by hypotension (40%). Few cases presented with tachypnea (29.23%), tachycardia (23.08%), and altered sensorium (6.15%). Deranged laboratory parameters noted were leukocytosis (73.85%), high C-RP value (56.92%), high creatinine value (49.23%), and hyperbilirubinemia (35.38%). Few cases revealed hyperlactatemia (29.23%), thrombocytopenia (18.46%), leucopenia (13.85%), and hyperglycemia (7.69%). Table 1 shows the distribution of cases according to the system involved. Approximately 82% of the mortality in sepsis was due to isolated system involvement, with the respiratory system being the most common (35.38%).

3.1. Morphology of organs in sepsis related deaths

In Tables 2, 3 and 4 are presented post-mortem findings of different organs, including the heart, lungs, kidney, brain, spleen, liver, and intestine. The internal organs showed both the site of sepsis and non-specific tissue alterations supposed to be sepsis-induced.

3.2. Site of infection

A site of infection was noted in all the cases. The lungs were the chief primary site of infection, mainly pneumonia (35.4%), and tuberculosis (7.7% cases), followed by the liver abscess (18%), renal abscess/ pyelonephritis (16.4%) and, peritonitis (16.4%). Besides the gluteal abscess, chest wall abscess, parotid abscess, epididymal-orchitis, axillary abscess, pancreatitis, cholangitis, meningitis, splenic abscess, splenic tuberculosis, intestine gangrene and fournier's gangrene were noted as other sites of infection.

3.3. Nonspecific post mortem findings (Table 5)

Red pulp congestion in the spleen (83.08%), was the most frequent non- specific organ changes presented grossly as diffluent/soft mushy spleen, (Figure 1) followed by mild to moderate cerebral edema (41.5%), and pulmonary edema (35. 4%). A few other important findings were hepatic portal space inflammation (Figure 2), focal hepatic necrosis (Figure 3), and hepatic intrasinusoidal/ intravenous leukostasis (29.2%; 21.5%; 21.5%, respectively). However, the p-value was not significant (0.06).

Table 1: Distribution of cases according to the underlying system involved

System	No. of cases (n=)	Percentage (100%)
Respiratory system (RS)	23	35.38
Hepatobiliary system (HB)	10	15.38
Renal system (renal)	8	12.31
Gastrointestinal system (GI)	7	10.76
Others (skin, soft tissue , glands)	6	9.23
Multiple organ failure	12	18.46
Total	65	100

Table 2: Post-mortem findings of heart [n=2] and lungs [n= 29]

Heart (n=2)	Lungs (n-29)
Histopathology n=	Histopathology n=
Interstitial edema (1)	Pneumonia (23)
Interstitial Hemorrhages(1)	Lung abscess (3)
Myocarditis (1)	Pulmonary TB (5)
Endocarditis (1)	Pulmonary edema(23)
Interstitial mononuclear cells (2)	Intrapulmonary hemorrhage (22)
Septic emboli (2)	Microthrombi (7)
	Intravenous leucostasis (6)
	Interstitial pneumonitis(1)

Table 3: Post-mortem findings of liver [n=15] and kidney [n= 13]

Liver (n=15)	Kidney (n=13)
Histopathology(n=)	Histopathology (n=)
Focal necrosis(14)	Acute tubular necrosis (ATN)(10)
Ductular inflammation (6)	Renal abscess (5)
Ductular proliferation (7)	Pyelonephritis (7)
Cholestasis (6)	Bacterial colonies (1)
Intrasinusoidal leucostasis/fibrin(14)	
Kupffer cell hyperplasia (1)	
Portal tract inflammation (13)	
Bacterial colonies (2)	
TB lesion (2)	

Table 4: Post-mortem findings of brain [n=28], spleen [n= 16], intestine [n=23]

Brain (n=28)	Spleen (16)	Intestine (n=23)
Histopathology (n=)	Histopathology (n=)	Histopathology (n=)
Meningitis (1)	Splenitis (6)	Serosal Exudates(18)
Cerebral edema (27)	White pulp atrophy(11)	Ulcer (9)
	TB spleen(2)	TB intestine (3)
		Gangrene (3)
		Microthrombi (1)

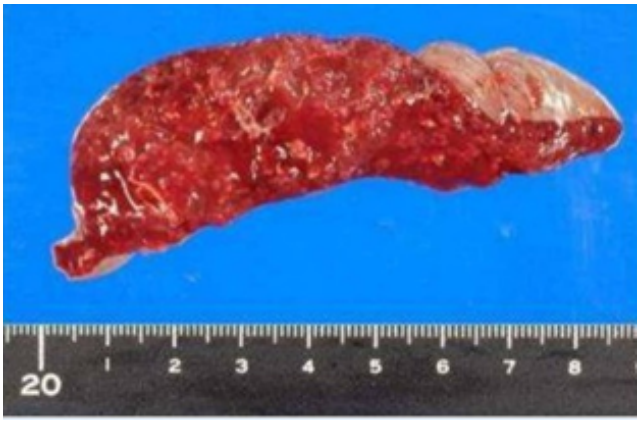

Fig. 1: Shows soft 'mushy' spleen characteristically seen in sepsis.

Table 5: Non-specific post-mortem findings in the study group [n=65]

Non-specific findings	No. of patients (65)	Percentage (100%)
Epicardial haemorrhages	1	1.5
Epicarditis/myocarditis	4	6.2
Portal inflammation liver	19	29.2
Splenitis	6	9.2
Interstitial inflammation kidney	12	18.6
Focal necrosis kidney	10	15.4
Focal necrosis liver	14	21.5
Cerebral edema	27	41.5
Pulmonary edema	23	35.4
Interstitial edema heart	1	1.5
Swollen kidney	10	15.4
Intravenous leucostasis lung	6	9.2
Intrasinusoidal leucostasis liver	14	21.5
Red pulp congestion spleen	54	83
White pulp atrophy spleen	11	16.9
Bacterial colony liver	2	3.1
Bacterial colony kidney	1	1.5

p value =.06(insignificant).

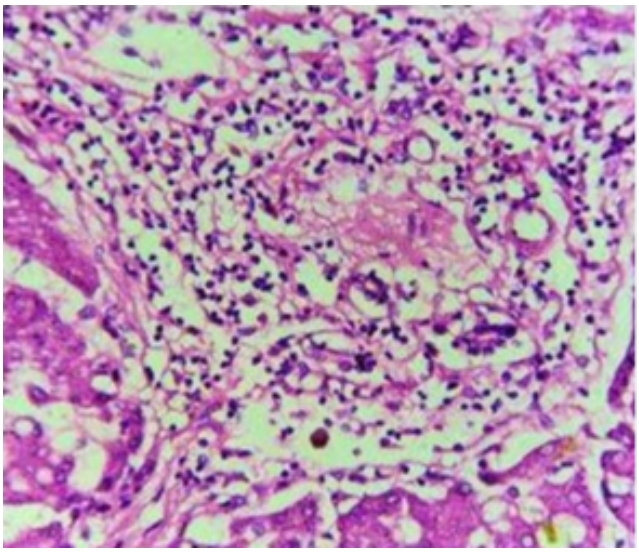

Fig. 2: (H&E, 100X) Shows portal tract inflammation liver

3.4. Significant post-mortem findings and complications that can cause death

The most frequent findings that contributed to death was intrapulmonary hemorrhage (33.8%), (Figure 4), acute tubular necrosis (17%), disseminated intravascular coagulation/ microthrombi (12.3%) and, acute respiratory distress syndrome (4.61%). However, p-value was not significant>0.5.

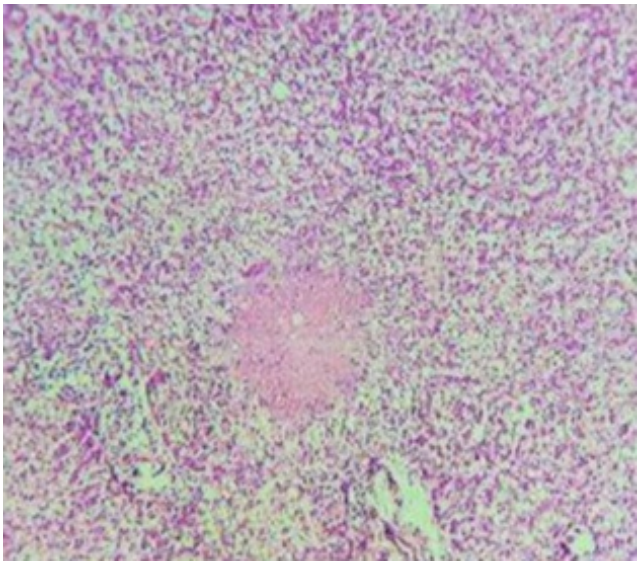

Fig. 3: (H&E, 100X) Shows centriacinar necrosis liver

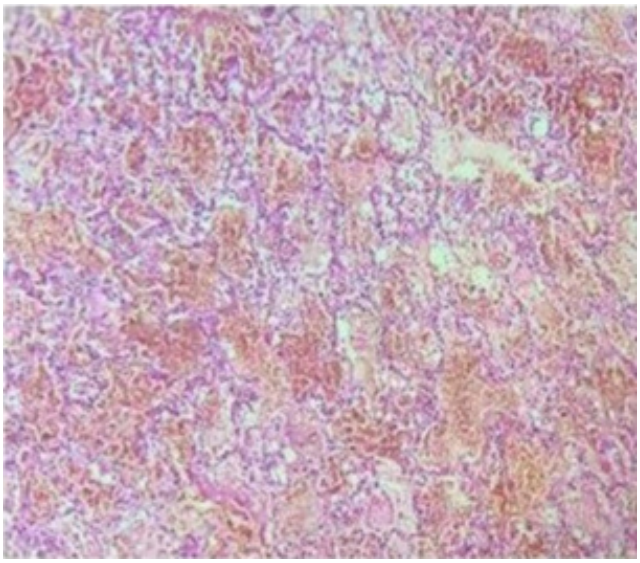

Fig. 4: (H&E, 100X) Shows marked haemorrhage in the alveoli (Intrapulmonary Haemorrhage)

3.5. Significant co-morbidities and conditions that can contribute to death

Fifteen (24.62%) cases had co-morbidities including chronic liver disease (15.38%), chronic kidney disease (3.08%), chronic heart disease (3.08%) and, chronic pulmonary disease (1.54%).

3.6. Microbiological culture in the study group

To confirm the clinical and radiological diagnosis, multiple ante mortem samples were sent for microbiology. A total of 96 samples, taken from different sites, were studied for microbiological studies. These included 11 respiratory samples of sputum or endotracheal secretions, 36 blood samples, 14urine samples, 24 samples of peritoneal fluid, 11 samples of pus or wound swab or tissue. 54 samples (56.25%) showed positive growth. The, most significant number of positive cultures was for the urine samples (78.57%) followed by respiratory samples, including sputum and endotracheal secretions (72.73%). Significant p-value < .05 was observed in urine samples. In this study population, the commonest organism obtained on culture was Pseudomonas spp (24.07%) followed by Escherichia coli. and Klebsiella spp (20.37% each). .

4. Discussion

In this study, sepsis-related death was seen more frequently in males (75.38%) in the age group of 41-60 years (43.08%) compared to females (24.61%) in the age group of 61-80 years.[10,11] The basis for these disparities has been postulated to relate to hormonal differences between genders. Estrogen levels and plasma cytokine imbalance may contribute to the differences in the inflammatory response and the development of sepsis.[11–13]

Elderly (>60yrs) age group have been reported to be most common age group affected by sepsis. In the current study, age group affected commonly was 41-60 years. Eleven out of 28 patients (39.3%) in the age group 41-60 years had co-morbidity like chronic liver disease or chronic kidney disease or heart disease. This differential distribution in the age groups can be attributed to the chronic co-morbid medical conditions that affect the immune system (diabetes, chronic renal failure, and HIV).[14]

In this study most common site of infection was lung and most frequent contributor for sepsis – related death was intrapulmonary hemorrhage. Intrapulmonary hemorrhage is a life threatening complication and needs a prompt treatment. Its pathophysiology is alveolar microcirculation injury.[15–17]

Red pulp congestion of spleen, cerebral edema and pulmonary edema were frequently observed non specific findings that supported the autopsy diagnosis of sepsis-related death.[18–21] Sepsis causes imbalance between proinflammatory and antiinflammatory repsonse and microbials and their products are recognised by immune cells initiating production of cytokines and a cascade of events leading to organ damage.[22]

5. Conclusion

This study highlights that a detailed and careful evaluation of the morphology of various organs at autopsy plays an important role in reaching a diagnosis of sepsis-related death and to understand the pathophysiology of sepsis better.

6. Source of Funding

No financial support was received for the work within this manuscript.

7. Conflict of Interest

The authors declare they have no conflict of interest.

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Cite this article: Chaturvedi M, Parihar A. Significance of detailed and careful morphological evaluation of organs in sepsis related deaths. *IP Arch Cytol Histopathology Res* 2021;6(2):76-80.